A QSP Model for Predicting Clinical Responses to Monotherapy, Combination and Sequential Therapy Following CTLA-4, PD-1, and PD-L1 Checkpoint Blockade

Oleg Milberg*[1], Chang Gong[1], Mohammad Jafarnejad[1], Imke H. Bartelink[2,5], Bing Wang[2], Paolo Vicini[3], Rajesh Narwal[4], Lorin Roskos[4], and Aleksander S. Popel[1,6]

[1]Department of Biomedical Engineering, Johns Hopkins University School of Medicine, Baltimore, Maryland
[2] Clinical Pharmacology, Pharmacometrics and DMPK (CPD), MedImmune, South San Francisco, California, USA

[3] Clinical Pharmacology, Pharmacometrics and DMPK, MedImmune, Cambridge, United Kingdom;
[4] MedImmune, Gaithersburg, Maryland, USA

[5] Department of Clinical Pharmacology and Pharmacy, Amsterdam UMC, Vrije Universiteit Amsterdam, The Netherlands

[6] The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, Maryland

Address for Correspondence:

Oleg Milberg, Ph.D.

Department of Biomedical Engineering

School of Medicine

Johns Hopkins University

720 Rutland Avenue

Baltimore, MD 21205

Telephone: 301-651-4868

Email: oleg.milberg@gmail.com

Keywords: Immuno-oncology, immunotherapy, melanoma, systems biology, computational model, T cell, quantitative systems pharmacology (QSP), pharmacokinetics (PK), pharmacodynamics (PD), checkpoint inhibitor therapies, virtual clinical trials, virtual patients, combination therapy, sequential therapy, multiscale modeling

Table S1 – Model Reactions (Start)

Reaction Number	Reaction
1	[Blood-Lymph].CTLA4_mabB <-> Lymph_Node.CTLA4_mab
2	[Blood-Lymph].CTLA4_mabB <-> Peripheral.CTLA4_mabP_leaky
3	[Blood-Lymph].CTLA4_mabB <-> Peripheral.CTLA4_mabP_tight
4	[Blood-Lymph].CTLA4_mabB <-> Tumor.CTLA4_mabt
5	[Blood-Lymph].CTLA4_mabB -> null
6	[Blood-Lymph].Effector_T_TB -> [Blood-Lymph].Effector_T_TB + [Blood-Lymph].Effector_TB
7	[Blood-Lymph].Effector_TB -> Liv_Spln_GI.EffT_GI_f_Vasc
8	[Blood-Lymph].Effector_TB -> Liv_Spln_GI.EffT_Liver_f_Vasc
9	[Blood-Lymph].Effector_TB -> Liv_Spln_GI.EffT_Spleen_f_Vasc
10	[Blood-Lymph].Effector_TB -> Lymph_Node.EffT_LN_f_Vasc
11	[Blood-Lymph].Effector_TB -> null
12	[Blood-Lymph].Effector_TB -> Peripheral.EffT_P_f_Vasc
13	[Blood-Lymph].Effector_TB -> Tumor.EffT_f_Vasc
14	[Blood-Lymph].PD1_mabb <-> Lymph_Node.PD1_mab
15	[Blood-Lymph].PD1_mabb <-> Peripheral.PD1_mabP_leaky
16	[Blood-Lymph].PD1_mabb <-> Peripheral.PD1_mabP_tight
17	[Blood-Lymph].PD1_mabb <-> Tumor.PD1_mabt
18	[Blood-Lymph].PD1_mabb -> null
19	[Blood-Lymph].PDL1_mabb <-> Lymph_Node.PDL1_mab
20	[Blood-Lymph].PDL1_mabb <-> Peripheral.PDL1_mabP_leaky
21	[Blood-Lymph].PDL1_mabb <-> Peripheral.PDL1_mabP_tight
22	[Blood-Lymph].PDL1_mabb <-> Tumor.PDL1_mabt
23	[Blood-Lymph].PDL1_mabb -> null
24	[Blood-Lymph].PDL1_mabb -> null
25	Liv_Spln_GI.EffT_GI_f_Vasc -> Liv_Spln_GI.EffT_Liver_f_Vasc
26	Liv_Spln_GI.EffT_GI_f_Vasc -> null
27	Liv_Spln_GI.EffT_Liver_AR_Vasc -> Liv_Spln_GI.EffT_LiverEx
28	Liv_Spln_GI.EffT_Liver_AR_Vasc -> null
29	Liv_Spln_GI.EffT_Liver_b_Vasc -> Liv_Spln_GI.EffT_Liver_AR_Vasc
30	Liv_Spln_GI.EffT_Liver_b_Vasc -> Liv_Spln_GI.EffT_Liver_f_Vasc
31	Liv_Spln_GI.EffT_Liver_b_Vasc -> null
32	Liv_Spln_GI.EffT_Liver_f_Vasc -> Lungs.EffT_f_LungsVasc
33	Liv_Spln_GI.EffT_Liver_f_Vasc -> null
34	Liv_Spln_GI.EffT_LiverEx -> Lymph_Node.EffT_LN_ExRec
35	Liv_Spln_GI.EffT_LiverEx -> null
36	Liv_Spln_GI.EffT_Spleen_AR_Vasc -> Liv_Spln_GI.EffT_SpleenEx
37	Liv_Spln_GI.EffT_Spleen_AR_Vasc -> null
38	Liv_Spln_GI.EffT_Spleen_b_Vasc -> Liv_Spln_GI.EffT_Spleen_AR_Vasc
39	Liv_Spln_GI.EffT_Spleen_b_Vasc -> Liv_Spln_GI.EffT_Spleen_f_Vasc
40	Liv_Spln_GI.EffT_Spleen_b_Vasc -> null
41	Liv_Spln_GI.EffT_Spleen_f_Vasc + Liv_Spln_GI.Spleen_Free_Sites -> Liv_Spln_GI.EffT_Spleen_b_Vasc + Liv_Spln_GI.Spleen_Free_Sites
42	Liv_Spln_GI.EffT_Spleen_f_Vasc -> Liv_Spln_GI.EffT_Liver_f_Vasc
43	Liv_Spln_GI.EffT_Spleen_f_Vasc -> null
44	Liv_Spln_GI.EffT_SpleenEx -> Lymph_Node.EffT_LN_ExRec
45	Liv_Spln_GI.EffT_SpleenEx -> null
46	Liv_Spln_GI.Liver_Free_Sites + Liv_Spln_GI.EffT_Liver_f_Vasc -> Liv_Spln_GI.EffT_Liver_b_Vasc + Liv_Spln_GI.Liver_Free_Sites
47	Lungs.EffT_AR_LungsVasc -> Lungs.EffT_LungsEx
48	Lungs.EffT_AR_LungsVasc -> null
49	Lungs.EffT_AR_LungsVasc -> null
50	Lungs.EffT_f_LungsVasc + Lungs.Lung_Free_Sites -> Lungs.EffT_r_LungsVasc + Lungs.Lung_Free_Sites
51	Lungs.EffT_f_LungsVasc -> [Blood-Lymph].Effector_TB
52	Lungs.EffT_f_LungsVasc -> null
53	Lungs.EffT_LungsEx -> Lymph_Node.EffT_LN_ExRec
54	Lungs.EffT_LungsEx -> null
55	Lungs.EffT_r_LungsVasc -> Lungs.EffT_AR_LungsVasc

Reaction Number	Reaction
56	Lungs.EffT_r_LungsVasc -> Lungs.EffT_f_LungsVasc
57	Lungs.EffT_r_LungsVasc -> null
58	Lungs.EffT_r_LungsVasc -> null
59	Lymph_Node.[PNT-Tr_CD80] + Lymph_Node.[Tr-PNT_PDL1] <-> Lymph_Node.[TrPNT_PDL1-CD80]
60	Lymph_Node.[PNT-Tr_CD80] -> null
61	Lymph_Node.[PNT-Tr_PD1] + Lymph_Node.[Tr-PNT_PDL1] <-> Lymph_Node.[TrPNT_PDL1-PD1]
62	Lymph_Node.[PNT-Tr_PD1] + Lymph_Node.PD1_mab <-> Lymph_Node.PNTTr_PD1_aPD1
63	Lymph_Node.[PNT-Tr_PD1] -> null
64	Lymph_Node.[PNT-Tr_PDL1] + Lymph_Node.PDL1_mab <-> Lymph_Node.PNTTr_PDL1_aPDL1
65	Lymph_Node.[PNT-Tr_PDL1] -> null
66	Lymph_Node.[TregLN-NT] + Lymph_Node.Naive_T -> null
67	Lymph_Node.[TregLN-NT] -> null
68	Lymph_Node.[TregLN-PNT] + Lymph_Node.Primed_Naive_T -> null
69	Lymph_Node.[TregLN-PNT] -> null
70	Lymph_Node.[TregLN-PNT1] -> Lymph_Node.[PNT-Tr_CD80] + Lymph_Node.[TregLN-PNT1]
71	Lymph_Node.[TregLN-PNT1] -> Lymph_Node.[PNT-Tr_PD1] + Lymph_Node.[TregLN-PNT1]
72	Lymph_Node.[TregLN-PNT1] -> Lymph_Node.[PNT-Tr_PDL1] + Lymph_Node.[TregLN-PNT1]
73	Lymph_Node.[TregLN-PNT1] -> Lymph_Node.[Tr-PNT_PD1] + Lymph_Node.[TregLN-PNT1]
74	Lymph_Node.[TregLN-PNT1] -> Lymph_Node.[Tr-PNT_PDL1] + Lymph_Node.[TregLN-PNT1]
75	Lymph_Node.[Tr-mAPC_CD80] -> null
76	Lymph_Node.[Tr-mAPC_CD86] -> null
77	Lymph_Node.[Tr-mAPC_CTLA4] + Lymph_Node.[Tr-mAPC_CD80] <-> Lymph_Node.TrALN_CT_CD80
78	Lymph_Node.[Tr-mAPC_CTLA4] + Lymph_Node.[Tr-mAPC_CD86] <-> Lymph_Node.TrALN_CT_CD86
79	Lymph_Node.[Tr-mAPC_CTLA4] + Lymph_Node.CTLA4_mab <-> Lymph_Node.TrALN_CT_aCT
80	Lymph_Node.[Tr-mAPC_CTLA4] -> null
81	Lymph_Node.[Tr-PNT_PD1] + Lymph_Node.[PNT-Tr_PDL1] <-> Lymph_Node.[TrPNT_PD1-L1]
82	Lymph_Node.[Tr-PNT_PD1] + Lymph_Node.PD1_mab <-> Lymph_Node.TrPNT_PD1_aPD1
83	Lymph_Node.[Tr-PNT_PD1] -> null
84	Lymph_Node.[Tr-PNT_PDL1] + Lymph_Node.PDL1_mab <-> Lymph_Node.TrPNT_PDL1_aPDL1
85	Lymph_Node.[Tr-PNT_PDL1] -> null
86	Lymph_Node.APCLN + Lymph_Node.C_DebrisLN -> Lymph_Node.mAPC
87	Lymph_Node.C_DebrisLN -> null
88	Lymph_Node.CTLA4_mab -> [Blood-Lymph].CTLA4_mabB
89	Lymph_Node.CTLA4_mab + Lymph_Node.PNT_CTLA4 <-> Lymph_Node.CTLA4_mAb_CTLA4
90	Lymph_Node.CTLA4_mAb_CTLA4 -> null
91	Lymph_Node.Effector_T -> null
92	Lymph_Node.EffT_LN_ExRec -> Lungs.EffT_f_LungsVasc
93	Lymph_Node.EffT_LN_ExRec -> null
94	Lymph_Node.EffT_LN_f_Vasc -> Lungs.EffT_f_LungsVasc
95	Lymph_Node.EffT_LN_f_Vasc -> null
96	Lymph_Node.mAPC -> Lymph_Node.mAPC_CD80 + Lymph_Node.mAPC
97	Lymph_Node.mAPC -> Lymph_Node.mAPC_CD86 + Lymph_Node.mAPC
98	Lymph_Node.mAPC -> Lymph_Node.mAPC_PD1 + Lymph_Node.mAPC
99	Lymph_Node.mAPC -> Lymph_Node.mAPC_PDL1 + Lymph_Node.mAPC
100	Lymph_Node.mAPC -> Lymph_Node.mAPC_PDL2 + Lymph_Node.mAPC
101	Lymph_Node.mAPC -> null
102	Lymph_Node.mAPC -> null
103	Lymph_Node.mAPC_CD80 -> null
104	Lymph_Node.mAPC_CD86 -> null
105	Lymph_Node.mAPC_Int_P1 -> Lymph_Node.mAPC_Int_P1 + Lymph_Node.mAPC_Int_P1_CD80
106	Lymph_Node.mAPC_Int_P1 -> Lymph_Node.mAPC_Int_P1 + Lymph_Node.mAPC_Int_P1_CD86
107	Lymph_Node.mAPC_Int_P1_CD80 -> null
108	Lymph_Node.mAPC_Int_P1_CD86 -> null
109	Lymph_Node.mAPC_Int_P2 -> Lymph_Node.mAPC_Int_P2_CD80 + Lymph_Node.mAPC_Int_P2
110	Lymph_Node.mAPC_Int_P2 -> Lymph_Node.mAPC_Int_P2_CD86 + Lymph_Node.mAPC_Int_P2
111	Lymph_Node.mAPC_Int_P2 -> Lymph_Node.mAPC_Int_P2_PD1 + Lymph_Node.mAPC_Int_P2
112	Lymph_Node.mAPC_Int_P2 -> Lymph_Node.mAPC_Int_P2_PDL1 + Lymph_Node.mAPC_Int_P2
113	Lymph_Node.mAPC_Int_P2 -> Lymph_Node.mAPC_Int_P2_PDL2 + Lymph_Node.mAPC_Int_P2
114	Lymph_Node.mAPC_Int_P2_CD80 + Lymph_Node.PNT_CTLA4 <-> Lymph_Node.NEG_Sig_PNT_CD80
115	Lymph_Node.mAPC_Int_P2_CD80 + Lymph_Node.PNT_Int_PDL1 <-> Lymph_Node.[PNT_PDL1-CD80]
116	Lymph_Node.mAPC_Int_P2_CD80 -> null
117	Lymph_Node.mAPC_Int_P2_CD86 + Lymph_Node.PNT_CTLA4 <-> Lymph_Node.NEG_Sig_PNT_CD86
118	Lymph_Node.mAPC_Int_P2_CD86 + Lymph_Node.PNT_Int_CD28 <-> Lymph_Node.POS_Sig_PNT_CD86
119	Lymph_Node.mAPC_Int_P2_CD86 -> null
120	Lymph_Node.mAPC_Int_P2_PD1 + Lymph_Node.PD1_mab <-> Lymph_Node.PD1mAb_mAPC_PD1
121	Lymph_Node.mAPC_Int_P2_PD1 -> null
122	Lymph_Node.mAPC_Int_P2_PDL1 -> null
123	Lymph_Node.mAPC_Int_P2_PDL2 + Lymph_Node.PNT_Int_PD1 <-> Lymph_Node.[PNT_PD1-PDL2]

Reaction Number	Reaction
124	Lymph_Node.mAPC_Int_P2_PDL2 -> null
125	Lymph_Node.mAPC_PD1 -> null
126	Lymph_Node.mAPC_PDL1 -> null
127	Lymph_Node.mAPC_PDL2 -> null
128	Lymph_Node.Naive_T -> Lymph_Node.Naive_T1
129	Lymph_Node.Naive_T -> null
130	Lymph_Node.Naive_T1 -> Lymph_Node.Naive_T
131	Lymph_Node.Naive_T1 -> Lymph_Node.Primed_Naive_T
132	Lymph_Node.NEG_Sig_PNT_CD80 -> null
133	Lymph_Node.NEG_Sig_PNT_CD86 -> null
134	Lymph_Node.NT_Int_CD28 + Lymph_Node.mAPC_Int_P1_CD80 <-> Lymph_Node.POS_Sig_NT_CD80
135	Lymph_Node.NT_Int_CD28 + Lymph_Node.mAPC_Int_P1_CD86 <-> Lymph_Node.POS_Sig_NT_CD86
136	Lymph_Node.NT_Int_CD28 -> null
137	Lymph_Node.NT1_Int1 -> Lymph_Node.NT1_Int1 + Lymph_Node.NT_Int_CD28
138	Lymph_Node.PD1_mab -> [Blood-Lymph].PD1_mabb
139	Lymph_Node.PDL1_mab -> [Blood-Lymph].PDL1_mabb
140	Lymph_Node.PDL1_mab + Lymph_Node.mAPC_Int_P2_PDL1 <-> Lymph_Node.[PDL1mAb-mAPC_PDL1]
141	Lymph_Node.PDL1_mab + Lymph_Node.PNT_Int_PDL1 <-> Lymph_Node.[PDL1mAb-PNT_PDL1]
142	Lymph_Node.PNT_CTLA4 -> null
143	Lymph_Node.PNT_Int_CD28 + Lymph_Node.mAPC_Int_P2_CD80 <-> Lymph_Node.POS_Sig_PNT_CD80
144	Lymph_Node.PNT_Int_CD28 -> null
145	Lymph_Node.PNT_Int_CD80 + Lymph_Node.mAPC_Int_P2_PDL1 <-> Lymph_Node.[PNT_CD80-PDL1]
146	Lymph_Node.PNT_Int_CD80 -> null
147	Lymph_Node.PNT_Int_PD1 + Lymph_Node.mAPC_Int_P2_PDL1 <-> Lymph_Node.[PNT_PD1-PDL1]
148	Lymph_Node.PNT_Int_PD1 + Lymph_Node.PD1_mab <-> Lymph_Node.PD1mAb_PNT_PD1
149	Lymph_Node.PNT_Int_PD1 -> null
150	Lymph_Node.PNT_Int_PDL1 + Lymph_Node.mAPC_Int_P2_PD1 <-> Lymph_Node.[PNT_PDL1-PD1]
151	Lymph_Node.PNT_Int_PDL1 -> null
152	Lymph_Node.PNT1_Int -> Lymph_Node.PNT_CTLA4 + Lymph_Node.PNT1_Int
153	Lymph_Node.PNT1_Int -> Lymph_Node.PNT_Int_CD28 + Lymph_Node.PNT1_Int
154	Lymph_Node.PNT1_Int -> Lymph_Node.PNT_Int_CD80 + Lymph_Node.PNT1_Int
155	Lymph_Node.PNT1_Int -> Lymph_Node.PNT1_Int + Lymph_Node.PNT_Int_PD1
156	Lymph_Node.PNT1_Int -> Lymph_Node.PNT1_Int + Lymph_Node.PNT_Int_PDL1
157	Lymph_Node.Primed_Naive_T -> Lymph_Node.Primed_Naive_T1
158	Lymph_Node.Primed_Naive_T1 -> Lymph_Node.Anergic_Naive_T
159	Lymph_Node.Primed_Naive_T1 -> Lymph_Node.Primed_Naive_T
160	Lymph_Node.Primed_Naive_T1 -> Lymph_Node.Prolif_Naive_T
161	Lymph_Node.Prolif_Naive_T -> Lymph_Node.Effector_T
162	Lymph_Node.Prolif_Naive_T -> null
163	Lymph_Node.TrALN_CT_aCT -> null
164	Lymph_Node.TrALN_CT_CD80 -> null
165	Lymph_Node.TrALN_CT_CD86 -> null
166	Lymph_Node.TregLN -> Lymph_Node.TregLN + Lymph_Node.TrLN_CTLA4
167	Lymph_Node.TregLN + Lymph_Node.mAPC1 -> Lymph_Node.TregLN_mAPC + Lymph_Node.TregLN + Lymph_Node.mAPC1
168	Lymph_Node.TregLN + Lymph_Node.Naive_T2 -> Lymph_Node.[TregLN-NT] + Lymph_Node.TregLN + Lymph_Node.Naive_T2
169	Lymph_Node.TregLN + Lymph_Node.Primed_Naive_T2 -> Lymph_Node.[TregLN-PNT] + Lymph_Node.TregLN + Lymph_Node.Primed_Naive_T2
170	Lymph_Node.TregLN_mAPC + Lymph_Node.mAPC -> null
171	Lymph_Node.TregLN_mAPC -> null
172	Lymph_Node.TregLN_mAPC1 -> Lymph_Node.[Tr-mAPC_CD80] + Lymph_Node.TregLN_mAPC1
173	Lymph_Node.TregLN_mAPC1 -> Lymph_Node.[Tr-mAPC_CD86] + Lymph_Node.TregLN_mAPC1
174	Lymph_Node.TregLN_mAPC1 -> Lymph_Node.[Tr-mAPC_CTLA4] + Lymph_Node.TregLN_mAPC1
175	Lymph_Node.TrLN_CTLA4 + Lymph_Node.CTLA4_mab <-> Lymph_Node.TrLN_CT_aCT
176	Lymph_Node.TrLN_CTLA4 -> null
177	null -> [Blood-Lymph].CTLA4_mabB
178	null -> [Blood-Lymph].PD1_mabb
179	null -> [Blood-Lymph].PDL1_mabb
180	null -> Lymph_Node.Naive_T
181	null -> Lymph_Node.Prolif_Naive_T
182	null -> Tumor.APC_T
183	null -> Tumor.Cancer
184	Peripheral.CTLA4_mabP_leaky <-> Lymph_Node.CTLA4_mab
185	Peripheral.CTLA4_mabP_tight <-> Lymph_Node.CTLA4_mab

Reaction Number	Reaction
186	Peripheral.EffT_P_f_Vasc -> Lungs.EffT_f_LungsVasc
187	Peripheral.EffT_P_f_Vasc -> null
188	Peripheral.PD1_mabP_leaky <-> Lymph_Node.PD1_mab
189	Peripheral.PD1_mabP_tight <-> Lymph_Node.PD1_mab
190	Peripheral.PDL1_mabP_leaky <-> Lymph_Node.PDL1_mab
191	Peripheral.PDL1_mabP_tight <-> Lymph_Node.PDL1_mab
192	Tumor.[C{CD80}] -> Tumor.[C{CD80}] + Tumor.[C5=CD80]
193	Tumor.[C{PD1}] -> Tumor.[C2=PD1] + Tumor.[C{PD1}]
194	Tumor.[C{PD1}{CD80}] -> Tumor.[C{PD1}{CD80}] + Tumor.[C9a=PD1]
195	Tumor.[C{PD1}{CD80}] -> Tumor.[C{PD1}{CD80}] + Tumor.[C9b=CD80]
196	Tumor.[C{PD1}{PDL1}] -> Tumor.[C6a=PD1] + Tumor.[C{PD1}{PDL1}]
197	Tumor.[C{PD1}{PDL1}] -> Tumor.[C6b=PDL1] + Tumor.[C{PD1}{PDL1}]
198	Tumor.[C{PD1}{PDL1}{CD80}] -> Tumor.[C{PD1}{PDL1}{CD80}] + Tumor.[C14a=PD1]
199	Tumor.[C{PD1}{PDL1}{CD80}] -> Tumor.[C{PD1}{PDL1}{CD80}] + Tumor.[C14b=PDL1]
200	Tumor.[C{PD1}{PDL1}{CD80}] -> Tumor.[C{PD1}{PDL1}{CD80}] + Tumor.[C14c=CD80]
201	Tumor.[C{PD1}{PDL1}{PDL2}] -> Tumor.[C{PD1}{PDL1}{PDL2}] + Tumor.[C10a=PD1]
202	Tumor.[C{PD1}{PDL1}{PDL2}] -> Tumor.[C{PD1}{PDL1}{PDL2}] + Tumor.[C10b=PDL1]
203	Tumor.[C{PD1}{PDL1}{PDL2}] -> Tumor.[C{PD1}{PDL1}{PDL2}] + Tumor.[C10c=PDL2]
204	Tumor.[C{PD1}{PDL1}{PDL2}{CD80}] -> Tumor.[C{PD1}{PDL1}{PDL2}{CD80}] + Tumor.[C16a=PD1]
205	Tumor.[C{PD1}{PDL1}{PDL2}{CD80}] -> Tumor.[C{PD1}{PDL1}{PDL2}{CD80}] + Tumor.[C16b=PDL1]
206	Tumor.[C{PD1}{PDL1}{PDL2}{CD80}] -> Tumor.[C{PD1}{PDL1}{PDL2}{CD80}] + Tumor.[C16c=PDL2]
207	Tumor.[C{PD1}{PDL1}{PDL2}{CD80}] -> Tumor.[C{PD1}{PDL1}{PDL2}{CD80}] + Tumor.[C16d=CD80]
208	Tumor.[C{PD1}{PDL2}] -> Tumor.[C{PD1}{PDL2}] + Tumor.[C7a=PD1]
209	Tumor.[C{PD1}{PDL2}] -> Tumor.[C{PD1}{PDL2}] + Tumor.[C7b=PDL2]
210	Tumor.[C{PD1}{PDL2}{CD80}] -> Tumor.[C{PD1}{PDL2}{CD80}] + Tumor.[C15a=PD1]
211	Tumor.[C{PD1}{PDL2}{CD80}] -> Tumor.[C{PD1}{PDL2}{CD80}] + Tumor.[C15b=PDL2]
212	Tumor.[C{PD1}{PDL2}{CD80}] -> Tumor.[C{PD1}{PDL2}{CD80}] + Tumor.[C15c=CD80]
213	Tumor.[C{PDL1}] -> Tumor.[C{PDL1}] + Tumor.[C3=PDL1]
214	Tumor.[C{PDL1}{CD80}] -> Tumor.[C{PDL1}{CD80}] + Tumor.[C11a=PDL1]
215	Tumor.[C{PDL1}{CD80}] -> Tumor.[C{PDL1}{CD80}] + Tumor.[C11b=CD80]
216	Tumor.[C{PDL1}{PDL2}] -> Tumor.[C{PDL1}{PDL2}] + Tumor.[C8a=PDL1]
217	Tumor.[C{PDL1}{PDL2}] -> Tumor.[C{PDL1}{PDL2}] + Tumor.[C8b=PDL2]
218	Tumor.[C{PDL1}{PDL2}{CD80}] -> Tumor.[C{PDL1}{PDL2}{CD80}] + Tumor.[C13a=PDL1]
219	Tumor.[C{PDL1}{PDL2}{CD80}] -> Tumor.[C{PDL1}{PDL2}{CD80}] + Tumor.[C13b=PDL2]
220	Tumor.[C{PDL1}{PDL2}{CD80}] -> Tumor.[C{PDL1}{PDL2}{CD80}] + Tumor.[C13c=CD80]
221	Tumor.[C{PDL2}] -> Tumor.[C{PDL2}] + Tumor.[C4=PDL2]
222	Tumor.[C{PDL2}{CD80}] -> Tumor.[C{PDL2}{CD80}] + Tumor.[C12a=PDL2]
223	Tumor.[C{PDL2}{CD80}] -> Tumor.[C{PDL2}{CD80}] + Tumor.[C12b=CD80]
224	Tumor.[C10a=PD1] + Tumor.PD1_mabt <-> Tumor.[C10a=PD1:aPD1]
225	Tumor.[C10a=PD1] -> null
226	Tumor.[C10b=PDL1] + Tumor.PDL1_mabt <-> Tumor.[C10b=PDL1:aPDL1]
227	Tumor.[C10b=PDL1] -> null
228	Tumor.[C10c=PDL2] -> null
229	Tumor.[C11a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[C11a=PDL1:aPDL1]
230	Tumor.[C11a=PDL1] -> null
231	Tumor.[C11b=CD80] -> null
232	Tumor.[C12a=PDL2] -> null
233	Tumor.[C12b=CD80] -> null
234	Tumor.[C13a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[C13a=PDL1:aPDL1]
235	Tumor.[C13a=PDL1] -> null
236	Tumor.[C13b=PDL2] -> null
237	Tumor.[C13c=CD80] -> null
238	Tumor.[C14a=PD1] + Tumor.[T14a=PDL1] <-> Tumor.[T14a=PDL1:PD1=C14a]
239	Tumor.[C14a=PD1] -> null
240	Tumor.[C14b=PDL1] + Tumor.[T14c=CD80] <-> Tumor.[T14c=CD80:PDL1=C14b]
241	Tumor.[C14b=PDL1] + Tumor.PDL1_mabt <-> Tumor.[C14b=PDL1:aPDL1]
242	Tumor.[C14b=PDL1] -> null
243	Tumor.[C14c=CD80] + Tumor.[T14a=PDL1] <-> Tumor.[T14a=PDL1:CD80=C14c]
244	Tumor.[C14c=CD80] -> null
245	Tumor.[C15a=PD1] + Tumor.PD1_mabt <-> Tumor.[C15a=PD1:aPD1]
246	Tumor.[C15a=PD1] -> null
247	Tumor.[C15b=PDL2] + Tumor.[T15b=PD1] <-> Tumor.[T15b=PD1:PDL2=C15b]
248	Tumor.[C15b=PDL2] -> null
249	Tumor.[C15c=CD80] + Tumor.[T15a=PDL1] <-> Tumor.[T15a=PDL1:CD80=C15c]
250	Tumor.[C15c=CD80] -> null
251	Tumor.[C16a=PD1] + Tumor.[T16a=PDL1] <-> Tumor.[T16a=PDL1:PD1=C16a]

Reaction Number	Reaction
252	Tumor.[C16a=PD1] + Tumor.PD1_mabt <-> Tumor.[C16a=PD1:aPD1]
253	Tumor.[C16a=PD1] -> null
254	Tumor.[C16b=PDL1] + Tumor.PDL1_mabt <-> Tumor.[C16b=PDL1:aPDL1]
255	Tumor.[C16b=PDL1] -> null
256	Tumor.[C16c=PDL2] + Tumor.[T16b=PD1] <-> Tumor.[T16b=PD1:PDL2=C16c]
257	Tumor.[C16c=PDL2] -> null
258	Tumor.[C16d=CD80] -> null
259	Tumor.[C2=PD1] -> null
260	Tumor.[C3=PDL1] -> null
261	Tumor.[C4=PDL2] -> null
262	Tumor.[C5=CD80] -> null
263	Tumor.[C6a=PD1] + Tumor.PD1_mabt <-> Tumor.[C6a=PD1:aPD1]
264	Tumor.[C6a=PD1] -> null
265	Tumor.[C6b=PDL1] + Tumor.[T6b=PD1] <-> Tumor.[T6b=PD1:PDL1=C6b]
266	Tumor.[C6b=PDL1] + Tumor.[T6c=CD80] <-> Tumor.[T6c=CD80:PDL1=C6b]
267	Tumor.[C6b=PDL1] + Tumor.PDL1_mabt <-> Tumor.[C6b=PDL1:aPDL1]
268	Tumor.[C6b=PDL1] -> null
269	Tumor.[C7a=PD1] -> null
270	Tumor.[C7b=PDL2] -> null
271	Tumor.[C8a=PDL1] + Tumor.[T8b=CD80] <-> Tumor.[T8b=CD80:PDL1=C8a]
272	Tumor.[C8a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[C8a=PDL1:aPDL1]
273	Tumor.[C8a=PDL1] -> null
274	Tumor.[C8b=PDL2] -> null
275	Tumor.[C9a=PD1] + Tumor.[T9=PDL1] <-> Tumor.[T9=PDL1-PD1=C9a]
276	Tumor.[C9a=PD1] -> null
277	Tumor.[C9b=CD80] -> null
278	Tumor.[CTLA4:CD80_TrAT] -> null
279	Tumor.[CTLA4:CD86_TrAT] -> null
280	Tumor.[CTLA4_CTLA4-Trt] -> null
281	Tumor.[T{PD1}{80}-{PDL1}{PDL2}C] -> Tumor.[T{PD1}{80}-{PDL1}{PDL2}C] + Tumor.[T8a=PD1]
282	Tumor.[T{PD1}{80}-{PDL1}{PDL2}C] -> Tumor.[T{PD1}{80}-{PDL1}{PDL2}C] + Tumor.[T8b=CD80]
283	Tumor.[T{PD1}{CD80}-{PDL1}C] -> Tumor.[T{PD1}{CD80}-{PDL1}C] + Tumor.[T3a=PD1]
284	Tumor.[T{PD1}{CD80}-{PDL1}C] -> Tumor.[T{PD1}{CD80}-{PDL1}C] + Tumor.[T3b=CD80]
285	Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C] + Tumor.[T16a=PDL1]
286	Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C] + Tumor.[T16b=PD1]
287	Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C] + Tumor.[T16c=CD80]
288	Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C] + Tumor.[T14a=PDL1]
289	Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C] + Tumor.[T14b=PD1]
290	Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C] + Tumor.[T14c=CD80]
291	Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C] + Tumor.[T10a=PDL1]
292	Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C] + Tumor.[T10b=PD1]
293	Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C] + Tumor.[T10c=CD80]
294	Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C] + Tumor.[T6a=PDL1]
295	Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C] + Tumor.[T6b=PD1]
296	Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C] -> Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C] + Tumor.[T6c=CD80]
297	Tumor.[T{PD1}{L1}-{PD1}{80}{PDL2}C] -> Tumor.[T{PD1}{L1}-{PD1}{80}{PDL2}C] + Tumor.[T15a=PDL1]
298	Tumor.[T{PD1}{L1}-{PD1}{80}{PDL2}C] -> Tumor.[T{PD1}{L1}-{PD1}{80}{PDL2}C] + Tumor.[T15b=PD1]
299	Tumor.[T{PD1}{L1}-{PD1}{L2}C] -> Tumor.[T{PD1}{L1}-{PD1}{L2}C] + Tumor.[T7a=PDL1]
300	Tumor.[T{PD1}{L1}-{PD1}{L2}C] -> Tumor.[T{PD1}{L1}-{PD1}{L2}C] + Tumor.[T7b=PD1]
301	Tumor.[T{PD1}{L1}-{PDL1}{80}{L2}C] -> Tumor.[T{PD1}{L1}-{PDL1}{80}{L2}C] + Tumor.[T13a=PDL1]
302	Tumor.[T{PD1}{L1}-{PDL1}{80}{L2}C] -> Tumor.[T{PD1}{L1}-{PDL1}{80}{L2}C] + Tumor.[T13b=PD1]
303	Tumor.[T{PD1}{L1}-{PDL1}{80}C] -> Tumor.[T{PD1}{L1}-{PDL1}{80}C] + Tumor.[T11a=PDL1]
304	Tumor.[T{PD1}{L1}-{PDL1}{80}C] -> Tumor.[T{PD1}{L1}-{PDL1}{80}C] + Tumor.[T11b=PD1]
305	Tumor.[T{PD1}{L1}-{PDL2}{80}C] -> Tumor.[T{PD1}{L1}-{PDL2}{80}C] + Tumor.[T12a=PDL1]
306	Tumor.[T{PD1}{L1}-{PDL2}{80}C] -> Tumor.[T{PD1}{L1}-{PDL2}{80}C] + Tumor.[T12b=PD1]
307	Tumor.[T{PD1}-{PDL2}C] -> Tumor.[T{PD1}-{PDL2}C] + Tumor.[T4=PD1]
308	Tumor.[T{PDL1}-{CD80}{PD1}C] -> Tumor.[T{PDL1}-{CD80}{PD1}C] + Tumor.[T9=PDL1]
309	Tumor.[T{PDL1}-{CD80}C] -> Tumor.[T{PDL1}-{CD80}C] + Tumor.[T5=PDL1]
310	Tumor.[T{PDL1}-{PD1}C] -> Tumor.[T{PDL1}-{PD1}C] + Tumor.[T2=PDL1]
311	Tumor.[T10a=PDL1] + Tumor.[C10a=PD1] <-> Tumor.[T10a=PDL1:PD1=C10a]
312	Tumor.[T10a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[T10a=PDL1:aPDL1]
313	Tumor.[T10a=PDL1] -> null
314	Tumor.[T10b=PD1] + Tumor.[C10b=PDL1] <-> Tumor.[T10b=PD1:PDL1=C10b]
315	Tumor.[T10b=PD1] + Tumor.[C10c=PDL2] <-> Tumor.[T10b=PD1:PDL2=C10c]
316	Tumor.[T10b=PD1] -> null

Reaction Number	Reaction
317	Tumor.[T10c=CD80] + Tumor.[C10b=PDL1] <-> Tumor.[T10c=CD80:PDL1=C10b]
318	Tumor.[T10c=CD80] -> null
319	Tumor.[T11a=PDL1] + Tumor.[C11b=CD80] <-> Tumor.[T11a=PDL1:CD80=C11b]
320	Tumor.[T11a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[T11a=PDL1:aPDL1]
321	Tumor.[T11a=PDL1] -> null
322	Tumor.[T11b=PD1] + Tumor.[C11a=PDL1] <-> Tumor.[T11b=PD1:PDL1=C11a]
323	Tumor.[T11b=PD1] -> null
324	Tumor.[T12a=PDL1] + Tumor.[C12b=CD80] <-> Tumor.[T12a=PDL1:CD80=C12b]
325	Tumor.[T12a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[T12a=PDL1:aPDL1]
326	Tumor.[T12a=PDL1] -> null
327	Tumor.[T12b=PD1] + Tumor.[C12a=PDL2] <-> Tumor.[T12b=PD1:PDL2=C12a]
328	Tumor.[T12b=PD1] -> null
329	Tumor.[T13a=PDL1] + Tumor.[C13c=CD80] <-> Tumor.[T13a=PDL1:CD80=C13c]
330	Tumor.[T13a=PDL1] -> null
331	Tumor.[T13b=PD1] + Tumor.[C13a=PDL1] <-> Tumor.[T13b=PD1:PDL1=C13a]
332	Tumor.[T13b=PD1] + Tumor.[C13b=PDL2] <-> Tumor.[T13b=PD1:PDL2=C13b]
333	Tumor.[T13b=PD1] + Tumor.PD1_mabt <-> Tumor.[T13b=PD1:aPD1]
334	Tumor.[T13b=PD1] -> null
335	Tumor.[T14a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[T14a=PDL1:aPDL1]
336	Tumor.[T14a=PDL1] -> null
337	Tumor.[T14b=PD1] + Tumor.[C14b=PDL1] <-> Tumor.[T14b=PD1:PDL1=C14b]
338	Tumor.[T14b=PD1] -> null
339	Tumor.[T14c=CD80] -> null
340	Tumor.[T15a=PDL1] + Tumor.[C15a=PD1] <-> Tumor.[T15a=PDL1:PD1=C15a]
341	Tumor.[T15a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[T15a=PDL1:aPDL1]
342	Tumor.[T15a=PDL1] -> null
343	Tumor.[T15b=PD1] + Tumor.PD1_mabt <-> Tumor.[T15b=PD1:aPD1]
344	Tumor.[T15b=PD1] -> null
345	Tumor.[T16a=PDL1] + Tumor.[C16d=CD80] <-> Tumor.[T16a=PDL1:CD80=C16d]
346	Tumor.[T16a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[T16a=PDL1:aPDL1]
347	Tumor.[T16a=PDL1] -> null
348	Tumor.[T16b=PD1] + Tumor.[C16b=PDL1] <-> Tumor.[T16b=PD1:PDL1=C16b]
349	Tumor.[T16b=PD1] + Tumor.PD1_mabt <-> Tumor.[T16b=PD1:aPD1]
350	Tumor.[T16b=PD1] -> null
351	Tumor.[T16c=CD80] + Tumor.[C16b=PDL1] <-> Tumor.[T16c=CD80:PDL1=C16b]
352	Tumor.[T16c=CD80] -> null
353	Tumor.[T2=PDL1] + Tumor.[C2=PD1] <-> Tumor.[T2=PDL1:PD1=C2]
354	Tumor.[T2=PDL1] -> null
355	Tumor.[T3a=PD1] + Tumor.[C3=PDL1] <-> Tumor.[T3a=PD1:PDL1=C3]
356	Tumor.[T3a=PD1] + Tumor.PD1_mabt <-> Tumor.[T3a=PD1:aPD1]
357	Tumor.[T3a=PD1] -> null
358	Tumor.[T3b=CD80] + Tumor.[C3=PDL1] <-> Tumor.[T3b=CD80:PDL1=C3]
359	Tumor.[T3b=CD80] -> null
360	Tumor.[T4=PD1] + Tumor.[C4=PDL2] <-> Tumor.[T4=PD1:PDL2=C4]
361	Tumor.[T4=PD1] + Tumor.PD1_mabt <-> Tumor.[T4=PD1:aPD1]
362	Tumor.[T4=PD1] -> null
363	Tumor.[T5=PDL1] + Tumor.[C5=CD80] <-> Tumor.[T5=PDL1:CD80=C5]
364	Tumor.[T5=PDL1] + Tumor.PDL1_mabt <-> Tumor.[T5=PDL1:aPDL1]
365	Tumor.[T5=PDL1] -> null
366	Tumor.[T6a=PDL1] + Tumor.[C6a=PD1] <-> Tumor.[T6a=PDL1:PD1=C6a]
367	Tumor.[T6a=PDL1] + Tumor.PDL1_mabt <-> Tumor.[T6a=PDL1:aPDL1]
368	Tumor.[T6a=PDL1] -> null
369	Tumor.[T6b=PD1] + Tumor.PD1_mabt <-> Tumor.[T6b=PD1:aPD1]
370	Tumor.[T6b=PD1] -> null
371	Tumor.[T6c=CD80] -> null
372	Tumor.[T7a=PDL1] + Tumor.[C7a=PD1] <-> Tumor.[T7a=PDL1:PD1=C7a]
373	Tumor.[T7a=PDL1] -> null
374	Tumor.[T7b=PD1] + Tumor.[C7b=PDL2] <-> Tumor.[T7b=PD1:PDL2=C7b]
375	Tumor.[T7b=PD1] -> null
376	Tumor.[T8a=PD1] + Tumor.[C8a=PDL1] <-> Tumor.[T8a=PD1:PDL1=C8a]
377	Tumor.[T8a=PD1] + Tumor.[C8b=PDL2] <-> Tumor.[T8a=PD1:PDL2=C8b]
378	Tumor.[T8a=PD1] -> null
379	Tumor.[T8b=CD80] -> null
380	Tumor.[T9=PDL1] + Tumor.[C9b=CD80] <-> Tumor.[T9=PDL1-CD80=C9b]
381	Tumor.[T9=PDL1] + Tumor.PDL1_mabt <-> Tumor.[T9=PDL1:aPDL1]
382	Tumor.[T9=PDL1] -> null
383	Tumor.APC_T -> null
384	Tumor.C_DebrisT + Tumor.APC_T -> Tumor.mAPC_T

Reaction Number	Reaction
385	Tumor.C_DebrisT -> Lymph_Node.C_DebrisLN
386	Tumor.C_DebrisT -> null
387	Tumor.C_DebrisT -> null
388	Tumor.C_DebrisT -> null
389	Tumor.Cancer -> (**AntSpread**) Tumor.C_DebrisT
390	Tumor.CD80_mAPCT -> null
391	Tumor.CD80_TeffT + Tumor.PDL1_TregT <-> Tumor.[PDL1:CD80_TrTeff]
392	Tumor.CD80_TeffT -> null
393	Tumor.CD80_TeffT1 -> null
394	Tumor.CD86_mAPCT -> null
395	Tumor.CTLA4_mabt <-> Lymph_Node.CTLA4_mab
396	Tumor.CTLA4_TregT + Tumor.CD80_mAPCT <-> Tumor.[CTLA4:CD80_TrAT]
397	Tumor.CTLA4_TregT + Tumor.CD86_mAPCT <-> Tumor.[CTLA4:CD86_TrAT]
398	Tumor.CTLA4_TregT + Tumor.CTLA4_mabt <-> Tumor.[CTLA4_CTLA4-Trt]
399	Tumor.CTLA4_TregT -> null
400	Tumor.Effector_TT -> null
401	Tumor.Effector_TT -> null
402	Tumor.Effector_TT -> Tumor.Effector_TT_Res
403	Tumor.Effector_TT_C_Eng + Tumor.Cancer1 -> Tumor.Effector_TT_C_Eng + Tumor.TC1 + Tumor.Cancer1
404	Tumor.EffT_AR_Vasc -> null
405	Tumor.EffT_AR_Vasc -> Tumor.Effector_TT
406	Tumor.EffT_b_Vasc -> null
407	Tumor.EffT_b_Vasc -> Tumor.EffT_AR_Vasc
408	Tumor.EffT_b_Vasc -> Tumor.EffT_f_Vasc
409	Tumor.EffT_f_Vasc + Tumor.Tmr_Free_Sites -> Tumor.EffT_b_Vasc + Tumor.Tmr_Free_Sites
410	Tumor.EffT_f_Vasc -> Lungs.EffT_f_LungsVasc
411	Tumor.EffT_f_Vasc -> null
412	Tumor.mAPC_T -> Lymph_Node.mAPC
413	Tumor.mAPC_T -> null
414	Tumor.mAPC_T -> null
415	Tumor.mAPCT_EngTregT -> Tumor.CD80_mAPCT + Tumor.mAPCT_EngTregT
416	Tumor.mAPCT_EngTregT -> Tumor.CD86_mAPCT + Tumor.mAPCT_EngTregT
417	Tumor.MDSC_T + Tumor.Effector_TT_MDSCs -> Tumor.MDSCsT_Teff + Tumor.Effector_TT_MDSCs + Tumor.MDSC_T
418	Tumor.MDSCsT_EngTeff -> Tumor.PD1_MDSCsT + Tumor.MDSCsT_EngTeff
419	Tumor.MDSCsT_EngTeff -> Tumor.PDL1_MDSCsT + Tumor.MDSCsT_EngTeff
420	Tumor.MDSCsT_Teff + Tumor.Effector_TT -> null
421	Tumor.MDSCsT_Teff -> null
422	Tumor.PD1_mabt <-> Lymph_Node.PD1_mab
423	Tumor.PD1_mabt + Tumor.[C14a=PD1] <-> Tumor.[C14a=PD1:aPD1]
424	Tumor.PD1_mabt + Tumor.[C2=PD1] <-> Tumor.[C2=PD1:aPD1]
425	Tumor.PD1_mabt + Tumor.[C7a=PD1] <-> Tumor.[C7a=PD1:aPD1]
426	Tumor.PD1_mabt + Tumor.[C9a=PD1] <-> Tumor.[C9a=PD1:aPD1]
427	Tumor.PD1_mabt + Tumor.[T10b=PD1] <-> Tumor.[T10b=PD1:aPD1]
428	Tumor.PD1_mabt + Tumor.[T11b=PD1] <-> Tumor.[T11b=PD1:aPD1]
429	Tumor.PD1_mabt + Tumor.[T12b=PD1] <-> Tumor.[T12b=PD1:aPD1]
430	Tumor.PD1_mabt + Tumor.[T14b=PD1] <-> Tumor.[T14b=PD1:aPD1]
431	Tumor.PD1_mabt + Tumor.[T7b=PD1] <-> Tumor.[T7b=PD1:aPD1]
432	Tumor.PD1_mabt + Tumor.[T8a=PD1] <-> Tumor.[T8a=PD1:aPD1]
433	Tumor.PD1_mabt + Tumor.PD1_TeffT <-> Tumor.[PD1:aPD1_Teff]
434	Tumor.PD1_MDSCsT + Tumor.PD1_mabt <-> Tumor.[PD1:aPD1_MDSCs]
435	Tumor.PD1_MDSCsT + Tumor.PDL1_TeffT1 <-> Tumor.[PD1:PDL1_MDSCT]
436	Tumor.PD1_MDSCsT -> null
437	Tumor.PD1_TeffT + Tumor.PDL1_TregT <-> Tumor.[PDL1:PD1_TrTeff]
438	Tumor.PD1_TeffT -> null
439	Tumor.PD1_TeffT1 + Tumor.PD1_mabt <-> Tumor.[PD1:aPD1_Teff1]
440	Tumor.PD1_TeffT1 -> null
441	Tumor.PD1_TregT + Tumor.PD1_mabt <-> Tumor.[PD1:aPD1_Treg]
442	Tumor.PD1_TregT -> null
443	Tumor.PDL1_mabt <-> Lymph_Node.PDL1_mab
444	Tumor.PDL1_mabt + Tumor.[C3=PDL1] <-> Tumor.[C3=PDL1:aPDL1]
445	Tumor.PDL1_mabt + Tumor.[T13a=PDL1] <-> Tumor.[T13a=PDL1:aPDL1]
446	Tumor.PDL1_mabt + Tumor.[T2=PDL1] <-> Tumor.[T2=PDL1:aPDL1]
447	Tumor.PDL1_mabt + Tumor.[T7a=PDL1] <-> Tumor.[T7a=PDL1:aPDL1]
448	Tumor.PDL1_mabt + Tumor.PDL1_TeffT <-> Tumor.[PDL1:aPDL1_Teff]
417	Tumor.PDL1_mabt + Tumor.PDL1_TeffT1 <-> Tumor.[PDL1:aPDL1_Teff1]
418	Tumor.PDL1_MDSCsT + Tumor.CD80_TeffT1 <-> Tumor.[PDL1:CD80_MDSCT]

Reaction Number	Reaction
419	Tumor.PDL1_MDSCsT + Tumor.PD1_TeffT1 <-> Tumor.[PDL1:PD1_MDSCT]
420	Tumor.PDL1_MDSCsT + Tumor.PDL1_mabt <-> Tumor.[PDL1:aPDL1_MDSCs]
421	Tumor.PDL1_MDSCsT -> null
422	Tumor.PDL1_TeffT + Tumor.PD1_TregT <-> Tumor.[PD1:PDL1_TrTeff]
423	Tumor.PDL1_TeffT -> null
424	Tumor.PDL1_TeffT1 -> null
425	Tumor.PDL1_TregT + Tumor.PDL1_mabt <-> Tumor.[PDL1:aPDL1_Treg]
426	Tumor.PDL1_TregT -> null
427	Tumor.T_Recover_Can_Dead -> null
428	Tumor.TC1 + Tumor.Cancer -> (**AntSpread**) Tumor.C_DebrisT
429	Tumor.TC1 -> Tumor.T_Recover_Can_Dead
430	Tumor.TC2 + Tumor.Effector_TT -> Tumor.TC2
431	Tumor.Teff_EngMDSC -> Tumor.Teff_EngMDSC + Tumor.CD80_TeffT1
432	Tumor.Teff_EngMDSC -> Tumor.Teff_EngMDSC + Tumor.PD1_TeffT1
433	Tumor.Teff_EngMDSC -> Tumor.Teff_EngMDSC + Tumor.PDL1_TeffT1
434	Tumor.Teff_EngTregT -> Tumor.CD80_TeffT + Tumor.Teff_EngTregT
435	Tumor.Teff_EngTregT -> Tumor.PD1_TeffT + Tumor.Teff_EngTregT
436	Tumor.Teff_EngTregT -> Tumor.PDL1_TeffT + Tumor.Teff_EngTregT
437	Tumor.TregT + Tumor.Effector_TT_TregT -> Tumor.TregT_Teff + Tumor.Effector_TT_TregT + Tumor.TregT
438	Tumor.TregT_EngAPC -> Tumor.CTLA4_TregT + Tumor.TregT_EngAPC
439	Tumor.TregT_EngTeff -> Tumor.PD1_TregT + Tumor.TregT_EngTeff
440	Tumor.TregT_EngTeff -> Tumor.PDL1_TregT + Tumor.TregT_EngTeff
441	Tumor.TregT_Teff + Tumor.Effector_TT -> null
442	Tumor.TregT_Teff -> null

Table S1 – Model Reactions (End)

Table S2 – Model Reaction Rates (Start)

Reaction Number	Reaction Rate
1	Kpa_LNB*S_LNB*VL*f_LN_CTLA4*([Blood-Lymph].CTLA4_mabB/Vc_CTLA4-Lymph_Node.CTLA4_mab/VL)
2	0.67*Q_L*[Blood-Lymph].CTLA4_mabB*(1-Sigma1_CTLA4)/Vc_CTLA4 - (Peripheral.CTLA4_mabP_leaky/(0.35*ISF*KP_CTLA4))*0.33*Q_L*(1-Sigma1_CTLA4)
3	0.33*Q_L*[Blood-Lymph].CTLA4_mabB*(1-Sigma2_CTLA4)/Vc_CTLA4-(Peripheral.CTLA4_mabP_tight/(0.65*ISF*KP_CTLA4))*0.33*Q_L*(1-Sigma2_CTLA4)
4	Kpa_TB*S_TB*Vt_avg_const*[Blood-Lymph].CTLA4_mabB/Vc_PD1-Kpa_TB*S_TB*Vt_avg_const*Tumor.CTLA4_mabt/(Vex_Tmr)
5	Cl_CTLA4*[Blood-Lymph].CTLA4_mabB
6	EffT_Migrate*[Blood-Lymph].Effector_T_TB
7	QC_GI*[Blood-Lymph].Effector_TB/Vc_Teff
8	(QC_Liver-QC_GI-QC_Spleen+LC_GI+LC_Spleen)*[Blood-Lymph].Effector_TB/Vc_Teff
9	QC_Spleen * [Blood-Lymph].Effector_TB/Vc_Teff
10	QC_LN*[Blood-Lymph].Effector_TB/Vc_Teff
11	EffT_Turnover*[Blood-Lymph].Effector_TB
12	QC_Periph*[Blood-Lymph].Effector_TB/Vc_Teff
13	QC_Tmr*TCytokineHoming*[Blood-Lymph].Effector_TB/Vc_Teff
14	Kpa_LNB*S_LNB*VL*f_LN_PD1*([Blood-Lymph].PD1_mabb/Vc_PD1-Lymph_Node.PD1_mab/VL)
15	0.67*Q_L*PD1_mabb*(1-Sigma1_PD1)/Vc_PD1-(Peripheral.PD1_mabP_leaky/(0.35*ISF*KP_PD1))*0.33*Q_L*(1-Sigma1_PD1)
16	0.33*Q_L*[Blood-Lymph].PD1_mabb*(1-Sigma2_PD1)/Vc_PD1-(Peripheral.PD1_mabP_tight/(0.65*ISF*KP_PD1))*0.33*Q_L*(1-Sigma2_PD1)
17	Kpa_TB*S_TB*Vt_avg_const*[Blood-Lymph].PD1_mabb/Vc_PD1-Kpa_TB*S_TB*Vt_avg_const*Tumor.PD1_mabt/(Vex_Tmr)
18	(Cl_PD1/Vc_PD1)*[Blood-Lymph].PD1_mabb
19	Kpa_LNB*S_LNB*VL*f_LN_PD1*([Blood-Lymph].PDL1_mabb/Vc_PDL1-Lymph_Node.PDL1_mab/VL)
20	0.67*Q_L*PDL1_mabb*(1-Sigma1_PDL1)/Vc_PDL1-(Peripheral.PDL1_mabP_leaky/(0.35*ISF*KP_PDL1))*0.33*Q_L*(1-Sigma1_PDL1)
21	0.33*Q_L*[Blood-Lymph].PDL1_mabb*(1-Sigma2_PDL1)/Vc_PDL1-(Peripheral.PDL1_mabP_tight/(0.65*ISF*KP_PDL1))*0.33*Q_L*(1-Sigma2_PDL1)

Reaction Number	Reaction Rate
22	Kpa_TB*S_TB*Vt_avg_const*[Blood-Lymph].PDL1_mabb/Vc_PDL1- Kpa_TB*S_TB*Vt_avg_const*Tumor.PDL1_mabt/(Vex_Tmr)
23	(Cl_PDL1/Vc_PDL1)*[Blood-Lymph].PDL1_mabb
24	(Vm/Durvalumab_MW)*[Blood-Lymph].PDL1_mabb/(Km*Vc_PDL1/Durvalumab_MW+[Blood-Lymph].PDL1_mabb)
25	(QC_GI - LC_GI)*Liv_Spln_GI.EffT_GI_f_Vasc/Vv_GI
26	EffT_Turnover*Liv_Spln_GI.EffT_GI_f_Vasc
27	J_Liver*Liv_Spln_GI.EffT_Liver_AR_Vasc
28	EffT_Turnover*Liv_Spln_GI.EffT_Liver_AR_Vasc
29	AR_Liver*[Liv_Spln_GI].EffT_Liver_b_Vasc
30	kr_Periph*Liv_Spln_GI.EffT_Liver_b_Vasc
31	EffT_Turnover*Liv_Spln_GI.EffT_Liver_b_Vasc
32	(QC_Liver - LC_Liver)*Liv_Spln_GI.EffT_Liver_f_Vasc/Vv_Liver
33	EffT_Turnover*Liv_Spln_GI.EffT_Liver_f_Vasc
34	LC_Liver*Delta_Liver*Liv_Spln_GI.EffT_LiverEx/Vext_Liver
35	EffT_Turnover*Liv_Spln_GI.EffT_LiverEx
36	J_Spleen*Liv_Spln_GI.EffT_Spleen_AR_Vasc
37	EffT_Turnover*Liv_Spln_GI.EffT_Spleen_AR_Vasc
38	AR_Spleen*[Liv_Spln_GI].EffT_Spleen_b_Vasc
39	kr_Periph*Liv_Spln_GI.EffT_Spleen_b_Vasc
40	EffT_Turnover*Liv_Spln_GI.EffT_Spleen_b_Vasc
41	kf_Spleen*Liv_Spln_GI.Spleen_Free_Sites*[Liv_Spln_GI].EffT_Spleen_f_Vasc/Vv_Spleen
42	(QC_Spleen - LC_Spleen)*Liv_Spln_GI.EffT_Spleen_f_Vasc/Vv_Spleen
43	EffT_Turnover*Liv_Spln_GI.EffT_Spleen_f_Vasc
44	LC_Spleen*Delta_Spleen*Liv_Spln_GI.EffT_SpleenEx/Vext_Spleen
45	EffT_Turnover*Liv_Spln_GI.EffT_SpleenEx
46	kf_Liver*Liver_Free_Sites*[Liv_Spln_GI].EffT_Liver_f_Vasc/Vv_Liver
47	J_Lungs*Lungs.EffT_AR_LungsVasc
48	EffT_Turnover*Lungs.EffT_AR_LungsVasc
49	E_Lungs*Lungs.EffT_AR_LungsVasc
50	kf_Lungs*Lung_Free_Sites*Lungs.EffT_f_LungsVasc/Vv_Lungs
51	(QC_Lungs - LC_Lungs)*Lungs.EffT_f_LungsVasc/Vv_Lungs
52	EffT_Turnover*Lungs.EffT_f_LungsVasc
53	LC_Lungs*Delta_Lungs*Lungs.EffT_LungsEx/Vext_Lungs
54	EffT_Turnover*Lungs.EffT_LungsEx
55	AR_Lungs*Lungs.EffT_r_LungsVasc
56	kr_Lungs*Lungs.EffT_r_LungsVasc
57	EffT_Turnover*Lungs.EffT_r_LungsVasc
58	E_Lungs*Lungs.EffT_r_LungsVasc
59	[kon_PDL1_CD80]*Lymph_Node.[PNT-Tr_CD80]*Lymph_Node.[Tr-PNT_PDL1]/[Vol_Cell-Rec_Tr-PNT] - [koff_PDL1_CD80]*Lymph_Node.[TrPNT_PDL1-CD80]
60	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.[PNT-Tr_CD80]+[TrPNT_PDL1-CD80])
61	[kon_PD1_PDL1]*Lymph_Node.[PNT-Tr_PD1]*Lymph_Node.[Tr-PNT_PDL1]/[Vol_Cell-Rec_Tr-PNT] - [koff_PD1_PDL1]*Lymph_Node.[TrPNT_PDL1-PD1]
62	[kon_PD1-PD1mAb]*Lymph_Node.[PNT-Tr_PD1]*Lymph_Node.PD1_mab/Vtdln - [koff_PD1- PD1mAb]*Lymph_Node.PNTTr_PD1_aPD1
63	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.[PNT-Tr_PD1]+PNTTr_PD1_aPD1+[TrPNT_PDL1-PD1])
64	[kon_PDL1-PDL1mAb]*Lymph_Node.[PNT-Tr_PDL1]*Lymph_Node.PDL1_mab/Vtdln - [koff_PDL1- PDL1mAb]*Lymph_Node.PNTTr_PDL1_aPDL1
65	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.[PNT-Tr_PDL1]+PNTTr_PDL1_aPDL1+[TrPNT_PD1-L1])
66	[Treg:T_IntTime]*Lymph_Node.[TregLN-NT]
67	[Treg:T_IntTime]*Lymph_Node.[TregLN-NT]
68	[Treg:T_IntTime]*Lymph_Node.[TregLN-PNT]*[Sig_TrPNT=PD1/L1/CD80]
69	[Treg:T_IntTime]*Lymph_Node.[TregLN-PNT]*(1-[Sig_TrPNT=PD1/L1/CD80])
70	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.[TregLN-PNT1]*(([%CD80_receptor_level_PNT]*[CD80_receptors-per- Tcell])/[Avagadro's_Num])*(1/Tr_per_T_cell)
71	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.[TregLN-PNT1]*(([%PD1_receptor_level_PNT]*[PD1_receptors-per- Tcell])/[Avagadro's_Num])*(1/Tr_per_T_cell)
72	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.[TregLN-PNT1]*(([%PDL1_receptor_level_PNT]*[PDL1_receptors-per- Tcell])/[Avagadro's_Num])*(1/Tr_per_T_cell)
73	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.[TregLN-PNT1]*([PD1_receptors-per- Tcell]/[Avagadro's_Num])*(1/T_per_Tr_cell)
74	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.[TregLN-PNT1]*([PDL1_receptors-per- Tcell]/[Avagadro's_Num])*(1/T_per_Tr_cell)
75	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.[Tr-mAPC_CD80]+TrALN_CT_CD80)
76	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.[Tr-mAPC_CD86]+TrALN_CT_CD86)
77	[kon_CTLA4_CD80]*Lymph_Node.[Tr-mAPC_CD80]*Lymph_Node.[Tr-mAPC_CTLA4]/[Vol_Cell-Rec_Tr-mAPC] - [koff_CTLA4_CD80]*Lymph_Node.TrALN_CT_CD80

Reaction Number	Reaction Rate
78	[kon_CTLA4_CD86]*Lymph_Node.[Tr-mAPC_CD86]*Lymph_Node.[Tr-mAPC_CTLA4]/[Vol_Cell-Rec_Tr-mAPC]-[koff_CTLA4_CD86]*Lymph_Node.TrALN_CT_CD86
79	kon_CTLA4mAb_CTLA4*Lymph_Node.[Tr-mAPC_CTLA4]*Lymph_Node.CTLA4_mab/Vtdln - koff_CTLA4mAb_CTLA4*Lymph_Node.TrALN_CT_aCT
80	[Exp_CTLA4]*(Lymph_Node.[Tr-mAPC_CTLA4]+[TrALN_CT_aCT]+[TrALN_CT_CD80]+[TrALN_CT_CD86])
81	[kon_PD1_PDL1]*Lymph_Node.[Tr-PNT_PD1]*Lymph_Node.[PNT-Tr_PDL1]/[Vol_Cell-Rec_Tr-PNT] - [koff_PD1_PDL1]*Lymph_Node.[TrPNT_PD1-L1]
82	[kon_PD1-PD1mAb]*Lymph_Node.[Tr-PNT_PD1]*Lymph_Node.PD1_mab/Vtdln - [koff_PD1-PD1mAb]*Lymph_Node.TrPNT_PD1_aPD1
83	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.[Tr-PNT_PD1]+TrPNT_PD1_aPD1+[TrPNT_PD1-L1])
84	[kon_PDL1-PDL1mAb]*Lymph_Node.[Tr-PNT_PDL1]*Lymph_Node.PDL1_mab/Vtdln - [koff_PDL1-PDL1mAb]*Lymph_Node.TrPNT_PDL1_aPDL1
85	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.[Tr-PNT_PDL1]+TrPNT_PDL1_aPDL1+[TrPNT_PDL1-PD1]+[TrPNT_PDL1-CD80])
86	Phago_Debris*Lymph_Node.APCLN*Lymph_Node.C_DebrisLN
87	Debris_Decay*Lymph_Node.C_DebrisLN
88	Q_L/VL*Lymph_Node.CTLA4_mab
89	kon_CTLA4mAb_CTLA4*Lymph_Node.CTLA4_mab*Lymph_Node.PNT_CTLA4/Vtdln-koff_CTLA4mAb_CTLA4*Lymph_Node.CTLA4_mAb_CTLA4
90	Endo_CTLA4*Lymph_Node.CTLA4_mAb_CTLA4
91	EffT_Migrate*Lymph_Node.Effector_T
92	LC_LN*Delta_LN*Lymph_Node.EffT_LN_ExRec/Vext_LN
93	EffT_Turnover*Lymph_Node.EffT_LN_ExRec
94	(QC_LN - LC_LN)*Lymph_Node.EffT_LN_f_Vasc/Vv_LN
95	EffT_Turnover*Lymph_Node.EffT_LN_f_Vasc
96	Exp_All_mAPCLN*(Lymph_Node.mAPC*([CD80_receptors-per-mAPC]/[Avagadro's_Num]))
97	Exp_All_mAPCLN*(Lymph_Node.mAPC*([CD86_receptors-per-mAPC]/[Avagadro's_Num]))
98	Exp_All_mAPCLN*Lymph_Node.mAPC*([PD1_receptors-per-mAPC]/[Avagadro's_Num])
99	Exp_All_mAPCLN*Lymph_Node.mAPC*([PDL1_receptors-per-mAPC]/[Avagadro's_Num])
100	Exp_All_mAPCLN*Lymph_Node.mAPC*([PDL2_receptors-per-mAPC]/[Avagadro's_Num])
101	kf_APC_turnover*Lymph_Node.mAPC
102	kf_TregLNS_Inact*Lymph_Node.mAPC*CTLA4Sig_Secrete
103	Exp_All_mAPCLN*(Lymph_Node.mAPC_CD80)
104	Exp_All_mAPCLN*(Lymph_Node.mAPC_CD86)
105	[Exp_CD28/80/86/PD1/L1/L2]*((Lymph_Node.mAPC_CD80)*(Lymph_Node.mAPC_Int_P1/(Lymph_Node.mAPC+ 1E-100*mole)))*(1/T_cells_per_mAPC)
106	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.mAPC_CD86*(Lymph_Node.mAPC_Int_P1/(Lymph_Node.mAPC+ 1E-100*mole)))*(1/T_cells_per_mAPC)
107	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.mAPC_Int_P1_CD80 + POS_Sig_NT_CD80)
108	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.mAPC_Int_P1_CD86 + POS_Sig_NT_CD86)
109	[Exp_CD28/80/86/PD1/L1/L2]*((Lymph_Node.mAPC_CD80)*(Lymph_Node.mAPC_Int_P2/(Lymph_Node.mAPC+1E-100*mole)))*(1/T_cells_per_mAPC)
110	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.mAPC_CD86*(Lymph_Node.mAPC_Int_P2/(Lymph_Node.mAPC+1E-100*mole)))*(1/T_cells_per_mAPC)
111	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.mAPC_PD1*(Lymph_Node.mAPC_Int_P2/(Lymph_Node.mAPC+1E-100*mole))*(1/T_cells_per_mAPC)
112	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.mAPC_PDL1*(Lymph_Node.mAPC_Int_P2/(Lymph_Node.mAPC+1E-100*mole))*(1/T_cells_per_mAPC)
113	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.mAPC_PDL2*(Lymph_Node.mAPC_Int_P2/(Lymph_Node.mAPC+1E-100*mole))*(1/T_cells_per_mAPC)
114	[kon_CTLA4_CD80]*Lymph_Node.mAPC_Int_P2_CD80*Lymph_Node.PNT_CTLA4/([Volume_PNT-Receptor_Int])-[koff_CTLA4_CD80]*Lymph_Node.NEG_Sig_PNT_CD80
115	[kon_PDL1_CD80]*Lymph_Node.mAPC_Int_P2_CD80*Lymph_Node.PNT_Int_PDL1/[Volume_PNT-Receptor_Int]-[koff_PDL1_CD80]*Lymph_Node.[PNT_PDL1-CD80]
116	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.mAPC_Int_P2_CD80+NEG_Sig_PNT_CD80+POS_Sig_PNT_CD80+[PNT_PDL1-CD80])
117	[kon_CTLA4_CD86]*Lymph_Node.mAPC_Int_P2_CD86*Lymph_Node.PNT_CTLA4/([Volume_PNT-Receptor_Int])-[koff_CTLA4_CD86]*Lymph_Node.NEG_Sig_PNT_CD86
118	[kon_CD28_CD86]*Lymph_Node.mAPC_Int_P2_CD86*Lymph_Node.PNT_Int_CD28/([Volume_PNT-Receptor_Int])-[koff_CD28_CD86]*Lymph_Node.POS_Sig_PNT_CD86
119	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.mAPC_Int_P2_CD86+NEG_Sig_PNT_CD86+POS_Sig_PNT_CD86)
120	[kon_PD1-PD1mAb]*Lymph_Node.mAPC_Int_P2_PD1*Lymph_Node.PD1_mab/Vtdln-[koff_PD1-PD1mAb]*[PD1mAb_mAPC_PD1]
121	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.mAPC_Int_P2_PD1+PD1mAb_mAPC_PD1+[PNT_PDL1-PD1])
122	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.mAPC_Int_P2_PDL1+[PDL1mAb-mAPC_PDL1]+[PNT_PD1-PDL1]+[PNT_CD80-PDL1])
123	[kon_PD1_PDL2]*Lymph_Node.mAPC_Int_P2_PDL2*Lymph_Node.PNT_Int_PD1/[Volume_PNT-Receptor_Int]-[koff_PD1_PDL2]*Lymph_Node.[PNT_PD1-PDL2]

Reaction Number	Reaction Rate
124	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.mAPC_Int_P2_PDL2+[PNT_PD1-PDL2])
125	Exp_All_mAPCLN*Lymph_Node.mAPC_PD1
126	Exp_All_mAPCLN*Lymph_Node.mAPC_PDL1
127	Exp_All_mAPCLN*Lymph_Node.mAPC_PDL2
128	PrimeNT_rate*Lymph_Node.Naive_T*[Prob_NT-mAPC_Interact]*[Sig_NT=CD28]
129	EffT_InOutLN*Lymph_Node.Naive_T
130	PrimeNT1_rate*Lymph_Node.Naive_T1*(1/Antigen_Intensity)*((mAPC_Int_P1)/(mAPC_Int_P1+Naive_T1*mAPC50_per_T_cell+0.001*mole))
131	PrimeNT1_rate*Lymph_Node.Naive_T1*Antigen_Intensity*((mAPC_Int_P1)/(mAPC_Int_P1+Naive_T1*mAPC50_per_T_cell+0.001*mole))
132	Endo_CTLA4*Lymph_Node.NEG_Sig_PNT_CD80
133	Endo_CTLA4*Lymph_Node.NEG_Sig_PNT_CD86
134	[kon_CD28_CD80]*Lymph_Node.NT_Int_CD28*Lymph_Node.mAPC_Int_P1_CD80/[Volume_NT-Receptor_Int] - [koff_CD28_CD80]*Lymph_Node.POS_Sig_NT_CD80
135	[kon_CD28_CD86]*Lymph_Node.NT_Int_CD28*Lymph_Node.mAPC_Int_P1_CD86/[Volume_NT-Receptor_Int] - [koff_CD28_CD86]*Lymph_Node.POS_Sig_NT_CD86
136	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.NT_Int_CD28+POS_Sig_NT_CD80+POS_Sig_NT_CD86)
137	[Exp_CD28/80/86/PD1/L1/L2]*(([CD28_receptors-per-Tcell]/[Avagadro's_Num]))*(mAPC_Int_P1/(mAPC_per_T_cell))
138	Q_L/VL*Lymph_Node.PD1_mab
139	Q_L/VL*Lymph_Node.PDL1_mab
140	[kon_PDL1-PDL1mAb]*Lymph_Node.PDL1_mab*Lymph_Node.mAPC_Int_P2_PDL1/Vtdln - [koff_PDL1-PDL1mAb]*Lymph_Node.[PDL1mAb-mAPC_PDL1]
141	[kon_PDL1-PDL1mAb]*Lymph_Node.PDL1_mab*Lymph_Node.PNT_Int_PDL1/Vtdln - [koff_PDL1-PDL1mAb]*Lymph_Node.[PDL1mAb-PNT_PDL1]
142	[Exp_CTLA4]*(Lymph_Node.PNT_CTLA4+NEG_Sig_PNT_CD80+[NEG_Sig_PNT_CD86]+[CTLA4_mAb_CTLA4])
143	[kon_CD28_CD80]*Lymph_Node.PNT_Int_CD28*Lymph_Node.mAPC_Int_P2_CD80/([Volume_PNT-Receptor_Int])-[koff_CD28_CD80]*Lymph_Node.POS_Sig_PNT_CD80
144	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.PNT_Int_CD28+POS_Sig_PNT_CD80+POS_Sig_PNT_CD86)
145	[kon_PDL1_CD80]*Lymph_Node.PNT_Int_CD80*Lymph_Node.mAPC_Int_P2_PDL1/[Volume_PNT-Receptor_Int]-[koff_PDL1_CD80]*Lymph_Node.[PNT_CD80-PDL1]
146	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.PNT_Int_CD80+[PNT_CD80-PDL1])
147	[kon_PD1_PDL1]*Lymph_Node.PNT_Int_PD1*Lymph_Node.mAPC_Int_P2_PDL1/[Volume_PNT-Receptor_Int]-[koff_PD1_PDL1]*Lymph_Node.[PNT_PD1-PDL1]
148	[kon_PD1-PD1mAb]*Lymph_Node.PNT_Int_PD1*Lymph_Node.PD1_mab/Vtdln-[koff_PD1-PD1mAb]*[PD1mAb_PNT_PD1]
149	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.PNT_Int_PD1+PD1mAb_PNT_PD1+[PNT_PD1-PDL2]+[PNT_PD1-PDL1])
150	[kon_PD1_PDL1]*Lymph_Node.PNT_Int_PDL1*Lymph_Node.mAPC_Int_P2_PD1/[Volume_PNT-Receptor_Int]-[koff_PD1_PDL1]*Lymph_Node.[PNT_PDL1-PD1]
151	[Exp_CD28/80/86/PD1/L1/L2]*(Lymph_Node.PNT_Int_PDL1+[PDL1mAb-PNT_PDL1]+[PNT_PDL1-CD80]+[PNT_PDL1-PD1])
152	[Exp_CTLA4]*(([CTLA4_receptors-Int-PNT]/[Avagadro's_Num]))*(mAPC_Int_P2/(mAPC_per_T_cell))
153	[Exp_CD28/80/86/PD1/L1/L2]*(([CD28_receptors-per-Tcell]/[Avagadro's_Num]))*(mAPC_Int_P2/(mAPC_per_T_cell))
154	[Exp_CD28/80/86/PD1/L1/L2]*((([%CD80_receptor_level_PNT]*[CD80_receptors-per-Tcell])/[Avagadro's_Num]))*(mAPC_Int_P2/(mAPC_per_T_cell))
155	[Exp_CD28/80/86/PD1/L1/L2]*((([%PD1_receptor_level_PNT]*[PD1_receptors-per-Tcell])/[Avagadro's_Num]))*(mAPC_Int_P2/(mAPC_per_T_cell))
156	[Exp_CD28/80/86/PD1/L1/L2]*((([%PDL1_receptor_level_PNT]*[PDL1_receptors-per-Tcell])/[Avagadro's_Num]))*(mAPC_Int_P2/(mAPC_per_T_cell))
157	kf_Phase2P*Lymph_Node.Primed_Naive_T*[Prob_PNT-mAPC_Interact]
158	kf_no_prolif*Lymph_Node.Primed_Naive_T1*[Sig_PNT=CTLA4/PD1/L1/CD80]
159	PrimeTLN2_rate*Lymph_Node.Primed_Naive_T1*(1/Antigen_Intensity)*((mAPC_Int_P2)/(mAPC_Int_P2+Primed_Naive_T1*mAPC50_per_T_cell+0.001*mole))
160	PrimeTLN2_rate*Lymph_Node.Primed_Naive_T1*(1-[Sig_PNT=CTLA4/PD1/L1/CD80])*Antigen_Intensity*((mAPC_Int_P2)/(mAPC_Int_P2 +Primed_Naive_T1*mAPC50_per_T_cell +0.001*mole))
161	kf_Prolif_end*Lymph_Node.Prolif_Naive_T
162	Lymph_Node.Prolif_Naive_T*[Prolif_Thresh]
163	Endo_CTLA4*Lymph_Node.TrALN_CT_aCT
164	Endo_CTLA4*Lymph_Node.TrALN_CT_CD80
165	Endo_CTLA4*Lymph_Node.TrALN_CT_CD86
166	[Exp_CTLA4]*Lymph_Node.TregLN*([CTLA4_receptors-Tr]/[Avagadro's_Num])
167	TregLN_Engage*Lymph_Node.mAPC1*((Lymph_Node.TregLN /(Lymph_Node.mAPC1 + 1E-100*mole))^gamma_TC_Assoc)/(s_Assoc + (Lymph_Node.TregLN /(Lymph_Node.mAPC1 + 1E-100*mole))^gamma_TC_Assoc)

Reaction Number	Reaction Rate
168	TregLN_Engage*Lymph_Node.Naive_T2*((Lymph_Node.TregLN /(Lymph_Node.Naive_T2 + 1E-100*mole))^gamma_TC_Assoc)/(s_Assoc + (Lymph_Node.TregLN /(Lymph_Node.Naive_T2 + 1E-100*mole))^gamma_TC_Assoc)
169	TregLN_Engage* Lymph_Node.Primed_Naive_T2*((Lymph_Node.TregLN /(Lymph_Node.Primed_Naive_T2+ 1E-100*mole))^gamma_TC_Assoc)/(s_Assoc + (Lymph_Node.TregLN /(Lymph_Node.Primed_Naive_T2+ 1E-100*mole))^gamma_TC_Assoc)
170	[Treg:mAPC_IntTime]*Lymph_Node.TregLN_mAPC*(1-[CTLA4Sig_TrLN-mAPC])
171	[Treg:mAPC_IntTime]*Lymph_Node.TregLN_mAPC*([CTLA4Sig_TrLN-mAPC])
172	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.TregLN_mAPC1*([CD80_receptors-per-mAPC]/[Avagadro's_Num])*(1/Tr_cells_per_mAPC)
173	[Exp_CD28/80/86/PD1/L1/L2]*Lymph_Node.TregLN_mAPC1*([CD86_receptors-per-mAPC]/[Avagadro's_Num])*(1/Tr_cells_per_mAPC)
174	[Exp_CTLA4]*Lymph_Node.TregLN_mAPC1*([CTLA4_receptors-Tr]/[Avagadro's_Num])*(1/mAPC_per_Tr_cell)
175	kon_CTLA4mAb_CTLA4*Lymph_Node.TrLN_CTLA4*Lymph_Node.CTLA4_mab/Vtdln - koff_CTLA4mAb_CTLA4*Lymph_Node.TrLN_CT_aCT
176	[Exp_CTLA4]*(Lymph_Node.TrLN_CTLA4+[TrLN_CT_aCT])
177	(k__DoseAdmin_AntiCTLA4*[BodyWeight (kg)]*CTLA4mAb)/(Ipilimumab_MW)
178	([BodyWeight (kg)]*PD1mAb)/(Nivolumab_MW)/T_IVinject
179	(k__DoseAdmin_AntiPDL1*[BodyWeight (kg)]*PDL1mAb)/(Durvalumab_MW)
180	EffT_InOutLN*Lymph_Node.Naive_T0
181	Lymph_Node.Prolif_Naive_T*[Prolif_Fract]
182	kf_Monocytes_intoT*Monocytes
183	Rate_Tumor_Growth*Tumor.Cancer
184	(Peripheral.CTLA4_mabP_leaky/(0.35*ISF*KP_PD1))*0.67*Q_L*(1-SigmaL)-Lymph_Node.CTLA4_mab*0.67*Q_L*(1-SigmaL)/VL
185	(Peripheral.CTLA4_mabP_tight/(0.65*ISF*KP_PD1))*0.33*Q_L*(1-SigmaL)-Lymph_Node.CTLA4_mab*0.33*Q_L*(1-SigmaL)/VL
186	(QC_Periph - LC_Periph)*Peripheral.EffT_P_f_Vasc/Vv_Periph
187	EffT_Turnover*Peripheral.EffT_P_f_Vasc
188	(Peripheral.PD1_mabP_leaky/(0.35*ISF*KP_PD1))*0.67*Q_L*(1-SigmaL)-Lymph_Node.PD1_mab*0.67*Q_L*(1-SigmaL)/VL
189	(Peripheral.PD1_mabP_tight/(0.65*ISF*KP_PD1))*0.33*Q_L*(1-SigmaL)-Lymph_Node.PD1_mab*0.33*Q_L*(1-SigmaL)/VL
190	(Peripheral.PDL1_mabP_leaky/(0.35*ISF*KP_PDL1))*0.67*Q_L*(1-SigmaL)-Lymph_Node.PDL1_mab*0.67*Q_L*(1-SigmaL)/VL
191	(Peripheral.PDL1_mabP_tight/(0.65*ISF*KP_PDL1))*0.33*Q_L*(1-SigmaL)-Lymph_Node.PDL1_mab*0.33*Q_L*(1-SigmaL)/VL
192	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{CD80}]*([CD80_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
193	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}]*([PD1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
194	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{CD80}]*([PD1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
195	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{CD80}]*([CD80_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
196	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}]*([PD1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
197	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}]*([PDL1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
198	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{CD80}]*([PD1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
199	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{CD80}]*([PDL1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
200	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{CD80}]*([CD80_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
201	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{PDL2}]*([PD1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
202	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{PDL2}]*([PDL1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
203	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{PDL2}]*([PDL2_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
204	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{PDL2}{CD80}]*([PD1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
205	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{PDL2}{CD80}]*([PDL1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
206	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{PDL2}{CD80}]*([PDL2_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])

Reaction Number	Reaction Rate
207	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL1}{PDL2}{CD80}]*([CD80_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
208	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL2}]*([PD1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
209	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL2}]*([PDL2_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
210	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL2}{CD80}]*([PD1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
211	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL2}{CD80}]*([PDL2_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
212	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PD1}{PDL2}{CD80}]*([CD80_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
213	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL1}]*([PDL1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
214	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL1}{CD80}]*([PDL1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
215	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL1}{CD80}]*([CD80_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
216	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL1}{PDL2}]*([PDL1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
217	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL1}{PDL2}]*([PDL2_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
218	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL1}{PDL2}{CD80}]*([PDL1_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
219	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL1}{PDL2}{CD80}]*([PDL2_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
220	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL1}{PDL2}{CD80}]*([CD80_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
221	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL2}]*([PDL2_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
222	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL2}{CD80}]*([PDL2_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
223	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[C{PDL2}{CD80}]*([CD80_receptors_per_C_Cl]/[Avagadro's_Num])*([T_per_Cancer_Cell_Int]/[T_per_Cancer_Cell_max])
224	[kon_PD1-PD1mAb]*Tumor.[C10a=PD1]*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[C10a=PD1:aPD1]
225	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C10a=PD1]+[C10a=PD1:aPD1]+[T10a=PDL1:PD1=C10a])
226	[kon_PDL1-PDL1mAb]*Tumor.[C10b=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[C10b=PDL1:aPDL1]
227	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C10b=PDL1]+[C10b=PDL1:aPDL1]+ [T10b=PD1:PDL1=C10b]+ [T10c=CD80:PDL1=C10b])
228	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C10c=PDL2] + [T10b=PD1:PDL2=C10c])
229	[kon_PDL1-PDL1mAb]*Tumor.[C11a=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[C11a=PDL1:aPDL1]
230	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C11a=PDL1]+[C11a=PDL1:aPDL1]+ [T11b=PD1:PDL1=C11a])
231	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C11b=CD80]+ [T11a=PDL1:CD80=C11b])
232	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C12a=PDL2]+ [T12b=PD1:PDL2=C12a])
233	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C12b=CD80]+ [T12a=PDL1:CD80=C12b])
234	[kon_PDL1-PDL1mAb]*Tumor.[C13a=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[C13a=PDL1:aPDL1]
235	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C13a=PDL1]+[C13a=PDL1:aPDL1]+ [T13b=PD1:PDL1=C13a])
236	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C13b=PDL2]+ [T13b=PD1:PDL2=C13b])
237	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C13c=CD80]+ [T13a=PDL1:CD80=C13c])
238	[kon_PD1_PDL1]*Tumor.[C14a=PD1]*Tumor.[T14a=PDL1]/[V_T:C_14] - [koff_PD1_PDL1]*Tumor.[T14a=PDL1:PD1=C14a]
239	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C14a=PD1]+[C14a=PD1:aPD1]+ [T14a=PDL1:PD1=C14a])
240	[kon_PDL1_CD80]*Tumor.[C14b=PDL1]*Tumor.[T14c=CD80]/[V_T:C_14] - [koff_PDL1_CD80]*Tumor.[T14c=CD80:PDL1=C14b]
241	[kon_PDL1-PDL1mAb]*Tumor.[C14b=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[C14b=PDL1:aPDL1]
242	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C14b=PDL1]+[C14b=PDL1:aPDL1]+ [T14b=PD1:PDL1=C14b]+ [T14c=CD80:PDL1=C14b])
243	[kon_PDL1_CD80]*Tumor.[C14c=CD80]*Tumor.[T14a=PDL1]/[V_T:C_14] - [koff_PDL1_CD80]*Tumor.[T14a=PDL1:CD80=C14c]
244	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C14c=CD80]+ [T14a=PDL1:CD80=C14c])
245	[kon_PD1-PD1mAb]*Tumor.[C15a=PD1]*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[C15a=PD1:aPD1]
246	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C15a=PD1]+[C15a=PD1:aPD1]+ [T15a=PDL1:PD1=C15a])
247	[kon_PD1_PDL2]*Tumor.[C15b=PDL2]*Tumor.[T15b=PD1]/[V_T:C_15] - [koff_PD1_PDL2]*Tumor.[T15b=PD1:PDL2=C15b]

Reaction Number	Reaction Rate
248	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C15b=PDL2] + [T15b=PD1:PDL2=C15b])
249	[kon_PDL1_CD80]*Tumor.[C15c=CD80]*Tumor.[T15a=PDL1]/[V_T:C_15] - [koff_PDL1_CD80]*Tumor.[T15a=PDL1:CD80=C15c]
250	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C15c=CD80]+ [T15a=PDL1:CD80=C15c])
251	[kon_PD1_PDL1]*Tumor.[C16a=PD1]*Tumor.[T16a=PDL1]/[V_T:C_16] - [koff_PD1_PDL1]*Tumor.[T16a=PDL1:PD1=C16a]
252	[kon_PD1-PD1mAb]*Tumor.[C16a=PD1]*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[C16a=PD1:aPD1]
253	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C16a=PD1]+[C16a=PD1:aPD1]+ [T16a=PDL1:PD1=C16a])
254	[kon_PDL1-PDL1mAb]*Tumor.[C16b=PDL1]*Tumor.PDL1_mabt/Vt-[koff_PDL1-PDL1mAb]*Tumor.[C16b=PDL1:aPDL1]
255	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C16b=PDL1]+[C16b=PDL1:aPDL1]+ [T16c=CD80:PDL1=C16b]+ [T16b=PD1:PDL1=C16b])
256	[kon_PD1_PDL2]*Tumor.[C16c=PDL2]*Tumor.[T16b=PD1]/[V_T:C_16] - [koff_PD1_PDL2]*Tumor.[T16b=PD1:PDL2=C16c]
257	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C16c=PDL2]+ [T16b=PD1:PDL2=C16c])
258	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C16d=CD80]+ [T16a=PDL1:CD80=C16d])
259	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C2=PD1]+[C2=PD1:aPD1]+[T2=PDL1:PD1=C2])
260	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C3=PDL1]+[C3=PDL1:aPDL1]+[T3a=PD1:PDL1=C3]+[T3b=CD80:PDL1=C3])
261	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C4=PDL2]+[T4=PD1:PDL2=C4])
262	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C5=CD80]+[T5=PDL1:CD80=C5])
263	[kon_PD1-PD1mAb]*Tumor.[C6a=PD1]*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[C6a=PD1:aPD1]
264	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C6a=PD1]+[C6a=PD1:aPD1]+[T6a=PDL1:PD1=C6a])
265	[kon_PD1_PDL1]*Tumor.[C6b=PDL1]*Tumor.[T6b=PD1]/[V_T:C_6] - [koff_PD1_PDL1]*Tumor.[T6b=PD1:PDL1=C6b]
266	[kon_PDL1_CD80]*Tumor.[C6b=PDL1]*Tumor.[T6c=CD80]/[V_T:C_6] - [koff_PDL1_CD80]*Tumor.[T6c=CD80:PDL1=C6b]
267	[kon_PDL1-PDL1mAb]*Tumor.[C6b=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[C6b=PDL1:aPDL1]
268	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C6b=PDL1]+[C6b=PDL1:aPDL1]+[T6b=PD1:PDL1=C6b]+[T6c=CD80:PDL1=C6b])
269	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C7a=PD1]+[C7a=PD1:aPD1]+[T7a=PDL1:PD1=C7a])
270	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C7b=PDL2]+[T7b=PD1:PDL2=C7b])
271	[kon_PDL1_CD80]*Tumor.[C8a=PDL1]*Tumor.[T8b=CD80]/[V_T:C_8] - [koff_PDL1_CD80]*Tumor.[T8b=CD80:PDL1=C8a]
272	[kon_PDL1-PDL1mAb]*Tumor.[C8a=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[C8a=PDL1:aPDL1]
273	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C8a=PDL1]+[C8a=PDL1:aPDL1]+[T8a=PD1:PDL1=C8a]+[T8b=CD80:PDL1=C8a])
274	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C8b=PDL2]+[T8a=PD1:PDL2=C8b])
275	[kon_PD1_PDL1]*Tumor.[C9a=PD1]*Tumor.[T9=PDL1]/[V_T:C_9] - [koff_PD1_PDL1]*Tumor.[T9=PDL1-PD1=C9a]
276	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C9a=PD1]+[C9a=PD1:aPD1]+[T9=PDL1-PD1=C9a])
277	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[C9b=CD80]+[T9=PDL1-CD80=C9b])
278	Endo_CTLA4*Tumor.[CTLA4:CD80_TrAT]
279	Endo_CTLA4*Tumor.[CTLA4:CD86_TrAT]
280	Endo_CTLA4*Tumor.[CTLA4_CTLA4-Trt]
281	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{80}-{PDL1}{PDL2}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
282	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{80}-{PDL1}{PDL2}C]*([CD80_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
283	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{CD80}-{PDL1}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
284	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{CD80}-{PDL1}C]*([CD80_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
285	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
286	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
287	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C]*([CD80_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
288	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
289	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
290	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C]*([CD80_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
291	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
292	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
293	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C]*([CD80_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
294	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])

Reaction Number	Reaction Rate
295	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
296	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C]*([CD80_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
297	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PD1}{80}{PDL2}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
298	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PD1}{80}{PDL2}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
299	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PD1}{L2}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
300	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PD1}{L2}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
301	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PDL1}{80}{L2}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
302	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PDL1}{80}{L2}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
303	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PDL1}{80}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
304	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PDL1}{80}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
305	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PDL2}{80}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
306	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}{L1}-{PDL2}{80}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
307	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PD1}-{PDL2}C]*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
308	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PDL1}-{CD80}{PD1}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
309	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PDL1}-{CD80}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
310	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.[T{PDL1}-{PD1}C]*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*([Cancer_per_T_Cell_Int]/[Cancer_per_T_Cell_max])
311	[kon_PD1_PDL1]*Tumor.[T10a=PDL1]*Tumor.[C10a=PD1]/[V_T:C_10] - [koff_PD1_PDL1]*Tumor.[T10a=PDL1:PD1=C10a]
312	[kon_PDL1-PDL1mAb]*Tumor.[T10a=PDL1]*Tumor.PDL1_mabt/Vt-[koff_PDL1-PDL1mAb]*Tumor.[T10a=PDL1:aPDL1]
313	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T10a=PDL1]+[T10a=PDL1:aPDL1]+[T10a=PDL1:PD1=C10a])
314	[kon_PD1_PDL1]*Tumor.[T10b=PD1]*Tumor.[C10b=PDL1]/[V_T:C_10] - [koff_PD1_PDL1]*Tumor.[T10b=PD1:PDL1=C10b]
315	[kon_PD1_PDL2]*Tumor.[T10b=PD1]*Tumor.[C10c=PDL2]/[V_T:C_10] - [koff_PD1_PDL2]*Tumor.[T10b=PD1:PDL2=C10c]
316	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T10b=PD1]+[T10b=PD1:aPD1]+ [T10b=PD1:PDL1=C10b]+ [T10b=PD1:PDL2=C10c])
317	[kon_PDL1_CD80]*Tumor.[T10c=CD80]*Tumor.[C10b=PDL1]/[V_T:C_10] - [koff_PDL1_CD80]*Tumor.[T10c=CD80:PDL1=C10b]
318	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T10c=CD80]+ [T10c=CD80:PDL1=C10b])
319	[kon_PDL1_CD80]*Tumor.[T11a=PDL1]*Tumor.[C11b=CD80]/[V_T:C_11] - [koff_PDL1_CD80]*Tumor.[T11a=PDL1:CD80=C11b]
320	[kon_PDL1-PDL1mAb]*Tumor.[T11a=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T11a=PDL1:aPDL1]
321	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T11a=PDL1]+[T11a=PDL1:aPDL1]+ [T11a=PDL1:CD80=C11b])
322	[kon_PD1_PDL1]*Tumor.[T11b=PD1]*Tumor.[C11a=PDL1]/[V_T:C_11] - [koff_PD1_PDL1]*Tumor.[T11b=PD1:PDL1=C11a]
323	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T11b=PD1]+[T11b=PD1:aPD1]+ [T11b=PD1:PDL1=C11a])
324	[kon_PDL1_CD80]*Tumor.[T12a=PDL1]*Tumor.[C12b=CD80]/[V_T:C_12] - [koff_PDL1_CD80]*Tumor.[T12a=PDL1:CD80=C12b]
325	[kon_PDL1-PDL1mAb]*Tumor.[T12a=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T12a=PDL1:aPDL1]
326	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T12a=PDL1]+[T12a=PDL1:aPDL1]+ [T12a=PDL1:CD80=C12b])
327	[kon_PD1_PDL2]*Tumor.[T12b=PD1]*Tumor.[C12a=PDL2]/[V_T:C_12] - [koff_PD1_PDL2]*Tumor.[T12b=PD1:PDL2=C12a]
328	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T12b=PD1]+[T12b=PD1:aPD1]+ [T12b=PD1:PDL2=C12a])
329	[kon_PDL1_CD80]*Tumor.[T13a=PDL1]*Tumor.[C13c=CD80]/[V_T:C_13] - [koff_PDL1_CD80]*Tumor.[T13a=PDL1:CD80=C13c]
330	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T13a=PDL1]+[T13a=PDL1:aPDL1]+ [T13a=PDL1:CD80=C13c])
331	[kon_PD1_PDL1]*Tumor.[T13b=PD1]*Tumor.[C13a=PDL1]/[V_T:C_13] - [koff_PD1_PDL1]*Tumor.[T13b=PD1:PDL1=C13a]
332	[kon_PD1_PDL2]*Tumor.[T13b=PD1]*Tumor.[C13b=PDL2]/[V_T:C_13] - [koff_PD1_PDL2]*Tumor.[T13b=PD1:PDL2=C13b]

Reaction Number	Reaction Rate
333	[kon_PD1-PD1mAb]*Tumor.[T13b=PD1]*Tumor.PD1_mabt/Vt-[koff_PD1-PD1mAb]*Tumor.[T13b=PD1:aPD1]
334	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T13b=PD1]+[T13b=PD1:aPD1]+ [T13b=PD1:PDL2=C13b]+ [T13b=PD1:PDL1=C13a])
335	[kon_PDL1-PDL1mAb]*Tumor.[T14a=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T14a=PDL1:aPDL1]
336	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T14a=PDL1]+[T14a=PDL1:aPDL1]+ [T14a=PDL1:PD1=C14a]+ [T14a=PDL1:CD80=C14c])
337	[kon_PD1_PDL1]*Tumor.[T14b=PD1]*Tumor.[C14b=PDL1]/[V_T:C_14] - [koff_PD1_PDL1]*Tumor.[T14b=PD1:PDL1=C14b]
338	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T14b=PD1]+[T14b=PD1:aPD1]+ [T14b=PD1:PDL1=C14b])
339	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T14c=CD80]+ [T14c=CD80:PDL1=C14b])
340	[kon_PD1_PDL1]*Tumor.[T15a=PDL1]*Tumor.[C15a=PD1]/[V_T:C_15] - [koff_PD1_PDL1]*Tumor.[T15a=PDL1:PD1=C15a]
341	[kon_PDL1-PDL1mAb]*Tumor.[T15a=PDL1]*Tumor.PDL1_mabt/Vt -[koff_PDL1-PDL1mAb]*Tumor.[T15a=PDL1:aPDL1]
342	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T15a=PDL1]+[T15a=PDL1:aPDL1]+ [T15a=PDL1:CD80=C15c]+ [T15a=PDL1:PD1=C15a])
343	[kon_PD1-PD1mAb]*Tumor.[T15b=PD1]*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[T15b=PD1:aPD1]
344	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T15b=PD1]+[T15b=PD1:aPD1]+ [T15b=PD1:PDL2=C15b])
345	[kon_PDL1_CD80]*Tumor.[T16a=PDL1]*Tumor.[C16d=CD80]/[V_T:C_16] - [koff_PDL1_CD80]*Tumor.[T16a=PDL1:CD80=C16d]
346	[kon_PDL1-PDL1mAb]*Tumor.[T16a=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T16a=PDL1:aPDL1]
347	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T16a=PDL1]+[T16a=PDL1:aPDL1]+ [T16a=PDL1:PD1=C16a]+ [T16a=PDL1:CD80=C16d])
348	[kon_PD1_PDL1]*Tumor.[T16b=PD1]*Tumor.[C16b=PDL1]/[V_T:C_16] - [koff_PD1_PDL1]*Tumor.[T16b=PD1:PDL1=C16b]
349	[kon_PD1-PD1mAb]*Tumor.[T16b=PD1]*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[T16b=PD1:aPD1]
350	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T16b=PD1]+[T16b=PD1:aPD1]+ [T16b=PD1:PDL2=C16c]+ [T16b=PD1:PDL1=C16b])
351	[kon_PDL1_CD80]*Tumor.[T16c=CD80]*Tumor.[C16b=PDL1]/[V_T:C_16] - [koff_PDL1_CD80]*Tumor.[T16c=CD80:PDL1=C16b]
352	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T16c=CD80]+ [T16c=CD80:PDL1=C16b])
353	[kon_PD1_PDL1]*Tumor.[T2=PDL1]*Tumor.[C2=PD1]/[V_T:C_2] - [koff_PD1_PDL1]*Tumor.[T2=PDL1:PD1=C2]
354	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T2=PDL1]+[T2=PDL1:aPDL1]+[T2=PDL1:PD1=C2])
355	[kon_PD1_PDL1]*Tumor.[T3a=PD1]*Tumor.[C3=PDL1]/[V_T:C_3] - [koff_PD1_PDL1]*Tumor.[T3a=PD1:PDL1=C3]
356	[kon_PD1-PD1mAb]*Tumor.[T3a=PD1]*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[T3a=PD1:aPD1]
357	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T3a=PD1]+[T3a=PD1:aPD1]+[T3a=PD1:PDL1=C3])
358	[kon_PDL1_CD80]*Tumor.[T3b=CD80]*Tumor.[C3=PDL1]/[V_T:C_3] - [koff_PDL1_CD80]*Tumor.[T3b=CD80:PDL1=C3]
359	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T3b=CD80]+[T3b=CD80:PDL1=C3])
360	[kon_PD1_PDL2]*Tumor.[T4=PD1]*Tumor.[C4=PDL2]/[V_T:C_4] - [koff_PD1_PDL2]*Tumor.[T4=PD1:PDL2=C4]
361	[kon_PD1-PD1mAb]*Tumor.[T4=PD1]*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[T4=PD1:aPD1]
362	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T4=PD1]+[T4=PD1:aPD1]+[T4=PD1:PDL2=C4])
363	[kon_PDL1_CD80]*Tumor.[T5=PDL1]*Tumor.[C5=CD80]/[V_T:C_5] - [koff_PDL1_CD80]*Tumor.[T5=PDL1:CD80=C5]
364	[kon_PDL1-PDL1mAb]*Tumor.[T5=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T5=PDL1:aPDL1]
365	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T5=PDL1]+[T5=PDL1:aPDL1]+[T5=PDL1:CD80=C5])
366	[kon_PD1_PDL1]*Tumor.[T6a=PDL1]*Tumor.[C6a=PD1]/[V_T:C_6] - [koff_PD1_PDL1]*Tumor.[T6a=PDL1:PD1=C6a]
367	[kon_PDL1-PDL1mAb]*Tumor.[T6a=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T6a=PDL1:aPDL1]
368	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T6a=PDL1]+[T6a=PDL1:aPDL1]+[T6a=PDL1:PD1=C6a])
369	[kon_PD1-PD1mAb]*Tumor.[T6b=PD1]*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[T6b=PD1:aPD1]
370	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T6b=PD1]+[T6b=PD1:aPD1]+[T6b=PD1:PDL1=C6b])
371	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T6c=CD80]+[T6c=CD80:PDL1=C6b])
372	[kon_PD1_PDL1]*Tumor.[T7a=PDL1]*Tumor.[C7a=PD1]/[V_T:C_7] - [koff_PD1_PDL1]*Tumor.[T7a=PDL1:PD1=C7a]
373	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T7a=PDL1]+[T7a=PDL1:aPDL1]+[T7a=PDL1:PD1=C7a])
374	[kon_PD1_PDL2]*Tumor.[T7b=PD1]*Tumor.[C7b=PDL2]/[V_T:C_7] - [koff_PD1_PDL2]*Tumor.[T7b=PD1:PDL2=C7b]
375	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T7b=PD1]+[T7b=PD1:aPD1]+[T7b=PD1:PDL2=C7b])
376	[kon_PD1_PDL1]*Tumor.[T8a=PD1]*Tumor.[C8a=PDL1]/[V_T:C_8] - [koff_PD1_PDL1]*Tumor.[T8a=PD1:PDL1=C8a]
377	[kon_PD1_PDL2]*Tumor.[T8a=PD1]*Tumor.[C8b=PDL2]/[V_T:C_8] - [koff_PD1_PDL2]*Tumor.[T8a=PD1:PDL2=C8b]
378	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T8a=PD1]+[T8a=PD1:aPD1]+[T8a=PD1:PDL1=C8a]+[T8a=PD1:PDL2=C8b])
379	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T8b=CD80]+[T8b=CD80:PDL1=C8a])
380	[kon_PDL1_CD80]*Tumor.[T9=PDL1]*Tumor.[C9b=CD80]/[V_T:C_9] - [koff_PDL1_CD80]*Tumor.[T9=PDL1-CD80=C9b]
381	[kon_PDL1-PDL1mAb]*Tumor.[T9=PDL1]*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T9=PDL1:aPDL1]
382	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.[T9=PDL1]+[T9=PDL1:aPDL1]+[T9=PDL1-PD1=C9a]+[T9=PDL1-CD80=C9b])
383	kf_RestingMacrophage*Tumor.APC_T
384	Phago_Debris*Tumor.C_DebrisT*Tumor.APC_T
385	Debris_Transport*Tumor.C_DebrisT*(1/[Num_TDLN_Considered])*(1-[mAPC_Debis_T_Inact])
386	Debris_Decay*Tumor.C_DebrisT

Reaction Number	Reaction Rate
387	Debris_Transport*Tumor.C_DebrisT*[mAPC_Debis_T_Inact]
388	Debris_Transport*Tumor.C_DebrisT*(1-1/[Num_TDLN_Considered])
389	kf_CanDecay*Tumor.Cancer
390	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.CD80_mAPCT+[CTLA4:CD80_TrAT])
391	[kon_PDL1_CD80]*Tumor.CD80_TeffT*Tumor.PDL1_TregT/[Vol_Cell-Rec_Tr-TeffT] - [koff_PDL1_CD80]*Tumor.[PDL1:CD80_TrTeff]
392	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.CD80_TeffT+[PDL1:CD80_TrTeff])
393	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.CD80_TeffT1+[PDL1:CD80_MDSCT])
394	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.CD86_mAPCT+[CTLA4:CD86_TrAT])
395	Kpa_TB*S_TB*Vt_avg_const*(1.43/1.63)*Tumor.CTLA4_mabt/(Vt_Teff*Tumor_Void_Fraction)- Kpa_TB*S_TB*Vt_avg_const*(1.43/1.63)*Lymph_Node.CTLA4_mab/(VL)
396	[kon_CTLA4_CD80]*Tumor.CTLA4_TregT*Tumor.CD80_mAPCT/[Vol_Cell-Rec_Tr-APCT] - [koff_CTLA4_CD80]*Tumor.[CTLA4:CD80_TrAT]
397	[kon_CTLA4_CD86]*Tumor.CTLA4_TregT*Tumor.CD86_mAPCT/[Vol_Cell-Rec_Tr-APCT] - [koff_CTLA4_CD86]*Tumor.[CTLA4:CD86_TrAT]
398	kon_CTLA4mAb_CTLA4*Tumor.CTLA4_TregT*Tumor.CTLA4_mabt/Vt - koff_CTLA4mAb_CTLA4*Tumor.[CTLA4_CTLA4-Trt]
399	[Exp_CTLA4]*(Tumor.CTLA4_TregT+[CTLA4:CD80_TrAT]+[CTLA4:CD86_TrAT]+[CTLA4_CTLA4-Trt])
400	EffT_Turnover*Tumor.Effector_TT
401	EffT_Res_Conversion*Tumor.Effector_TT*(1-TheEnd)*.9
402	EffT_Res_Conversion*Tumor.Effector_TT*(1-TheEnd)*.1
403	CancerTEng * Tumor.Cancer1 * ((Tumor.Effector_TT_C_Eng/(Tumor.Cancer1+1E-100*mole))^gamma_TC_Assoc)/(s_Assoc + (Tumor.Effector_TT_C_Eng/(Tumor.Cancer1+1E-100*mole))^gamma_TC_Assoc)
404	EffT_Turnover*Tumor.EffT_AR_Vasc
405	J_Tmr*Tumor.EffT_AR_Vasc
406	EffT_Turnover*Tumor.EffT_b_Vasc
407	AR_Tmr*Tumor.EffT_b_Vasc
408	kr_Tmr*Tumor.EffT_b_Vasc
409	kf_Tmr*Tmr_Free_Sites*Tumor.EffT_f_Vasc/Vv_Tmr
410	(QC_Tmr - LC_Tmr)*Tumor.EffT_f_Vasc/Vv_Tmr
411	EffT_Turnover*Tumor.EffT_f_Vasc
412	mAPC_Migrate*Tumor.mAPC_T*(1/[Num_TDLN_Considered])*(1-[mAPC_Debis_T_Inact])
413	mAPC_Migrate*Tumor.mAPC_T*(1-1/[Num_TDLN_Considered])
414	mAPC_Migrate*Tumor.mAPC_T*[mAPC_Debis_T_Inact]
415	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.mAPCT_EngTregT*([CD80_receptors-per-mAPC]/[Avagadro's_Num])*(1/Tr_cells_per_mAPC)
416	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.mAPCT_EngTregT*([CD86_receptors-per-mAPC]/[Avagadro's_Num])*(1/Tr_cells_per_mAPC)
417	TregTMDSCEng*Tumor.Effector_TT_MDSCs*((Tumor.MDSC_T/(Tumor.Effector_TT_MDSCs + 1E-100*mole))^gamma_TC_Assoc)/(s_Assoc + (Tumor.MDSC_T/(Tumor.Effector_TT_MDSCs + 1E-100*mole))^gamma_TC_Assoc)
418	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.MDSCsT_EngTeff*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*(1/T_per_Tr_cell)
419	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.MDSCsT_EngTeff*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*(1/T_per_Tr_cell)
420	[Treg:T_IntTime]*Tumor.MDSCsT_Teff*[Sig_MDSCTeff=Total]
421	[Treg:T_IntTime]*Tumor.MDSCsT_Teff*(1-[Sig_MDSCTeff=Total])
422	Kpa_TB*S_TB*Vt_avg_const*(1.43/1.63)*Tumor.PD1_mabt/(Vt_Teff*Tumor_Void_Fraction)- Kpa_TB*S_TB*Vt_avg_const*(1.43/1.63)*Lymph_Node.PD1_mab/(VL)
423	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[C14a=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[C14a=PD1:aPD1]
424	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[C2=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[C2=PD1:aPD1]
425	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[C7a=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[C7a=PD1:aPD1]
426	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[C9a=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[C9a=PD1:aPD1]
427	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[T10b=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[T10b=PD1:aPD1]
428	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[T11b=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[T11b=PD1:aPD1]
429	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[T12b=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[T12b=PD1:aPD1]
430	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[T14b=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[T14b=PD1:aPD1]
431	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[T7b=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[T7b=PD1:aPD1]
432	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.[T8a=PD1]/Vt - [koff_PD1-PD1mAb]*Tumor.[T8a=PD1:aPD1]
433	[kon_PD1-PD1mAb]*Tumor.PD1_mabt*Tumor.PD1_TeffT/Vt - [koff_PD1-PD1mAb]*Tumor.[PD1:aPD1_Teff]
434	[kon_PD1-PD1mAb]*Tumor.PD1_MDSCsT*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[PD1:aPD1_MDSCs]
435	[kon_PD1_PDL1]*Tumor.PD1_MDSCsT*Tumor.PDL1_TeffT1/[Vol_Cell-Rec_MDSC-TeffT] - [koff_PD1_PDL1]*Tumor.[PD1:PDL1_MDSCT]
436	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.PD1_MDSCsT+[PD1:PDL1_MDSCT]+[PD1:aPD1_MDSCs])
437	[kon_PD1_PDL1]*Tumor.PD1_TeffT*Tumor.PDL1_TregT/[Vol_Cell-Rec_Tr-TeffT] - [koff_PD1_PDL1]*Tumor.[PDL1:PD1_TrTeff]
438	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.PD1_TeffT+[PDL1:PD1_TrTeff]+[PD1:aPD1_Teff])
439	[kon_PD1-PD1mAb]*Tumor.PD1_TeffT1*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[PD1:aPD1_Teff1]
440	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.PD1_TeffT1+[PDL1:PD1_MDSCT]+[PD1:aPD1_Teff1])

Reaction Number	Reaction Rate
441	[kon_PD1-PD1mAb]*Tumor.PD1_TregT*Tumor.PD1_mabt/Vt - [koff_PD1-PD1mAb]*Tumor.[PD1:aPD1_Treg]
442	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.PD1_TregT+[PD1:PDL1_TrTeff]+[PD1:aPD1_Treg])
443	Kpa_TB*S_TB*Vt_avg_const*(1.43/1.63)*Tumor.PDL1_mabt/(Vt_Teff*Tumor_Void_Fraction)-Kpa_TB*S_TB*Vt_avg_const*(1.43/1.63)*Lymph_Node.PDL1_mab/(VL)
444	[kon_PDL1-PDL1mAb]*Tumor.PDL1_mabt*Tumor.[C3=PDL1]/Vt - [koff_PDL1-PDL1mAb]*Tumor.[C3=PDL1:aPDL1]
445	[kon_PDL1-PDL1mAb]*Tumor.PDL1_mabt*Tumor.[T13a=PDL1]/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T13a=PDL1:aPDL1]
446	[kon_PDL1-PDL1mAb]*Tumor.PDL1_mabt*Tumor.[T2=PDL1]/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T2=PDL1:aPDL1]
447	[kon_PDL1-PDL1mAb]*Tumor.PDL1_mabt*Tumor.[T7a=PDL1]/Vt - [koff_PDL1-PDL1mAb]*Tumor.[T7a=PDL1:aPDL1]
448	[kon_PDL1-PDL1mAb]*Tumor.PDL1_mabt*Tumor.PDL1_TeffT/Vt - [koff_PDL1-PDL1mAb]*Tumor.[PDL1:aPDL1_Teff]
417	[kon_PDL1-PDL1mAb]*Tumor.PDL1_mabt*Tumor.PDL1_TeffT1/Vt -[koff_PDL1-PDL1mAb]*Tumor.[PDL1:aPDL1_Teff1]
418	[kon_PDL1_CD80]*Tumor.PDL1_MDSCsT*Tumor.CD80_TeffT1/[Vol_Cell-Rec_MDSC-TeffT] - [koff_PDL1_CD80]*Tumor.[PDL1:CD80_MDSCT]
419	[kon_PD1_PDL1]*Tumor.PDL1_MDSCsT*Tumor.PD1_TeffT1/[Vol_Cell-Rec_MDSC-TeffT] - [koff_PD1_PDL1]*Tumor.[PDL1:PD1_MDSCT]
420	[kon_PDL1-PDL1mAb]*Tumor.PDL1_MDSCsT*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[PDL1:aPDL1_MDSCs]
421	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.PDL1_MDSCsT+[PDL1:CD80_MDSCT]+[PDL1:PD1_MDSCT]+[PDL1:aPDL1_MDSCs])
422	[kon_PD1_PDL1]*Tumor.PDL1_TeffT*Tumor.PD1_TregT/[Vol_Cell-Rec_Tr-TeffT] - [koff_PD1_PDL1]*Tumor.[PD1:PDL1_TrTeff]
423	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.PDL1_TeffT+[PD1:PDL1_TrTeff]+[PDL1:aPDL1_Teff])
424	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.PDL1_TeffT1+[PD1:PDL1_MDSCT]+[PDL1:aPDL1_Teff1])
425	[kon_PDL1-PDL1mAb]*Tumor.PDL1_TregT*Tumor.PDL1_mabt/Vt - [koff_PDL1-PDL1mAb]*Tumor.[PDL1:aPDL1_Treg]
426	[Exp_CD28/80/86/PD1/L1/L2]*(Tumor.PDL1_TregT+[PDL1:CD80_TrTeff]+[PDL1:PD1_TrTeff]+[PDL1:aPDL1_Treg])
427	kf_TRecover*Tumor.T_Recover_Can_Dead*(1-Total_TC_Sig)
428	CancerTInt*Tumor.TC1*(1-Total_TC_Sig*[%Sig_Inhibit_Cancer])
429	CancerTInt*Tumor.TC1*Total_TC_Sig*[%Sig_Inhibit_Cancer]
430	CancerTInt*Tumor.TC2* Total_TC_Sig*[%Sig_Inhibit_Cancer]
431	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.Teff_EngMDSC*([CD80_receptors-per-Tcell]/[Avagadro's_Num])*(1/Tr_per_T_cell)
432	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.Teff_EngMDSC*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*(1/Tr_per_T_cell)
433	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.Teff_EngMDSC*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*(1/Tr_per_T_cell)
434	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.Teff_EngTregT*([CD80_receptors-per-Tcell]/[Avagadro's_Num])*(1/Tr_per_T_cell)
435	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.Teff_EngTregT*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*(1/Tr_per_T_cell)
436	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.Teff_EngTregT*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*(1/Tr_per_T_cell)
437	TregTMDSCEng*Tumor.Effector_TT_TregT *((TregT/(Tumor.Effector_TT_TregT + 1E-20*mole))^gamma_TC_Assoc)/(s_Assoc + (TregT/(Tumor.Effector_TT_TregT + 1E-20*mole))^gamma_TC_Assoc)
438	[Exp_CTLA4]*Tumor.TregT_EngAPC*([CTLA4_receptors-Tr]/[Avagadro's_Num])*(1/mAPC_per_Tr_cell)
439	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.TregT_EngTeff*([PD1_receptors-per-Tcell]/[Avagadro's_Num])*(1/T_per_Tr_cell)
440	[Exp_CD28/80/86/PD1/L1/L2]*Tumor.TregT_EngTeff*([PDL1_receptors-per-Tcell]/[Avagadro's_Num])*(1/T_per_Tr_cell)
441	[Treg:T_IntTime]*Tumor.TregT_Teff*[Sig_TrTeff=Total]
442	[Treg:T_IntTime]*Tumor.TregT_Teff*(1-[Sig_TrTeff=Total])

Table S2 – Model Reaction Rates (End)

Table S3 – Model Reaction and Rate Descriptions (Start)

Reaction Number	Reaction Description
1	Distribution of Anti-CTLA-4 mAb between the central and lymph node compartments
2	Distribution of Anti-CTLA-4 mAb between the central and leaky tissues
3	Distribution of Anti-CTLA-4 mAb between the central and tight tissues
4	Distribution of Anti-CTLA-4 mAb between the central and tumor compartments
5	Clearance of Anti-CTLA-4 mAb from the central compartment
6	The generation of Effector T cells and their migration into the blood/plasma from the designated number of lymph nodes as a multiple of that from a single lymph node
7	Trafficking of free Effector T cells from blood to GI vasculature
8	Trafficking of free Effector T cells from blood to Liver vasculature
9	Trafficking of free Effector T cells from blood to Spleen vasculature
10	Trafficking of free Effector T cells from blood to Lymph Node vasculature
11	The natural turnover of Effector T cells in the blood
12	Trafficking of free Effector T cells from blood to Peripheral (other tissues not directly accounted for) vasculature
13	Trafficking of free Effector T cells from blood to Tumor vasculature
14	Distribution of Anti-PD-1 mAb between the central and lymph node compartments
15	Distribution of Anti-PD-1 mAb between the central and leaky tissues
16	Distribution of Anti-PD-1 mAb between the central and tight tissues
17	Distribution of Anti-PD-1 mAb between the central and tumor compartments

Reaction Number	Reaction Description
18	Clearance of Anti-PD-1 mAb from the central compartment
19	Distribution of Anti-PD-L1 mAb between the central and lymph node compartments
20	Distribution of Anti-PD-L1 mAb between the central and leaky tissues
21	Distribution of Anti-PD-L1 mAb between the central and tight tissues
22	Distribution of Anti-PD-L1 mAb between the central and tumor compartments
23	Clearance of Anti-PD-L1 mAb from the central compartment
24	Saturation of Anti-PD-L1 mAb clearance from the central compartment
25	Trafficking of Effector T cells from GI to Liver vasculature
26	Turnover of free Effector T cells in the GI vasculature
27	Extravasation of arrested Effector T cells from the Liver vasculature
28	Turnover of arrested Effector T cells in the Liver vasculature
29	Arrest of bound Effector T cells in the Liver vasculature
30	Detachment of bound Effector T cells in the Liver vasculature
31	Turnover of bound Effector T cells in the liver vasculature
32	Trafficking of free Effector T cells from Liver to Lung vasculature
33	Turnover of free Effector T cells in the liver vasculature
34	Trafficking of free Effector T cells from Liver to lymph node extravascular space
35	Turnover of Effector T cells in the Liver extravascular space
36	Extravasation of arrested Effector T cells from the Spleen vasculature
37	Turnover of arrested Effector T cells in the Spleen vasculature
38	Arrest of bound Effector T cells in the Spleen vasculature
39	Detachment of bound Effector T cells in the Spleen vasculature
40	Turnover of bound Effector T cells in the Spleen vasculature
41	Binding or free Effector T cells to the Spleen vasculature
42	Trafficking of free Effector T cells from Spleen to Liver vasculature
43	Turnover of free Effector T cells in the Spleen vasculature
44	Trafficking of free Effector T cells from Spleen to lymph node extravascular space
45	Turnover of Effector T cells in the Spleen extravascular space
46	Binding or free Effector T cells to the Liver vasculature
47	Extravasation of arrested Effector T cells from the Lungs vasculature
48	Turnover of arrested Effector T cells in the Lungs vasculature
49	Depletion of arrested Effector T cells in the Lungs vasculature
50	Binding or free Effector T cells to the Lungs vasculature
51	Trafficking of free Effector T cells from Lungs to (arterial) Blood
52	Turnover of free Effector T cells in the Lungs vasculature
53	Trafficking of free Effector T cells from Lungs to lymph node extravascular space
54	Turnover of Effector T cells in the Lungs extravascular space
55	Arrest of bound Effector T cells in the Lungs vasculature
56	Detachment of bound Effector T cells in the Lungs vasculature
57	Turnover of bound Effector T cells in the Lungs vasculature
58	Depletion of bound Effector T cells in the Lungs vasculature
59	Interaction at the immunological synapse between CD80 on Primed Naive T cells and PD-L1 on T Regulatory cells in the lymph node
60	CD80 expression threshold on Primed Naive T cells for interaction with T Regulatory cells in the lymph node
61	Interaction at the immunological synapse between PD-1 on Primed Naive T cells and PD-L1 on T Regulatory cells in the lymph node
62	Interaction at the immunological synapse between PD-1 on Primed Naive T cells and Anti-PD-1 mAb in the lymph node
63	PD-1 expression threshold on Primed Naive T cells for interaction with T Regulatory cells in the lymph node
64	Interaction at the immunological synapse between PD-L1 on Primed Naive T cells and Anti-PD-L1 mAb in the lymph node
65	PD-L1 expression threshold on Primed Naive T cells for interaction with T Regulatory cells in the lymph node
66	Inactivation of Naïve T cells by T Regulatory cells in the lymph node
67	Dissociation of T Regulatory cells from Naïve T cells in the lymph node without inactivation of the latter
68	Inactivation of Primed Naïve T cells by T Regulatory cells in the lymph node
69	Dissociation of T Regulatory cells from Primed Naïve T cells in the lymph node without inactivation of the latter
70	CD80 expression by Primed Naive T cells for interaction with T Regulatory cells in the lymph node
71	PD-1 expression by Primed Naive T cells for interaction with T Regulatory cells in the lymph node
72	PD-L1 expression by Primed Naive T cells for interaction with T Regulatory cells in the lymph node
73	PD-1 expression by T Regulatory cells for interaction with Primed Naive T cells in the lymph node
74	PD-L1 expression by T Regulatory cells for interaction with Primed Naive T cells in the lymph node
75	CD80 expression threshold on mAPCs for interaction with T Regulatory cells in the lymph node
76	CD86 expression threshold on mAPCs for interaction with T Regulatory cells in the lymph node
77	Interaction at the immunological synapse between CD80 on mAPCs and CTLA-4 on T Regulatory cells in the lymph node
78	Interaction at the immunological synapse between CD86 on mAPCs and CTLA-4 on T Regulatory cells in the lymph node
79	Interaction at the immunological synapse between CTLA-4 on T Regulatory cells and Anti-CTLA-4 mAb in the lymph node
80	CTLA-4 expression threshold on T Regulatory cells for interaction with mAPCs in the lymph node
81	Interaction at the immunological synapse between PD-L1 on Primed Naive T cells and PD-1 on T Regulatory cells in the lymph node
82	Interaction at the immunological synapse between PD-1 on T Regulatory cells and Anti-PD-1 mAb in the lymph node

Reaction Number	Reaction Description
83	PD-1 expression threshold on Regulatory cells for interaction with Primed Naive T cells in the lymph node
84	Interaction at the immunological synapse between PD-L1 on T Regulatory cells and Anti-PD-L1 mAb in the lymph node
85	Interaction at the immunological synapse between PD-L1 on T Regulatory cells and Anti-PD-1 mAb in the lymph node
86	Phagocytosis of tumor debris by resident APCs in the lymph node
87	Decay of tumor debris in the lymph nodes
88	Lymph return of Anti-CTLA-4 to the blood
89	Interaction at the immunological synapse between CTLA-4 on Primed Naïve T cells during priming interactions with mAPCS and Anti-CTLA-4 mAb in the lymph node
90	Internalization of the CTLA-4 receptor on Primed Naïve T cells following its binding to Anti-CTLA-4 mAb
91	Migration of Effector T cells from the lymph node into the blood (removal linked to regeneration by algebraic equation below)
92	Return of Effector T cells from lymph node extravascular space to the Lungs vascular space
93	Turnover of Effector T cells in the lymph node extravascular space
94	Trafficking of free Effector T cells from lymph node vascular space to the Lungs vascular space
95	Turnover of free Effector T cells in the lymph node vascular space
96	CD80 expression by total mAPCs in the lymph node
97	CD86 expression by total mAPCs in the lymph node
98	PD-1 expression by total mAPCs in the lymph node
99	PD-L1 expression by total mAPCs in the lymph node
100	PD-L2 expression by total mAPCs in the lymph node
101	Natural turnover of mAPCs in the lymph node
102	Inactivation of mAPCs in the lymph node as a result of CTLA-4 secreted from T Regulatory cells in the lymph nodes binding to CD80 and CD86
103	CD80 expression threshold on mAPCs in the lymph node
104	CD86 expression threshold on mAPCs in the lymph node
105	CD80 expression by mAPCs that interact with Naive T cells in the lymph node
106	CD86 expression by mAPCs that interact with Naive T cells in the lymph node
107	CD80 expression threshold on mAPCs for interaction with Naive T cells in the lymph node
108	CD86 expression threshold on mAPCs for interaction with Naive T cells in the lymph node
109	CD80 expression by mAPCs that interact with Primed Naive T cells in the lymph node
110	CD86 expression by mAPCs that interact with Primed Naive T cells in the lymph node
111	PD-1 expression by mAPCs that interact with Primed Naive T cells in the lymph node
112	PD-L1 expression by mAPCs that interact with Primed Naive T cells in the lymph node
113	PD-L2 expression by mAPCs that interact with Primed Naive T cells in the lymph node
114	Interaction at the immunological synapse between CD80 on mAPCs and CTLA-4 on Primed Naïve T cells in the lymph node
115	Interaction at the immunological synapse between CD80 on mAPCs and PD-L1 on Primed Naïve T cells in the lymph node
116	CD80 expression threshold on mAPCs for interaction with Primed Naive T cells in the lymph node
117	Interaction at the immunological synapse between CD86 on mAPCs and CTLA-4 on Primed Naïve T cells in the lymph node
118	Interaction at the immunological synapse between CD86 on mAPCs and CD28 on Primed Naïve T cells in the lymph node
119	CD86 expression threshold on mAPCs for interaction with Primed Naive T cells in the lymph node
120	Interaction at the immunological synapse between PD-1 on mAPCs cells during priming interactions with Primed Naïve T cells and Anti-PD-1 mAb in the lymph node
121	PD-1 expression threshold on mAPCs for interaction with Primed Naive T cells in the lymph node
122	PD-L1 expression threshold on mAPCs for interaction with Primed Naive T cells in the lymph node
123	Interaction at the immunological synapse between PD-L2 on mAPCs and PD-1 on Primed Naïve T cells in the lymph node
124	PD-L2 expression threshold on mAPCs for interaction with Primed Naive T cells in the lymph node
125	PD-1 expression threshold on total mAPCs in the lymph node
126	PD-L1 expression threshold on total mAPCs in the lymph node
127	PD-L2 expression threshold on total mAPCs in the lymph node
128	Engagement of Naïve T cells in the first priming phase in the lymph node
129	Naïve T cells cycling out of the lymph node
130	Naïve T cells being disengaged in the first priming phase without undergoing successful priming in the lymph node
131	Naïve T cells successfully undergoing the first priming phase in the lymph node
132	Transendocytosis of the CD80 receptors on mAPCs through CTLA-4 binding and internalization on Primed Naïve T cells in the lymph node
133	Transendocytosis of the CD86 receptors on mAPCs through CTLA-4 binding and internalization on Primed Naïve T cells in the lymph node
134	Interaction at the immunological synapse between CD80 on mAPCs cells and CD28 on Naïve T cells in the lymph node
135	Interaction at the immunological synapse between CD86 on mAPCs cells and CD28 on Naïve T cells in the lymph node
136	CD28 expression threshold on Naïve T cells in the lymph node
137	Naïve T cells expressing CD28 in the lymph node
138	Lymph return of Anti-PD-1 to the blood
139	Lymph return of Anti-PD-L1 to the blood
140	Interaction at the immunological synapse between PD-L1 on mAPCs involved in the second priming phase and Anti-PD-L1 mAb in the lymph node
141	Interaction at the immunological synapse between PD-L1 on Primed Naïve T cells involved in the second priming phase with mAPCs and Anti-PD-L1 mAb in the lymph node
142	CTLA-4 expression threshold on Primed Naïve T cells for interaction with mAPCs in the lymph node
143	Interaction at the immunological synapse between CD80 on mAPCs and CD28 on Primed Naïve T cells in the lymph node

Reaction Number	Reaction Description
144	CD28 expression threshold on Primed Naïve T cells for interaction with mAPCs in the lymph node
145	Interaction at the immunological synapse between PD-L1 on mAPCs and CD80 on Primed Naïve T cells in the lymph node
146	CD80 expression threshold on Primed Naïve T cells for interaction with mAPCs in the lymph node
147	Interaction at the immunological synapse between PD-L1 on mAPCs and PD-1 on Primed Naïve T cells in the lymph node
148	Interaction at the immunological synapse between PD-1 on Primed Naïve T cells involved in the second priming phase with mAPCs and Anti-PD-1 mAb in the lymph node
149	PD-1 expression threshold on Primed Naïve T cells for interaction with mAPCs in the lymph node
150	Interaction at the immunological synapse between PD-1 on mAPCs and PD-L1 on Primed Naïve T cells in the lymph node
151	PD-L1 expression threshold on Primed Naïve T cells for interaction with mAPCs in the lymph node
152	CTLA-4 expression by Primed Naïve T cells for interaction with mAPCs in the lymph node
153	CD28 expression by Primed Naïve T cells for interaction with mAPCs in the lymph node
154	CD80 expression by Primed Naïve T cells for interaction with mAPCs in the lymph node
155	PD-1 expression by Primed Naïve T cells for interaction with mAPCs in the lymph node
156	PD-L1 expression by Primed Naïve T cells for interaction with mAPCs in the lymph node
157	Primed Naïve T cells engaging in the second priming phase in the lymph node
158	Primed Naïve T cells unsuccessfully undergoing the second priming phase to become anergic T cells in the lymph node
159	Primed Naïve T cells engaged in the second priming phase disengaging form being primed in the lymph node
160	Primed Naïve T cells engaged in the second priming phase successfully undergoing priming to become Proliferating T cells in the lymph node
161	Proliferating T cells becoming fully activated Effector T cells in the lymph node
162	Sets the proliferation threshold for Proliferating T cells in the lymph node
163	Internalization of the Anti-CTLA-4 antibodies bound to CTLA-4 receptors on T Regulatory cells in the lymph node
164	Transendocytosis of the CD80 receptors on mAPCs through CTLA-4 binding and internalization on T Regulatory cells in the lymph node
165	Transendocytosis of the CD86 receptors on mAPCs through CTLA-4 binding and internalization on T Regulatory cells in the lymph node
166	CTLA-4 expression on the surface of non-interacting T Regulatory cells in the lymph node
167	Interaction between T Regulatory cells and mAPCs in lymph node
168	Interaction between T Regulatory cells and Naïve T cells in lymph node
169	Interaction between T Regulatory cells and Primed Naïve T cells in lymph node
170	Dissociation of T Regulatory cells from mAPCs in the lymph node with inactivation of the latter
171	Dissociation of T Regulatory cells from mAPCs in the lymph node without inactivation of the latter
172	CD80 expression by mAPCs for interaction with T Regulatory cells in the lymph node
173	CD86 expression by mAPCs for interaction with T Regulatory cells in the lymph node
174	CTLA-4 expression by T Regulatory cells for interaction with mAPCs in the lymph node
175	Binding of Anti-CTLA-4 to CTLA-4 expressed on the surface of non-interacting T Regulatory in the lymph node
176	CTLA-4 expression threshold on non-interacting T Regulatory cells in the lymph node
177	Administration of Anti-CTLA-4 mAb into the central compartment
178	Administration of Anti-PD-1 mAb into the central compartment
179	Administration of Anti-PD-L1 mAb into the central compartment
180	Naïve T cells cycling into the lymph node
181	The proliferation rate of the Proliferating T cells in the lymph node
182	Appearance of monocytes in the tumor
183	Proliferation of cancer cells in the tumor
184	Distribution of Anti-CTLA-4 mAb between leaky tissues and lymph node
185	Distribution of Anti-CTLA-4 mAb between tight tissues and lymph node
186	Trafficking of free Effector T cells from Peripheral tissues vasculature to the lung vasculature
187	Turnover of free Effector T cells in the Peripheral tissues vasculature
188	Distribution of Anti-PD-1 mAb between leaky tissues and lymph node
189	Distribution of Anti-PD-1 mAb between tight tissues and lymph node
190	Distribution of Anti-PD-L1 mAb between leaky tissues and lymph node
191	Distribution of Anti-PD-L1 mAb between tight tissues and lymph node
192	CD80 expression by the T5 subtype of cancer cells in the tumor
193	PD-1 expression by the T2 subtype of cancer cells in the tumor
194	PD-1 expression by the T9 subtype of cancer cells in the tumor
195	CD80 expression by the T9 subtype of cancer cells in the tumor
196	PD-1 expression by the T6 subtype of cancer cells in the tumor
197	PD-L1 expression by the T6 subtype of cancer cells in the tumor
198	PD-1 expression by the T14 subtype of cancer cells in the tumor
199	PD-L1 expression by the T14 subtype of cancer cells in the tumor
200	CD80 expression by the T14 subtype of cancer cells in the tumor
201	PD-1 expression by the T10 subtype of cancer cells in the tumor
202	PD-L1 expression by the T10 subtype of cancer cells in the tumor
203	PD-L2 expression by the T10 subtype of cancer cells in the tumor
204	PD-1 expression by the T16 subtype of cancer cells in the tumor
205	PD-L1 expression by the T16 subtype of cancer cells in the tumor
206	PD-L2 expression by the T16 subtype of cancer cells in the tumor
207	CD80 expression by the T16 subtype of cancer cells in the tumor

Reaction Number	Reaction Description
208	PD-1 expression by the T7 subtype of cancer cells in the tumor
209	PD-L2 expression by the T7 subtype of cancer cells in the tumor
210	PD-1 expression by the T15 subtype of cancer cells in the tumor
211	PD-L2 expression by the T15 subtype of cancer cells in the tumor
212	CD80 expression by the T15 subtype of cancer cells in the tumor
213	PD-L1 expression by the T3 subtype of cancer cells in the tumor
214	PD-L1 expression by the T11 subtype of cancer cells in the tumor
215	CD80 expression by the T11 subtype of cancer cells in the tumor
216	PD-L1 expression by the T8 subtype of cancer cells in the tumor
217	PD-L2 expression by the T8 subtype of cancer cells in the tumor
218	PD-L1 expression by the T13 subtype of cancer cells in the tumor
219	PD-L2 expression by the T13 subtype of cancer cells in the tumor
220	CD80 expression by the T13 subtype of cancer cells in the tumor
221	PD-L2 expression by the T4 subtype of cancer cells in the tumor
222	PD-L2 expression by the T12 subtype of cancer cells in the tumor
223	CD80 expression by the T12 subtype of cancer cells in the tumor
224	Interaction at the immunological synapse between PD-1 expressed by the T10 subtype of cancer cells and Anti-PD-1 in the tumor
225	PD-1 expression threshold by the T10 subtype of cancer cells in the tumor
226	Interaction at the immunological synapse between PD-L1 expressed by the T10 subtype of cancer cells and Anti-PD-L1 in the tumor
227	PD-L1 expression threshold by the T10 subtype of cancer cells in the tumor
228	PD-L2 expression threshold by the T10 subtype of cancer cells in the tumor
229	Interaction at the immunological synapse between PD-L1 expressed by the T11 subtype of cancer cells and Anti-PD-L1 in the tumor
230	PD-L1 expression threshold by the T11 subtype of cancer cells in the tumor
231	CD80 expression threshold by the T11 subtype of cancer cells in the tumor
232	PD-L2 expression threshold by the T12 subtype of cancer cells in the tumor
233	CD80 expression threshold by the T12 subtype of cancer cells in the tumor
234	Interaction at the immunological synapse between PD-L1 expressed by the T13 subtype of cancer cells and Anti-PD-L1 in the tumor
235	PD-L1 expression threshold by the T13 subtype of cancer cells in the tumor
236	PD-L2 expression threshold by the T13 subtype of cancer cells in the tumor
237	CD80 expression by the T13 subtype of cancer cells in the tumor
238	Interaction at the immunological synapse between PD-1 expressed by the T14 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
239	PD-1 expression threshold by the T14 subtype of cancer cells in the tumor
240	Interaction at the immunological synapse between PD-L1 expressed by the T14 subtype of cancer cells and CD80 on the complementary Effector T cells in the tumor
241	Interaction at the immunological synapse between PD-L1 expressed by the T14 subtype of cancer cells and Anti-PD-L1 in the tumor
242	PD-L1 expression threshold by the T14 subtype of cancer cells in the tumor
243	Interaction at the immunological synapse between CD80 expressed by the T14 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
244	CD80 expression threshold by the T14 subtype of cancer cells in the tumor
245	Interaction at the immunological synapse between PD-1 expressed by the T15 subtype of cancer cells and Anti-PD-1 in the tumor
246	PD-1 expression threshold by the T15 subtype of cancer cells in the tumor
247	Interaction at the immunological synapse between PD-L2 expressed by the T15 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
248	PD-L2 expression threshold by the T15 subtype of cancer cells in the tumor
249	Interaction at the immunological synapse between CD80 expressed by the T15 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
250	CD80 expression threshold by the T15 subtype of cancer cells in the tumor
251	Interaction at the immunological synapse between PD-1 expressed by the T16 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
252	Interaction at the immunological synapse between PD-1 expressed by the T16 subtype of cancer cells and Anti-PD-1 in the tumor
253	PD-1 expression threshold by the T16 subtype of cancer cells in the tumor
254	Interaction at the immunological synapse between PD-L1 expressed by the T16 subtype of cancer cells and Anti-PD-L1 in the tumor
255	PD-L1 expression threshold by the T16 subtype of cancer cells in the tumor
256	Interaction at the immunological synapse between PD-L2 expressed by the T16 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
257	PD-L2 expression threshold by the T16 subtype of cancer cells in the tumor
258	CD80 expression threshold by the T16 subtype of cancer cells in the tumor
259	PD-1 expression threshold by the T2 subtype of cancer cells in the tumor
260	PD-L1 expression threshold by the T3 subtype of cancer cells in the tumor

Reaction Number	Reaction Description
261	PD-L2 expression threshold by the T4 subtype of cancer cells in the tumor
262	CD80 expression threshold by the T5 subtype of cancer cells in the tumor
263	Interaction at the immunological synapse between PD-L2 expressed by the T6 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
264	PD-1 expression threshold by the T6 subtype of cancer cells in the tumor
265	Interaction at the immunological synapse between PD-L1 expressed by the T6 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
266	Interaction at the immunological synapse between PD-L1 expressed by the T6 subtype of cancer cells and CD80 on the complementary Effector T cells in the tumor
267	Interaction at the immunological synapse between PD-L1 expressed by the T6 subtype of cancer cells and Anti-PD-L1 in the tumor
268	PD-L1 expression threshold by the T6 subtype of cancer cells in the tumor
269	PD-1 expression threshold by the T7 subtype of cancer cells in the tumor
270	PD-L2 expression threshold by the T7 subtype of cancer cells in the tumor
271	Interaction at the immunological synapse between PD-L1 expressed by the T8 subtype of cancer cells and CD80 on Effector T cells in the tumor
272	Interaction at the immunological synapse between PD-L1 expressed by the T8 subtype of cancer cells and Anti-PD-L1 in the tumor
273	PD-L1 expression threshold by the T8 subtype of cancer cells in the tumor
274	PD-L2 expression threshold by the T8 subtype of cancer cells in the tumor
275	Interaction at the immunological synapse between PD-1 expressed by the T9 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
276	PD-1 expression threshold by the T9 subtype of cancer cells in the tumor
277	CD80 expression threshold by the T9 subtype of cancer cells in the tumor
278	Transendocytosis of the CD80 receptors on mAPCs through CTLA-4 binding and internalization on T Regulatory cells in the tumor
279	Transendocytosis of the CD86 receptors on mAPCs through CTLA-4 binding and internalization on T Regulatory cells in the tumor
280	Internalization of the Anti-CTLA-4 antibodies bound to CTLA-4 receptors on T Regulatory cells in the tumor
281	PD-1 expression by Effector T cells interacting with the T8 subtype of cancer cells in the tumor
282	CD80 expression by Effector T cells interacting with the T8 subtype of cancer cells in the tumor
283	PD-1 expression by Effector T cells interacting with the T3 subtype of cancer cells in the tumor
284	CD80 expression by Effector T cells interacting with the T3 subtype of cancer cells in the tumor
285	PD-L1 expression by Effector T cells interacting with the T16 subtype of cancer cells in the tumor
286	PD-1 expression by Effector T cells interacting with the T16 subtype of cancer cells in the tumor
287	CD80 expression by Effector T cells interacting with the T16 subtype of cancer cells in the tumor
288	PD-L1 expression by Effector T cells interacting with the T14 subtype of cancer cells in the tumor
289	PD-1 expression by Effector T cells interacting with the T14 subtype of cancer cells in the tumor
290	CD80 expression by Effector T cells interacting with the T14 subtype of cancer cells in the tumor
291	PD-L1 expression by Effector T cells interacting with the T10 subtype of cancer cells in the tumor
292	PD-1 expression by Effector T cells interacting with the T10 subtype of cancer cells in the tumor
293	CD80 expression by Effector T cells interacting with the T10 subtype of cancer cells in the tumor
294	PD-L1 expression by Effector T cells interacting with the T6 subtype of cancer cells in the tumor
295	PD-1 expression by Effector T cells interacting with the T6 subtype of cancer cells in the tumor
296	CD80 expression by Effector T cells interacting with the T6 subtype of cancer cells in the tumor
297	PD-L1 expression by Effector T cells interacting with the T15 subtype of cancer cells in the tumor
298	PD-1 expression by Effector T cells interacting with the T15 subtype of cancer cells in the tumor
299	PD-L1 expression by Effector T cells interacting with the T7 subtype of cancer cells in the tumor
300	PD-1 expression by Effector T cells interacting with the T7 subtype of cancer cells in the tumor
301	PD-L1 expression by Effector T cells interacting with the T13 subtype of cancer cells in the tumor
302	PD-1 expression by Effector T cells interacting with the T13 subtype of cancer cells in the tumor
303	PD-L1 expression by Effector T cells interacting with the T11 subtype of cancer cells in the tumor
304	PD-1 expression by Effector T cells interacting with the T11 subtype of cancer cells in the tumor
305	PD-L1 expression by Effector T cells interacting with the T12 subtype of cancer cells in the tumor
306	PD-1 expression by Effector T cells interacting with the T12 subtype of cancer cells in the tumor
307	PD-1 expression by Effector T cells interacting with the T4 subtype of cancer cells in the tumor
308	PD-L1 expression by Effector T cells interacting with the T9 subtype of cancer cells in the tumor
309	PD-L1 expression by Effector T cells interacting with the T5 subtype of cancer cells in the tumor
310	PD-L1 expression by Effector T cells interacting with the T2 subtype of cancer cells in the tumor
311	Interaction at the immunological synapse between PD-1 expressed by the T10 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
312	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T10 subtype of cancer cells and Anti-PD-L1 in the tumor
313	PD-L1 expression threshold by the Effector T cells interacting with the T10 subtype of cancer cells in the tumor
314	Interaction at the immunological synapse between PD-L1 expressed by the T10 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
315	Interaction at the immunological synapse between PD-L2 expressed by the T10 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor

Reaction Number	Reaction Description
316	PD-1 expression threshold by the Effector T cells interacting with the T10 subtype of cancer cells in the tumor
317	Interaction at the immunological synapse between PD-L1 expressed by the T10 subtype of cancer cells and CD80 on the complementary Effector T cells in the tumor
318	CD80 expression threshold by the Effector T cells interacting with the T10 subtype of cancer cells in the tumor
319	Interaction at the immunological synapse between PD-L1 expressed by the T11 subtype of cancer cells and CD80 on the complementary Effector T cells in the tumor
320	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T11 subtype of cancer cells and Anti-PD-L1 in the tumor
321	PD-L1 expression threshold by the Effector T cells interacting with the T11 subtype of cancer cells in the tumor
322	Interaction at the immunological synapse between PD-L1 expressed by the T11 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
323	PD-1 expression threshold by the Effector T cells interacting with the T11 subtype of cancer cells in the tumor
324	Interaction at the immunological synapse between CD80 expressed by the T12 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
325	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T12 subtype of cancer cells and Anti-PD-L1 in the tumor
326	PD-L1 expression threshold by the Effector T cells interacting with the T12 subtype of cancer cells in the tumor
327	Interaction at the immunological synapse between PD-L2 expressed by the T12 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
328	PD-1 expression threshold by the Effector T cells interacting with the T12 subtype of cancer cells in the tumor
329	Interaction at the immunological synapse between CD80 expressed by the T13 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
330	PD-L1 expression threshold by the Effector T cells interacting with the T13 subtype of cancer cells in the tumor
331	Interaction at the immunological synapse between PD-L1 expressed by the T13 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
332	Interaction at the immunological synapse between PD-L2 expressed by the T13 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
333	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T13 subtype of cancer cells and Anti-PD-1 in the tumor
334	PD-1 expression threshold by the Effector T cells interacting with the T13 subtype of cancer cells in the tumor
335	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T14 subtype of cancer cells and Anti-PD-L1 in the tumor
336	PD-L1 expression threshold by the Effector T cells interacting with the T14 subtype of cancer cells in the tumor
337	Interaction at the immunological synapse between PD-L1 expressed by the T14 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
338	PD-1 expression threshold by the Effector T cells interacting with the T14 subtype of cancer cells in the tumor
339	CD80 expression threshold by the Effector T cells interacting with the T14 subtype of cancer cells in the tumor
340	Interaction at the immunological synapse between PD-1 expressed by the T15 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
341	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T15 subtype of cancer cells and Anti-PD-L1 in the tumor
342	PD-L1 expression threshold by the Effector T cells interacting with the T15 subtype of cancer cells in the tumor
343	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T15 subtype of cancer cells and Anti-PD-1 in the tumor
344	PD-1 expression threshold by the Effector T cells interacting with the T15 subtype of cancer cells in the tumor
345	Interaction at the immunological synapse between CD80 expressed by the T16 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
346	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T16 subtype of cancer cells and Anti-PD-L1 in the tumor
347	PD-L1 expression threshold by the Effector T cells interacting with the T16 subtype of cancer cells in the tumor
348	Interaction at the immunological synapse between PD-L1 expressed by the T16 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
349	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T16 subtype of cancer cells and Anti-PD-1 in the tumor
350	PD-1 expression threshold by the Effector T cells interacting with the T16 subtype of cancer cells in the tumor
351	Interaction at the immunological synapse between PD-L1 expressed by the T16 subtype of cancer cells and CD80 on the complementary Effector T cells in the tumor
352	CD80 expression threshold by the Effector T cells interacting with the T16 subtype of cancer cells in the tumor
353	Interaction at the immunological synapse between PD-1 expressed by the T2 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
354	PD-L1 expression threshold by the Effector T cells interacting with the T2 subtype of cancer cells in the tumor
355	Interaction at the immunological synapse between PD-L1 expressed by the T3 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
356	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T3 subtype of cancer cells and Anti-PD-1 in the tumor
357	PD-1 expression threshold by the Effector T cells interacting with the T3 subtype of cancer cells in the tumor
358	Interaction at the immunological synapse between PD-L1 expressed by the T3 subtype of cancer cells and CD80 on the complementary Effector T cells in the tumor

Reaction Number	Reaction Description
359	CD80 expression threshold by the Effector T cells interacting with the T3 subtype of cancer cells in the tumor
360	Interaction at the immunological synapse between PD-L2 expressed by the T4 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
361	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T4 subtype of cancer cells and Anti-PD-1 in the tumor
362	PD-1 expression threshold by the Effector T cells interacting with the T4 subtype of cancer cells in the tumor
363	Interaction at the immunological synapse between CD80 expressed by the T5 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
364	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T5 subtype of cancer cells and Anti-PD-L1 in the tumor
365	PD-L1 expression threshold by the Effector T cells interacting with the T5 subtype of cancer cells in the tumor
366	Interaction at the immunological synapse between PD-1 expressed by the T6 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
367	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T6 subtype of cancer cells and Anti-PD-L1 in the tumor
368	PD-L1 expression threshold by the Effector T cells interacting with the T6 subtype of cancer cells in the tumor
369	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T6 subtype of cancer cells and Anti-PD-1 in the tumor
370	PD-1 expression threshold by the Effector T cells interacting with the T6 subtype of cancer cells in the tumor
371	CD80 expression threshold by the Effector T cells interacting with the T6 subtype of cancer cells in the tumor
372	Interaction at the immunological synapse between PD-1 expressed by the T7 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
373	PD-L1 expression threshold by the Effector T cells interacting with the T7 subtype of cancer cells in the tumor
374	Interaction at the immunological synapse between PD-L2 expressed by the T7 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
375	PD-1 expression threshold by the Effector T cells interacting with the T7 subtype of cancer cells in the tumor
376	Interaction at the immunological synapse between PD-L1 expressed by the T8 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
377	Interaction at the immunological synapse between PD-L2 expressed by the T8 subtype of cancer cells and PD-1 on the complementary Effector T cells in the tumor
378	PD-1 expression threshold by the Effector T cells interacting with the T8 subtype of cancer cells in the tumor
379	CD80 expression threshold by the Effector T cells interacting with the T8 subtype of cancer cells in the tumor
380	Interaction at the immunological synapse between CD80 expressed by the T9 subtype of cancer cells and PD-L1 on the complementary Effector T cells in the tumor
381	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T9 subtype of cancer cells and Anti-PD-L1 in the tumor
382	PD-L1 expression threshold by the Effector T cells interacting with the T9 subtype of cancer cells in the tumor
383	Turnover of resting macrophages
384	Phagocytosis of tumor debris by resting APCs in the lymph node
385	Transport of tumor debris from the tumor to the lymph node
386	Decay of tumor debris in the tumor
387	The distribution of tumor debris away from any of the considered lymph nodes
388	Accounting for the distribution of tumor debris from the tumor to the lymph nodes other than the lymph node compartment in the model
389	Natural turnover of cancer cells in the tumor
390	CD80 expression threshold by the mAPCs interacting with the T Regulatory cells in the tumor
391	Interaction at the immunological synapse between CD80 expressed by the Effector T cells and PD-L1 on the T Regulatory cells in the tumor
392	CD80 expression threshold by the Effector T cells interacting with the T Regulatory cells in the tumor
393	CD80 expression threshold by the Effector T cells interacting with the MDSCs in the tumor
394	CD86 expression threshold by the mAPCs interacting with the T Regulatory cells in the tumor
395	Flow of Anti-CTLA-4 mAb between the tumor and lymph node
396	Interaction at the immunological synapse between CD80 expressed by the mAPCs and CTLA-4 on the T Regulatory cells in the tumor
397	Interaction at the immunological synapse between CD86 expressed by the mAPCs and CTLA-4 on the T Regulatory cells in the tumor
398	Interaction at the immunological synapse between CTLA-4 expressed by the T Regulatory cells and Anti-CTLA-4 in the tumor
399	CTLA-4 expression threshold by the T Regulatory cells interacting with the mAPCs in the tumor
400	Turnover of Effector T cells in the tumor
401	Apoptosis of Effector T cells following complete cancer cell death in the tumor
402	Conversion of Effector T cells into Resident Effector Memory cells following complete cancer cell death in the tumor
403	Association of Effector T cells with cancer cells in the tumor
404	Turnover of arrested Effector T cells in Tumor vasculature
405	Extravasation of arrested Effector T cells into Tumor interstitium
406	Turnover of bound Effector T cells in Tumor vasculature
407	Arrest of bound Effector T cells in the Tumor vasculature
408	Detachment of bound Effector T cells in the Tumor vasculature

Reaction Number	Reaction Description
409	Binding or free Effector T cells to the Tumor vasculature
410	Trafficking of free Effector T cells from the Tumor vasculature to the Lungs vasculature
411	Turnover of free Effector T cells in Tumor vasculature
412	Transport of mAPCs from the tumor to the lymph node
413	Accounting for the distribution of mAPCs from the tumor to the lymph nodes other than the lymph node compartment in the model
414	The distribution of mAPCs away from any of the considered lymph nodes
415	CD80 expression by mAPCs interacting with the T Regulatory cells in the tumor
416	CD86 expression by mAPCs interacting with the T Regulatory cells in the tumor
417	Association of Effector T cells with MDSCs in the tumor
418	PD-1 expression by MDSCs interacting with the Effector T cells in the tumor
419	PD-L1 expression by MDSCs interacting with the Effector T cells in the tumor
420	Dissociation of MDSCs from Effector T cells with inactivation of the latter in the tumor
421	Dissociation of MDSCs from Effector T cells without inactivation of the latter in the tumor
422	Distribution of Anti-PD-1 mAb between Tumor and Lymph Node
423	Interaction at the immunological synapse between PD-1 expressed by the T14 subtype of cancer cells and Anti-PD-1 in the tumor
424	Interaction at the immunological synapse between PD-1 expressed by the T2 subtype of cancer cells and Anti-PD-1 in the tumor
425	Interaction at the immunological synapse between PD-1 expressed by the T7 subtype of cancer cells and Anti-PD-1 in the tumor
426	Interaction at the immunological synapse between PD-1 expressed by the T9 subtype of cancer cells and Anti-PD-1 in the tumor
427	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T10 subtype of cancer cells and Anti-PD-1 in the tumor
428	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T11 subtype of cancer cells and Anti-PD-1 in the tumor
429	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T12 subtype of cancer cells and Anti-PD-1 in the tumor
430	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T14 subtype of cancer cells and Anti-PD-1 in the tumor
431	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T7 subtype of cancer cells and Anti-PD-1 in the tumor
432	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T8 subtype of cancer cells and Anti-PD-1 in the tumor
433	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the T Regulatory cells and Anti-PD-1 in the tumor
434	Interaction at the immunological synapse between PD-1 expressed by the MDSCs interacting with Effector T cells and Anti-PD-1 in the tumor
435	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells and PD-1 on the MDSCs in the tumor
436	PD-1 expression threshold by the MDSCs interacting with the Effector T cells in the tumor
437	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells and PD-L1 on the T Regulatory cells in the tumor
438	PD-1 expression threshold by the Effector T cells interacting with the T Regulatory cells in the tumor
439	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells interacting with the MDSCs and Anti-PD-1 in the tumor
440	PD-1 expression threshold by the Effector T cells interacting with the MDSCs in the tumor
441	Interaction at the immunological synapse between PD-1 expressed by the T Regulatory cells interacting with the Effector T cells and Anti-PD-1 in the tumor
442	PD-1 expression threshold by the T Regulatory cells interacting with the Effector T cells in the tumor
443	Distribution of Anti-PD-L1 mAb between Tumor and Lymph Node
444	Interaction at the immunological synapse between PD-L1 expressed by the T3 subtype of cancer cells and Anti-PD-L1 in the tumor
445	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T13 subtype of cancer cells and Anti-PD-L1 in the tumor
446	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T2 subtype of cancer cells and Anti-PD-L1 in the tumor
447	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T7 subtype of cancer cells and Anti-PD-L1 in the tumor
448	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the T Regulatory cells and Anti-PD-L1 in the tumor
417	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells interacting with the MDSCs and Anti-PD-L1 in the tumor
418	Interaction at the immunological synapse between CD80 expressed by the Effector T cells and PD-L1 on the MDSCs in the tumor
419	Interaction at the immunological synapse between PD-1 expressed by the Effector T cells and PD-L1 on the MDSCs in the tumor

Reaction Number	Reaction Description
420	Interaction at the immunological synapse between PD-L1 expressed by the MDSCs interacting with the Effector T cells and Anti-PD-L1 in the tumor
421	PD-L1 expression threshold by the MDSCs interacting with the Effector T cells in the tumor
422	Interaction at the immunological synapse between PD-L1 expressed by the Effector T cells and PD-1 on the T Regulatory cells in the tumor
423	PD-L1 expression threshold by the Effector T cells interacting with the T Regulatory cells in the tumor
424	PD-1 expression threshold by the Effector T cells interacting with the MDSCs in the tumor
425	Interaction at the immunological synapse between PD-L1 expressed by the T Regulatory cells interacting with the Effector T cells and Anti-PD-L1 in the tumor
426	PD-1 expression threshold by the T Regulatory cells interacting with the Effector T cells in the tumor
427	Recovery of Effector T cells from the delay state following interaction with cancer cells in the tumor
428	Generation of cancer debris by killing of the cancer cells by the Effector T cells in the tumor
429	Dissociation of Effector T cells from the cancer cells into a delay state in the tumor
430	Inactivation of Effector T cells as a result of interactions with the cancer cells in the tumor
431	CD80 expression by Effector T cells interacting with the MDSCs in the tumor
432	PD-1 expression by Effector T cells interacting with the MDSCs in the tumor
433	PD-L1 expression by Effector T cells interacting with the MDSCs in the tumor
434	CD80 expression by Effector T cells interacting with the T Regulatory cells in the tumor
435	PD-1 expression by Effector T cells interacting with the T Regulatory cells in the tumor
436	PD-L1 expression by Effector T cells interacting with the T Regulatory cells in the tumor
437	Association of Effector T cells with T Regulatory cells in the tumor
438	CTLA-4 expression by T Regulatory cells interacting with the mAPCs in the tumor
439	PD-1 expression by T Regulatory cells interacting with the Effector T cells in the tumor
440	PD-L1 expression by T Regulatory cells interacting with the Effector T cells in the tumor
441	Dissociation of T Regulatory cells from Effector T cells with inactivation of the latter in the tumor
442	Dissociation of T Regulatory cells from Effector T cells without inactivation of the latter in the tumor

Table S3 – Model Reaction and Rate Descriptions (End)

Table S4 – Definition of species in the model (Start)

Compartment Location	Variable Name	Units	Variable Definition
Blood-Lymph	CTLA4_mabB	mole	Anti-CTLA-4 antibody in the blood
Blood-Lymph	CTLA4_mabB_ugml	µg/ml	Serum concentration of Anti-CTLA-4
Blood-Lymph	PD1_mabb	mole	Anti-PD-1 antibody in the blood
Blood-Lymph	PDL1_mabb	mole	Anti-PD-L1 antibody in the blood
Blood-Lymph	PDL1_mabB_ugml	µg/ml	Serum concentration of Anti-PD-L1
Blood-Lymph	PD1_mabB_ugml	µg/ml	Serum concentration of Anti-PD-1
Blood-Lymph	Effector_TB	cell	Effector T cells that have been generated from all the lymph nodes considered that have migrated into the blood
Blood-Lymph	Effector_T_TOTAL	cell	The total number of Effector T cells present that have exited the lymph nodes
Blood-Lymph	Effector_T_TB	cell	Effector T cells that have been generated from all the lymph nodes considered that are in the process of migrating into the blood
Lungs	EffT_f_LungsVasc	cell	Free effector T cells in the Lung vasculature
Lungs	EffT_r_LungsVasc	cell	Bound effector T cells in the Lung vasculature
Lungs	EffT_AR_LungsVasc	cell	Arrested effector T cells in the Lung vasculature
Lungs	EffT_LungsEx	cell	Effector T cells in the Lung interstitium
Lungs	Lung_Free_Sites	cell	Available binding sites for cells in the Lung vasculature
Liv_Spln_GI	EffT_Liver_f_Vasc	cell	Free effector T cells in the Liver vasculature
Liv_Spln_GI	EffT_LiverEx	cell	Effector T cells in the Liver interstitium
Liv_Spln_GI	EffT_Liver_b_Vasc	cell	Bound effector T cells in the Liver vasculature
Liv_Spln_GI	EffT_Liver_AR_Vasc	cell	Arrested effector T cells in the Liver vasculature
Liv_Spln_GI	Liver_Free_Sites	cell	Available binding sites for cells in the Liver vasculature
Liv_Spln_GI	EffT_Spleen_f_Vasc	cell	Free effector T cells in the Spleen vasculature
Liv_Spln_GI	EffT_GI_f_Vasc	cell	Free effector T cells in the GI vasculature
Liv_Spln_GI	EffT_SpleenEx	cell	Effector T cells in the Spleen interstitium
Liv_Spln_GI	EffT_Spleen_b_Vasc	cell	Bound effector T cells in the Spleen vasculature
Liv_Spln_GI	EffT_Spleen_AR_Vasc	cell	Arrested effector T cells in the Spleen vasculature
Liv_Spln_GI	Spleen_Free_Sites	cell	Available binding sites for cells in the Spleen vasculature
Lymph_Node	Naive_T	cell	Naïve T cells that undergo the first phase of priming in the Lymph Nodes
Lymph_Node	Primed_Naive_T	cell	Primed Naive T cells that undergo the second phase of priming in the Lymph Nodes

Compartment Location	Variable Name	Units	Variable Definition
Lymph_Node	PNT_Int_CD28	mole	CD28 expressed by interacting Primed Naive T cells engaged in the second priming phase
Lymph_Node	mAPC	cell	Total number of mature antigen presenting cells (mAPCs) in the lymph node compartment
Lymph_Node	Effector_T	cell	Effector T cells that are generate in the lymph node compartment (considering one lymph node)
Lymph_Node	CTLA4_mab	mole	Anti-CTLA-4 antibody in the lymph node
Lymph_Node	Naive_T0	cell	Naive T cells that can undergo priming in the lymph node
Lymph_Node	Prolif_Naive_T	cell	Proliferating Naive T cells that have undergone the second phase of priming in the lymph node
Lymph_Node	Anergic_Naive_T	cell	Primed Naive T cells that do not undergo proliferation following the second phase of priming and are deemed to be anergic T cells in the lymph node
Lymph_Node	PD1_mabLN_ugml	µg/ml	Concentration of anti-PD-1 antibody in the lymph node
Lymph_Node	CTLA4_mab_ugml	µg/ml	Concentration of anti-CTLA-4 antibody in the lymph node
Lymph_Node	PDL1_mabLN_ugml	µg/ml	Concentration of anti-PD-L1 antibody in the lymph node
Lymph_Node	EffT_LN_ExRec	cell	Effector T cells in the lymph node interstitium
Lymph_Node	EffT_LN_f_Vasc	cell	Free effector T cells in the lymph node vasculature
Lymph_Node	mAPC1	cell	mAPCs in lymph node interacting with T regulatory cells
Lymph_Node	Naive_T2	cell	Naïve T cells in the lymph node interacting with T regulatory cells
Lymph_Node	Primed_Naive_T2	cell	Primed naïve T cells in the lymph node interacting with T regulatory cells
Lymph_Node	mAPC_cells_per_ml	cell/ml	Calculation of mAPC in the lymph node
Lymph_Node	PD1_mab	mole	Anti-PD-1 antibody in the lymph node
Lymph_Node	PDL1_mab	mole	Anti-PD-L1 antibody in the lymph node
Lymph_Node	Naive_T1	cell	Naive T cells engaged in the first priming phase in the lymph node
Lymph_Node	Primed_Naive_T1	cell	Primed Naive T cells engaged in the second priming phase in the lymph node
Lymph_Node	mAPC_Total_Calc_Pr	cell	mAPCs in the lymph node that are not engaged in priming
Lymph_Node	Total_T_CD8-CD4	cell	Total number of all T cells in the lymph node
Lymph_Node	PNT1_Int	cell	Primed Naive T cells engaged in the second priming phase in the lymph node that are accounting for the expression of immune checkpoints
Lymph_Node	PNT_CTLA4	mole	CTLA-4 expressed by interacting Primed Naive T cells engaged in the second priming phase
Lymph_Node	mAPC_Int_P1	cell	mAPCs interacting with Naive T cells in the first phase of priming
Lymph_Node	mAPC_Int_P2	cell	mAPCs interacting with Primed Naive T cells in the second phase of priming
Lymph_Node	mAPC_Int_P2_CD80	mole	CD80 receptors expressed by mAPCs that are involved in the second priming phase interactions
Lymph_Node	mAPC_Int_P2_CD86	mole	CD86 receptors expressed by mAPCs that are involved in the second priming phase interactions
Lymph_Node	POS_Sig_PNT_CD80	mole	Receptor-receptor interactions at the immunological synapse between CD28 expressed on Primed Naive T cells and CD80 expressed on mAPCs during the second phase of priming
Lymph_Node	POS_Sig_PNT_CD86	mole	Receptor-receptor interactions at the immunological synapse between CD28 expressed on Primed Naive T cells and CD86 expressed on mAPCs during the second phase of priming
Lymph_Node	NEG_Sig_PNT_CD80	mole	Receptor-receptor interactions at the immunological synapse between CTLA-4 expressed on Primed Naive T cells and CD80 expressed on mAPCs during the second phase of priming
Lymph_Node	NEG_Sig_PNT_CD86	mole	Receptor-receptor interactions at the immunological synapse between CTLA-4 expressed on Primed Naive T cells and CD80 expressed on mAPCs during the second phase of priming
Lymph_Node	CTLA4_mAb_CTLA4	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between CTLA-4 expressed on Primed Naive T cells during the second priming phase and

Compartment Location	Variable Name	Units	Variable Definition
			Anti-CTLA-4 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	mAPC_Int_P2_PDL1	mole	PD-L1 receptors expressed by mAPCs that are involved in the second priming phase interactions
Lymph_Node	mAPC_Int_P2_PDL2	mole	PD-L2 receptors expressed by mAPCs that are involved in the second priming phase interactions
Lymph_Node	mAPC_Int_P2_PD1	mole	PD-1 receptors expressed by mAPCs that are involved in the second priming phase interactions
Lymph_Node	PNT_Int_CD80	mole	CD80 expressed by interacting Primed Naive T cells engaged in the second priming phase
Lymph_Node	PNT_Int_PD1	mole	PD-1 expressed by interacting Primed Naive T cells engaged in the second priming phase
Lymph_Node	PNT_Int_PDL1	mole	PD-L1 expressed by interacting Primed Naive T cells engaged in the second priming phase
Lymph_Node	PNT_CD80-PDL1	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed on Primed Naive T cells and PD-L1 expressed on mAPCs during the second phase of priming
Lymph_Node	PNT_PD1-PDL2	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed on Primed Naive T cells and PD-L2 expressed on mAPCs during the second phase of priming
Lymph_Node	PNT_PD1-PDL1	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed on Primed Naive T cells and PD-L1 expressed on mAPCs during the second phase of priming
Lymph_Node	PNT_PDL1-CD80	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed on Primed Naive T cells and CD80 expressed on mAPCs during the second phase of priming
Lymph_Node	PNT_PDL1-PD1	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed on Primed Naive T cells and PD-1 expressed on mAPCs during the second phase of priming
Lymph_Node	PDL1mAb-PNT_PDL1	mole	Heterogenous receptor-antibody interactions at the immunological synapse between PD-L1 expressed on Primed Naive T cells during the second priming phase and Anti-PD-L1 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	PDL1mAb-mAPC_PDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed on mAPCs during the second priming phase and Anti-PD-L1 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	PD1mAb_mAPC_PD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed on mAPCs during the second priming phase and Anti-PD-1 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	PD1mAb_PNT_PD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed on Primed Naive T cells during the second priming phase and Anti-PD-1 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	mAPC_PD1	mole	Total PD-1 expression by all mAPCs in the lymph node
Lymph_Node	mAPC_PDL2	mole	Total PD-L2 expression by all mAPCs in the lymph node
Lymph_Node	mAPC_PDL1	mole	Total PD-L1 expression by all mAPCs in the lymph node
Lymph_Node	mAPC_CD86	mole	Total CD86 expression by all mAPCs in the lymph node
Lymph_Node	mAPC_CD80	mole	Total CD80 expression by all mAPCs in the lymph node
Lymph_Node	TregLN-NT	cell	T Regulatory cells in the lymph node that have engaged in interacting with Naïve T cells
Lymph_Node	TregLN-PNT	cell	T Regulatory cells in the lymph node that have engaged in interacting with Primed Naïve T cells
Lymph_Node	TregLN_mAPC	cell	T Regulatory cells in the lymph node that have engaged in interacting with mAPCs

Compartment Location	Variable Name	Units	Variable Definition
Lymph_Node	TregLN	cell	Total number of T Regulatory cells that able to engage with other cell types in the lymph node
Lymph_Node	Tr-mAPC_CTLA4	mole	CTLA-4 receptors expressed by T Regulatory cells in the lymph node
Lymph_Node	Tr-PNT_PD1	mole	PD-1 receptors expressed by T Regulatory cells in the lymph node
Lymph_Node	Tr-PNT_PDL1	mole	PD-L1 receptors expressed by T Regulatory cells in the lymph node
Lymph_Node	PNT-Tr_PDL1	mole	PD-L1 receptors expressed by Primed Naïve T cells in the lymph node during engagement with T Regulatory cells
Lymph_Node	PNT-Tr_PD1	mole	PD-1 receptors expressed by Primed Naïve T cells in the lymph node during engagement with T Regulatory cells
Lymph_Node	PNT-Tr_CD80	mole	CD80 receptors expressed by Primed Naïve T cells in the lymph node during engagement with T Regulatory cells
Lymph_Node	TrALN_CT_CD80	mole	Receptor-receptor interactions at the immunological synapse between CTLA-4 expressed on T Regulatory cells and CD80 expressed on mAPCs in the lymph node
Lymph_Node	TrALN_CT_CD86	mole	Receptor-receptor interactions at the immunological synapse between CTLA-4 expressed on T Regulatory cells and CD86 expressed on mAPCs in the lymph node
Lymph_Node	TrPNT_PD1-L1	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed on T Regulatory cells and PD-L1 expressed on Primed Naïve T cells in the lymph node
Lymph_Node	TrPNT_PDL1-PD1	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed on T Regulatory cells and PD-1 expressed on Primed Naïve T cells in the lymph node
Lymph_Node	TrPNT_PDL1-CD80	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed on T Regulatory cells and CD80 expressed on Primed Naïve T cells in the lymph node
Lymph_Node	TrALN_CT_aCT	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between CTLA-4 expressed on T Regulatory cells and Anti-CTLA-4 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	TrPNT_PD1_aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed on T Regulatory cells and Anti-PD-1 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	PNTTr_PDL1_aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed on Primed Naïve T cells and Anti-PD-L1 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	TrPNT_PDL1_aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed on T Regulatory cells and Anti-PD-L1 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	PNTTr_PD1_aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed on Primed Naïve T cells and Anti-PD-1 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	Tr-mAPC_CD80	mole	CD80 receptors expressed by mACPs that are interacting with T Regulatory cells in the lymph node
Lymph_Node	Tr-mAPC_CD86	mole	CD86 receptors expressed by mACPs that are interacting with T Regulatory cells in the lymph node
Lymph_Node	TregLN_mAPC1	cell	T Regulatory cells in the lymph node that have engaged in interacting with mAPCs in the lymph node that are accounting for the expression of immune checkpoints
Lymph_Node	TregLN-PNT1	cell	T Regulatory cells in the lymph node that have engaged in interacting with Primed Naïve T cells in the lymph node that are accounting for the expression of immune checkpoints
Lymph_Node	C_DebrisLN	cell	Cancer debris that has been transported to the lymph node
Lymph_Node	APCLN	cell	Resident antigen presenting cells in the lymph node that have not yet phagocytosed tumor debris

Compartment Location	Variable Name	Units	Variable Definition
Lymph_Node	TrLN_CTLA4	mole	CTLA-4 expressed on the surface of non-interacting T Regulatory cells
Lymph_Node	TrLN_CT_aCT	mole	Receptor-antibody interactions between CTLA-4 expressed on T Regulatory cells and Anti-CTLA-4 mAb delivered to the lymph node by way of IV injection into the blood
Lymph_Node	PNT1_Int1	cell	Naive T cells undergoing the first priming phase in the lymph node that are accounting for the expression of immune checkpoints
Lymph_Node	NT1_Int1	cell	Naive T cells undergoing the first priming phase in the lymph node that are accounting for the expression of CD28
Lymph_Node	NT_Int_CD28	mole	CD28 expressed to the immunological synapse of Naive T cells that are undergoing the first phase of priming
Lymph_Node	mAPC_Int_P1_CD86	mole	CD86 receptors expressed by mAPCs that are involved in the first priming phase interactions with Naïve T cells
Lymph_Node	mAPC_Int_P1_CD80	mole	CD80 receptors expressed by mAPCs that are involved in the first priming phase interactions with Naïve T cells
Lymph_Node	POS_Sig_NT_CD86	mole	Receptor-receptor interactions at the immunological synapse between CD28 expressed on Naive T cells and CD86 expressed on mAPCs during the first phase of priming
Lymph_Node	POS_Sig_NT_CD80	mole	Receptor-receptor interactions at the immunological synapse between CD28 expressed on Naive T cells and CD86 expressed on mAPCs during the first phase of priming
Peripheral	CTLA4_leaky_ugml	µg/ml	Concentration of anti-CTLA-4 in leaky tissue
Peripheral	CTLA4_mabP_leaky	mole	Amount of anti-CTLA-4 in leaky tissue
Peripheral	CTLA4_mabP_tight	mole	Amount of anti-CTLA-4 in tight tissue
Peripheral	CTLA4_tight_ugml	µg/ml	Concentration of anti-CTLA-4 in tight tissue
Peripheral	EffT_P_f_Vasc	cell	Free effector T cells in the peripheral vasculature
Peripheral	PD1_leaky_ugml	µg/ml	Concentration of anti-PD-1 in leaky tissue
Peripheral	PD1_mabP_leaky	mole	Amount of anti-PD-1 in leaky tissue
Peripheral	PD1_mabP_tight	mole	Amount of anti-PD-1 in tight tissue
Peripheral	PD1_tight_ugml	µg/ml	Concentration of anti-PD-1 in tight tissue
Peripheral	PDL1_leaky_ugml	µg/ml	Concentration of anti-PD-L1 in leaky tissue
Peripheral	PDL1_mabP_leaky	mole	Amount of anti-PD-L1 in leaky tissue
Peripheral	PDL1_mabP_tight	mole	Amount of anti-PD-L1 in tight tissue
Peripheral	PDL1_tight_ugml	µg/ml	Concentration of anti-PD-L1 in tight tissue
Tumor	PD1_mabt	mole	Anti-PD-1 antibody in the tumor compartment
Tumor	PDL1_mabt	mole	Anti-PD-L1 antibody in the tumor compartment
Tumor	CTLA4_mabt	mole	Anti-CTLA-4 antibody in the tumor compartment
Tumor	Effector_TT	cell	Effector T cells in the tumor microenvironment
Tumor	Cancer	cell	Cancer cells in the tumor
Tumor	Effector_TT_C_Eng	cell	Effector T cells that can engage with cancer cells in the tumor microenvironment
Tumor	TC1	cell	Cancer cells that are engaged with Effector T cells in the tumor microenvironment
Tumor	T_Recover_Can_Dead	cell	Effector T cells that have disengaged from the cancer cells in the tumor and are in delay state prior to being able to bind other cancer cells
Tumor	C_DebrisT	cell	Cancer debris in the tumor that has resulted from cancer death
Tumor	TC2	cell	Effector T cells that are engaged with cancer cells in the tumor microenvironment
Tumor	Monocytes	cell	Monocytes that migrate into the tumor and differentiate into APCs
Tumor	APC_T	cell	Antigen Presenting Cells (APCs) in the tumor that can phagocytose tumor debris (tumor antigens) and become mature APCs
Tumor	mAPC_T	cell	Mature Antigen Presenting Cells (mAPCs) in the tumor that resulted from APCs that have phagocytosed tumor debris
Tumor	PD1_mabt	mole	Moles of anti-PD-1 antibody in the tumor interstitium
Tumor	PD1_mabT_ugml	µg/ml	Concentration of anti-PD-1 antibody in the tumor interstitium

Compartment Location	Variable Name	Units	Variable Definition
Tumor	CTLA4_mabt_ugml	µg/ml	Concentration of anti-CTLA-4 antibody in the tumor interstitium
Tumor	PDL1_mabT_ugml	µg/ml	Concentration of anti-PD-L1 antibody in the tumor interstitium
Tumor	EffT_f_Vasc	cell	Free effector T cells in the tumor vasculature
Tumor	Tmr_Free_Sites	cell	Available binding sites for cells in the tumor vasculature
Tumor	EffT_b_Vasc	cell	Bound effector T cells in the tumor vasculature
Tumor	EffT_AR_Vasc	cell	Arrested effector T cells in the tumor vasculature
Tumor	Cancer1	cell	Cancer cells that can engage with Effector T cells in the tumor
Tumor	T{PD1}{CD80}-{PDL1}C	cell	Effector T cells in the tumor that interact with the T3 subgroup of cancer cells expressing PD-L1 only, and other unknown factors
Tumor	T{PD1}-{PDL2}C	cell	Effector T cells in the tumor that interact with the T4 subgroup of cancer cells expressing PD-L2 only, and other unknown factors
Tumor	T{PDL1}-{PD1}C	cell	Effector T cells in the tumor that interact with the T2 subgroup of cancer cells expressing PD-1 only, and other unknown factors
Tumor	T{PDL1}-{CD80}C	cell	Effector T cells in the tumor that interact with the T5 subgroup of cancer cells expressing CD80 only, and other unknown factors
Tumor	T{PD1}{L1}{80}-{PD1}{L1}C	cell	Effector T cells in the tumor that interact with the T6 subgroup of cancer cells expressing PD-1 and PD-L1 only, and other unknown factors
Tumor	T{PD1}{80}-{PDL1}{PDL2}C	cell	Effector T cells in the tumor that interact with the T8 subgroup of cancer cells expressing PD-L1 and PD-L2 only, and other unknown factors
Tumor	T{PD1}{L1}-{PD1}{L2}C	cell	Effector T cells in the tumor that interact with the T7 subgroup of cancer cells expressing PD-1 and PD-L2 only, and other unknown factors
Tumor	T{PD1}{L1}{80}-{PD1}{L1}{L2}C	cell	Effector T cells in the tumor that interact with the T10 subgroup of cancer cells expressing PD-1, PD-L1 and PD-L2 only, and other unknown factors
Tumor	T{PDL1}-{CD80}{PD1}C	cell	Effector T cells in the tumor that interact with the T9 subgroup of cancer cells expressing CD80 and PD-1 only, and other unknown factors
Tumor	T{PD1}{L1}-{PDL1}{80}C	cell	Effector T cells in the tumor that interact with the T11 subgroup of cancer cells expressing PD-L1 and CD80 only, and other unknown factors
Tumor	T{PD1}{L1}-{PDL2}{80}C	cell	Effector T cells in the tumor that interact with the T12 subgroup of cancer cells expressing PD-L2 and CD80 only, and other unknown factors
Tumor	T{PD1}{L1}-{PDL1}{80}{L2}C	cell	Effector T cells in the tumor that interact with the T13 subgroup of cancer cells expressing PD-L1, CD80 and PD-L2 only, and other unknown factors
Tumor	T{PD1}{L1}{80}-{PD1}{80}{L1}C	cell	Effector T cells in the tumor that interact with the T14 subgroup of cancer cells expressing PD-1, CD80 and PD-L1 only, and other unknown factors
Tumor	T{PD1}{L1}-{PD1}{80}{PDL2}C	cell	Effector T cells in the tumor that interact with the T15 subgroup of cancer cells expressing PD-1, CD80 and PD-L2 only, and other unknown factors
Tumor	T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C	cell	Effector T cells in the tumor that interact with the T16 subgroup of cancer cells expressing PD-1, CD80, PD-L1 and PD-L2 only, and other unknown factors
Tumor	T2=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T2 subgroup of cancer cells
Tumor	T3a=PD1	mole	PD-1 expressed by Effector T cells that interact with T3 subgroup of cancer cells
Tumor	T4=PD1	mole	PD-1 expressed by Effector T cells that interact with T4 subgroup of cancer cells
Tumor	T5=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T5 subgroup of cancer cells
Tumor	T3b=CD80	mole	CD80 expressed by Effector T cells that interact with T3 subgroup of cancer cells

Compartment Location	Variable Name	Units	Variable Definition
Tumor	T7a=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T7 subgroup of cancer cells
Tumor	T10b=PD1	mole	PD-1 expressed by Effector T cells that interact with T10 subgroup of cancer cells
Tumor	T7b=PD1	mole	PD-1 expressed by Effector T cells that interact with T7 subgroup of cancer cells
Tumor	T6a=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T6 subgroup of cancer cells
Tumor	T6c=CD80	mole	CD80 expressed by Effector T cells that interact with T6 subgroup of cancer cells
Tumor	T6b=PD1	mole	PD-1 expressed by Effector T cells that interact with T6 subgroup of cancer cells
Tumor	T11a=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T11 subgroup of cancer cells
Tumor	T11b=PD1	mole	PD-1 expressed by Effector T cells that interact with T11 subgroup of cancer cells
Tumor	T10c=CD80	mole	CD80 expressed by Effector T cells that interact with T10 subgroup of cancer cells
Tumor	T12b=PD1	mole	PD-1 expressed by Effector T cells that interact with T12 subgroup of cancer cells
Tumor	T13a=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T13 subgroup of cancer cells
Tumor	T12a=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T12 subgroup of cancer cells
Tumor	T14c=CD80	mole	CD80 expressed by Effector T cells that interact with T14 subgroup of cancer cells
Tumor	T15b=PD1	mole	PD-1 expressed by Effector T cells that interact with T15 subgroup of cancer cells
Tumor	T15a=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T15 subgroup of cancer cells
Tumor	T13b=PD1	mole	PD-1 expressed by Effector T cells that interact with T13 subgroup of cancer cells
Tumor	T14b=PD1	mole	PD-1 expressed by Effector T cells that interact with T14 subgroup of cancer cells
Tumor	T14a=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T14 subgroup of cancer cells
Tumor	T16b=PD1	mole	PD-1 expressed by Effector T cells that interact with T16 subgroup of cancer cells
Tumor	T16c=CD80	mole	CD80 expressed by Effector T cells that interact with T16 subgroup of cancer cells
Tumor	T16a=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T16 subgroup of cancer cells
Tumor	T8a=PD1	mole	PD-1 expressed by Effector T cells that interact with T8 subgroup of cancer cells
Tumor	T8b=CD80	mole	CD80 expressed by Effector T cells that interact with T8 subgroup of cancer cells
Tumor	T9=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T9 subgroup of cancer cells
Tumor	T10a=PDL1	mole	PD-L1 expressed by Effector T cells that interact with T10 subgroup of cancer cells
Tumor	C10a=PD1	mole	PD-1 expressed by the T10 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C9b=CD80	mole	CD80 expressed by the T9 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C9a=PD1	mole	PD-1 expressed by the T9 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C8b=PDL2	mole	PD-L2 expressed by the T8 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C16a=PD1	mole	PD-1 expressed by the T16 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C16c=PDL2	mole	PD-L2 expressed by the T16 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C16b=PDL1	mole	PD-L1 expressed by the T16 subtype of cancer cells that interact with Effector T cells in the tumor

Compartment Location	Variable Name	Units	Variable Definition
Tumor	C14a=PD1	mole	PD-1 expressed by the T14 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C14b=PDL1	mole	PD-L1 expressed by the T14 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C13b=PDL2	mole	PD-L2 expressed by the T13 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C15a=PD1	mole	PD-1 expressed by the T15 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C15b=PDL2	mole	PD-L2 expressed by the T15 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C14c=CD80	mole	CD80 expressed by the T14 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C12a=PDL2	mole	PD-L2 expressed by the T12 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C13a=PDL1	mole	PD-L1 expressed by the T13 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C12b=CD80	mole	CD80 expressed by the T12 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C10c=PDL2	mole	PD-L2 expressed by the T10 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C11b=CD80	mole	CD80 expressed by the T11 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C11a=PDL1	mole	PD-L1 expressed by the T11 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C6b=PDL1	mole	PD-L1 expressed by the T6 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C7a=PD1	mole	PD-1 expressed by the T7 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C6a=PD1	mole	PD-1 expressed by the T6 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C8a=PDL1	mole	PD-L1 expressed by the T8 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C10b=PDL1	mole	PD-L1 expressed by the T10 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C7b=PDL2	mole	PD-L2 expressed by the T7 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C5=CD80	mole	CD80 expressed by the T5 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C4=PDL2	mole	PD-L2 expressed by the T4 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C3=PDL1	mole	PD-L1 expressed by the T3 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C2=PD1	mole	PD-1 expressed by the T2 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C{PD1}	cell	T2 subgroup of cancer cells expressing PD-1 only, and other unknown factors
Tumor	C{PDL1}	cell	T3 subgroup of cancer cells expressing PD-L1 only, and other unknown factors
Tumor	C{PDL2}	cell	T4 subgroup of cancer cells expressing PD-L2 only, and other unknown factors
Tumor	C{CD80}	cell	T5 subgroup of cancer cells expressing CD80 only, and other unknown factors
Tumor	C{PD1}{PDL1}	cell	T6 subgroup of cancer cells expressing PD-1 and PD-L1 only, and other unknown factors
Tumor	C{PD1}{PDL2}	cell	T7 subgroup of cancer cells expressing PD-1 and PD-L2 only, and other unknown factors
Tumor	C{PDL1}{PDL2}	cell	T8 subgroup of cancer cells expressing PD-L1 and PD-L2 only, and other unknown factors
Tumor	C{PD1}{CD80}	cell	T9 subgroup of cancer cells expressing PD-1 and CD80 only, and other unknown factors
Tumor	C{PD1}{PDL1}{PDL2}	cell	T10 subgroup of cancer cells expressing PD-1, PD-L1 and PD-L2 only, and other unknown factors
Tumor	C{PDL1}{CD80}	cell	T11 subgroup of cancer cells expressing PD-L1 and CD80 only, and other unknown factors

Compartment Location	Variable Name	Units	Variable Definition
Tumor	C{PDL2}{CD80}	cell	T12 subgroup of cancer cells expressing PD-L2 and CD80 only, and other unknown factors
Tumor	C{PDL1}{PDL2}{CD80}	cell	T13 subgroup of cancer cells expressing PD-L1, PDL-L2 and CD80 only, and other unknown factors
Tumor	C{PD1}{PDL1}{CD80}	cell	T14 subgroup of cancer cells expressing PD-1, PD-L1 and CD80 only, and other unknown factors
Tumor	C{PD1}{PDL2}{CD80}	cell	T15 subgroup of cancer cells expressing PD-1, PD-L2 and CD80 only, and other unknown factors
Tumor	C{PD1}{PDL1}{PDL2}{CD80}	cell	T16 subgroup of cancer cells expressing PD-1, PD-L1, PD-L2 and CD80 only, and other unknown factors
Tumor	C13c=CD80	mole	CD80 expressed by the T13 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C15c=CD80	mole	CD80 expressed by the T15 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	C16d=CD80	mole	CD80 expressed by the T16 subtype of cancer cells that interact with Effector T cells in the tumor
Tumor	T2=PDL1:PD1=C2	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the T2 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T3a=PD1:PDL1=C3	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T3 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T3b=CD80:PDL1=C3	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T3 subtype of cancer cells and CD80 expressed on Effector T cells
Tumor	T4=PD1:PDL2=C4	mole	Receptor-receptor interactions at the immunological synapse between PD-L2 expressed by the T4 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T5=PDL1:CD80=C5	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the T5 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T6a=PDL1:PD1=C6a	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the T6 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T6c=CD80:PDL1=C6b	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T6 subtype of cancer cells and CD80 expressed on Effector T cells
Tumor	T6b=PD1:PDL1=C6b	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T6 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T7a=PDL1:PD1=C7a	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the T7 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T7b=PD1:PDL2=C7b	mole	Receptor-receptor interactions at the immunological synapse between PD-L2 expressed by the T7 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T8a=PD1:PDL2=C8b	mole	Receptor-receptor interactions at the immunological synapse between PD-L2 expressed by the T8 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T8a=PD1:PDL1=C8a	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T8 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T8b=CD80:PDL1=C8a	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T8 subtype of cancer cells and CD80 expressed on Effector T cells
Tumor	T9=PDL1-PD1=C9a	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the T9 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T9=PDL1-CD80=C9b	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the T9 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T10a=PDL1:PD1=C10a	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the T10 subtype of cancer cells and PD-L1 expressed on Effector T cells

Compartment Location	Variable Name	Units	Variable Definition
Tumor	T10b=PD1:PDL1=C10b	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T10 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T10b=PD1:PDL2=C10c	mole	Receptor-receptor interactions at the immunological synapse between PD-L2 expressed by the T10 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T10c=CD80:PDL1=C10b	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T10 subtype of cancer cells and CD80 expressed on Effector T cells
Tumor	T11b=PD1:PDL1=C11a	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T11 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T11a=PDL1:CD80=C11b	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the T11 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T12b=PD1:PDL2=C12a	mole	Receptor-receptor interactions at the immunological synapse between PD-L2 expressed by the T12 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T12a=PDL1:CD80=C12b	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the T12 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T13b=PD1:PDL1=C13a	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T13 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T13a=PDL1:CD80=C13c	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the T13 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T13b=PD1:PDL2=C13b	mole	Receptor-receptor interactions at the immunological synapse between PD-L2 expressed by the T13 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T14a=PDL1:PD1=C14a	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the T14 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T14a=PDL1:CD80=C14c	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the T14 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T14b=PD1:PDL1=C14b	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T14 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T14c=CD80:PDL1=C14b	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the T14 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T15a=PDL1:CD80=C15c	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the T15 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T15a=PDL1:PD1=C15a	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the T15 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T15b=PD1:PDL2=C15b	mole	Receptor-receptor interactions at the immunological synapse between PD-L2 expressed by the T15 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T16b=PD1:PDL2=C16c	mole	Receptor-receptor interactions at the immunological synapse between PD-L2 expressed by the T15 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T16b=PD1:PDL1=C16b	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T15 subtype of cancer cells and PD-1 expressed on Effector T cells
Tumor	T16c=CD80:PDL1=C16b	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the T15 subtype of cancer cells and CD80 expressed on Effector T cells
Tumor	T16a=PDL1:PD1=C16a	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the T15 subtype of cancer cells and PD-L1 expressed on Effector T cells
Tumor	T16a=PDL1:CD80=C16d	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the T15 subtype of cancer cells and PD-L1 expressed on Effector T cells

Compartment Location	Variable Name	Units	Variable Definition
Tumor	T2=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T2 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T3a=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T3 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C3=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by the T3 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T5=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T5 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T6a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T6 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C6b=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by the T6 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T10a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T10 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C10b=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by the T10 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C11a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by the T11 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T11a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T11 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T12a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T12 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T7a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T7 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C8a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by the T8 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T9=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T9 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood

Compartment Location	Variable Name	Units	Variable Definition
Tumor	C13a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by the T13 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T13a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T13 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T14a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T14 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C14b=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by the T14 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T15a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T15 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T16a=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T16 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C16b=PDL1:aPDL1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by the T16 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C2=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by the T2 subtype of cancer cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T4=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T4 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C6a=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by the T6 subtype of cancer cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T6b=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T6 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C7a=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by the T7 subtype of cancer cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T7b=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T7 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T8a=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T8 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood

Compartment Location	Variable Name	Units	Variable Definition
Tumor	C9a=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by the T9 subtype of cancer cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C10a=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by the T10 subtype of cancer cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T10b=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T10 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T11b=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T11 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T13b=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T13 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C14a=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by the T14 subtype of cancer cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T14b=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T14 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C15a=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by the T15 subtype of cancer cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T15b=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T15 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	C16a=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by the T16 subtype of cancer cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T16b=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T16 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	T12b=PD1:aPD1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T12 subtype of cancer cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	TregT	cell	Total number of T Regulatory cells that able to engage with Effector T cells and mAPCs in the tumor
Tumor	TregT_Teff	cell	T Regulatory cells in the tumor that have engaged in interacting with Effector T cells
Tumor	MDSC_T	cell	Total number of MDSCs that able to engage with Effector T cells in the tumor
Tumor	MDSCsT_Teff	cell	MDSCs in the tumor that have engaged in interacting with Effector T cells
Tumor	MDSCsT_EngTeff	cell	MDSCs in the tumor that have engaged in interacting with Effector T cells that are accounting for the expression of PD-1 and PD-L1

Compartment Location	Variable Name	Units	Variable Definition
Tumor	TregT_EngAPC	cell	T Regulatory cells in the tumor that have engaged in interacting with mAPCs that are accounting for the expression of CTLA-4
Tumor	mAPCT_EngTregT	cell	mAPCs in the tumor that have engaged in interacting with T Regulatory cells that are accounting for the expression of CD80 and CD86
Tumor	Teff_EngTregT	cell	Effector T cells in the tumor that have engaged in interacting with T Regulatory cells that are accounting for the expression of CD80, PD-1 and PD-L1
Tumor	PD1_TeffT	mole	PD-1 expressed by Effector T cells that interact with T Regulatory cells in the tumor
Tumor	PDL1_TeffT	mole	PD-L1 expressed by Effector T cells that interact with T Regulatory cells in the tumor
Tumor	CD80_TeffT	mole	CD80 expressed by Effector T cells that interact with T Regulatory cells in the tumor
Tumor	CD80_mAPCT	mole	CD80 expressed by mAPCs that interact with T Regulatory cells in the tumor
Tumor	PDL1_MDSCsT	mole	PD-L1 expressed by MDSCs that interact with Effector T cells in the tumor
Tumor	PD1_MDSCsT	mole	PD-1 expressed by MDSCs that interact with Effector T cells in the tumor
Tumor	CD86_mAPCT	mole	CD86 expressed by mAPCs that interact with T Regulatory cells in the tumor
Tumor	PD1_TregT	mole	PD-1 expressed by T Regulatory cells that interact with Effector T cells in the tumor
Tumor	PDL1_TregT	mole	PD-L1 expressed by T Regulatory cells that interact with Effector T cells in the tumor
Tumor	CTLA4_TregT	mole	CTLA-4 expressed by T Regulatory cells that interact with mAPCs in the tumor
Tumor	CTLA4:CD80_TrAT	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by mAPCs and CTLA-4 expressed on T Regulatory cells in the tumor
Tumor	CTLA4:CD86_TrAT	mole	Receptor-receptor interactions at the immunological synapse between CD86 expressed by mAPCs and CTLA-4 expressed on T Regulatory cells in the tumor
Tumor	CTLA4_CTLA4-Trt	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between CTLA-4 expressed by T Regulatory cells that interact with the mAPCs and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	PDL1:PD1_TrTeff	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the Effector T cells and PD-L1 expressed on T Regulatory cells in the tumor
Tumor	PDL1:CD80_TrTeff	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the Effector T cells and PD-L1 expressed on T Regulatory cells in the tumor
Tumor	PD1:PDL1_TrTeff	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the Effector T cells and PD-1 expressed on T Regulatory cells in the tumor
Tumor	PDL1:CD80_MDSCT	mole	Receptor-receptor interactions at the immunological synapse between CD80 expressed by the Effector T cells and PD-L1 expressed on MDSCs in the tumor
Tumor	PDL1:PD1_MDSCT	mole	Receptor-receptor interactions at the immunological synapse between PD-1 expressed by the Effector T cells and PD-L1 expressed on MDSCs cells in the tumor
Tumor	PD1:PDL1_MDSCT	mole	Receptor-receptor interactions at the immunological synapse between PD-L1 expressed by the Effector T cells and PD-1 expressed on MDSCs in the tumor
Tumor	PD1:aPD1_Teff	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the T Regulatory cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	PDL1:aPDL1_Teff	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the T Regulatory cells

Compartment Location	Variable Name	Units	Variable Definition
			and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	PDL1:aPDL1_Treg	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by T Regulatory cells that interact with Effector T cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	PD1:aPD1_Treg	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by T Regulatory cells that interact with Effector T cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	PD1:aPD1_MDSCs	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by MDSCs that interact with Effector T cells and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	PDL1:aPDL1_MDSCs	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by MDSCs that interact with Effector T cells and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	TregT_EngTeff	cell	T Regulatory cells in the tumor that have engaged in interacting with Effector T cells that are accounting for the expression of PD-1 and PD-L1
Tumor	Teff_EngMDSC	cell	Effector T cells in the tumor that have engaged in interacting with MDSCs that are accounting for the expression of CD80, PD-1 and PD-L1
Tumor	CD80_TeffT1	mole	CD80 expressed by Effector T cells that interact with MDSCs in the tumor
Tumor	PDL1_TeffT1	mole	PD-L1 expressed by Effector T cells that interact with MDSCs in the tumor
Tumor	PD1_TeffT1	mole	PD-1 expressed by Effector T cells that interact with MDSCs in the tumor
Tumor	PD1:aPD1_Teff1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-1 expressed by Effector T cells that interact with the MDSCs and Anti-PD-1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	PDL1:aPDL1_Teff1	mole	Heterogeneous receptor-antibody interactions at the immunological synapse between PD-L1 expressed by Effector T cells that interact with the MDSCs and Anti-PD-L1 mAb delivered to the tumor by way of IV injection into the blood
Tumor	Effector_TT_TregT	cell	Total number of Effector T cells that able to engage with T Regulatory cells in the tumor
Tumor	Effector_TT_MDSCs	cell	Total number of Effector T cells that able to engage with MDSCs in the tumor
Tumor	Effector_TT_Res	cell	Effector T cells that have become Resident Effector Memory cells after the tumor has died
Tumor	Effector_TT_Count	cell	The total number of Effector and Resident Effector Memory cells
Tumor	Effector_TT_per_Treg	cell/ cell	The number of Effector T cells per T Regulatory cells in the tumor
Tumor	Effector_TT_per_mL	cell/ mm^3	The volumetric density of Effector T cells per milliliter in the tumor

Table S4 – Definition of species in the model (End)

Table S5 – Model Parameters (Start)

Variable	Value	Units	Source	Description
%_NT_LN	55	dimensionless	[1, 2]	Percent Naïve T cells of total T cells in each lymph node (taken as all CD3+ cells)

Variable	Value	Units	Source	Description
%_Tr_LN	5-35	dimensionless	[1, 3-5]	Percent Regulatory T cells of total T cells in each lymph node
%{CD80}{PD1}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing CD80 and PD-1 checkpoint receptors only
%{CD80}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing the CD80 checkpoint receptor only
%{Other}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing only unknown factors, other than CD80, PD-1, PD-L1 and PD-L2
%{PD1}{80}{L1}{L2}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing CD80, PD-1, PD-L1 and PD-L2 checkpoint receptors only
%{PD1}{80}{L1}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing CD80, PD-1, and PD-L1 checkpoint receptors only
%{PD1}{80}{PDL2}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing CD80, PD-1, and PD-L2 checkpoint receptors only
%{PD1}{L1}{L2}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing PD-1, PD-L1 and PD-L2 checkpoint receptors only
%{PD1}{L1}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing PD-1, and PD-L1 checkpoint receptors only
%{PD1}{L2}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing PD-1, and PD-L2 checkpoint receptors only
%{PD1}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing the PD-1 checkpoint receptor only
%{PDL1}{80}{L2}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing CD80, PD-L1, and PD-L1 checkpoint receptors only
%{PDL1}{80}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing CD80 and PD-L1 checkpoint receptors only
%{PDL1}{PDL2}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing PD-L1, and PD-L2 checkpoint receptors only
%{PDL1}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing the PD-L1 checkpoint receptor only
%{PDL2}{80}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing CD80 and PD-L2 checkpoint receptors only
%{PDL2}C	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of cancer cells expressing the PD-L2 checkpoint receptor only
%CD80_Exp_Cancer	5 (mean)	dimensionless	[6-8]	Percent of cancer cells of total cancer cells that are CD80 positive that interact with the Effector T cells in the tumor compartment
%CD80_receptor_level_PNT	10	dimensionless	Assumed low	Percent of maximum CD80 receptor expression on Primed Naive T cells in the lymph nodes
%PD1_Exp_Cancer	10 (mean)	dimensionless	[9]	Percent of cancer cells of total cancer cells that are PD-1 positive that interact with the Effector T cells in the tumor compartment
%PD1_receptor_level_PNT	25	dimensionless	[10]	Percent of maximum PD-1 receptor expression on Primed Naive T cells in the lymph nodes
%PDL1_Exp_Cancer	60	dimensionless	[11]	Percent of cancer cells of total cancer cells that are PD-L1 positive that interact with the Effector T cells in the tumor compartment
%PDL1_receptor_level_PNT	25	dimensionless	Assumed low	Percent of maximum PD-L1 receptor expression on Primed Naive T cells in the lymph nodes
%PDL2_Exp_Cancer	20 (mean)	dimensionless	[12]	Percent of cancer cells of total cancer cells that are PD-L2 positive that interact with the Effector T cells in the tumor compartment

Variable	Value	Units	Source	Description
%Sig_Inhibit_Cancer	0.65	dimensionless	Set to fit response	The percent effect that total immune checkpoints on the cancer cells have on inactivating the Effector T cells in the tumor
%T_Tregs_per_Cancer	0-0.25	dimensionless	Assumed	Defines the percentage of Regulatory T cells in the tumor compartment as a percent of total tumor cells
Adhesion_D_Lung_Liv_spln	1E9	cell/ml	[13]	Effector T cell adhesion density in Lung, Liver, or Spleen vasculature
Adhesion_Density_Tmr	5E8	cell/ml	[13]	Effector T cell adhesion density in Tumor vasculature
AntSpread	x = 1 to 5 (Where it is used as 10^x)	dimensionless	Estimated during fitting to anti-PD-1 data and varied across range	Sets the number of TAA/TSA released per cancer cell upon natural death and decay or following cytotoxic killing. The value is used to set a multiple of cancer cells in the formation of debris for APC maturation.
Antigen_Intensity	Assigned from 0.8-1.0 for melanoma	dimensionless	Upper range of cancer types [14]	The strength of the tumor antigens that are involved in priming of the T cells in the lymph nodes
AR_Liver	1.5	1/minute	[13]	Effector T cell arrest rate in Liver vasculature
AR_Lungs	0.0027	1/minute	[13]	Effector T cell arrest rate in Lungs vasculature
AR_Spleen	0.0036	1/minute	[13]	Effector T cell arrest rate in Spleen vasculature
AR_Tmr	1	1/minute	[13]	Effector T cell arrest rate in Tumor vasculature
Avogadro's_Num	6.022E+23	molecules /mole	Exact value	Avogadro's number – converts receptor numbers to moles
BodyWeight (kg)	80	kg	[15]	Body weight of an average human being
Cancer_Cell_Diam_um	12	µm	[16, 17]	Diameter of each cancer cell when considering each cell's volume to be represented by a sphere
Cancer_Cell_Vol_mm3	9.0478E-7	mm^3	Calculated; see algebraic equations below	Volume of each cancer cell when the diameter is that of a sphere
Cancer_Diam_mm	Calculated	mm	Calculated; see algebraic equations below	Diameter of the entire tumor – considering all cells and a void fraction
Cancer_mm_Start_Therapy	Assigned	mm	Assigned	Diameter of the tumor when to start the therapeutic regimen
Cancer_per_T_Cell_Int	Set to 1	cell/cell	Variable	Number of cancer cells that interact with each Effector T cell in the model
Cancer_per_T_Cell_max	4	cell/cell	[18, 19]	Maximum number of cancer cells that can interact with each Effector T cell in the model; assuming that each Effector T cell uses 25% of its surface area to interact with each cancer cell (can be up to 50%) [19].
Cancer_Vol_cm3	Calculated	cm^3	Calculated; see algebraic equations below	Volume of the entire tumor – considering all cells and a void fraction
CancerTEng	2.079	1/hour	[20]	Rate constant defining the half-life of engagement between cancer cells and Effector T cells in the tumor (at a migration rate of 5-10 µm/min, T cells encounter and engage with a cancer cell approximately every 15 minutes to 1 hour).
CancerTInt	0.03465	1/minute	[20]	Rate constant defining the half-life of dissociation between Effector T cells and cancer cells (thus, determining total time of interaction)
CD28_POS-Sig_NT	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of total CD28 receptors on Naïve T cells that are involved in interacting with the CD80 and CD86 receptors on mAPCs during priming in the lymph nodes
CD28_POS-to-Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of total CD28 receptors on Primed Naïve T cells that are involved in interacting with the CD80 and CD86 receptors on mAPCs during priming in the lymph nodes
CD28_receptors-per-Tcell	15000	molecules/cell	[21]	Number of CD28 receptors expressed on each T cell during priming
CD80_PNT_NEG-to-Max	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of total CD80 receptors on Primed Naïve T cells that are involved in interacting with the PD-L1 receptors on mAPCs during priming in the lymph nodes

Variable	Value	Units	Source	Description
CD80_receptors_per_C_Cl	30000	molecules/cell	Assumed same as T cells	Number of CD80 receptors expressed on each cancer cell (assumed same as for T cells).
CD80_receptors-per-mAPC	130000	molecules/cell	[22]	Maximum number of CD80 receptors expressed on each mAPC
CD80_receptors-per-Tcell	30000	molecules/cell	[23, 24]	Number of CD80 receptors expressed on each T cell (by acquisition of CD80 from mAPCs over two rounds of priming) [24].
CD80Sig_Tr-PNT	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of total CD80 receptors on Primed Naïve T cells that are involved in interacting with the PD-L1 receptors on Regulatory T cells during priming in the lymph nodes
CD86_receptors-per-mAPC	208000	molecules/cell	[22]	Maximum number of CD86 receptors expressed on each mAPC
Chemokine	100	dimensionless	Estimated during anti-PD-1 therapy fitting; varied in sensitivity analysis	The chemokine factor to promote extravasation of effector T cells into the tumor
Cl_CTLA4	0.003736141	1/hour	[15]	Clearance rate of Anti-CTLA-4 mAb from the central compartment
Cl_PD1	0.014570722	liter/hour	[25]	Clearance rate of Anti-PD-1 mAb from the central compartment
Cl_PDL1	0.016530129	liter/hour	[26, 27]	Clearance rate of Anti-PD-L1 mAb from the central compartment
Copies-per-T_Cell_Clone	10-130	dimensionless	[28-30]	Number of copies of each Naïve T cell clone in the lymph nodes.
CTLA4_change_schedule	Based on regimen	day	[15] Based on regimen	Time in simulation to switch schedule in regimen for Anti-CTLA-4 therapy
CTLA4_counter_off	Based on regimen	day	[15] Based on regimen	Time in simulation to stop Anti-CTLA-4 dose
CTLA4_counter_on	Based on regimen	day	[15] Based on regimen	Time in simulation to start Anti-CTLA-4 dose
CTLA4_DoseSet	Based on regimen	mg/kg	Set dose	Dose of anti-CTLA-4 therapy
CTLA4_NEG-to-Total	Calculated; see algebraic equations below	dimensionless	Calculated with RO; see algebraic equations below	Fraction of total CTLA-4 receptors on Primed Naïve T cells that are involved in interacting with the CD80 and CD86 receptors on mAPCs during priming in the lymph nodes
CTLA4_receptors-Int-PNT	Calculated; see algebraic equations below	molecules/cell	[31]	Maximum number of CTLA-4 receptors that can be recruited to the immunological synapse by Primed Naive T cells when interacting with mAPCs
CTLA4_receptors-nInt-PNT	Calculated; see algebraic equations below	molecules/cell	[32]	Number of CTLA-4 receptors that are expressed on the surface of non-interacting Primed Naive T cells
CTLA4_receptors-Tr	Calculated; see algebraic equations below	molecules/cell	Assumed dependent on CD28/CTLA4 ratio	Maximum number of CTLA-4 receptors on T-regulatory cells
CTLA4mAb	Based on regimen	mg/kg	[15] Based on regimen	Dose of Anti-CTLA-4 being delivered
CTLA4mAb_Dose	Based on regimen	mg/kg	[15] Based on regimen	Dose of Anti-CTLA-4 to deliver based on the current schedule
CTLA4mAb_New_Dose	Based on regimen	mg/kg	[15] Based on regimen	Dose of Anti-CTLA-4 to be delivered when schedule is changed
CTLA4Sig_TrLN	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CTLA-4 receptors expressed on T Regulatory cells that are occupied by Anti-CTLA-4 mAb in the lymph nodes
CTLA4Sig_TrLN-mAPC	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CTLA-4 receptors expressed on T Regulatory cells that are interacting with CD80 and CD86 on the mAPCs in the lymph nodes
CTLA4-to-CD28_Ratio_Int	Calculated	dimensionless	[31]	Ratio of CTLA-4 to CD28 expression on interacting Primed Naive T cells
CTLA4-to-CD28_Ratio_nInt	0.035	dimensionless	[32]	Ratio of CTLA-4 to CD28 expression on non-interacting Primed Naive T cells

Variable	Value	Units	Source	Description
CTLA4-to-CD28_Ratio_Tr	0.5	dimensionless	[33]	CTLA-4 expression levels on T Regulatory cells relative to CD28 expression on Primed Naive T cells
day	1	day	Unit assignment	Assigns value of 1 day to the term day in the model
Debris_Decay	2	1/day	[34, 35]	Half-life of tumor debris and non-phagocytosed tumor antigens
Debris_Transport	3	1/day	[34]	Transport rate of tumor debris by the lymphatics to the lymph nodes (based on "permeation of tumor debris and the blood")
Delta_Liver	1	dimensionless	[13]	Fraction of Effector T cells in extravascular space of Liver that can recirculate
Delta_LN	0.018	dimensionless	[13]	Fraction of Effector T cells in extravascular space of Lymph Nodes that can recirculate
Delta_Lungs	1	dimensionless	[13]	Fraction of Effector T cells in extravascular space of Lungs that can recirculate
Delta_Spleen	1	dimensionless	[13]	Fraction of Effector T cells in extravascular space of Spleen that can recirculate
Dose_sched_CTLA4	Based on regimen	day	[15] Based on regimen	Time between sequential doses of Anti-CTLA-4 in a regimen
Dose_sched_PD1	Based on regimen	day	[25] Based on regimen	Time between sequential doses of Anti-PD-1 in a regimen
Dose_sched_PDL1	Based on regimen	day	[26, 27] Based on regimen	Time between sequential doses of Anti-PD-L1 in a regimen
Durvalumab_MW	146300000	mg/mole	[36-39]	Molecular weight of Anti-PD-L1 antibody, Durvalumab
E_Lungs	0.0019	1/minute	[13]	Effector T cell depletion rate
EffT_InOutLN	0.0693	1/hour	[40]	Rate constant defining the half-life of Naïve T cell migration into and out of the lymph nodes
EffT_Migrate	0.9	1/day	[34, 41]	Rate constant defining the half-life of Effector T cell migration from the lymph nodes to the blood
EffT_Res_Conversion	0.1155	1/minute	[42, 43]	Rate constant defining the half-life by which Effector T cells in the tumor compartment undergo apoptosis (90%) and become resident Effector T cells (10%) following the death of the tumor [42].
EffT_Turnover	0.02	1/day	[34, 35, 44, 45]	Rate constant defining the half-life of Effector T cells
Endo_CTLA4	0.3465	1/minute	[46, 47]	Rate constant defining the half-life of (trans)endocytosis of CTLA-4 on T cells
EndTherapy	1	dimensionless	Assigned when to stop therapy	Parameter used to define when to stop therapy after tumor becomes smaller than a certain size
Exp_All_mAPCLN	69.3	1/second	Assumed to be very fast	Rate constant defining the half-life of expression of receptors on mAPCs that are part of the mAPC count
Exp_CD28/80/86/PD1/L1/L2	2.772	1/minute	[31, 48]	Rate constant defining the half-life of expression of CD28, CD80, CD86, PD-1, PD-L1 and PD-L2 to the immunological synapse by all interacting T cells, mAPCs and cancer cells
Exp_CTLA4	0.0462	1/minute	[49]	Rate constant defining the half-life of expression of CTLA-4 to the immunological synapse by all interacting T cells
f_LN_CTLA4	0.2	dimensionless	[50]	Assume that due to high cell numbers and packing, that the LN only allows for 3% interstitial space for antibody transport.
f_LN_PD1	0.1	dimensionless	[50]	Assume that due to high cell numbers and packing, that the LN only allows for 3% interstitial space for antibody transport.
Frac_CD80_Exp_Cancer	Set value	dimensionless	Varied parameter	Fraction form of %CD80_Exp_Cancer
Frac_PD1_Exp_Cancer	Set value	dimensionless	Varied parameter	Fraction form of %PD1_Exp_Cancer
Frac_PDL1_Exp_Cancer	Set value	dimensionless	Varied parameter	Fraction form of %PDL1_Exp_Cancer
Frac_PDL2_Exp_Cancer	Set value	dimensionless	Varied parameter	Fraction form of %PDL2_Exp_Cancer
Frac_Vv_Tmr	0.07	dimensionless	[13]	Fraction of vascular of total Tumor
gamma_Sig	3	dimensionless	Set for RO-based dose response potency	Gamma for total CTLA4 signaling in Tumor
gamma_Sig1	7	dimensionless	Set for RO-based dose response potency	Gamma for total CD80/PD1/PDL1 total signaling in Tumor

Variable	Value	Units	Source	Description
gamma_SigTr	3	dimensionless	Set for RO-based dose response potency	Gamma for total CD80/PD1/PDL1 total signaling in Lymph Node
gamma_TC_Assoc	0.9	dimensionless	[51]	Potency of Effector engagement/killing between Effector and target cells
Ipilimumab_MW	148634914	mg/mole	[52, 53]	Molecular weight of Anti-CTLA-4 antibody, Ipilimumab
IS_Scaling	2	dimensionless	[54, 55]	Sets the immunological synapse diameter to 30nm, from 15nm.
ISF	15.9	liter	[56]	Volume of interstitial fluid (ISF) is tissues
J_Liver	0.0029	1/minute	[13]	Effector T cell transmigration rate in Liver
J_Lungs	0.0029	1/minute	[13]	Effector T cell transmigration rate in Lungs
J_Spleen	0.0029	1/minute	[13]	Effector T cell transmigration rate in Spleen
J_Tmr	0.0029	1/minute	[13]	Effector T cell transmigration rate in Tumor
k__DoseAdmin_AntiCTLA4	0.6666666	1/hour	[15]	Zero-order rate constant for the delivery of Anti-CTLA-4 into the central compartment for a designated dose
k__DoseAdmin_AntiPDL1	1	1/hour	[26, 27]	Zero-order rate constant for the delivery of Anti-PD-L1 into the central compartment for a designated dose
k_DoseAdmin_AntiPD1	1	1/hour	[25]	Zero-order rate constant for the delivery of Anti-PD-1 into the central compartment for a designated dose
kf_APC_turnover	0.462	1/day	[57]	Half-life of mAPC turnover in the lymph nodes
kf_CanDecay	0.001	1/day	[34, 35]	Rate constant defining the half-life decay of cancer cells by natural death
kf_Liver	7.6E-9	ml/cell/minute	[13]	Attachment rate for free Effector T cells in Liver vasculature
kf_Lungs	0.0000031	ml/cell/minute	[13]	Attachment rate for free Effector T cells in Lung vasculature
kf_Monocytes_intoT	0.0231	1/minute	[58]	Rate constant defining the half-life of the appearance of monocytes in the tumor following the appearance of tumor antigens
kf_no_prolif	99.72	1/day	Estimated in proportion to cells dividing 3 times a day for about 1 week as baseline	Rate constant defining the half-life for the fraction of Primed Naive T cells that will not successfully undergo the second phase of priming, and will therefore be considered anergic
kf_Phase2P	0.1155	1/hour	[59-61]	Rate constant defining the approximate half-life of the entire second phase of priming in the lymph nodes, considering that the Primed Naïve T cells are\in the deep T-cell areas in the lymph node. This, along with the second priming phase, accounts for T cells starting to proliferate 1.5-2 days following the encounter of antigens on mAPCs [61].
kf_Prolif_end	15000	1/day	[19, 60, 62]	Rate constant defining the half-life for conversion of proliferating Naive T cells into Effector T cells in the lymph nodes. The T cells were optimized to account for 3 divisions per day over 5 days.
kf_RestingMacrophage	0.01	1/day	[34, 41]	Rate constant defining the half-life for turnover of resting macrophages
kf_Spleen	0.0000081	ml/cell/minute	[13]	Attachment rate for free Effector T cells in Spleen vasculature
kf_Tmr	6.9E-9	ml/cell/minute	[13]	Attachment rate for free Effector T cells in Tumor vasculature
kf_TRecover	0.1386	1/minute	Estimated	Rate constant defining the half-life of Effector T cell recovery following their interaction with cancer cells in the tumor
kg	1	kilogram	Unit assignment	Assigns value of 1 kilogram to the term kg in the model
Km	0.344	µg/ml	[63]	EC50 Durvalumab saturation for ADA
koff_CD28_CD80	1.6	1/second	[64]	Dissociation rate constant for the interaction of CD28 with CD80
koff_CD28_CD86	28	1/second	[64]	Dissociation rate constant for the interaction of CD28 with CD86
koff_CTLA4_CD80	0.43	1/second	[64]	Dissociation rate constant for the interaction of CTLA-4 with CD80

Variable	Value	Units	Source	Description
koff_CTLA4_CD86	5.1	1/second	[64]	Dissociation rate constant for the interaction of CTLA-4 with CD86
koff_CTLA4mAb_CTLA4	0.3	1/second	[65]	Dissociation rate constant for the interaction of CTLA-4 with Anti-CTLA-4 (considering a Kd of 5.25+/-3.62 nM)
koff_PD1_PDL1	1.44	1/second	[66]	Dissociation rate constant for the interaction of PD-1 with PD-L1
koff_PD1_PDL2	0.55	1/second	[66]	Dissociation rate constant for the interaction of PD-1 with PD-L2
koff_PD1-PD1mAb	0.000768	1/second	[67]	Dissociation rate constant for the interaction of PD-1 with Anti-PD-1
koff_PDL1_CD80	5.94	1/second	[66]	Dissociation rate constant for the interaction of PD-L1 with CD80
koff_PDL1-PDL1mAb	0.000025	1/second	[26]	Dissociation rate constant for the interaction of PD-L1 with Anti-PD-L1 (considering a Kd of 100 pM)
kon_CD28_CD80	660000	1/(molarity*second)	[64]	Association rate constant for the interaction of CD28 with CD80
kon_CD28_CD86	1400000	1/(molarity*second)	[64]	Association rate constant for the interaction of CD28 with CD86
kon_CTLA4_CD80	2150000	1/(molarity*second)	[64]	Association rate constant for the interaction of CTLA-4 with CD80
kon_CTLA4_CD86	1960000	1/(molarity*second)	[64]	Association rate constant for the interaction of CTLA-4 with CD86
kon_CTLA4mAb_CTLA4	40900000	1/(molarity*second)	[65]	Association rate constant for the interaction of CTLA-4 with Anti-CTLA-4 (considering a Kd of 5.25+/-3.62 nM)
kon_PD1_PDL1	184000	1/(molarity*second)	[66]	Association rate constant for the interaction of PD-1 with PD-L1
kon_PD1_PDL2	250000	1/(molarity*second)	[66]	Association rate constant for the interaction of PD-1 with PD-L2
kon_PD1-PD1mAb	250000	1/(molarity*second)	[67]	Association rate constant for the interaction of PD-1 with Anti-PD-1
kon_PDL1_CD80	316000	1/(molarity*second)	[66]	Association rate constant for the interaction of PD-L1 with CD80
kon_PDL1-PDL1mAb	250000	1/(molarity*second)	[26]	Association rate constant for the interaction of PD-L1 with Anti-PD-L1 (considering a Kd of 100 pM)
KP_CTLA4	0.8	dimensionless	[56]	Available fraction of ISF for antibody distribution
KP_PD1	0.4	dimensionless	[56]	Available fraction of ISF for antibody distribution
KP_PDL1	0.4	dimensionless	[56]	Available fraction of ISF for antibody distribution
Kpa_LNB	9.87E-8	cm/second	[68]	Transport of antibody between Serum and Lymph Node
Kpa_TB	9.86E-8	cm/second	[68]	Transport of antibody between Serum and Tumor
kr_Lungs	2.3	1/second	[13]	Detachment rate of Effector T cells in the Lung vasculature
kr_Periph	3.3	1/second	[13]	Detachment rate of Effector T cells in the Peripheral vasculature
kr_Tmr	3.3	1/second	[13]	Detachment rate of Effector T cells in the Tumor vasculature
L	1	liter	Unit assignment	Assigns value of 1 liter to the term L in the model
LC_GI	0.3	ml/minute	[13]	Lymph flow rate of GI
LC_Liver	0.087	ml/minute	[13]	Lymph flow rate of Liver
LC_LN	0.77	ml/minute	[13]	Lymph flow rate of Lymph Node
LC_Lungs	0.043	ml/minute	[13]	Lymph flow rate of Lungs
LC_Periph	0.369	ml/minute	[13]	Lymph flow rate of Peripheral tissues
LC_Spleen	0.00087	ml/minute	[13]	Lymph flow rate of Spleen
LC_Tmr	0.03	ml/minute	[13]	Lymph flow rate of Tumor
mAPC_activation_level	1 (unless varied)	dimensionless	[13]	The fraction of CD80 and CD86 expression on the mAPCs from 0-1.
mAPC_Debis_T_Inact	0.05-0.95	dimensionless	Varied across range (5-95%) and estimated during fitting to anti-PD-1 data	The fraction of tumor debris that is considered to not be transported to the lymph nodes, and is removed from the system
mAPC_Migrate	0.2	1/day	[34, 41, 69]	Maximum migration rate of mAPCs
mAPC_per_T_cell	10	cell/cell	[19, 70-72]	Maximum number of mAPCs that can interact with each Naive and Primed Naive T cell. Note: all T cells were estimated to be the same size, and a surface area analysis was used for this estimation.

Variable	Value	Units	Source	Description
mAPC_per_Tr_cell	10	cell/cell	[19, 70-72]	Maximum number of mAPCs that can interact with each Effector T cell. Note: all T cells were estimated to be the same size, and a surface area analysis was used for this estimation.
mAPC50_per_T_cell	3	cell/cell	[40]	Number of mAPCs that should interact with each Naive and Primed Naive T cell to achieve a 50% priming rate
MDSCs_per_Treg	3	cell/cell	[73]	The ratio of MDSCs per T Regulatory cells in the tumor
mg	1	milligram	Unit assignment	Assigns value of 1 miligram to the term mg in the model
mole	1	mole	Unit assignment	Assigns value of 1 mole to the term mole in the model
New_sched_CTLA4	Based on regimen	day	[15] Based on regimen	New time between sequential doses of Anti-CTLA-4 in a regimen
New_sched_PD1	Based on regimen	day	[25] Based on regimen	New time between sequential doses of Anti-PD-1 in a regimen
New_sched_PDL1	Based on regimen	day	[26, 27] Based on regimen	New time between sequential doses of Anti-PD-L1 in a regimen
Nivolumab_MW	143600000	mg/mole	[36-38, 74]	Molecular weight of Anti-PD-1 antibody, Nivolumab
Num_TDLN_Considered	35	dimensionless	[75-78] Estimated	The number of total different lymph nodes (or lobules receiving a variety of antigens) in a region near the tumor (can be >9cm) that can produce an immune response against the tumor.
PD1_change_schedule	Based on regimen	day	[25] Based on regimen	Time in simulation to switch schedule in regimen for Anti-PD-1 therapy
PD1_counter_off	Based on regimen	day	[25] Based on regimen	Time in simulation to stop Anti-PD-1 dose
PD1_counter_on	Based on regimen	day	[25] Based on regimen	Time in simulation to start Anti-PD-1 dose
PD1_DoseSet	0-10	mg/kg	Based on regimen	Dose administered of anti-PD-1 therapy
PD1_PNT_NEG-to-Max	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of total PD-1 receptors on Primed Naïve T cells that are involved in interacting with the PD-L1 and PD-L2 receptors on mAPCs during priming in the lymph nodes
PD1_receptors_per_C_Cl	9288	molecules/cell	Assumed same as on T cells	Number of PD-1 receptors expressed on each cancer cell
PD1_receptors-per-mAPC	9288	molecules/cell	Assumed same as on T cells	Maximum number of PD-1 receptors expressed on each mAPC (maximum taken as max from mAPC levels)
PD1_receptors-per-Tcell	3096	molecules/cell	[66]	Maximum number of PD-1 receptors expressed on each T cell
PD1mAb	Based on regimen	milligram/kilogram	[25] Based on regimen	Dose of Anti-PD-1 being delivered
PD1mAb_Dose	Based on regimen	milligram/kilogram	[25] Based on regimen	Dose of Anti-PD-1 to deliver based on the current schedule
PD1mAb_New_Dose	Based on regimen	milligram/kilogram	[25] Based on regimen	Dose of Anti-PD-1 to be delivered when schedule is changed
PD1Sig_Tr-PNT	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of total PD-1 receptors on Primed Naïve T cells that are involved in interacting with the PD-L1 receptors on Regulatory T cells during priming in the lymph nodes
PDL1_change_schedule	Based on regimen	day	[26, 27] Based on regimen	Time in simulation to switch schedule in regimen for Anti-PD-L1 therapy
PDL1_counter_off	Based on regimen	day	[26, 27] Based on regimen	Time in simulation to stop Anti-PD-L1 dose
PDL1_counter_on	Based on regimen	day	[26, 27] Based on regimen	Time in simulation to start Anti-PD-L1 dose
PDL1_DoseSet	0-20	mg/kg	Based on regimen	Dose administered of anti-PD-L1 therapy
PDL1_PNT_NEG-to-Max	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of total PD-L1 receptors on Primed Naïve T cells that are involved in interacting with the PD-1 and CD80 receptors on mAPCs during priming in the lymph nodes
PDL1_receptors_per_C_Cl	80372	molecules/cell	[66]	Number of PD-L1 receptors expressed on each cancer cell (maximum taken as max from mAPC levels)
PDL1_receptors-per-mAPC	80372	molecules/cell	[66]	Maximum number of PD-L1 receptors expressed on each mAPC

Variable	Value	Units	Source	Description
PDL1_receptors-per-Tcell	9282	molecules/cell	[66]	Maximum number of PD-L1 receptors expressed on each T cell
PDL1mAb	Based on regimen	milligram/kilogram	[26, 27] Based on regimen	Dose of Anti-PD-L1 being delivered
PDL1mAb_Dose	Based on regimen	milligram/kilogram	[26, 27] Based on regimen	Dose of Anti-PD-L1 to deliver based on the current schedule
PDL1mAb_New_Dose	Based on regimen	milligram/kilogram	[26, 27] Based on regimen	Dose of Anti-PD-L1 to be delivered when schedule is changed
PDL1Sig_Tr-PNT	Calculated	dimensionless	Calculated; see algebraic equations below	Fraction of total PD-L1 receptors on Primed Naïve T cells that are involved in interacting with the PD-1 receptors on Regulatory T cells during priming in the lymph nodes
PDL2_receptors_per_C_Cl	5243	molecules/cell	[66]	Number of PD-L2 receptors expressed on each cancer cell (maximum taken as max from mAPC levels)
PDL2_receptors-per-mAPC	5243	molecules/cell	[66]	Maximum number of PD-L2 receptors expressed on each mAPC
Phago_Debris	1E-7	1/(mole*day)	[34, 41]	Tumor antigen uptake rate by APCs
Precursor_Frequen_NT	Calculated	dimensionless	[72, 79]	Calculates the ratio of available Naive T cells for priming phase 1 to total T cells in the lymph nodes
Precursor_Frequen_PNT	Calculated	dimensionless	[72, 79]	Calculates the ratio of available Primed Naive T cells for priming phase 2 to total T cells in the lymph nodes
PrimeNT_rate	0.05775	1/hour	[59-61]	Rate constant defining the approximate half-life of the entire first phase of priming in the lymph nodes, including the priming of all of the superficial Naïve T cells and those in the deep T-cell areas in the lymph node. This, along with the second priming phase, accounts for T cells starting to proliferate 1.5-2 days following the encounter of antigens on mAPCs [61].
PrimeNT1_rate	2.772	1/hour	[59, 60, 80]	Rate constant defining the approximate half-life of each interaction between Naive T cells and mAPCs during the first phase of priming in the lymph nodes, including the formation time of mature synapses between the Naïve T cells and the mAPCs.
PrimeTLN2_rate	1.386	1/hour	[59, 60]	Rate constant defining the approximate half-life of each interaction between Primed Naive T cells and mAPCs during the second phase of priming in the lymph nodes, which was dominated by stable T-cell-mAPC interactions.
Prob_NT-mAPC_Interact	Calculated	dimensionless	[72]	Calculates the probability in a deterministic manner that at least one successful priming interaction will occur between Naive T cells and mAPCs during the first phase of priming
Prob_PNT-mAPC_Interact	Calculated	dimensionless	[72]	Calculates the probability in a deterministic manner that at least one successful priming interaction will occur between Primed Naive T cells and mAPCs during the second phase of priming
Prolif_Fract	718.30381081261	1/hour	[19, 60, 62]	Proliferation threshold for fully primed and activated T cells in the lymph nodes that are undergoing proliferation. The T cells were optimized to account for 3 divisions per day over 5 days.
Prolif_Thresh	93.322881497449 91	1/hour	[19, 60, 62]	Proliferation level for fully primed and activated T cells in the lymph nodes that are undergoing proliferation. The T cells were optimized to account for 3 divisions per day over 5 days.
Q_L	8.000498419	L/day	[56]	Lymph flow rate for antibody transport
QC_GI	468	ml/minute	[13]	Blood flow rate in GI
QC_Liver	800	ml/minute	[13]	Blood flow rate in Liver
QC_LN	138	ml/minute	[13]	Blood flow rate in Lymph Node
QC_Lungs	3000	ml/minute	[13]	Blood flow rate in Lungs
QC_Periph	1521	ml/minute	[13]	Blood flow rate in Periphery
QC_Spleen	138	ml/minute	[13]	Blood flow rate in Spleen
QC_Tmr	0.564	ml/minute	[13]	Blood flow rate in Tumor

Variable	Value	Units	Source	Description
Rate_Tumor_Growth	64/144 day doubling: see description	1/day	[81]	Proliferation rate of cancer cells that defines the volumetric doubling time of the tumor. 64 day metastatic doubling: 0.010955675075414 144 day non-metastatic doubling: 0.004913635262592
s_Assoc	5.27	Dimensionless	[51]	Effector:Target cell association/killing EC50
S_LNB	166	cm^2/cm^3	[68]	Surface are of vasculature per volume Lymph Node for antibody transport
S_TB	108	cm^2/cm^3	[68]	Surface are of vasculature per volume Tumor for antibody transport
Sig_MDSCTeff = Other	0.15	dimensionless	Assumed	Fraction of inhibitory effect that other factors expressed by MDSCs have on the Effector T cells in the tumor
Sig_MDSCTeff=CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CD80 receptors expressed on Effector T cells that are interacting with PD-L1 on the MDSCs in the lymph nodes
Sig_MDSCTeff=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors expressed on Effector T cells that are interacting with PD-L1 on the MDSCs in the lymph nodes
Sig_MDSCTeff=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors expressed on Effector T cells that are interacting with PD-1 on the MDSCs in the lymph nodes
Sig_MDSCTeff=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total inhibitory fraction that MDSCs have on the Effector T cells in the tumor following their interaction
Sig_NT=CD28	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Positive CD28 co-receptor fraction signaling on Naive T cells by CD80 and CD86 on mAPC in the lymph nodes following their interaction
Sig_PNT=CTLA4/PD1/L1/CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total inhibitory fraction that mAPCs have on the Effector T cells during priming following their interaction
Sig_T=Other	0.15	dimensionless	Calculated with RO; see algebraic equations below	Fraction of inhibitory effect that other factors expressed by all cancer cells have on the Effector T cells in the tumor
Sig_T1=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing only other factors have on the Effector T cells in the tumor
Sig_T10=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-1, PD-L1, PD-L2 and other factors have on the Effector T cells in the tumor
Sig_T10a=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T10 subset of cancer cells in the tumor
Sig_T10b=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T10 subset of cancer cells in the tumor
Sig_T10c=CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T10 subset of cancer cells in the tumor
Sig_T11=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-L1, CD80 and other factors have on the Effector T cells in the tumor
Sig_T11a=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T11 subset of cancer cells in the tumor
Sig_T11b=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T11 subset of cancer cells in the tumor
Sig_T12=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-L2, CD80 and other factors have on the Effector T cells in the tumor
Sig_T12a=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T12 subset of cancer cells in the tumor
Sig_T12b=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T12 subset of cancer cells in the tumor

Variable	Value	Units	Source	Description
Sig_T13=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-L1, PD-L2, CD80 and other factors have on the Effector T cells in the tumor
Sig_T13a=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T13 subset of cancer cells in the tumor
Sig_T13b=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T13 subset of cancer cells in the tumor
Sig_T14=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-1, PD-L1, CD80 and other factors have on the Effector T cells in the tumor
Sig_T14a=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 and PD-1 expressed on the T14 subset of cancer cells in the tumor
Sig_T14b=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T14 subset of cancer cells in the tumor
Sig_T14c=CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T14 subset of cancer cells in the tumor
Sig_T15=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-1, PD-L2, CD80 and other factors have on the Effector T cells in the tumor
Sig_T15a=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 and PD-1 expressed on the T15 subset of cancer cells in the tumor
Sig_T15b=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T15 subset of cancer cells in the tumor
Sig_T16=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-1, PD-L1, PD-L2, CD80 and other factors have on the Effector T cells in the tumor
Sig_T16a=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 and PD-1 expressed on the T16 subset of cancer cells in the tumor
Sig_T16b=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T16 subset of cancer cells in the tumor
Sig_T16c=CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T16 subset of cancer cells in the tumor
Sig_T2=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T2 subset of cancer cells in the tumor
Sig_T2=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-1 and other factors have on the Effector T cells in the tumor
Sig_T3=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-L1 and other factors have on the Effector T cells in the tumor
Sig_T3a=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T3 subset of cancer cells in the tumor
Sig_T3b=CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T3 subset of cancer cells in the tumor
Sig_T4=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T4 subset of cancer cells in the tumor
Sig_T4=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-L2 and other factors have on the Effector T cells in the tumor
Sig_T5=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T5 subset of cancer cells in the tumor
Sig_T5=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing CD80 and other factors have on the Effector T cells in the tumor

Variable	Value	Units	Source	Description
Sig_T6=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-1, PD-L1 and other factors have on the Effector T cells in the tumor
Sig_T6a=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T6 subset of cancer cells in the tumor
Sig_T6b=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T6 subset of cancer cells in the tumor
Sig_T6c=CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T6 subset of cancer cells in the tumor
Sig_T7=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-1, PD-L2 and other factors have on the Effector T cells in the tumor
Sig_T7a=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T7 subset of cancer cells in the tumor
Sig_T7b=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T7 subset of cancer cells in the tumor
Sig_T8=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-L1, PD-L2 and other factors have on the Effector T cells in the tumor
Sig_T8a=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T8 subset of cancer cells in the tumor
Sig_T8b=CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T8 subset of cancer cells in the tumor
Sig_T9=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 and CD80 expressed on the T9 subset of cancer cells in the tumor
Sig_T9=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total fraction of inhibitory effect that cancer cells expressing PD-1, CD80 and other factors have on the Effector T cells in the tumor
Sig_TrAPC = Other	0	dimensionless	Calculated with RO; see algebraic equations below	Fraction of inhibitory effect that other factors expressed by T Regulatory cells have on the mAPCs in the tumor
Sig_TrAPCT=CTLA4	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CD80 and CD86 receptors on mAPCs that are occupied by CTLA-4 expressed on T Regulatory cells in the tumor
Sig_TrAPCT=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total inhibitory fraction that T Regulatory cells have on the mAPCs in the tumor following their interaction
Sig_TrPNT=PD1/L1/CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total inhibitory fraction that T Regulatory cells have on the Primed Naive T cells in the lymph nodes following their interaction
Sig_TrTeff = Other	0.15	dimensionless	Calculated with RO; see algebraic equations below	Fraction of inhibitory effect that other factors expressed by T Regulatory cells have on the Effector T cells in the tumor
Sig_TrTeff=CD80	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of CD80 receptors expressed on Effector T cells that are interacting with PD-L1 on the T Regulatory cells in the lymph nodes
Sig_TrTeff=PD1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-1 receptors expressed on Effector T cells that are interacting with PD-L1 on the T Regulatory cells in the lymph nodes
Sig_TrTeff=PDL1	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Fraction of PD-L1 receptors expressed on Effector T cells that are interacting with PD-1 on the T Regulatory cells in the lymph nodes
Sig_TrTeff=Total	Calculated	dimensionless	Calculated with RO; see algebraic equations below	Total inhibitory fraction that T Regulatory cells have on the Effector T cells in the tumor following their interaction
Sigma1_CTLA4	0.996839823	dimensionless	[56]	Estimated leaky tissue reflection coefficient for anti-CTLA-4 therapy
Sigma1_PD1	0.912199893	dimensionless	[56]	Estimated leaky tissue reflection coefficient for anti-PD-1 therapy
Sigma1_PDL1	0.990145236	dimensionless	[56]	Estimated leaky tissue reflection coefficient for anti-PD-L1 therapy

Variable	Value	Units	Source	Description
Sigma2_CTLA4	0.97448852	dimensionless	[56]	Estimated tight tissue reflection coefficient for anti-CTLA-4 therapy
Sigma2_PD1	0.89230685	dimensionless	[56]	Estimated tight tissue reflection coefficient for anti-PD-1 therapy
Sigma2_PDL1	0.98870285 7	dimensionless	[56]	Estimated tight tissue reflection coefficient for anti-PD-L1 therapy
SigmaL	0.2	dimensionless	[56]	Lymphatic tissue reflection coefficient
Sigmax_MDSCTeff=CD80	0.03393437 8	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD80 receptors expressed on Effector T cells that are interacting with PD-L1 on the MDSCs in the lymph nodes
Sigmax_MDSCTeff=PD1	0.07390316 4	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors expressed on Effector T cells that are interacting with PD-L1 on the MDSCs in the lymph nodes
Sigmax_MDSCTeff=PDL1	0.02853033 9	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors expressed on Effector T cells that are interacting with PD-1 on the MDSCs in the lymph nodes
Sigmax_NT=CD28	0.83953994 5	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD28 co-receptor interaction on Naive T cells by CD80 and CD86 on mAPC in the lymph nodes
Sigmax_PNT=CD80	0.013125	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of total CD80 receptors on Primed Naïve T cells that can interact with the PD-L1 receptors on mAPCs during priming in the lymph nodes
Sigmax_PNT=CTLA4	0.564375	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of total CTLA-4 receptors on Primed Naïve T cells that can interact with the CD80 and CD86 receptors on mAPCs during priming in the lymph nodes
Sigmax_PNT=PD1	0.02625	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of total PD-1 receptors on Primed Naïve T cells that can interact with the PD-L1 and PD-L2 receptors on mAPCs during priming in the lymph nodes
Sigmax_PNT=PDL1	0.02625	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of total PD-L1 receptors on Primed Naïve T cells that can interact with the PD-1 and CD80 receptors on mAPCs during priming in the lymph nodes
Sigmax_T10a=PDL1	0.03399172 7	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T10 subset of cancer cells in the tumor
Sigmax_T10b=PD1	0.24079052	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T10 subset of cancer cells in the tumor
Sigmax_T10c=CD80	0.10654076 3	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T10 subset of cancer cells in the tumor
Sigmax_T11a=PDL1	0.04820050 1	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T11 subset of cancer cells in the tumor
Sigmax_T11b=PD1	0.22918360 7	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T11 subset of cancer cells in the tumor
Sigmax_T12a=PDL1	0.04820050 1	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T12 subset of cancer cells in the tumor
Sigmax_T12b=PD1	0.06413499 1	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T12 subset of cancer cells in the tumor
Sigmax_T13a=PDL1	0.04820050 1	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T13 subset of cancer cells in the tumor
Sigmax_T13b=PD1	0.26059594	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T13 subset of cancer cells in the tumor
Sigmax_T14a=PDL1	0.07809972 9	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 and PD-1 expressed on the T14 subset of cancer cells in the tumor

Variable	Value	Units	Source	Description
Sigmax_T14b=PD1	0.206595509	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T14 subset of cancer cells in the tumor
Sigmax_T14c=CD80	0.106540762	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T14 subset of cancer cells in the tumor
Sigmax_T15a=PDL1	0.078099729	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 and PD-1 expressed on the T15 subset of cancer cells in the tumor
Sigmax_T15b=PD1	0.064134991	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T15 subset of cancer cells in the tumor
Sigmax_T16a=PDL1	0.078099729	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 and PD-1 expressed on the T16 subset of cancer cells in the tumor
Sigmax_T16b=PD1	0.24079052	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T16 subset of cancer cells in the tumor
Sigmax_T16c=CD80	0.106540763	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T16 subset of cancer cells in the tumor
Sigmax_T2=PDL1	0.033991727	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T2 subset of cancer cells in the tumor
Sigmax_T3a=PD1	0.206595509	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T3 subset of cancer cells in the tumor
Sigmax_T3b=CD80	0.106540753	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T3 subset of cancer cells in the tumor
Sigmax_T4=PD1	0.064134991	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T4 subset of cancer cells in the tumor
Sigmax_T5=PDL1	0.048200501	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T5 subset of cancer cells in the tumor
Sigmax_T6a=PDL1	0.033991727	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T6 subset of cancer cells in the tumor
Sigmax_T6b=PD1	0.206595509	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T6 subset of cancer cells in the tumor
Sigmax_T6c=CD80	0.106540761	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T6 subset of cancer cells in the tumor
Sigmax_T7a=PDL1	0.033991727	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T7 subset of cancer cells in the tumor
Sigmax_T7b=PD1	0.064134991	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T7 subset of cancer cells in the tumor
Sigmax_T8a=PD1	0.24079052	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T8 subset of cancer cells in the tumor
Sigmax_T8b=CD80	0.104091855	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T8 subset of cancer cells in the tumor
Sigmax_T9=PDL1	0.078099729	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors on Effector T cells that are occupied by PD-1 and CD80 expressed on the T9 subset of cancer cells in the tumor
Sigmax_TrAPCT=CTLA4	0.0008355	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD80 and CD86 receptors on mAPCs that are occupied by CTLA-4 expressed on T Regulatory cells in the tumor

Variable	Value	Units	Source	Description
Sigmax_TrPNT=CD80	0.020305139	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of total CD80 receptors on Primed Naïve T cells that are involved in interacting with the PD-L1 receptors on Regulatory T cells during priming in the lymph nodes
Sigmax_TrPNT=Other	1	dimensionless	Calculated with RO; see algebraic equations below	Maximum level of inhibitory effects against Primed Naive T cells by other factors expressed by T Regulatory cells
Sigmax_TrPNT=PD1	0.034241129	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of total PD-1 receptors on Primed Naïve T cells that are involved in interacting with the PD-L1 receptors on Regulatory T cells during priming in the lymph nodes
Sigmax_TrPNT=PDL1	0.010435276	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of total PD-L1 receptors on Primed Naïve T cells that are involved in interacting with the PD-1 receptors on Regulatory T cells during priming in the lymph nodes
Sigmax_TrTeff=CD80	0.033934413	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of CD80 receptors expressed on Effector T cells that are interacting with PD-L1 on the T Regulatory cells in the tumor
Sigmax_TrTeff=PD1	0.073903236	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-1 receptors expressed on Effector T cells that are interacting with PD-L1 on the T Regulatory cells in the tumor
Sigmax_TrTeff=PDL1	0.028530371	dimensionless	Calculated with RO; see algebraic equations below	Maximum fraction of PD-L1 receptors expressed on Effector T cells that are interacting with PD-1 on the T Regulatory cells in the tumor
Sigweight_MDSCTeff=CD80	0.248844361	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through CD80 receptors expressed on Effector T cells that are interacting with PD-L1 on the MDSCs in the tumor
Sigweight_MDSCTeff=PD1	0.541939663	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors expressed on Effector T cells that are interacting with PD-L1 on the MDSCs in the tumor
Sigweight_MDSCTeff=PDL1	0.209215976	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors expressed on Effector T cells that are interacting with PD-1 on the MDSCs in the tumor
SigWeight_PNT=CD80	0.020833333	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Primed Naive T cell inhibition by signaling through CD80 receptors on Primed Naïve T cells that can interact with the PD-L1 receptors on mAPCs during priming in the lymph nodes
SigWeight_PNT=CTLA4	0.895833333	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Primed Naive T cell inhibition by signaling through CTLA-4 receptors on Primed Naïve T cells that can interact with the CD80 and CD86 receptors on mAPCs during priming in the lymph nodes
SigWeight_PNT=PD1	0.041666667	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Primed Naive T cell inhibition by signaling through PD-1 receptors on Primed Naïve T cells that can interact with the PD-L1 and PD-L2 receptors on mAPCs during priming in the lymph nodes
SigWeight_PNT=PDL1	0.041666667	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Primed Naive T cell inhibition by signaling through PD-L1 receptors on Primed Naïve T cells that can interact with the PD-1 and CD80 receptors on mAPCs during priming in the lymph nodes
Sigweight_T10a=PDL1	0.089141557	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T10 subset of cancer cells in the tumor
Sigweight_T10b=PD1	0.631460767	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T10 subset of cancer cells in the tumor

Variable	Value	Units	Source	Description
Sigweight_T10c=CD80	0.279397677	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T10 subset of cancer cells in the tumor
Sigweight_T11a=PDL1	0.173768069	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T11 subset of cancer cells in the tumor
Sigweight_T11b=PD1	0.826231931	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T11 subset of cancer cells in the tumor
Sigweight_T12a=PDL1	0.429076332	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T12 subset of cancer cells in the tumor
Sigweight_T12b=PD1	0.570923668	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T12 subset of cancer cells in the tumor
Sigweight_T13a=PDL1	0.156091504	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T13 subset of cancer cells in the tumor
Sigweight_T13b=PD1	0.843908496	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T13 subset of cancer cells in the tumor
Sigweight_T14a=PDL1	0.199623063	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by CD80 and PD-1 expressed on the T14 subset of cancer cells in the tumor
Sigweight_T14b=PD1	0.528058536	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T14 subset of cancer cells in the tumor
Sigweight_T14c=CD80	0.272318401	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T14 subset of cancer cells in the tumor
Sigweight_T15a=PDL1	0.549090467	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by CD80 and PD-1 expressed on the T15 subset of cancer cells in the tumor
Sigweight_T15b=PD1	0.450909533	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T15 subset of cancer cells in the tumor
Sigweight_T16a=PDL1	0.183577893	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by CD80 and PD-1 expressed on the T16 subset of cancer cells in the tumor
Sigweight_T16b=PD1	0.565991931	dimensionless	Calculated as fraction of RO per total RO; see	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T16 subset of cancer cells in the tumor

Variable	Value	Units	Source	Description
			algebraic equations below	
Sigweight_T16c=CD80	0.250430176	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T16 subset of cancer cells in the tumor
Sigweight_T2=PDL1	1	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T2 subset of cancer cells in the tumor
Sigweight_T3a=PD1	0.659762327	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T3 subset of cancer cells in the tumor
Sigweight_T3b=CD80	0.340237673	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T3 subset of cancer cells in the tumor
Sigweight_T4=PD1	1	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T4 subset of cancer cells in the tumor
Sigweight_T5=PDL1	1	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by CD80 expressed on the T5 subset of cancer cells in the tumor
Sigweight_T6a=PDL1	0.097922746	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T6 subset of cancer cells in the tumor
Sigweight_T6b=PD1	0.595156574	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L1 expressed on the T6 subset of cancer cells in the tumor
Sigweight_T6c=CD80	0.30692068	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T6 subset of cancer cells in the tumor
Sigweight_T7a=PDL1	0.346406438	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that are occupied by PD-1 expressed on the T7 subset of cancer cells in the tumor
Sigweight_T7b=PD1	0.653593562	dimensionless	Calculated as fraction of RO of total ROs in signaling equation	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L2 expressed on the T7 subset of cancer cells in the tumor
Sigweight_T8a=PD1	0.698181576	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors on Effector T cells that are occupied by PD-L1 and PD-L2 expressed on the T8 subset of cancer cells in the tumor
Sigweight_T8b=CD80	0.301818424	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through CD80 receptors on Effector T cells that are occupied by PD-L1 expressed on the T8 subset of cancer cells in the tumor
Sigweight_T9=PDL1	1	dimensionless	Calculated as fraction of RO per	Weight of Effector T cell inhibition by signaling through PD-L1 receptors on Effector T cells that

Variable	Value	Units	Source	Description
			total RO; see algebraic equations below	are occupied by PD-1 and CD80 expressed on the T9 subset of cancer cells in the tumor
SigWeight_TrPNT=CD80	0.266666667	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Primed Naive T cell inhibition by signaling through CD80 receptors on Primed Naïve T cells that are involved in interacting with the PD-L1 receptors on Regulatory T cells during priming in the lymph nodes
SigWeight_TrPNT=Other	0.2	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of of inhibitory effects against Primed Naive T cells by other factors expressed by T Regulatory cells
SigWeight_TrPNT=PD1	0.266666667	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Primed Naive T cell inhibition by signaling through PD-1 receptors on Primed Naïve T cells that are involved in interacting with the PD-L1 receptors on Regulatory T cells during priming in the lymph nodes
SigWeight_TrPNT=PDL1	0.266666667	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Primed Naive T cell inhibition by signaling through PD-L1 receptors on Primed Naïve T cells that are involved in interacting with the PD-1 receptors on Regulatory T cells during priming in the lymph nodes
Sigweight_TrTeff=CD80	0.248844363	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through CD80 receptors expressed on Effector T cells that are interacting with PD-L1 on the T Regulatory cells in the tumor
Sigweight_TrTeff=PD1	0.54193964	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-1 receptors expressed on Effector T cells that are interacting with PD-L1 on the T Regulatory cells in the tumor
Sigweight_TrTeff=PDL1	0.209215997	dimensionless	Calculated as fraction of RO per total RO; see algebraic equations below	Weight of Effector T cell inhibition by signaling through PD-L1 receptors expressed on Effector T cells that are interacting with PD-1 on the T Regulatory cells in the tumor
Starting_Cancer_Diam_mm	15-80	mm	Set value; varied	The diameter of the tumor at which to start its growth in the simulation
Success_NT-mAPC	500	dimensionless	[60, 62, 72, 79, 82, 83]	The number of Naive T:mAPC interactions that would occur prior to a successful priming interaction
Success_PNT-mAPC	50	dimensionless	[60, 62, 72, 79, 82, 84]	The number of Primed Naive T:mAPC interactions that would occur prior to a successful priming interaction. The difference between the number of successful interactions prior to priming between the first and second stage is estimated by enhanced immunity through chemokines that attract the CD8+ T cells where the APCs and T cells have gathered in a more localized area during priming [84].
T_Cell_Clonality	10-130	cell	[28, 30, 85]	Number of Naïve T cells populations specific for different tumor antigens; in other words; the number of anti-tumor T cell clones in each lymph node.
T_Cell_Diffusion	10	$\mu m^2/min$	[62, 72, 79, 86]	The diffusion coefficient of Naive and Primed Naive T cells in the lymph nodes during priming
T_cells_per_mAPC	75	cell/cell	[19, 40, 71, 72, 87, 88]	The maximum number of Naïve and Primed Naïve T cells that can interact with an mAPC at once (surface area of APCs is ~900μm^2 as a sphere – from ~2500 μm^3 [88] per APC – and APC:T contact area is ~50μm^2[40], but have been shown to range from 1um^2 to >70um^2 and even as much as 50% of a cell's surface area [19]). Note: all T cells were estimated to be the same size, and a surface area analysis was used for this estimation. Furthermore, the available surface area on the

Variable	Value	Units	Source	Description
				mAPCs was multiplied by a factor of 3-4-fold [19] to consider dendritic projections, which would increase the surface area relative to the volume.
T_Density	Calculated	cell/μm^3	[72]	The density of total T cells in the lymph nodes
T_IVinject	1	hour	Can be varied	Injection time of antibody
T_per_Cancer_Cell_Int	1	cell/cell	Can be varied	The number of Effector T cells that interact with each cancer cell at once
T_per_Cancer_Cell_max	10	cell/cell	[71, 72]	The maximum number of Effector T cells that can interact with a cancer at once. Note: all T cells were estimated to be the same size, and a surface area analysis was used for this estimation.
T_per_Tr_cell	10	cell/cell	[71, 72, 89]	The maximum number of T (Naive, Primed Naive and Effector) cells that can interact with a T regulatory cell at once. Note: all T cells were estimated to be the same size, and a surface area analysis was used for this estimation.
TCytokineHoming	100	dimensionless	[90, 91]; estimated with fitting to PD1 monotherapy tumor response	The factor specifying homing of Effector T cells to extravasate into the tumor more so than into the peripheral tissues, or to remain in the blood
TDLN_Radius	6203.504909	µm	[72]	The radius of the lymph node region where T cell priming and interactions occur
TheEnd	1	dimensionless	Assigned	Factor that is 0 or 1, which stops the immune response when the tumor has died, former, or allows the immune response to be active, latter
Time_Start_Therapy	Calculated	day	Function of tumor diameter	Recorded time when therapy began
Time_Tumor_Death	Calculated	day	Function of tumor diameter	Recorded time when tumor was sufficiently killed by the immune response
T-mAPC_Cell_Size	12	µm	[72]	The diameter of a T cell undergoing priming
T-mAPC_Inter_tmax_min	1440	min	[72]	The maximum time (24 hours) over which interaction during each priming stage are considered.
Total_T_per_TDLN	5000000	cell	[3]	The total number of T cells in each lymph node
Total_TC_Sig	Calculated	dimensionless	Sum of all cancer checkpoint signaling modules	The total immune checkpoint inhibiting effect on the Effector T cells by the tumor
Tr_cells_per_mAPC	75	cell/cell	[19, 71, 72, 87, 88]	The maximum number of T Regulatory cells that can interact with a mAPC cell at once. Note: all T cells were estimated to be the same size, and an approximate surface area analysis was used for this estimation. Furthermore, the available surface area on the mAPCs was multiplied by a factor of 3-4-fold [19] to consider dendritic projections, which would increase the surface area relative to the volume.
Tr_per_T_cell	10	cell/cell	[71, 72, 89]	The maximum number of T Regulatory cells that can interact with a T (Naive, Primed Naive and Effector) cell at once. Note: all T cells were estimated to be the same size, and a surface area analysis was used for this estimation.
Treg:mAPC_IntTime	0.0924	1/minute	[89]	Rate constant defining the half-life of interaction between T Regulatory cells or MDSCs and mAPCs
Treg:T_IntTime	0.1386	1/minute	[89]	Rate constant defining the half-life of interaction between T Regulatory cells or MDSCs and T (Naive, Primed Naive and Effector) cells
TregLN_Engage	0.05775	1/(mole*hour)	[59-61]; assumed the same	Rate constant defining the half-life of engagement between T Regulatory cells and mAPCs or T (Naive, Primed Naive and Effector) cells
TregTMDSCEng	0.2079	1/hour	Assumed 0.1 of Effect:Target engagement time	Rate constant defining the half-life of engagement between mAPCs or Effector T cells, and T Regulatory cells or MDSCs in the tumor
TrLN-mAPC_Cell_Size	12	µm	[72, 89]	The diameter of a T Regulatory cell interacting with mAPCs
TrLN-PNT_Cell_Size	12	µm	[72, 89]	The diameter of a T Regulatory cell interacting with Primed Naive T cells
Total_Tumor_Void_Frac	0.57	dimensionless	[13, 16]	The fraction of tumor volume that is not occupied by cancer cells, consider vasculature

Variable	Value	Units	Source	Description
Tumor_Void_Fraction	0.5	dimensionless	[16]	The fraction of tumor volume that is not occupied by cancer cells, not consider vasculature
Tumor_Vol_Ellipse_c_ratio	0.5	dimensionless	[92]	The approximate shortest radius of the ellipsoid tumor
V_T:C_10	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T10 subgroup at the immunological synapse
V_T:C_11	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T11 subgroup at the immunological synapse
V_T:C_12	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T12 subgroup at the immunological synapse
V_T:C_13	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T13 subgroup at the immunological synapse
V_T:C_14	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T14 subgroup at the immunological synapse
V_T:C_15	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T15 subgroup at the immunological synapse
V_T:C_16	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T16 subgroup at the immunological synapse
V_T:C_2	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T2 subgroup at the immunological synapse
V_T:C_3	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T3 subgroup at the immunological synapse
V_T:C_4	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T4 subgroup at the immunological synapse
V_T:C_5	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T5 subgroup at the immunological synapse
V_T:C_6	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T6 subgroup at the immunological synapse
V_T:C_7	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T7 subgroup at the immunological synapse
V_T:C_8	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T8 subgroup at the immunological synapse
V_T:C_9	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and cancer cells in the T9 subgroup at the immunological synapse
Vc_CTLA4	2.727814034	liter	[15]	Volume of the central compartment for Anti-CTLA-4
Vc_PD1	2.716739643	liter	[25]	Volume of the central compartment for Anti-PD-1

Variable	Value	Units	Source	Description
Vc_PDL1	4.051599814	liter	[26, 27]	Volume of the central compartment for Anti-PD-L1
Vc_Teff	2.7	liter	[13, 93]	Volume of blood through which Effector T cells circulate throughout the body
Vex_Tmr	~50% (void space) of total tumor volume	ml	[13] Calculated dynamically	Volume of Tumor interstitium
Vext_Liver	361.8	ml	[13]	Volume of Liver interstitium
Vext_LN	34.7	ml	[13]	Volume of Lymph Node interstitium
Vext_Lungs	299.7	ml	[13]	Volume of Lungs interstitium
Vext_Spleen	34.7	ml	[13]	Volume of Spleen interstitium
VL	5.2	liter	[56]	Volume of Lymph
Vm	0.824	mg/day	[63]	Vmax for ADA saturation for Durvalumab
Vol_Cell-Rec_MDSC-TeffT	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and MDSCs at the immunological synapse in the tumor
Vol_Cell-Rec_Tr-APCT	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between mAPCs and T Regulatory cells at the immunological synapse in the tumor
Vol_Cell-Rec_Tr-mAPC	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between mAPCs and T Regulatory cells at the immunological synapse in the lymph nodes
Vol_Cell-Rec_Tr-PNT	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Primed Naive T cells and T Regulatory cells at the immunological synapse in the lymph nodes
Vol_Cell-Rec_Tr-TeffT	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Effector T cells and T Regulatory cells at the immunological synapse in the tumor
Vol_per_TDLN	1	ml	[94]	Volume of a single human lymph node (represented as a sphere) where the T cells reside and undergo priming for probability calculations
Volume_NT-Receptor_Int	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Naive T cells and mAPCs at the immunological synapse in the lymph nodes during priming
Volume_PNT-Receptor_Int	Calculated	liter	Calculated (cell SA times synapse diameter); see equations below	Volume of receptor interactions between Primed Naive T cells and mAPCs at the immunological synapse in the lymph nodes during priming
Vt	0.01	liter	Estimated	Volume of the tumor compartment for PK calculations
Vt_avg_const	33.5	cm^3	[68]	Average tumor volume considered diffusive transport
Vtdln	5.2	liter	[56, 94]	Volume of total lymph
Vt_Teff	Based on Cancer_Vol_cm3	liter	Calculated dynamically	Total tumor volume based on cancer cell number, void space and tumor vasculature
Vv_GI	43	ml	[13]	Vasculature volume of GI
Vv_Liver	180.9	ml	[13]	Vasculature volume of Liver
Vv_LN	17	ml	[13]	Vasculature volume of Lymph Node
Vv_Lungs	99.9	ml	[13]	Vasculature volume of Lungs
Vv_Periph	1355.4	ml	[13]	Vasculature volume of Peripheral for Effector T cell trafficking
Vv_Spleen	17	ml	[13]	Vasculature volume of Spleen
Vv_Tmr	~7% of total tumor volume	ml	[13] Calculated dynamically	Vasculature volume of Tumor based on fraction of total tumor volume

Table S5 – Model Parameters (End)

Table S6 – Model Algebraic Equations (Start)

Parameter and Species Assignment Equation	Assignment Type
[%{CD80}{PD1}C] = Frac_PD1_Exp_Cancer*Frac_CD80_Exp_Cancer*(1-Frac_PDL2_Exp_Cancer)*(1-Frac_PDL1_Exp_Cancer)	Repeated
[%{CD80}C] = Frac_CD80_Exp_Cancer*(1-Frac_PDL1_Exp_Cancer)*(1-Frac_PDL2_Exp_Cancer)*(1-Frac_PD1_Exp_Cancer)	Repeated
[%{Other}C] = (1-Frac_PDL1_Exp_Cancer)*(1-Frac_CD80_Exp_Cancer)*(1-Frac_PDL2_Exp_Cancer)*(1-Frac_PD1_Exp_Cancer)	Repeated
[%{PD1}{80}{L1}{L2}C] = Frac_PDL1_Exp_Cancer*Frac_CD80_Exp_Cancer*Frac_PDL2_Exp_Cancer*Frac_PD1_Exp_Cancer	Repeated
[%{PD1}{80}{L1}C] = Frac_PD1_Exp_Cancer*Frac_CD80_Exp_Cancer*Frac_PDL1_Exp_Cancer*(1-Frac_PDL2_Exp_Cancer)	Repeated
[%{PD1}{80}{PDL2}C] = Frac_PD1_Exp_Cancer*Frac_CD80_Exp_Cancer*Frac_PDL2_Exp_Cancer*(1-Frac_PDL1_Exp_Cancer)	Repeated
[%{PD1}{L1}{L2}C] = Frac_PD1_Exp_Cancer*Frac_PDL1_Exp_Cancer*Frac_PDL2_Exp_Cancer*(1-Frac_CD80_Exp_Cancer)	Repeated
[%{PD1}{L1}C] = Frac_PD1_Exp_Cancer*Frac_PDL1_Exp_Cancer*(1-Frac_PDL2_Exp_Cancer)*(1-Frac_CD80_Exp_Cancer)	Repeated
[%{PD1}{L2}C] = Frac_PD1_Exp_Cancer*Frac_PDL2_Exp_Cancer*(1-Frac_PDL1_Exp_Cancer)*(1-Frac_CD80_Exp_Cancer)	Repeated
[%{PD1}C] = Frac_PD1_Exp_Cancer*(1-Frac_PDL1_Exp_Cancer)*(1-Frac_PDL2_Exp_Cancer)*(1-Frac_CD80_Exp_Cancer)	Repeated
[%{PDL1}{80}{L2}C] = Frac_PDL1_Exp_Cancer*Frac_CD80_Exp_Cancer*Frac_PDL2_Exp_Cancer*(1-Frac_PD1_Exp_Cancer)	Repeated
[%{PDL1}{80}C] = Frac_CD80_Exp_Cancer*Frac_PDL1_Exp_Cancer*(1-Frac_PDL2_Exp_Cancer)*(1-Frac_PD1_Exp_Cancer)	Repeated
[%{PDL1}{PDL2}C] = Frac_PDL1_Exp_Cancer*Frac_PDL2_Exp_Cancer*(1-Frac_PD1_Exp_Cancer)*(1-Frac_CD80_Exp_Cancer)	Repeated
[%{PDL1}C] = Frac_PDL1_Exp_Cancer*(1-Frac_PD1_Exp_Cancer)*(1-Frac_PDL2_Exp_Cancer)*(1-Frac_CD80_Exp_Cancer)	Repeated
[%{PDL2}{80}C] = Frac_CD80_Exp_Cancer*Frac_PDL2_Exp_Cancer*(1-Frac_PDL1_Exp_Cancer)*(1-Frac_PD1_Exp_Cancer)	Repeated
[%{PDL2}C] = Frac_PDL2_Exp_Cancer*(1-Frac_PDL1_Exp_Cancer)*(1-Frac_PD1_Exp_Cancer)*(1-Frac_CD80_Exp_Cancer)	Repeated
[Blood-Lymph].CTLA4_mabB_ugml = ([Blood-Lymph].CTLA4_mabB*Ipilimumab_MW)/(Vc_CTLA4)	Repeated
[Blood-Lymph].Effector_T_Blood_Con = Effector_TB/(Vc_Teff * 5/2.7)	Repeated
[Blood-Lymph].Effector_T_TB = Effector_T * [Num_TDLN_Considered]	Repeated
[Blood-Lymph].Effector_T_TOTAL = EffT_P_f_Vasc+Effector_TT_Count+Effector_TB	Repeated
[Blood-Lymph].PD1_mabB_ugml = ([Blood-Lymph].PD1_mabb*Nivolumab_MW)/Vc_PD1	Repeated
[Blood-Lymph].PDL1_mabB_ugml = ([Blood-Lymph].PDL1_mabb*Durvalumab_MW)/Vc_PDL1	Repeated
[CD28_POS-Sig_NT] = (POS_Sig_NT_CD80+POS_Sig_NT_CD86)/(POS_Sig_NT_CD80+POS_Sig_NT_CD86+NT_Int_CD28+1E-100*mole)	Repeated
[CD28_POS-to-Total] = (POS_Sig_PNT_CD80+POS_Sig_PNT_CD86)/(POS_Sig_PNT_CD80+POS_Sig_PNT_CD86+PNT_Int_CD28+1E-100*mole)	Repeated
[CD80_PNT_NEG-to-Max] = [PNT_CD80-PDL1]/([PNT_Int_CD80] + [PNT_CD80-PDL1]+1E-100*mole)	Repeated
[CD80_receptors-per-mAPC] = 130000*mAPC_activation_level	Repeated
[CD80Sig_Tr-PNT] = [TrPNT_PDL1-CD80]/([TrPNT_PDL1-CD80] + [PNT-Tr_CD80] +1E-100*mole)	Repeated
[CD86_receptors-per-mAPC] = 208000*mAPC_activation_level	Repeated
[CTLA4_NEG-to-Total] = (NEG_Sig_PNT_CD80+NEG_Sig_PNT_CD86)/(NEG_Sig_PNT_CD80+NEG_Sig_PNT_CD86+PNT_CTLA4+CTLA4_mAb_CTLA4+1E-100*mole)	Repeated
[CTLA4_receptors-Int-PNT] = [CD28_receptors-per-Tcell]*[CTLA4-to-CD28_Ratio_Int]	Repeated
[CTLA4_receptors-nInt-PNT] = [CD28_receptors-per-Tcell]*[CTLA4-to-CD28_Ratio_nInt]	Repeated
[CTLA4_receptors-Tr] = [CD28_receptors-per-Tcell]*[CTLA4-to-CD28_Ratio_Tr]	Repeated
[CTLA4Sig_TrLN-mAPC] = ([TrALN_CT_aCT])/([TrALN_CT_CD80] + [TrALN_CT_CD86] + [Tr-mAPC_CTLA4] + [TrALN_CT_aCT]+1E-100*mole)	Repeated
[CTLA4-to-CD28_Ratio_Int] = 0.035*(1+Antigen_Intensity*2)	Repeated
[CTLA4-to-CD28_Ratio_nInt] = 0.035	Repeated
[Max_#Cells_per_mm^3] = 1/[Cancer_Cell_Vol_mm3]	Initial
[PD1_PNT_NEG-to-Max] = ([PNT_PD1-PDL2]+[PNT_PD1-PDL1])/([PNT_Int_PD1] + [PNT_PD1-PDL2]+[PNT_PD1-PDL1] + [PD1mAb_PNT_PD1]+1E-100*mole)	Repeated
[PD1Sig_Tr-PNT] = ([TrPNT_PDL1-PD1])/([TrPNT_PDL1-PD1] + [PNT-Tr_PD1] + [PNTTr_PD1_aPD1] +1E-100*mole)	Repeated
[PDL1_PNT_NEG-to-Max] = ([PNT_PDL1-CD80]+[PNT_PDL1-PD1])/([PNT_Int_PDL1] +[PNT_PDL1-CD80]+[PNT_PDL1-PD1] + [PDL1mAb-PNT_PDL1]+1E-100*mole)	Repeated
[PDL1Sig_Tr-PNT] = ([TrPNT_PD1-L1])/([TrPNT_PD1-L1] +[PNT-Tr_PDL1]+[PNTTr_PDL1_aPDL1] + 1E-100*mole)	Repeated

Parameter and Species Assignment Equation	Assignment Type
[Prob_NT-mAPC_Interact] = (1-exp((-4*pi*[T-mAPC_Cell_Size]*T_Cell_Diffusion*mAPC_Total_Calc_Pr*Precursor_Frequen_NT*T_Density*[T-mAPC_Inter_tmax_min]*Antigen_Intensity)/(T_Cell_Clonality*[Success_NT-mAPC])))	Repeated
[Prob_PNT-mAPC_Interact] = (1-exp((-4*pi*[T-mAPC_Cell_Size]*T_Cell_Diffusion*mAPC_Total_Calc_Pr*Precursor_Frequen_PNT*T_Density*[T-mAPC_Inter_tmax_min]*Antigen_Intensity)/(T_Cell_Clonality*[Success_PNT-mAPC])))	Repeated
[Sig_MDSCTeff=CD80] = ([PDL1:CD80_MDSCT])/([PDL1:CD80_MDSCT] +[CD80_TeffT1] + 1E-100*mole)	Repeated
[Sig_MDSCTeff=PD1] = ([PDL1:PD1_MDSCT])/([PDL1:PD1_MDSCT] + [PD1_TeffT1] + [PD1:aPD1_Teff1] + 1E-100*mole)	Repeated
[Sig_MDSCTeff=PDL1] = ([PD1:PDL1_MDSCT])/([PD1:PDL1_MDSCT] + [PDL1_TeffT1] + [PDL1:aPDL1_Teff1] + 1E-100*mole)	Repeated
[Sig_MDSCTeff=Total] = (([Sigweight_MDSCTeff=CD80]*([Sig_MDSCTeff=CD80]/[Sigmax_MDSCTeff=CD80])+[Sigweight_MDSCTeff=PD1]*([Sig_MDSCTeff=PD1]/[Sigmax_MDSCTeff=PD1])+[Sigweight_MDSCTeff=PDL1]*([Sig_MDSCTeff=PDL1]/[Sigmax_MDSCTeff=PDL1]))^gamma_Sig1 / (1 + ([Sigweight_MDSCTeff=CD80]*([Sig_MDSCTeff=CD80]/[Sigmax_MDSCTeff=CD80])+[Sigweight_MDSCTeff=PD1]*([Sig_MDSCTeff=PD1]/[Sigmax_MDSCTeff=PD1])+[Sigweight_MDSCTeff=PDL1]*([Sig_MDSCTeff=PDL1]/[Sigmax_MDSCTeff=PDL1]))^gamma_Sig1))*(1-[Sig_MDSCTeff = Other])+[Sig_MDSCTeff = Other]	Repeated
[Sig_NT=CD28] = ([CD28_POS-Sig_NT]/[Sigmax_NT=CD28])	Repeated
[Sig_PNT=CTLA4/PD1/L1/CD80] = ([SigWeight_PNT=CTLA4]*[CTLA4_NEG-to-Total]/[Sigmax_PNT=CTLA4]+[SigWeight_PNT=PD1]*[PD1_PNT_NEG-to-Max]/[Sigmax_PNT=PD1]+[SigWeight_PNT=PDL1]*[PDL1_PNT_NEG-to-Max]/[Sigmax_PNT=PDL1]+[SigWeight_PNT=CD80]*[CD80_PNT_NEG-to-Max]/[Sigmax_PNT=CD80])^gamma_Sig/(1+([SigWeight_PNT=CTLA4]*[CTLA4_NEG-to-Total]/[Sigmax_PNT=CTLA4]+[SigWeight_PNT=PD1]*[PD1_PNT_NEG-to-Max]/[Sigmax_PNT=PD1]+[SigWeight_PNT=PDL1]*[PDL1_PNT_NEG-to-Max]/[Sigmax_PNT=PDL1]+[SigWeight_PNT=CD80]*[CD80_PNT_NEG-to-Max]/[Sigmax_PNT=CD80])^gamma_Sig)	Repeated
[Sig_T1=Total] = 1	Repeated
[Sig_T10=Total] = (([Sigweight_T10a=PDL1]*[Sig_T10a=PDL1]/[Sigmax_T10a=PDL1] + [Sigweight_T10b=PD1]*[Sig_T10b=PD1]/[Sigmax_T10b=PD1] + [Sigweight_T10c=CD80]*[Sig_T10c=CD80]/[Sigmax_T10c=CD80]) ^gamma_Sig1/(1 + ([Sigweight_T10a=PDL1]*[Sig_T10a=PDL1]/[Sigmax_T10a=PDL1] + [Sigweight_T10b=PD1]*[Sig_T10b=PD1]/[Sigmax_T10b=PD1] + [Sigweight_T10c=CD80]*[Sig_T10c=CD80]/[Sigmax_T10c=CD80])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T10a=PDL1] = ([T10a=PDL1:PD1=C10a])/([T10a=PDL1:PD1=C10a] +[T10a=PDL1]+[T10a=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T10b=PD1] = ([T10b=PD1:PDL1=C10b] + [T10b=PD1:PDL2=C10c])/([T10b=PD1:PDL1=C10b] + [T10b=PD1:PDL2=C10c] +[T10b=PD1]+[T10b=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T10c=CD80] = ([T10c=CD80:PDL1=C10b])/([T10c=CD80:PDL1=C10b] +[T10c=CD80] +1E-100*mole)	Repeated
[Sig_T11=Total] = (([Sigweight_T11a=PDL1]*[Sig_T11a=PDL1]/[Sigmax_T11a=PDL1] + [Sigweight_T11b=PD1]*[Sig_T11b=PD1]/[Sigmax_T11b=PD1]) ^gamma_Sig1/(1 + ([Sigweight_T11a=PDL1]*[Sig_T11a=PDL1]/[Sigmax_T11a=PDL1] + [Sigweight_T11b=PD1]*[Sig_T11b=PD1]/[Sigmax_T11b=PD1])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T11a=PDL1] = ([T11a=PDL1:CD80=C11b])/([T11a=PDL1:CD80=C11b] +[T11a=PDL1]+[T11a=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T11b=PD1] = ([T11b=PD1:PDL1=C11a])/([T11b=PD1:PDL1=C11a] +[T11b=PD1]+[T11b=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T12=Total] = (([Sigweight_T12a=PDL1]*[Sig_T12a=PDL1]/[Sigmax_T12a=PDL1] + [Sigweight_T12b=PD1]*[Sig_T12b=PD1]/[Sigmax_T12b=PD1]) ^gamma_Sig1/(1 + ([Sigweight_T12a=PDL1]*[Sig_T12a=PDL1]/[Sigmax_T12a=PDL1] + [Sigweight_T12b=PD1]*[Sig_T12b=PD1]/[Sigmax_T12b=PD1])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T12a=PDL1] = ([T12a=PDL1:CD80=C12b])/([T12a=PDL1:CD80=C12b] +[T12a=PDL1]+[T12a=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T12b=PD1] = ([T12b=PD1:PDL2=C12a])/([T12b=PD1:PDL2=C12a] +[T12b=PD1]+[T12b=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T13=Total] = (([Sigweight_T13a=PDL1]* [Sig_T13a=PDL1]/[Sigmax_T13a=PDL1] + [Sigweight_T13b=PD1]*[Sig_T13b=PD1]/[Sigmax_T13b=PD1]) ^gamma_Sig1/(1 + ([Sigweight_T13a=PDL1]* [Sig_T13a=PDL1]/[Sigmax_T13a=PDL1] + [Sigweight_T13b=PD1]*[Sig_T13b=PD1]/[Sigmax_T13b=PD1])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T13a=PDL1] = ([T13a=PDL1:CD80=C13c])/([T13a=PDL1:CD80=C13c] +[T13a=PDL1]+[T13a=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T13b=PD1] = ([T13b=PD1:PDL2=C13b] + [T13b=PD1:PDL1=C13a])/([T13b=PD1:PDL2=C13b] + [T13b=PD1:PDL1=C13a] +[T13b=PD1]+[T13b=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T14=Total] = (([Sigweight_T14a=PDL1]*[Sig_T14a=PDL1]/[Sigmax_T14a=PDL1] + [Sigweight_T14b=PD1]*[Sig_T14b=PD1]/[Sigmax_T14b=PD1] + [Sigweight_T14c=CD80]*[Sig_T14c=CD80]/[Sigmax_T14c=CD80]) ^gamma_Sig1/(1 +	Repeated

Parameter and Species Assignment Equation	Assignment Type
([Sigweight_T14a=PDL1]*[Sig_T14a=PDL1]/[Sigmax_T14a=PDL1] + [Sigweight_T14b=PD1]*[Sig_T14b=PD1]/[Sigmax_T14b=PD1] + [Sigweight_T14c=CD80]*[Sig_T14c=CD80]/[Sigmax_T14c=CD80])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	
[Sig_T14a=PDL1] = ([T14a=PDL1:PD1=C14a] + [T14a=PDL1:CD80=C14c])/([T14a=PDL1:PD1=C14a] + [T14a=PDL1:CD80=C14c] +[T14a=PDL1]+[T14a=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T14b=PD1] = ([T14b=PD1:PDL1=C14b])/([T14b=PD1:PDL1=C14b] +[T14b=PD1]+[T14b=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T14c=CD80] = ([T14c=CD80:PDL1=C14b])/([T14c=CD80:PDL1=C14b] +[T14c=CD80] +1E-100*mole)	Repeated
[Sig_T15=Total] = (([Sigweight_T15a=PDL1]*[Sig_T15a=PDL1]/[Sigmax_T15a=PDL1] + [Sigweight_T15b=PD1]*[Sig_T15b=PD1]/[Sigmax_T15b=PD1]) ^gamma_Sig1/(1 + ([Sigweight_T15a=PDL1]*[Sig_T15a=PDL1]/[Sigmax_T15a=PDL1] + [Sigweight_T15b=PD1]*[Sig_T15b=PD1]/[Sigmax_T15b=PD1])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T15a=PDL1] = ([T15a=PDL1:CD80=C15c] + [T15a=PDL1:PD1=C15a])/([T15a=PDL1:CD80=C15c]+[T15a=PDL1:PD1=C15a] +[T15a=PDL1]+[T15a=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T15b=PD1] = ([T15b=PD1:PDL2=C15b])/([T15b=PD1:PDL2=C15b] +[T15b=PD1]+[T15b=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T16=Total] = (([Sigweight_T16a=PDL1]*[Sig_T16a=PDL1]/[Sigmax_T16a=PDL1] + [Sigweight_T16b=PD1]*[Sig_T16b=PD1]/[Sigmax_T16b=PD1] + [Sigweight_T16c=CD80]*[Sig_T16c=CD80]/[Sigmax_T16c=CD80]) ^gamma_Sig1/(1 + ([Sigweight_T16a=PDL1]*[Sig_T16a=PDL1]/[Sigmax_T16a=PDL1] + [Sigweight_T16b=PD1]*[Sig_T16b=PD1]/[Sigmax_T16b=PD1] + [Sigweight_T16c=CD80]*[Sig_T16c=CD80]/[Sigmax_T16c=CD80])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T16a=PDL1] = ([T16a=PDL1:PD1=C16a] + [T16a=PDL1:CD80=C16d])/([T16a=PDL1:PD1=C16a]+[T16a=PDL1:CD80=C16d] +[T16a=PDL1]+[T16a=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T16b=PD1] = ([T16b=PD1:PDL2=C16c]+[T16b=PD1:PDL1=C16b])/([T16b=PD1:PDL2=C16c]+[T16b=PD1:PDL1=C16b] +[T16b=PD1]+[T16b=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T16c=CD80] = ([T16c=CD80:PDL1=C16b])/([T16c=CD80:PDL1=C16b] +[T16c=CD80]+1E-100*mole)	Repeated
[Sig_T2=PDL1] = ([T2=PDL1:PD1=C2])/([T2=PDL1:PD1=C2] +[T2=PDL1]+[T2=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T2=Total] = (([Sigweight_T2=PDL1]*[Sig_T2=PDL1]/[Sigmax_T2=PDL1]) ^gamma_Sig1/(1 + ([Sigweight_T2=PDL1]*[Sig_T2=PDL1]/[Sigmax_T2=PDL1])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T3=Total] = (([Sigweight_T3a=PD1]*[Sig_T3a=PD1]/[Sigmax_T3a=PD1] + [Sigweight_T3b=CD80]*[Sig_T3b=CD80]/[Sigmax_T3b=CD80]) ^gamma_Sig1/(1 + ([Sigweight_T3a=PD1]*[Sig_T3a=PD1]/[Sigmax_T3a=PD1] + [Sigweight_T3b=CD80]*[Sig_T3b=CD80]/[Sigmax_T3b=CD80])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T3a=PD1] = ([T3a=PD1:PDL1=C3])/([T3a=PD1:PDL1=C3] +[T3a=PD1]+[T3a=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T3b=CD80] = ([T3b=CD80:PDL1=C3])/([T3b=CD80:PDL1=C3] +[T3b=CD80] +1E-100*mole)	Repeated
[Sig_T4=PD1] = ([T4=PD1:PDL2=C4])/([T4=PD1:PDL2=C4] +[T4=PD1]+[T4=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T4=Total] = (([Sigweight_T4=PD1]*[Sig_T4=PD1]/[Sigmax_T4=PD1])^ gamma_Sig1/(1 + ([Sigweight_T4=PD1]*[Sig_T4=PD1]/[Sigmax_T4=PD1])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T5=PDL1] = ([T5=PDL1:CD80=C5])/([T5=PDL1:CD80=C5] +[T5=PDL1]+[T5=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T5=Total] = (([Sigweight_T5=PDL1]*[Sig_T5=PDL1]/[Sigmax_T5=PDL1])^ gamma_Sig1/(1 + ([Sigweight_T5=PDL1]*[Sig_T5=PDL1]/[Sigmax_T5=PDL1])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T6=Total] = (([Sigweight_T6a=PDL1]*[Sig_T6a=PDL1]/[Sigmax_T6a=PDL1] + [Sigweight_T6b=PD1]*[Sig_T6b=PD1]/[Sigmax_T6b=PD1] + [Sigweight_T6c=CD80]*[Sig_T6c=CD80]/[Sigmax_T6c=CD80])^ gamma_Sig1/(1 + ([Sigweight_T6a=PDL1]*[Sig_T6a=PDL1]/[Sigmax_T6a=PDL1] + [Sigweight_T6b=PD1]*[Sig_T6b=PD1]/[Sigmax_T6b=PD1] + [Sigweight_T6c=CD80]*[Sig_T6c=CD80]/[Sigmax_T6c=CD80])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T6a=PDL1] = ([T6a=PDL1:PD1=C6a])/([T6a=PDL1:PD1=C6a] +[T6a=PDL1]+[T6a=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T6b=PD1] = ([T6b=PD1:PDL1=C6b])/([T6b=PD1:PDL1=C6b] +[T6b=PD1]+[T6b=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T6c=CD80] = ([T6c=CD80:PDL1=C6b])/([T6c=CD80:PDL1=C6b] +[T6c=CD80] +1E-100*mole)	Repeated
[Sig_T7=Total] = (([Sigweight_T7a=PDL1]*[Sig_T7a=PDL1]/[Sigmax_T7a=PDL1] + [Sigweight_T7b=PD1]*[Sig_T7b=PD1]/[Sigmax_T7b=PD1]) ^gamma_Sig1/(1 + ([Sigweight_T7a=PDL1]*[Sig_T7a=PDL1]/[Sigmax_T7a=PDL1] + [Sigweight_T7b=PD1]*[Sig_T7b=PD1]/[Sigmax_T7b=PD1])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T7a=PDL1] = ([T7a=PDL1:PD1=C7a])/([T7a=PDL1:PD1=C7a] +[T7a=PDL1]+[T7a=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T7b=PD1] = ([T7b=PD1:PDL2=C7b])/([T7b=PD1:PDL2=C7b] +[T7b=PD1]+[T7b=PD1:aPD1] +1E-100*mole)	Repeated
[Sig_T8=Total] = (([Sigweight_T8a=PD1]*[Sig_T8a=PD1]/[Sigmax_T8a=PD1] + [Sigweight_T8b=CD80]*[Sig_T8b=CD80]/[Sigmax_T8b=CD80]) ^gamma_Sig1/(1 + ([Sigweight_T8a=PD1]*[Sig_T8a=PD1]/[Sigmax_T8a=PD1] + [Sigweight_T8b=CD80]*[Sig_T8b=CD80]/[Sigmax_T8b=CD80])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_T8a=PD1] = ([T8a=PD1:PDL1=C8a] + [T8a=PD1:PDL2=C8b])/([T8a=PD1:PDL1=C8a] +[T8a=PD1:PDL2=C8b] + [T8a=PD1]+[T8a=PD1:aPD1] +1E-100*mole)	Repeated

Parameter and Species Assignment Equation	Assignment Type
[Sig_T8b=CD80] = ([T8b=CD80:PDL1=C8a])/([T8b=CD80:PDL1=C8a] +[T8b=CD80] +1E-100*mole)	Repeated
[Sig_T9=PDL1] = ([T9=PDL1-PD1=C9a] + [T9=PDL1-CD80=C9b])/([T9=PDL1-PD1=C9a] + [T9=PDL1-CD80=C9b] +[T9=PDL1]+[T9=PDL1:aPDL1] +1E-100*mole)	Repeated
[Sig_T9=Total] = (([Sigweight_T9=PDL1]*[Sig_T9=PDL1]/[Sigmax_T9=PDL1]) ^gamma_Sig1/(1 + ([Sigweight_T9=PDL1]*[Sig_T9=PDL1]/[Sigmax_T9=PDL1])^gamma_Sig1))*(1-[Sig_T=Other])+[Sig_T=Other]	Repeated
[Sig_TrAPCT=CTLA4] = ([CTLA4:CD80_TrAT] + [CTLA4:CD86_TrAT])/ ([CTLA4:CD80_TrAT] + [CTLA4:CD86_TrAT] + [CD80_mAPCT] + [CD86_mAPCT] + [CTLA4_CTLA4-Trt] + 1E-100*mole)	Repeated
[Sig_TrAPCT=Total] = (([Sig_TrAPCT=CTLA4]/[Sigmax_TrAPCT=CTLA4])^gamma_Sig / (1 + ([Sig_TrAPCT=CTLA4]/[Sigmax_TrAPCT=CTLA4])^gamma_Sig))*(1-[Sig_TrAPC = Other])+[Sig_TrAPC = Other]	Repeated
[Sig_TrPNT=PD1/L1/CD80] = (([SigWeight_TrPNT=CD80]*[CD80Sig_Tr-PNT]/[Sigmax_TrPNT=CD80] + [SigWeight_TrPNT=PD1]*[PD1Sig_Tr-PNT]/[Sigmax_TrPNT=PD1] + [SigWeight_TrPNT=PDL1]*[PDL1Sig_Tr-PNT]/[Sigmax_TrPNT=PDL1])^gamma_SigTr / (1 + ([SigWeight_TrPNT=CD80]*[CD80Sig_Tr-PNT]/[Sigmax_TrPNT=CD80] + [SigWeight_TrPNT=PD1]*[PD1Sig_Tr-PNT]/[Sigmax_TrPNT=PD1] + [SigWeight_TrPNT=PDL1]*[PDL1Sig_Tr-PNT]/[Sigmax_TrPNT=PDL1]))^gamma_SigTr)*(1-[SigWeight_TrPNT=Other]*([Sigmax_TrPNT=Other]))+ [SigWeight_TrPNT=Other]*([Sigmax_TrPNT=Other])	Repeated
[Sig_TrTeff=CD80] = ([PDL1:CD80_TrTeff])/([PDL1:CD80_TrTeff] + [CD80_TeffT] + 1E-100*mole)	Repeated
[Sig_TrTeff=PD1] = ([PDL1:PD1_TrTeff])/([PDL1:PD1_TrTeff] + [PD1_TeffT] + [PD1:aPD1_Teff] + 1E-100*mole)	Repeated
[Sig_TrTeff=PDL1] = ([PD1:PDL1_TrTeff])/([PD1:PDL1_TrTeff] + [PDL1_TeffT] + [PDL1:aPDL1_Teff] + 1E-100*mole)	Repeated
[Sig_TrTeff=Total] = (([Sigweight_TrTeff=PD1]*[Sig_TrTeff=PD1]/[Sigmax_TrTeff=PD1] +[Sigweight_TrTeff=PDL1]*[Sig_TrTeff=PDL1]/[Sigmax_TrTeff=PDL1] +[Sigweight_TrTeff=CD80]*[Sig_TrTeff=CD80]/[Sigmax_TrTeff=CD80])^gamma_Sig1/(1+([Sigweight_TrTeff=PD1]*[Sig_TrTeff=PD1]/[Sigmax_TrTeff=PD1] +[Sigweight_TrTeff=PDL1]*[Sig_TrTeff=PDL1]/[Sigmax_TrTeff=PDL1] +[Sigweight_TrTeff=CD80]*[Sig_TrTeff=CD80]/[Sigmax_TrTeff=CD80])^gamma_Sig1)) *(1-[Sig_TrTeff = Other])+[Sig_TrTeff = Other]	Repeated
[Success_NT-mAPC] = 500	Repeated
[Success_PNT-mAPC] = 50	Repeated
[V_T:C_10] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{L1}{80}-{PD1}{L1}{L2}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_11] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{L1}-{PDL1}{80}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_12] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{L1}-{PDL2}{80}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_13] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{L1}-{PDL1}{80}{L2}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_14] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{L1}{80}-{PD1}{80}{L1}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_15] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{L1}-{PD1}{80}{PDL2}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_16] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_2] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PDL1}-{PD1}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_3] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{CD80}-{PDL1}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_4] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}-{PDL2}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_5] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PDL1}-{CD80}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_6] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{L1}{80}-{PD1}{L1}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_7] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{L1}-{PD1}{L2}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_8] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PD1}{80}-{PDL1}{PDL2}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[V_T:C_9] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*([T{PDL1}-{CD80}{PD1}C])*(Cancer_per_T_Cell_Int/Cancer_per_T_Cell_max)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[Vol_Cell-Rec_MDSC-TeffT] = ((4*pi*(([TrLN-PNT_Cell_Size]/2)^2)*(MDSCsT_EngTeff/T_per_Tr_cell)*15E-3))*(1E-15)*(IS_Scaling)*(L/mole)	Repeated
[Vol_Cell-Rec_Tr-APCT] = ((4*pi*(([TrLN-mAPC_Cell_Size]/2)^2)*(TregT_EngAPC/mAPC_per_Tr_cell)*15E-3))*(1E-15)*(IS_Scaling)*(L/mole)	Repeated
[Vol_Cell-Rec_Tr-mAPC] = ((4*pi*(([TrLN-mAPC_Cell_Size]/2)^2)*(TregLN_mAPC1/mAPC_per_Tr_cell)*15E-3))*(1E-15)*(IS_Scaling)*(L/mole)	Repeated
[Vol_Cell-Rec_Tr-PNT] = ((4*pi*(([TrLN-PNT_Cell_Size]/2)^2)*([TregLN-PNT1]/T_per_Tr_cell)*15E-3))*(1E-15)*(IS_Scaling)*(L/mole)	Repeated
[Vol_Cell-Rec_Tr-TeffT] = ((4*pi*(([TrLN-PNT_Cell_Size]/2)^2)*(TregT_EngTeff/T_per_Tr_cell)*15E-3))*(1E-15)*(IS_Scaling)*(L/mole)	Repeated

Parameter and Species Assignment Equation	Assignment Type
[Volume_NT-Receptor_Int] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*((mAPC_Int_P1)/mAPC_per_T_cell)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
[Volume_PNT-Receptor_Int] = ((4*pi*(([T-mAPC_Cell_Size]/2)^2)*((mAPC_Int_P2)/mAPC_per_T_cell)*15E-3)*(L/mole))*(1E-15)*(IS_Scaling)	Repeated
Cancer_Cell_Vol_mm3 = (4/3)*pi*(([Cancer_Cell_Diam_um]/2000)^3)	Initial
Cancer_Diam_mm = ((6*Cancer)/(pi*Tumor_Vol_Ellipse_c_ratio*(1/((4/3)*pi*((Cancer_Cell_Diam_um/2000)^3)))*(1-Total_Tumor_Void_Frac)*mole))^(1/3)	Repeated
Cancer_Vol_cm3 = (4/3)*pi*(([Cancer_Diam_mm]/2)^2)*(([Cancer_Diam_mm]*[Tumor_Vol_Ellipse_c_ratio])/2000)	Repeated
CTLA4Sig_TrLN = [TrLN_CT_aCT]/([TrLN_CT_aCT] + [TrLN_CTLA4] +1E-100*mole)	Repeated
Frac_CD80_Exp_Cancer = [%CD80_Exp_Cancer]/100	Repeated
Frac_PD1_Exp_Cancer = [%PD1_Exp_Cancer]/100	Repeated
Frac_PDL1_Exp_Cancer = [%PDL1_Exp_Cancer]/100	Repeated
Frac_PDL2_Exp_Cancer = [%PDL2_Exp_Cancer]/100	Repeated
Liv_Spln_GI.Liver_Free_Sites = Adhesion_D_Lung_Liv_spln*Vv_Liver - EffT_Liver_b_Vasc-EffT_Liver_AR_Vasc	Repeated
Liv_Spln_GI.Spleen_Free_Sites = Adhesion_D_Lung_Liv_spln*Vv_Spleen-EffT_Spleen_b_Vasc-EffT_Spleen_AR_Vasc	Repeated
Lungs.Lung_Free_Sites = Adhesion_D_Lung_Liv_spln*Vv_Lungs - EffT_r_LungsVasc - EffT_AR_LungsVasc	Repeated
Lymph_Node.[Total_T_CD8-CD4] = Total_T_per_TDLN	Repeated
Lymph_Node.[TregLN-PNT1] = Lymph_Node.[TregLN-PNT]+0.001*mole	Repeated
Lymph_Node.CTLA4_mab_ugml = (Lymph_Node.CTLA4_mab*Ipilimumab_MW)/VL	Repeated
Lymph_Node.mAPC_cells_per_ml = mAPC/Vext_LN	Repeated
Lymph_Node.mAPC_Int_P1 = 0.001*mole+gt(Naive_T1,0)*gt(Primed_Naive_T1+Naive_T1,0)*(Naive_T1*[mAPC_per_T_cell] * gt(((Naive_T1 * mAPC)/(Primed_Naive_T1 + Naive_T1+1E-100*mole)) / (Naive_T1 *[mAPC_per_T_cell]+ 1E-100*mole),1) + (Naive_T1/(Primed_Naive_T1 + Naive_T1+1E-100*mole)) *mAPC* le(((Naive_T1 * mAPC)/(Primed_Naive_T1 + Naive_T1+1E-100*mole)) / (Naive_T1 *[mAPC_per_T_cell]+ 1E-100*mole),1))	Repeated
Lymph_Node.mAPC_Int_P2 = 0.001*mole+gt(Primed_Naive_T1,0)*gt(Primed_Naive_T1+Naive_T1,0)*(Primed_Naive_T1*[mAPC_per_T_cell] * gt(((Primed_Naive_T1 * mAPC)/(Primed_Naive_T1 + Naive_T1+1E-100*mole)) / (Primed_Naive_T1 *[mAPC_per_T_cell]+ 1E-100*mole),1) + (Primed_Naive_T1/(Primed_Naive_T1 + Naive_T1+1E-100*mole)) *mAPC* le(((Primed_Naive_T1 * mAPC)/(Primed_Naive_T1 + Naive_T1+1E-100*mole)) / (Primed_Naive_T1 *[mAPC_per_T_cell]+ 1E-100*mole),1))	Repeated
Lymph_Node.mAPC_nInt = (mAPC - mAPC_Int_P1 - mAPC_Int_P2) * ge(mAPC - mAPC_Int_P1 - mAPC_Int_P2,0)	Repeated
Lymph_Node.mAPC_Total_Calc_Pr = (mAPC-mAPC_Int_P1-mAPC_Int_P2)*ge(mAPC-mAPC_Int_P1-mAPC_Int_P2,0)	Repeated
Lymph_Node.mAPC1 = mAPC - [TregLN_mAPC]	Repeated
Lymph_Node.Naive_T = Lymph_Node.Naive_T0	Initial
Lymph_Node.Naive_T0 = T_Cell_Clonality * [Copies-per-T_Cell_Clone]	Repeated
Lymph_Node.Naive_T2 = Naive_T - [TregLN-NT]	Repeated
Lymph_Node.NT1_Int1 = Naive_T+0.001*mole	Repeated
Lymph_Node.PD1_mabLN_ugml = (Lymph_Node.PD1_mab*Nivolumab_MW)/VL	Repeated
Lymph_Node.PDL1_mabLN_ugml = (Lymph_Node.PDL1_mab*Durvalumab_MW)/VL	Repeated
Lymph_Node.PNT1_Int = Lymph_Node.Primed_Naive_T1+0.001*mole	Repeated
Lymph_Node.Primed_Naive_T2 = Primed_Naive_T - [TregLN-PNT]	Repeated
Lymph_Node.TregLN = ((Naive_T0)*([%_Tr_LN]/[%_NT_LN]) - TregLN_mAPC - [TregLN-NT] - [TregLN-PNT])*gt(mAPC,0)*(1-[CTLA4Sig_TrLN])	Repeated
Lymph_Node.TregLN_mAPC1 = Lymph_Node.TregLN_mAPC + 0.001*mole	Repeated
Peripheral.CTLA4_leaky_ugml = (Peripheral.CTLA4_mabP_leaky*Ipilimumab_MW)/(0.35*ISF)	Repeated
Peripheral.CTLA4_tight_ugml = (Peripheral.CTLA4_mabP_tight*Ipilimumab_MW)/(0.65*ISF)	Repeated
Peripheral.PD1_leaky_ugml = (Peripheral.PD1_mabP_leaky*Nivolumab_MW)/(0.35*ISF)	Repeated
Peripheral.PD1_tight_ugml = (Peripheral.PD1_mabP_tight*Nivolumab_MW)/(0.65*ISF)	Repeated
Peripheral.PDL1_leaky_ugml = (Peripheral.PDL1_mabP_leaky*Durvalumab_MW)/(0.35*ISF)	Repeated
Peripheral.PDL1_tight_ugml = (Peripheral.PDL1_mabP_tight*Durvalumab_MW)/(0.65*ISF)	Repeated
Precursor_Frequen_NT = Naive_T/[Total_T_CD8-CD4]	Repeated
Precursor_Frequen_PNT = Primed_Naive_T/[Total_T_CD8-CD4]	Repeated
Starting_Cancer_Diam_mm = Cancer_mm_Start_Therapy*0.95	Repeated
T_Density = [Total_T_CD8-CD4]/((4/3)*pi*TDLN_Radius^3)	Repeated
TDLN_Radius = 10000*([Vol_per_TDLN]*(3/(4*pi)))^(1/3)	Repeated
Total_TC_Sig = [Sig_T1=Total]*[%{Other}C] + [Sig_T2=Total]*[%{PD1}C] + [Sig_T3=Total]*[%{PDL1}C] + [Sig_T4=Total]*[%{PDL2}C] + [Sig_T5=Total]*[%{CD80}C] + [Sig_T6=Total]*[%{PD1}{L1}C] + [Sig_T7=Total]*[%{PD1}{L2}C] + [Sig_T8=Total]*[%{PDL1}{PDL2}C] + [Sig_T9=Total]*[%{CD80}{PD1}C] + [Sig_T10=Total]*[%{PD1}{L1}{L2}C] + [Sig_T11=Total]*[%{PDL1}{80}C] + [Sig_T12=Total]*[%{PDL2}{80}C] + [Sig_T13=Total]*[%{PDL1}{80}{L2}C] + [Sig_T14=Total]*[%{PD1}{80}{L1}C] + [Sig_T15=Total]*[%{PD1}{80}{PDL2}C] + [Sig_T16=Total]*[%{PD1}{80}{L1}{L2}C]	Repeated
Total_Tumor_Void_Frac = Tumor_Void_Fraction + Frac_Vv_Tmr	Repeated
Tumor.[C{CD80}] = 0.001*mole+TC1*[%{CD80}C]	Repeated
Tumor.[C{PD1}] = 0.001*mole+TC1*[%{PD1}C]	Repeated
Tumor.[C{PD1}{CD80}] = 0.001*mole+TC1*[%{CD80}{PD1}C]	Repeated

Parameter and Species Assignment Equation	Assignment Type
Tumor.[C{PD1}{PDL1}] = 0.001*mole+TC1*[%{PD1}{L1}C]	Repeated
Tumor.[C{PD1}{PDL1}{CD80}] = 0.001*mole+TC1*[%{PD1}{80}{L1}C]	Repeated
Tumor.[C{PD1}{PDL1}{PDL2}] = 0.001*mole+TC1*[%{PD1}{L1}{L2}C]	Repeated
Tumor.[C{PD1}{PDL1}{PDL2}{CD80}] = 0.001*mole+TC1*[%{PD1}{80}{L1}{L2}C]	Repeated
Tumor.[C{PD1}{PDL2}] = 0.001*mole+TC1*[%{PD1}{L2}C]	Repeated
Tumor.[C{PD1}{PDL2}{CD80}] = 0.001*mole+TC1*[%{PD1}{80}{PDL2}C]	Repeated
Tumor.[C{PDL1}] = 0.001*mole+TC1*[%{PDL1}C]	Repeated
Tumor.[C{PDL1}{CD80}] = 0.001*mole+TC1*[%{PDL1}{80}C]	Repeated
Tumor.[C{PDL1}{PDL2}] = 0.001*mole+TC1*[%{PDL1}{PDL2}C]	Repeated
Tumor.[C{PDL1}{PDL2}{CD80}] = 0.001*mole+TC1*[%{PDL1}{80}{L2}C]	Repeated
Tumor.[C{PDL2}] = 0.001*mole+TC1*[%{PDL2}C]	Repeated
Tumor.[C{PDL2}{CD80}] = 0.001*mole+TC1*[%{PDL2}{80}C]	Repeated
Tumor.[T{PD1}{80}-{PDL1}{PDL2}C] = 0.001*mole+TC2*[%{PDL1}{PDL2}C]	Repeated
Tumor.[T{PD1}{CD80}-{PDL1}C] = 0.001*mole+TC2*[%{PDL1}C]	Repeated
Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}{L2}C] = 0.001*mole+TC2*[%{PD1}{80}{L1}{L2}C]	Repeated
Tumor.[T{PD1}{L1}{80}-{PD1}{80}{L1}C] = 0.001*mole+TC2*[%{PD1}{80}{L1}C]	Repeated
Tumor.[T{PD1}{L1}{80}-{PD1}{L1}{L2}C] = 0.001*mole+TC2*[%{PD1}{L1}{L2}C]	Repeated
Tumor.[T{PD1}{L1}{80}-{PD1}{L1}C] = 0.001*mole+TC2*[%{PD1}{L1}C]	Repeated
Tumor.[T{PD1}{L1}-{PD1}{80}{PDL2}C] = 0.001*mole+TC2*[%{PD1}{80}{PDL2}C]	Repeated
Tumor.[T{PD1}{L1}-{PD1}{L2}C] = 0.001*mole+TC2*[%{PD1}{L2}C]	Repeated
Tumor.[T{PD1}{L1}-{PDL1}{80}{L2}C] = 0.001*mole+TC2*[%{PDL1}{80}{L2}C]	Repeated
Tumor.[T{PD1}{L1}-{PDL1}{80}C] = 0.001*mole+TC2*[%{PDL1}{80}C]	Repeated
Tumor.[T{PD1}{L1}-{PDL2}{80}C] = 0.001*mole+TC2*[%{PDL2}{80}C]	Repeated
Tumor.[T{PD1}-{PDL2}C] = 0.001*mole+TC2*[%{PDL2}C]	Repeated
Tumor.[T{PDL1}-{CD80}{PD1}C] = 0.001*mole+TC2*[%{CD80}{PD1}C]	Repeated
Tumor.[T{PDL1}-{CD80}C] = 0.001*mole+TC2*[%{CD80}C]	Repeated
Tumor.[T{PDL1}-{PD1}C] = 0.001*mole+TC2*[%{PD1}C]	Repeated
Tumor.Cancer = (4/3)*pi*((Starting_Cancer_Diam_mm/2)^2)*((Starting_Cancer_Diam_mm*Tumor_Vol_Ellipse_c_ratio)/2)*(1/((4/3)*pi*((Cancer_Cell_Diam_um/2000)^3)))*(1-Total_Tumor_Void_Frac)*mole	Initial
Tumor.Cancer1 = (Cancer-TC1)*ge(Cancer-TC1,0)	Repeated
Tumor.CTLA4_mabt_ugml = (Tumor.CTLA4_mabt*Ipilimumab_MW)/Vex_Tmr	Repeated
Tumor.Effector_TT_C_Eng = (Effector_TT-TregT_Teff - MDSCsT_Teff - TC2-T_Recover_Can_Dead)*ge(Effector_TT-TC2-T_Recover_Can_Dead,0)	Repeated
Tumor.Effector_TT_Count = Effector_TT + Effector_TT_Res	Repeated
Tumor.Effector_TT_MDSCs = Effector_TT-TregT_Teff - MDSCsT_Teff - TC1	Repeated
Tumor.Effector_TT_per_mL = Effector_TT_Count/Vex_Tmr	Repeated
Tumor.Effector_TT_per_Treg = (Effector_TT_Count/(Cancer*[%T_Tregs_per_Cancer]/100))*ge(Cancer,10*mole)	Repeated
Tumor.Effector_TT_TregT = Effector_TT-TregT_Teff - MDSCsT_Teff - TC1	Repeated
Tumor.mAPCT_EngTregT = mAPC_T+0.001*mole	Repeated
Tumor.MDSC_T = (Cancer*[%T_Tregs_per_Cancer]/100)*[MDSCs_per_Treg] -MDSCsT_Teff	Repeated
Tumor.MDSCsT_EngTeff = MDSCsT_Teff+0.001*mole	Repeated
Tumor.PD1_mabT_ugml = (Tumor.PD1_mabt*Nivolumab_MW)/Vex_Tmr	Repeated
Tumor.PDL1_mabT_ugml = (Tumor.PDL1_mabt*Durvalumab_MW)/Vex_Tmr	Repeated
Tumor.TC2 = TC1*T_per_Cancer_Cell_Int	Repeated
Tumor.Teff_EngMDSC = MDSCsT_Teff+0.001*mole	Repeated
Tumor.Teff_EngTregT = TregT_Teff+0.001*mole	Repeated
Tumor.Tmr_Free_Sites = Vv_Tmr*Adhesion_Density_Tmr-EffT_b_Vasc-EffT_AR_Vasc	Repeated
Tumor.TregT = (((Cancer*[%T_Tregs_per_Cancer]/100)) - TregT_Teff)*(1-[Sig_TrAPCT=Total])	Repeated
Tumor.TregT_EngAPC = mAPC_T+0.001*mole	Repeated
Tumor.TregT_EngTeff = TregT_Teff+0.001*mole	Repeated
Vex_Tmr = (Total_Tumor_Void_Frac - Frac_Vv_Tmr)*Vt_Teff	Repeated
Vt = Vex_Tmr + ml_correct	Repeated
Vt_Teff = ([Cancer_Vol_cm3]*0.001+1E-20)*L	Repeated
Vv_Tmr = Vt_Teff*Frac_Vv_Tmr	Repeated

Table S6 – Model Algebraic Equations (End)

Table S7 – Model Discontinuous Equation Sets (Start)

Trigger	Event Functions	Description
CTLA4_counter_on<=time	CTLA4_counter_off = time+0.0625*day;CTLA4mAb = CTLA4mAb_Dose*EndTherapy	CTLA4 counter for dosing

Trigger	Event Functions	Description
CTLA4_counter_off<=time	CTLA4_counter_on = time+Dose_sched_CTLA4 - 0.0625*day;CTLA4mAb = 0*(mg/kg)	CTLA4 counter for dosing
time>=CTLA4_change_schedule	CTLA4mAb = 0*(mg/kg);CTLA4mAb_Dose = CTLA4mAb_New_Dose;New_sched_CTLA4 = 365*day + time;Dose_sched_CTLA4 = New_sched_CTLA4	CTLA4 change schedule for dosing
PD1_counter_on<=time	PD1_counter_off = time+0.0416666*day;PD1mAb = PD1mAb_Dose*EndTherapy	PD1 counter for dosing
PD1_counter_off<=time	PD1_counter_on = time+Dose_sched_PD1 - 0.0416666*day;PD1mAb = 0*(mg/kg)	PD1 counter for dosing
time>=PD1_change_schedule	PD1mAb = 0*(mg/kg);PD1mAb_Dose = PD1mAb_New_Dose;Dose_sched_PD1 = New_sched_PD1;PD1_change_schedule = 1500*day	PD1 change schedule for dosing
PDL1_counter_off<=time	PDL1_counter_on = time+Dose_sched_PDL1 - 0.0416666*day;PDL1mAb = 0*(mg/kg)	PDL1 counter for dosing
time>=PDL1_change_schedule	PDL1mAb = 0*(mg/kg);PDL1mAb_Dose = PDL1mAb_New_Dose;Dose_sched_PDL1 = New_sched_PDL1;PDL1_change_schedule = 1500*day	PDL1 change schedule for dosing
PDL1_counter_on<=time	PDL1_counter_off = time+0.0416666*day;PDL1mAb = PDL1mAb_Dose*EndTherapy	PDL1 counter for dosing
Cancer<=1*mole	TheEnd = 0	End extravasation at tumor death
Cancer<=1.446759259259259e+05*mole	EndTherapy = 0;Time_Tumor_Death = time	Stop therapy at tumor death
Cancer_Diam_mm>=Cancer_mm_Start_Therapy	CTLA4mAb_Dose = CTLA4_DoseSet*(mg/kg);CTLA4_counter_on = time+0.0001*day;CTLA4_counter_off = CTLA4_counter_on + 0.0625*day;CTLA4_change_schedule = time + 64*day;Cancer_mm_Start_Therapy = Cancer_mm_Start_Therapy*100;Time_Start_Therapy = time;TCytokineHoming = 100	CTLA4 dosing
Cancer_Diam_mm>=Cancer_mm_Start_Therapy	CTLA4mAb_Dose = CTLA4_DoseSet* (mg/kg);CTLA4_counter_on = time+0.0001*day;CTLA4_counter_off = CTLA4_counter_on + 0.0625*day;CTLA4_change_schedule = time + 64*day;PD1_counter_on = time+0.0001*day;PD1_counter_off = PD1_counter_on + 0.0416666*day;PD1mAb_Dose = PD1_DoseSet* (mg/kg);PD1_change_schedule = time + 64*day;Cancer_mm_Start_Therapy = Cancer_mm_Start_Therapy*100;Time_Start_Therapy = time;TCytokineHoming = 100	CTLA4 and PD1 dosing
Cancer_Diam_mm>=Cancer_mm_Start_Therapy	CTLA4mAb_Dose = CTLA4_DoseSet* (mg/kg);CTLA4_counter_on = time+0.0001*day;CTLA4_counter_off = CTLA4_counter_on + 0.0625*day;CTLA4_change_schedule = time + 64*day;PD1_counter_on = time+85.0001*day;PD1_counter_off = PD1_counter_on + 0.0416666*day;PD1mAb_Dose = PD1_DoseSet* (mg/kg);Cancer_mm_Start_Therapy = Cancer_mm_Start_Therapy*100;Time_Start_Therapy = time;TCytokineHoming = 100	CTLA4 then PD1 dosing
Cancer_Diam_mm>=Cancer_mm_Start_Therapy && time<=150*day	PD1mAb_Dose = PD1_DoseSet* (mg/kg);PD1_counter_on = time+0.0001*day;PD1_counter_off = PD1_counter_on + 0.0416666*day;PD1_change_schedule = time + 71.0001*day;CTLA4_counter_on = time+85.0001*day;CTLA4_counter_off = CTLA4_counter_on + 0.0625*day;CTLA4_change_schedule = time + 64*day + 85.0001*day;CTLA4mAb_Dose = CTLA4_DoseSet* (mg/kg);Cancer_mm_Start_Therapy = Cancer_mm_Start_Therapy*100;Time_Start_Therapy = time;TCytokineHoming = 100	PD1 then CTLA4 dosing: set CTLA4 and PD1 dosing

Trigger	Event Functions	Description
Cancer_Diam_mm>=Cancer_mm_Start_Therapy	PD1_counter_on = time+0.0001*day;PD1_counter_off = PD1_counter_on + 0.0416666*day;PD1mAb_Dose = PD1_DoseSet*(mg/kg);Cancer_mm_Start_Therapy = Cancer_mm_Start_Therapy*100;Time_Start_Therapy = time;TCytokineHoming = 100	PD1 dosing
Cancer_Diam_mm>=Cancer_mm_Start_Therapy	PDL1mAb_Dose = PDL1_DoseSet* (mg/kg);PD1mAb_Dose = PD1_DoseSet* (mg/kg);PDL1_counter_on = time+0.0001*day;PD1_counter_on = time+0.0001*day;PDL1_counter_off = PDL1_counter_on + 0.0416666*day;PD1_counter_off = PD1_counter_on + 0.0416666*day;Cancer_mm_Start_Therapy = Cancer_mm_Start_Therapy*100;Time_Start_Therapy = time;TCytokineHoming = 100	PD1 and PDL1 dosing
Cancer_Diam_mm>=Cancer_mm_Start_Therapy	PDL1_counter_on = time+0.0001*day;PDL1_counter_off = PDL1_counter_on + 0.0416666*day;PDL1mAb_Dose = PDL1_DoseSet*(mg/kg);Cancer_mm_Start_Therapy = Cancer_mm_Start_Therapy*100;Time_Start_Therapy = time;TCytokineHoming = 100	PDL1 dosing
Cancer_Diam_mm>=Cancer_mm_Start_Therapy	CTLA4mAb_Dose = CTLA4_DoseSet* (mg/kg);CTLA4_counter_on = time+0.0001*day;CTLA4_counter_off = CTLA4_counter_on + 0.0625*day;CTLA4_change_schedule = time + 64*day;PDL1_counter_on = time+0.0001*day;PDL1_counter_off = PDL1_counter_on + 0.0416666*day;PDL1mAb_Dose = PDL1_DoseSet* (mg/kg);PDL1_change_schedule = time + 64*day;Cancer_mm_Start_Therapy = Cancer_mm_Start_Therapy*100;Time_Start_Therapy = time;TCytokineHoming = 100	CTLA4 and PDL1 dosing
Cancer_Diam_mm>=Cancer_mm_Start_Therapy	CTLA4mAb_Dose = CTLA4_DoseSet* (mg/kg);CTLA4_counter_on = time+0.0001*day;CTLA4_counter_off = CTLA4_counter_on + 0.0625*day;CTLA4_change_schedule = time + 64*day;PDL1_counter_on = time+0.0001*day;PDL1_counter_off = PDL1_counter_on + 0.0416666*day;PDL1mAb_Dose = PDL1_DoseSet* (mg/kg);PDL1_change_schedule = time + 64*day;PD1_counter_on = time+0.0001*day;PD1_counter_off = PD1_counter_on + 0.0416666*day;PD1mAb_Dose = PD1_DoseSet* (mg/kg);PD1_change_schedule = time + 64*day;Cancer_mm_Start_Therapy = Cancer_mm_Start_Therapy*100;Time_Start_Therapy = time;TCytokineHoming = 100	CTLA4, PD1 and PDL1 dosing
time>=Time_Start_Therapy + 163*day	PD1mAb_New_Dose = PD1_DoseSet* (mg/kg);PD1_change_schedule = 2000*day;PD1mAb_Dose = PD1_DoseSet* (mg/kg);TCytokineHoming = 100	PD1 then CTLA4 therapy: set delayed PD1 dosing
Cancer_Diam_mm>=Cancer_mm_Start_Therapy	Time_Start_Therapy = time	Time to start therapy once tumor diameter reaches a certain threshold

Table S7 – Model Discontinuous Equation Sets (End)

Table S8 – Model Compartment Volumes (Start)

Compartment	Variable	Volume	Units	Reference	Description
Blood-Lymph	Vc_CTLA4	2.727814034	liter	[15]	Volume of the central compartment for Anti-CTLA-4
Blood-Lymph	Vc_PD1	2.716739643	liter	[25]	Volume of the central compartment for Anti-PD-1
Blood-Lymph	Vc_PDL1	4.051599814	liter	[26, 27]	Volume of the central compartment for Anti-PD-L1

Compartment	Variable	Volume	Units	Reference	Description
Blood-Lymph	Vc_Teff	2.7	liter	[13, 93]	Volume of blood through which Effector T cells circulate throughout the body
Liv_Spln_GI	Vv_GI	43	ml	[13]	Vasculature volume of GI for Effector T cell trafficking
Liv_Spln_GI	Vext_Liver	361.8	ml	[13]	Volume of Liver interstitium for Effector T cell trafficking
Liv_Spln_GI	Vv_Liver	180.9	ml	[13]	Vasculature volume of Liver for Effector T cell trafficking
Liv_Spln_GI	Vext_Spleen	34.7	ml	[13]	Volume of Spleen interstitium for Effector T cell trafficking
Liv_Spln_GI	Vv_Spleen	17	ml	[13]	Vasculature volume of Spleen for Effector T cell trafficking
Lungs	Vext_Lungs	299.7	ml	[13]	Volume of Lungs interstitium for Effector T cell trafficking
Lungs	Vv_Lungs	99.9	ml	[13]	Vasculature volume of Lungs for Effector T cell trafficking
Lymph_Node	Vext_LN	34.7	ml	[13]	Volume of Lymph Node interstitium for Effector T cell trafficking
Lymph_Node	VL	5.2	liter	[56, 94]	Volume of total Lymph for antibody PK
Lymph_Node	Vtdln	5.2	liter	[56, 94]	Volume of total Lymph for antibody PK
Lymph_Node	Vv_LN	17	ml	[13]	Vasculature volume of Lymph Node for Effector T cell trafficking
Peripheral	ISF	15.9	liter	[56]	Volume of interstitial fluid (ISF) is tissues for antibody PK
Peripheral	Vv_Periph	1355.4	ml	[13]	Vasculature volume of Peripheral (other tissue not accounted for) for Effector T cell trafficking
Tumor	Vex_Tmr	~50% (void space) of total tumor volume	ml	[13] Calculated dynamically	Volume of Tumor interstitium
Tumor	Vt_Teff	Based on Cancer_Vol_cm3	liter	Calculated dynamically	Total tumor volume calculated from cancer cell number, void space and tumor vasculature
Tumor	Vv_Tmr	~7% of total tumor volume	ml	[13] Calculated dynamically	Vasculature volume of Tumor based on fraction of total tumor volume

Table S8 – Model Compartment Volumes (End)

Table S9 – Parameters Varied in Virtual Clinical Trials (Start)

Parameter Name in Model	Value Range	Units	Source	Description
%PDL1_Exp_Cancer	40-90; Median: 75	dimensionless	[11]	Percent of cancer cells of total cancer cells that are PD-L1 positive that interact with the Effector T cells in the tumor compartment.
%T_Tregs_per_Cancer	0-0.25; Median: 0.13	dimensionless	Assumed as recruited by tumor	Defines the percentage of Regulatory T cells in the tumor compartment as a percent of total tumor cells.
%_Tr_LN	5-35; Median: 20	dimensionless	[1, 3-5]	Percent Regulatory T cells of total T cells in each lymph node.
Antigen_Intensity	Assigned from 0.8-1.0 for melanoma (on a scale of 0.1-1.0); Median: 0.9	dimensionless	Upper range of cancer types [14]	Defines the strength of the TAA/TSA that are involved in priming of the T cells in the lymph nodes. Also known as antigen strength.
AntSpread	x = 2 (Where it is used as 10^x)	dimensionless	Estimated during fitting to anti-PD-1 data	Sets the number of TAA/TSA released per cancer cell upon natural death and decay or following cytotoxic killing. The value is used to set a multiple of cancer cells in the formation of debris for APC maturation.
Cancer_mm_Start_Therapy	15-80; Median: 40	mm	Approximated based on reported literature range	Diameter of the tumor when to start the therapeutic regimen.
Chemokine	100	dimensionless	Estimated during fitting to anti-PD-1 data	The chemokine factor to promote extravasation of effector T cells into the tumor.

Parameter Name in Model	Value Range	Units	Source	Description
T_Cell_Clonality	10-130; Median: 70	cell	[28, 30, 85]	Number of Naïve T cells populations specific for different tumor antigens; in other words; the number of anti-tumor T cell clones in each lymph node.

Table S9 – Parameters Varied in Virtual Clinical Trials (End)

Table S10 – Parameters Varied in Sensitivity Analysis (Start)

Parameter Name in Model	Value Range	Units	Source	Description
%CD80_Exp_Cancer	1-100	dimensionless	[6-8]	Percent of cancer cells of total cancer cells that are CD80 positive that interact with the Effector T cells in the tumor compartment.
%PD1_Exp_Cancer	1-100	dimensionless	[9]	Percent of cancer cells of total cancer cells that are PD-1 positive that interact with the Effector T cells in the tumor compartment.
%PDL1_Exp_Cancer	1-100	dimensionless	[11]	Percent of cancer cells of total cancer cells that are PD-L1 positive that interact with the Effector T cells in the tumor compartment.
%PDL2_Exp_Cancer	1-100	dimensionless	[12]	Percent of cancer cells of total cancer cells that are PD-L2 positive that interact with the Effector T cells in the tumor compartment.
%T_Tregs_per_Cancer	0-0.25	dimensionless	Assumed as recruited by tumor	Defines the percentage of Regulatory T cells in the tumor compartment as a percent of total tumor cells.
%_Tr_LN	5-35	dimensionless	[1, 3-5]	Percent Regulatory T cells of total T cells in each lymph node.
Antigen_Intensity	Assigned from 0.8-1.0 for melanoma (on a scale of 0.1-1.0)	dimensionless	Upper range of cancer types [14]	Defines the strength of the TAA/TSA that are involved in priming of the T cells in the lymph nodes. Also known as antigen strength.
AntSpread	x = 1-5 (Where it is used as 10^x)	dimensionless	Estimated during fitting to anti-PD-1 data and varied across range	Sets the number of TAA/TSA released per cancer cell upon natural death and decay or following cytotoxic killing. The value is used to set a multiple of cancer cells in the formation of debris for APC maturation.
Cancer_mm_Start_Therapy	5-80	mm	Assigned based on reported literature range	Longest diameter of the tumor when to start the therapeutic regimen.
Chemokine	50-500	dimensionless	Estimated during anti-PD-1 therapy fitting; varied in sensitivity analysis	The chemokine factor to promote extravasation of effector T cells into the tumor.
CTLA4_DoseSet	0.3-10	mg/kg	Based on regimen	Dose of anti-CTLA-4 therapy
mAPC_activation_level	0.1-1.0	dimensionless	[13]	The fraction of CD80 and CD86 expression on the mAPCs from 0.1-1.
mAPC_Debis_T_Inact	0.05-0.95	dimensionless	Varied across range (5-95%) and estimated during fitting to anti-PD-1 data	The fraction of tumor debris that is considered to not be transported to the lymph nodes and is removed from the system.
PD1_DoseSet	0.03-2	mg/kg	Based on regimen	Dose administered of anti-PD-1 therapy.
PDL1_DoseSet	0.003-0.1	mg/kg	Based on regimen	Dose administered of anti-PD-L1 therapy.
Rate_Tumor_Growth	64-144 day doubling time	1/day	[81]	Proliferation rate of cancer cells that defines the volumetric doubling time of the tumor. 64 day metastatic doubling: 0.010955675075414 144 day non-metastatic doubling: 0.004913635262592.

Parameter Name in Model	Value Range	Units	Source	Description
T_Cell_Clonality	5-130	cell	[28, 30, 85]	Number of Naïve T cells populations specific for different tumor antigens; in other words; the number of anti-tumor T cell clones in each lymph node.

Table S10 Parameters Varied in Sensitivity Analysis (End)

Table S11 – Conditions Specific to Each Clinical Scenario Simulated (Start)

Fig.	Tiral	Dose/Regimen	Patients Simulated	Parameter ranges and medians
2	Anti-PD-1	3 mg/kg, Q2W	200	Same for all simulations: Table S9 for references and ranges. Latin Hypercube Sampling (LHS) with equal distribution was utilized for simulations.
3	Anti-PD-1 with Anti-CTLA-4	3 mg/kg anti-CTLA-4 and 1 mg/kg anti-PD-1 Q3W, 4 doses combo; while anti-PD-1, 8 doses; then, combo Q12W	47	
4	Anti-PD-L1	20 mg/kg, Q2W	200	
5	Anti-PD-1 and Anti-CTLA-4 Sequential Therapy	3 mg/kg anti-CTLA-4 and 3 mg/kg anti-PD-1 a) Q3W anti-CTLA-4, 4 doses; Q2W anti-PD-1 b) Q2W anti-PD-1, 6 doses; Q3W anti-CTLA-4, 4 doses; Q2W anti-PD-1	200	
S1	Anti-CTLA-4	3 and 10 mg/kg, Q3W, 4 doses; then, Q12W	200	
S2	Anti-PD-L1 with Anti-CTLA-4	1 mg/kg anti-CTLA-4 and 20 mg/kg anti-PD-L1 Q3W, 4 doses combo; anti-PD-L1 Q2W	200	
S3	Anti-PD-1 with Anti-PD-L1	3 mg/kg anti-PD-1 and 20 mg/kg anti-PD-L1, Q2W	200	

Table S11 – Conditions Specific to Each Clinical Scenario Simulated (End)

References:

1. Battaglia, A., et al., *Lymphocyte populations in human lymph nodes. Alterations in CD4+ CD25+ T regulatory cell phenotype and T-cell receptor Vß repertoire.* Immunology, 2003. **110**(3): p. 304-12.
2. Backteman, K., et al., *Lymphocyte subpopulations in lymph nodes and peripheral blood: a comparison between patients with stable angina and acute coronary syndrome.* PLoS One, 2012. **7**(3): p. e32691.
3. Höfer, T., O. Krichevsky, and G. Altan-Bonnet, *Competition for IL-2 between Regulatory and Effector T Cells to Chisel Immune Responses.* Front Immunol., 2012. **3**: p. 1-9.
4. Viguier, M., et al., *Foxp3 Expressing CD4+CD25high Regulatory T Cells Are Overrepresented in Human Metastatic Melanoma Lymph Nodes and Inhibit the Function of Infiltrating T Cells.* J Immunol., 2004. **173**(2): p. 1444-53.
5. Jandus, C., et al., *Selective accumulation of differentiated FOXP3+ CD4+ T cells in metastatic tumor lesions from melanoma patients compared to peripheral blood.* Cancer Immunol Immunother., 2008. **57**(12): p. 1795-805.
6. Tirapu, I., et al., *Low surface expression of B7-1 (CD80) is an immunoescape mechanism of colon carcinoma.* Cancer Res., 2006. **66**(4): p. 2442-50.
7. *CD80 in Melanoma*. 2015; Available from: http://www.proteinatlas.org/ENSG00000121594-CD80/cancer/tissue/melanoma.
8. Uhlén, M., et al., *Proteomics. Tissue-based map of the human proteome.* Science, 2015. **347**(6220): p. 1260419.

9. Kleffel, S., et al., *Melanoma cell-intrinsic PD-1 receptor functions promote tumor growth.* Cell, 2015. **162**(6): p. 1242-56.
10. Chemnitz, J.M., et al., *SHP-1 and SHP-2 associate with immunoreceptor tyrosine-based switch motif of programmed death 1 upon primary human T cell stimulation, but only receptor ligation prevents T cell activation.* J Immunol., 2004. **173**(2): p. 945-54.
11. Madore, J., et al., *PD-L1 expression in melanoma shows marked heterogeneity within and between patients: implications for anti-PD-1/PD-L1 clinical trials.* Pigment Cell Melanoma Res., 2015. **28**(3): p. 245-53.
12. Obeid, J.M., et al., *PD-L1, PD-L2 and PD-1 expression in metastatic melanoma: Correlation with tumor-infiltrating immune cells and clinical outcome.* Oncoimmunology, 2016. **5**(11): p. e1235107.
13. Zhu, H., et al., *Physiologically based kinetic model of effector cell biodistribution in mammals: implications for adoptive immunotherapy.* Cancer Res., 1996. **56**(16): p. 3771-81.
14. Yarchoan, M., A. Hopkins, and E.M. Jaffee, *Tumor Mutational Burden and Response Rate to PD-1 Inhibition.* N Engl J Med., 2017. **377**(25): p. 2500-2501.
15. Feng, Y., et al., *Model-based clinical pharmacology profiling of ipilimumab in patients with advanced melanoma.* Br J Clin Pharmacol., 2014. **78**(1): p. 106-17.
16. Lyng, H., O. Haraldseth, and E.K. Rofstad, *Measurement of Cell Density and Necrotic Fraction in Human Melanoma Xenografts by Diffusion Weighted Magnetic Resonance Imaging.* Magn Reson Med., 2000. **43**(6): p. 828-36.
17. Thurber, G.M., M.M. Schmidt, and K.D. Wittrup, *Antibody tumor penetration: transport opposed by systemic and antigen-mediated clearance.* Adv Drug Deliv Rev., 2008. **60**(12): p. 1421-34.
18. Ritter, A.T., et al., *Actin Depletion Initiates Events Leading to Granule Secretion at the Immunological Synapse.* Immunity, 2015. **42**(5): p. 864-76.
19. Miller, M.J., et al., *T cell repertoire scanning is promoted by dynamic dendritic cell behavior and random T cell motility in the lymph node.* Proc Natl Acad Sci U S A., 2004. **101**(4): p. 998–1003.
20. Mrass, P., et al., *Random migration precedes stable target cell interactions of tumor-infiltrating T cells.* J Exp Med., 2006. **203**(12): p. 2749-61.
21. Ewa Bryl, et al., *Modulation of CD28 expression with anti-tumor necrosis factor alpha therapy in rheumatoid arthritis.* Arthritis Rheum., 2005. **52**(10): p. 2996-3003.
22. Unternaehrer, J.J., et al., *The tetraspanin CD9 mediates lateral association of MHC class II molecules on the dendritic cell surface.* Proc Natl Acad Sci U S A., 2007. **104**(1): p. 234-9.
23. Haile, S.T., et al., *Tumor Cell Programmed Death Ligand 1-Mediated T Cell Suppression Is Overcome by Coexpression of CD80.* J Immunol., 2011. **186**(12): p. 6822-9.
24. Tatari-Calderone, Z., et al., *Acquisition of CD80 by human T cells at early stages of activation: functional involvement of CD80 acquisition in T cell to T cell interaction.* J Immunol., 2002. **169**(11): p. 6162-9.
25. BMS, *Clinical Pharmacology BLA Review - Opdivo (nivolumab)*. 2014, CENTER FOR DRUG EVALUATION AND RESEARCH (CDER): CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S). p. 1-28.
26. Cogswell, J.P., et al., *Cancer immunotherapy by disrupting pd-1/pd-l1 signaling*. 2013, Google Patents.
27. Deng, R., et al., *Preclinical pharmacokinetics, pharmacodynamics, tissue distribution, and tumor penetration of anti-PD-L1 monoclonal antibody, an immune checkpoint inhibitor.* MAbs, 2016. **8**(3): p. 593-603.
28. Qia, Q., et al., *Diversity and clonal selection in the human T-cell repertoire.* Proc Natl Acad Sci U S A., 2014. **111**(36): p. 13139–44.

29. Jenkins, M.K. and J.J. Moon, *The Role of Naive T Cell Precursor Frequency and Recruitment in Dictating Immune Response Magnitude.* J Immunol., 2012. **188**(9): p. 4135-40.
30. Zarnitsyna, V.I., et al., *Estimating the diversity, completeness, and cross-reactivity of the T cell repertoire.* Front Immunol., 2013. **4**.
31. Egen, J.G. and J.P. Allison, *Cytotoxic T Lymphocyte Antigen-4 Accumulation in the Immunological Synapse Is Regulated by TCR Signal Strength.* Immunity, 2002. **16**(1): p. 23-35.
32. Linsley, P.S., et al., *Coexpression and functional cooperation of CTLA-4 and CD28 on activated T lymphocytes.* J Exp Med., 1992. **176**(6): p. 1595-604.
33. Read S, G.R., Izcue A, Robinson N, Mandelbrot D, Francisco L, Sharpe AH, Powrie F, *Blockade of CTLA-4 on CD4+CD25+ regulatory T cells abrogates their function in vivo.* J Immunol., 2006. **177**(7): p. 4376-83.
34. Palsson, S., et al., *The development of a fully-integrated immune response model (FIRM) simulator of the immune response through integration of multiple subset models.* BMC Syst Biol., 2013. **7**.
35. De Boer RJ, H.P., Dullens HF, De Weger RA, Den Otter W., *Macrophage T lymphocyte interactions in the anti-tumor immune response: a mathematical model.* J Immunol., 1985. **134**(4): p. 2748-58.
36. Kanehisa, M., et al., *KEGG: new perspectives on genomes, pathways, diseases and drugs.* Nucleic Acids Res., 2017. **45**(D1): p. D353-D361.
37. Kanehisa, M., et al., *KEGG as a reference resource for gene and protein annotation.* Nucleic Acids Res., 2016. **44**(D1): p. D457-62.
38. Kanehisa, M. and S. Goto, *KEGG: kyoto encyclopedia of genes and genomes.* Nucleic Acids Res., 2000. **28**(1): p. 27-30.
39. Wikipedia contributors. *Durvalumab*. 2016 8 December 2016 18:37 UTC; Available from: https://en.wikipedia.org/wiki/Durvalumab.
40. Henrickson, S.E., et al., *T cell sensing of antigen dose governs interactive behavior with dendritic cells and sets a threshold for T cell activation.* Nat Immunol., 2008. **9**(3): p. 282-291.
41. Marino, S. and D.E. Kirschner, *The human immune response to Mycobacterium tuberculosis in lung and lymph node.* J Theor Biol., 2004. **227**(4): p. 463-86.
42. Klebanoff, C.A., L. Gattinoni, and N.P. Restif, *CD8+ T-cell memory in tumor immunology and immunotherapy.* Immunol Rev., 2006. **211**: p. 214-24.
43. Northrop, J.K. and H. Shen, *CD8+ T-cell memory: only the good ones last.* Curr Opin Immunol., 2004. **16**(4): p. 451-5.
44. Macallan, D.C., et al., *Rapid Turnover of Effector–Memory CD4+ T Cells in Healthy Humans.* J Exp Med., 2004. **200**(2): p. 255-60.
45. De Boer RJ, et al., *Turnover rates of B cells, T cells, and NK cells in simian immunodeficiency virus-infected and uninfected rhesus macaques.* J Immunol., 2003. **170**(5): p. 2479-87.
46. Qureshi, O.S., et al., *Constitutive Clathrin-mediated Endocytosis of CTLA-4 Persists during T Cell Activation.* J Biol Chem., 2012. **287**(12): p. 9429-40.
47. Kaur, S., O.S. Qureshi, and D.M. Sansom, *Comparison of the Intracellular Trafficking Itinerary of CTLA-4 Orthologues.* PLoS One, 2013. **8**(4): p. e60903.
48. Pentcheva-Hoang, T., et al., *Programmed death-1 concentration at the immunological synapse is determined by ligand affinity and availability.* Proc Natl Acad Sci U S A., 2007. **104**(45): p. 17765-70.
49. Linsley, P.S., et al., *Intracellular Trafficking of CTLA-4 and Focal Localization Towards Sites of TCR Engagement.* Immunity, 1996. **4**(6): p. 535-43.
50. Jafarnejad, M., et al., *Modeling Lymph Flow and Fluid Exchange with Blood Vessels in Lymph Nodes.* Lymphat Res Biol., 2015. **13**(4): p. 234-247.

51. Pillis, L.G.d., A.E. Radunskaya, and C.L. Wiseman, *A validated mathematical model of cell-mediated immune response to tumor growth.* Cancer Res., 2005. **65**(17): p. 7950-8.
52. Patel, S.P. and S.E. Woodman, *Profile of ipilimumab and its role in the treatment of metastatic melanoma.* Drug Des Devel Ther., 2011. **5**: p. 489-95.
53. Wikipedia contributors. *Ipilimumab*. 2017 26 February 2017 03:23 UTC; Available from: https://en.wikipedia.org/w/index.php?title=Ipilimumab&oldid=767469815.
54. Wild, M.K., et al., *Dependence of T Cell Antigen Recognition on the Dimensions of an Accessory Receptor–Ligand Complex.* J Exp Med., 1999. **190**(1): p. 31-41.
55. Burroughs, N.J. and C. Wulfing, *Differential Segregation in a Cell-Cell Contact Interface: The Dynamics of the Immunological Synapse.* Biophys J., 2002. **83**(4): p. 1784-96.
56. Cao, Y., J.P. Balthasar, and W.J. Jusko, *Second-generation minimal physiologically-based pharmacokinetic model for monoclonal antibodies.* J Pharmacokinet Pharmacodyn., 2013. **40**(5): p. 597-607.
57. Ruedl C, K.P., Bachmann M, Hess M, Karjalainen K., *Anatomical origin of dendritic cells determines their life span in peripheral lymph nodes.* 165, 2000. **9**(4910-6).
58. Domínguez PM, A.C., *Differentiation and function of mouse monocyte-derived dendritic cells in steady state and inflammation.* Immunol Rev., 2010. **234**(1): p. 90-104.
59. Henrickson, S.E., et al., *In vivo imaging of T cell priming.* Sci Signal, 2008. **1**(12): p. pt2.
60. Mempel, T.R., S.E. Henrickson, and U.H.v. Andrian, *T-cell priming by dendritic cells in lymph nodes occurs in three distinct phases.* Nature, 2004. **427**(6970): p. 154-9.
61. Stoll, S., et al., *Dynamic imaging of T cell-dendritic cell interactions in lymph nodes.* Science, 2002. **296**(5574): p. 1873-6.
62. Miller, M.J., et al., *Imaging the Single Cell Dynamics of CD4+ T Cell Activation by Dendritic Cells in Lymph Nodes.* J Exp Med., 2004. **200**(7): p. 847-56.
63. Baverel, P.G., et al., *Population Pharmacokinetics of Durvalumab in Cancer Patients and Association With Longitudinal Biomarkers of Disease Status.* Clin Pharmacol Ther., 2018. **103**(4): p. 631-642.
64. Collins, A.V., et al., *The Interaction Properties of Costimulatory Molecules Revisited.* Immunity, 2002. **17**(2): p. 201-10.
65. EMA, *Assessment Report For Yervoy (ipilimumab)* 2011, European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use (CHMP).
66. Cheng, X., et al., *Structure and Interactions of the Human Programmed Cell Death 1 Receptor.* J Biol Chem., 2013. **288**(17): p. 11771-85.
67. EMA, *Nivolumab BMS, INN-nivolumab*. 2015, European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use (CHMP).
68. Finley, S.D., et al., *Pharmacokinetics and pharmacodynamics of VEGF-neutralizing antibodies.* BMC Syst Biol. , 2011. **5**.
69. Norbury, C.C., et al., *Visualizing priming of virus-specific CD8+ T cells by infected dendritic cells in vivo.* Nat Immunol., 2002. **3**(3): p. 265-71.
70. Haghighi, H.R., et al., *Identification of a Dual-Specific T Cell Epitope of the Hemagglutinin Antigen of an H5 Avian Influenza Virus in Chickens.* PLoS ONE, 2009. **4**(11): p. e7772.
71. Sims, T.N., et al., *Opposing effects of PKCtheta and WASp on symmetry breaking and relocation of the immunological synapse.* Cell, 2007. **129**(4): p. 773-85.
72. Celli, S., et al., *How many dendritic cells are required to initiate a T-cell response?* Blood, 2012. **120**(19): p. 3945-8.
73. Currana, M.A., et al., *PD-1 and CTLA-4 combination blockade expands infiltrating T cells and reduces regulatory T and myeloid cells within B16 melanoma tumors.* Proc Natl Acad Sci U S A., 2010. **107**(9): p. 4275-80.

74. Wikipedia contributors. *Nivolumab*. 2017 27 February 2017 13:59 UTC; Available from: https://en.wikipedia.org/wiki/Nivolumab.
75. Farzad, Z., et al., *Lymphocyte subset alterations in nodes regional to human melanoma.* Cancer Res., 1990. **50**(12): p. 3585-8.
76. Willard-Mack, C.L., *Normal Structure, Function, and Histology of Lymph Nodes.* Toxicol Pathol., 2006. **34**(5): p. 409-24.
77. Native American Cancer Researc (NACR). *Introduction to Lymphedema Branch*. 2016; Available from: http://natamcancer.org/lymphedema-intro.html.
78. Wikipedia contributors. *List of lymph nodes of the human body*. 2016 11 December 2016 00:14 UTC; Available from: https://en.wikipedia.org/wiki/List_of_lymph_nodes_of_the_human_body.
79. Bousso, P. and E. Robey, *Dynamics of CD8+ T cell priming by dendritic cells in intact lymph nodes.* Nat Immunol., 2003. **4**(6): p. 579-85.
80. Lee, K.-H., et al., *T cell receptor signaling precedes immunological synapse formation.* Science, 2002. **295**(5559): p. 1539-42.
81. Carlson, J.A., *Tumor doubling time of cutaneous melanoma and its metastasis.* Am J Dermatopathol., 2003. **25**(4): p. 291-9.
82. Bousso, P., *T-cell activation by dendritic cells in the lymph node: lessons from the movies.* Nat Rev Immunol., 2008. **8**(9): p. 675-84.
83. Obst, R., *The timing of T cell priming and cycling.* Front Immunol., 2015. **6**.
84. Castellino, F., et al., *Chemokines enhance immunity by guiding naive CD81 T cells to sites of CD41 T cell–dendritic cell interaction.* Nature, 2006. **440**(7086): p. 890-5.
85. Tumeh, P.C., et al., *PD-1 blockade induces responses by inhibiting adaptive immune resistance.* Nature, 2014. **515**(7528): p. 568-71.
86. Miller, M.J., et al., *Two-Photon Imaging of Lymphocyte Motility and Antigen Response in Intact Lymph Node.* Science, 2002. **296**(5574): p. 1869-73.
87. Baey, A.d. and A. Lanzavecchia, *The role of aquaporins in dendritic cell macropinocytosis.* J Exp Med., 2000. **191**(4): p. 743-8.
88. Sallusto, F., et al., *Dendritic cells use macropinocytosis and the mannose receptor to concentrate macromolecules in the major histocompatibility complex class II compartment: downregulation by cytokines and bacterial products.* J Exp Med., 1995. **182**(2): p. 389-400.
89. Matheu, M.P., et al., *Imaging regulatory T cell dynamics and suppression of T cell priming mediated by CTLA4.* Nat Commun., 2015. **6**: p. 6219.
90. Papatriantafyllou, M., *Trafficking: Effector T cells cross the line.* Nat Rev Immunol., 2011. **12**(2): p. 74.
91. Shulman, Z., et al., *Transendothelial migration of lymphocytes mediated by intraendothelial vesicle stores rather than by extracellular chemokine depots.* Nat Immunol., 2011. **13**(1): p. 67-76.
92. Voss, B., et al., *Tumor Volume as a Prognostic Factor in Resectable Malignant Melanoma.* Dermatology, 2014. **228**(1): p. 66-70.
93. Dean, L., *Chapter 1, Blood and the cells it contains*, in *Blood Groups and Red Cell Antigens*. 2005, Bethesda (MD): National Center for Biotechnology Information (US): Internet.
94. Baldazzi, V., et al., *Modeling lymphocyte homing and encounters in lymph nodes.* BMC Bioinformatics, 2009. **10**: p. 1-11.

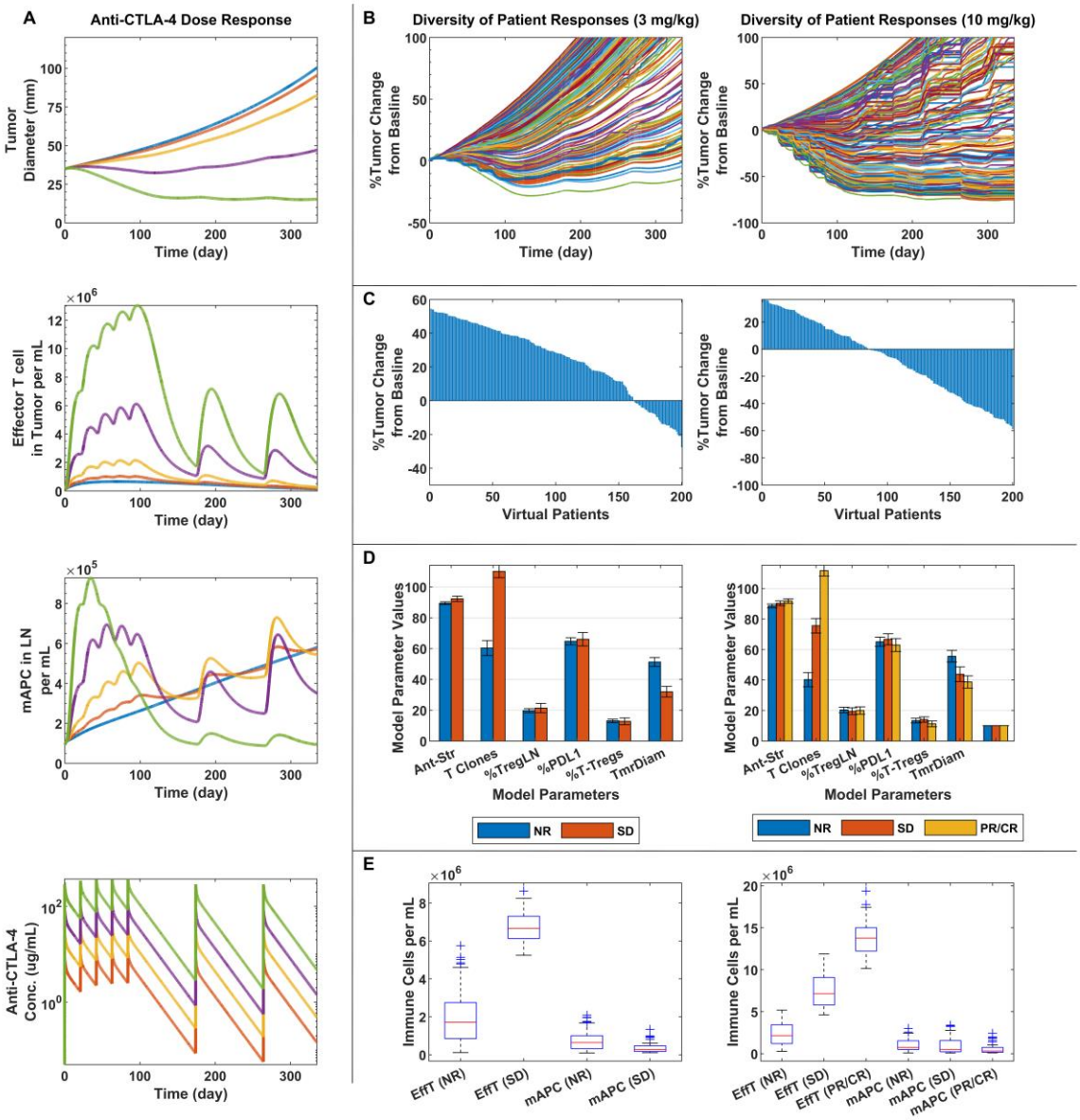

Figure S1. Dose response anti-CTLA-4 mono-therapy. A) From top to bottom: Tumor response to anti-CTLA-4 therapy at doses of 0.3, 1, 3 and 10 mg/kg as represented by the colors in the bottom figure in ascending order; the blue line indicates no therapy in the top figure. Then, Effector T cell density in the tumor (second from the top), mAPC density in the lymph nodes (third from the top) and finally, the PK of anti-CTLA-4 at the given doses. **B)** Diversity of tumor response for 3 mg/kg (left) and 10 mg/kg (right). **C)** Waterfall plot of VPs at 3 mg/kg (left) and 10 mg/kg (right). **D)** Bar graph comparison parameters varied in model for each type of responder at 3 mg/kg (left) and 10 mg/kg (right). **E)** Max Effector T cell density in the tumor and average mAPC density in the lymph nodes for each responder category at 3 mg/kg (left) and 10 mg/kg (right).

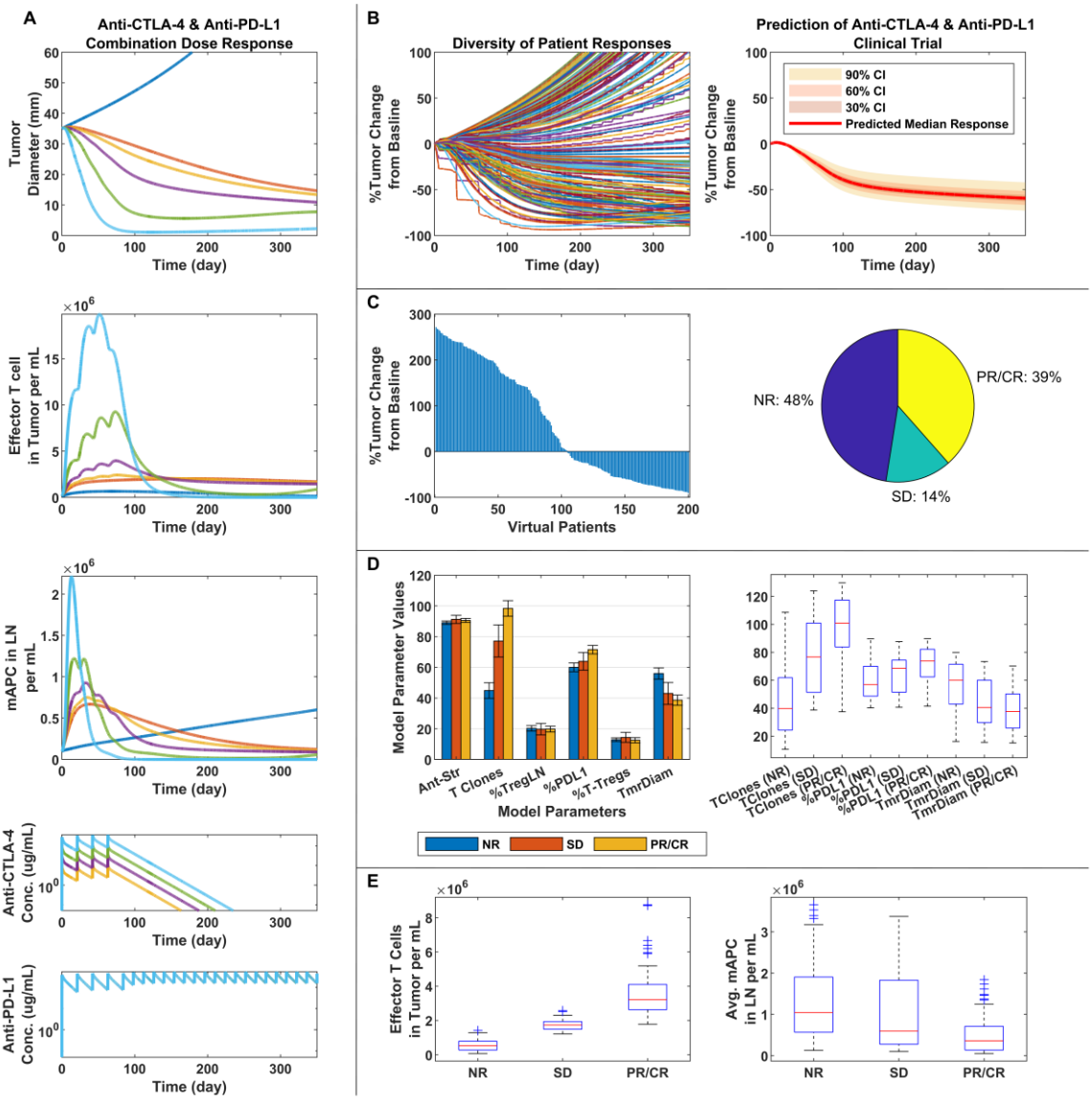

Figure S2. Dose response and clinical validation of anti-CTLA-4/anti-PD-L1 combo-therapy. A) From top to bottom: Tumor response to combination therapy at doses of 0.3, 1, 3 and 10 mg/kg of anti-CTLA-4, as represented by the colors in the second from the bottom figure in ascending order and 20 mg/kg for anti-PD-L1 was used for all simulations; the blue line indicates no therapy (top figure), and orange indicates only anti-PD-L1. Then, Effector T cell density in the tumor (second from the top), mAPC density in the lymph nodes (third from the top) and finally, the PK of anti-CTLA-4 and lastly, anti-PD-L1 at the given doses. For all following figures, 20 mg/kg anti-PD-L1 and 1 mg/kg anti-CTLA-4 were used, following the same regimen. **B)** Diversity of tumor response (left), prediction of median clinical response data (right). **C)** Waterfall plot of VPs (left) and pie chart (right) with percent of virtual non-responders (NR), stable disease (SD) and partial or complete responders (PR/CR). **D)** Bar graph comparison parameters varied in model for each responder type (left) and box plots of significant differentiators (right). **E)** Max

Effector T cell density in the tumor (left) and average mAPC density in the lymph nodes (right) for each responder category.

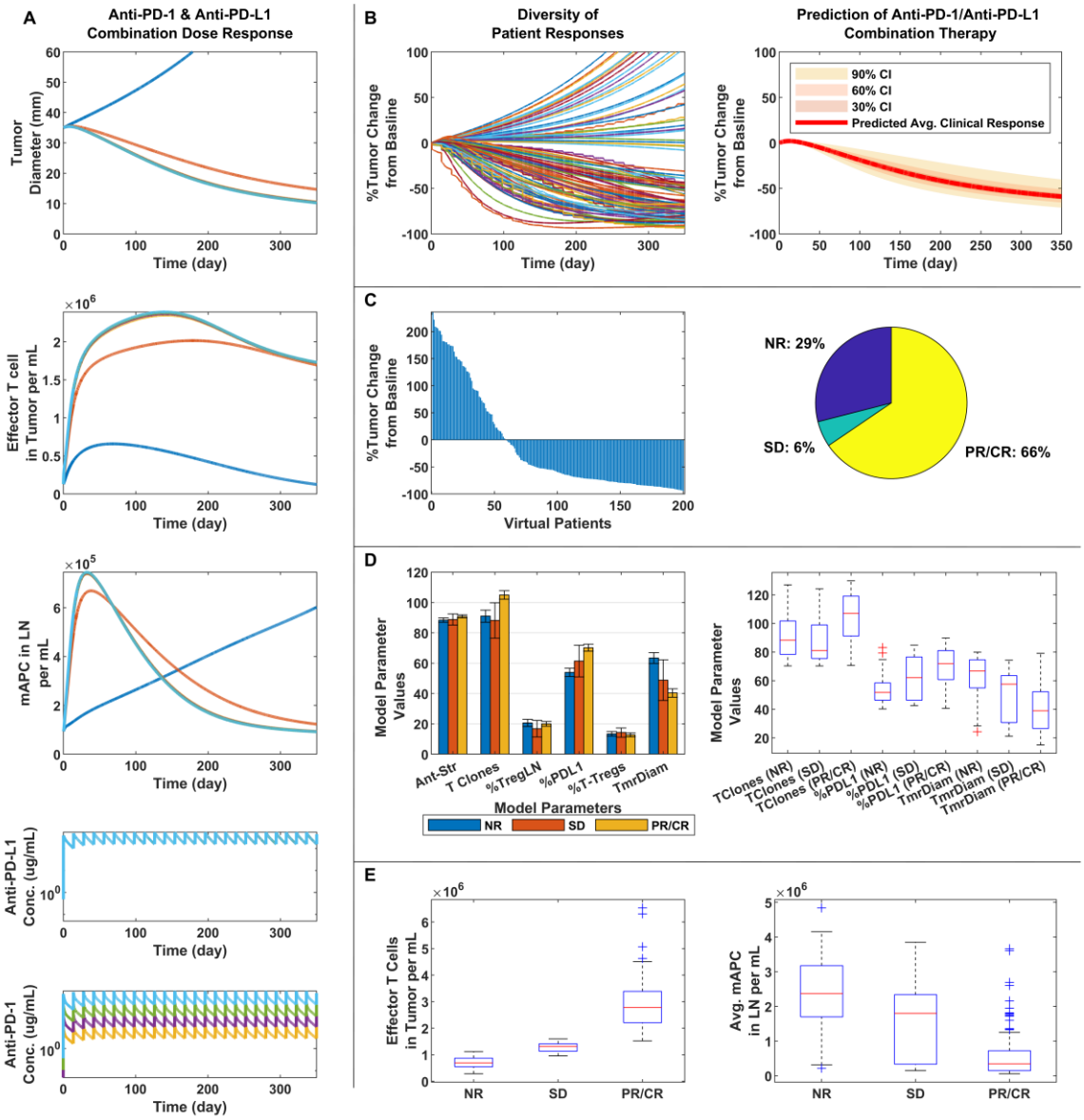

Figure S3. Dose response and clinical validation of anti-PD-1/anti-PD-L1 combo-therapy. A) From top to bottom: Tumor response to combination therapy at doses of 0.3, 1, 3 and 10 mg/kg of anti-PD-1, as represented by the colors in the bottom figure in ascending order and 20 mg/kg for anti-PD-L1 was used for all simulations; the blue line indicates no therapy (top figure), and orange indicates only anti-PD-L1. Then, Effector T cell density in the tumor (second from the top), mAPC density in the lymph nodes (third from the top) and finally, the PK of anti-PD-L1 and lastly, anti-PD-1 at the given doses. For all following

figures, 20 mg/kg anti-PD-L1 and 3 mg/kg anti-PD-1 was used, following the same regimen. **B)** Diversity of tumor response (left), prediction of median clinical response data (right). **C)** Waterfall plot of VPs (left) and pie chart (right) with percent of virtual non-responders (NR), stable disease (SD) and partial or complete responders (PR/CR). **D)** Bar graph comparison parameters varied in model for each responder type (left) and box plots of significant differentiators (right). **E)** Max Effector T cell density in the tumor (left) and average mAPC density in the lymph nodes (right) for each responder category.

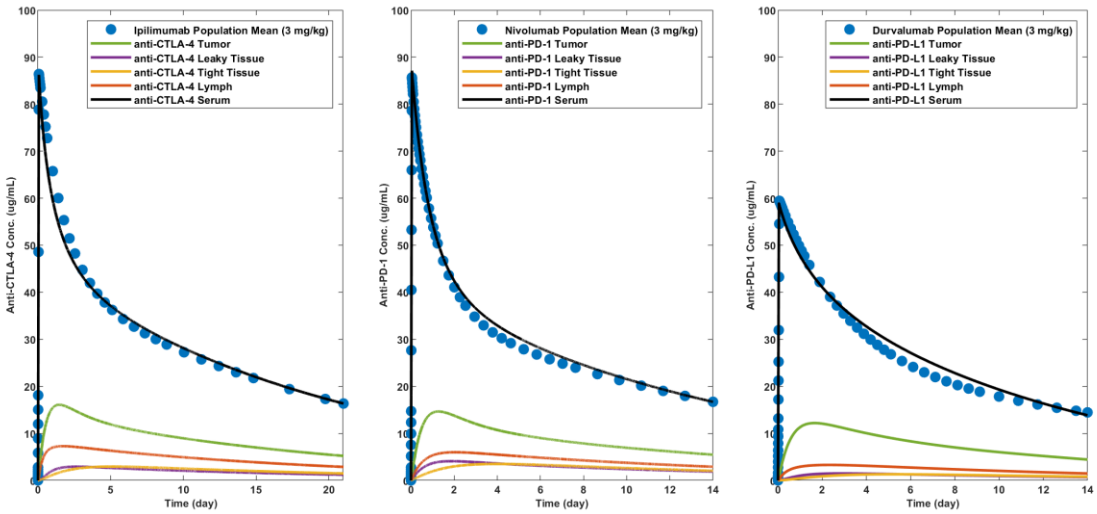

Figure S4. Pharmacokinetics of A) anti-CTLA-4, B) anti-PD-1 and C) anti-PD-L1 at 3 mg/kg each in the serum, tumor, leaky and tight tissues, lymph and serum. Results are based on a minimal-PBPK model, combined with tumor transport equations with diffusion across the vascular surface area.

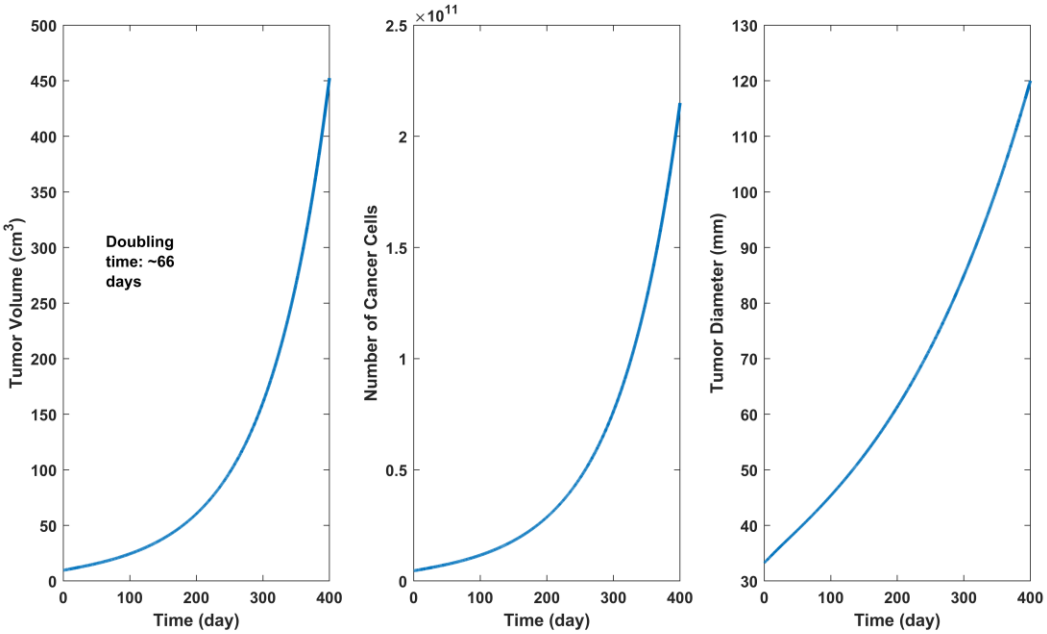

Figure S5. Simulation of tumor volume doubling time (left) and associated number of cancer cells (middle) and tumor diameter (right). A tumor doubling time of ~66 days was used for all model simulations. Variability in tumor growth was an emergent outcome for each simulation in the model.

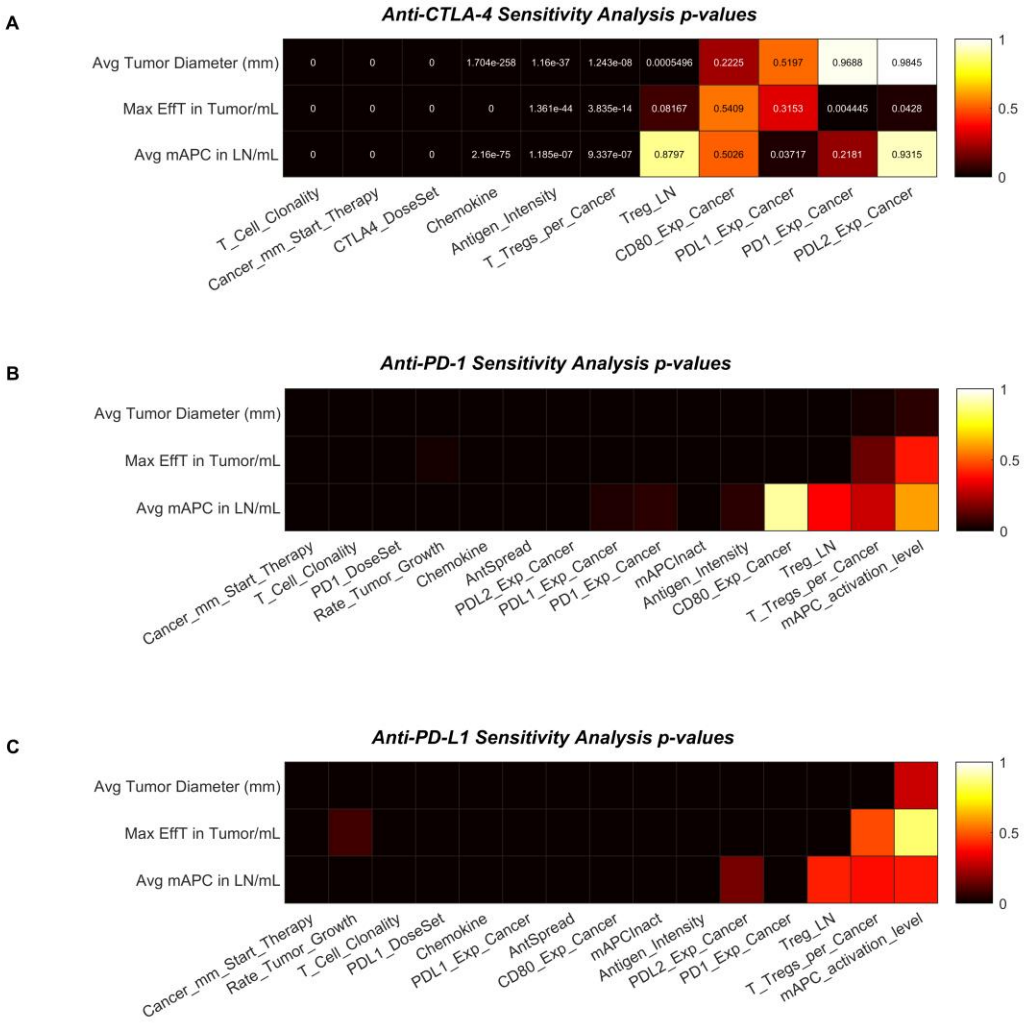

Figure S6. Sensitivity analysis p-values for A) anti-CTLA-4, B) anti-PD-1 and C) anti-PD-L1.

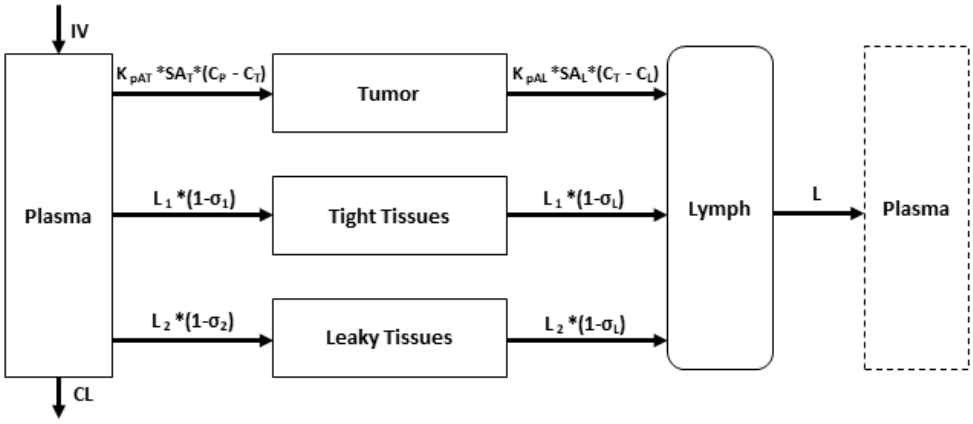

Figure S7. Minimal PBPK model of antibody distribution used in the QSP model.

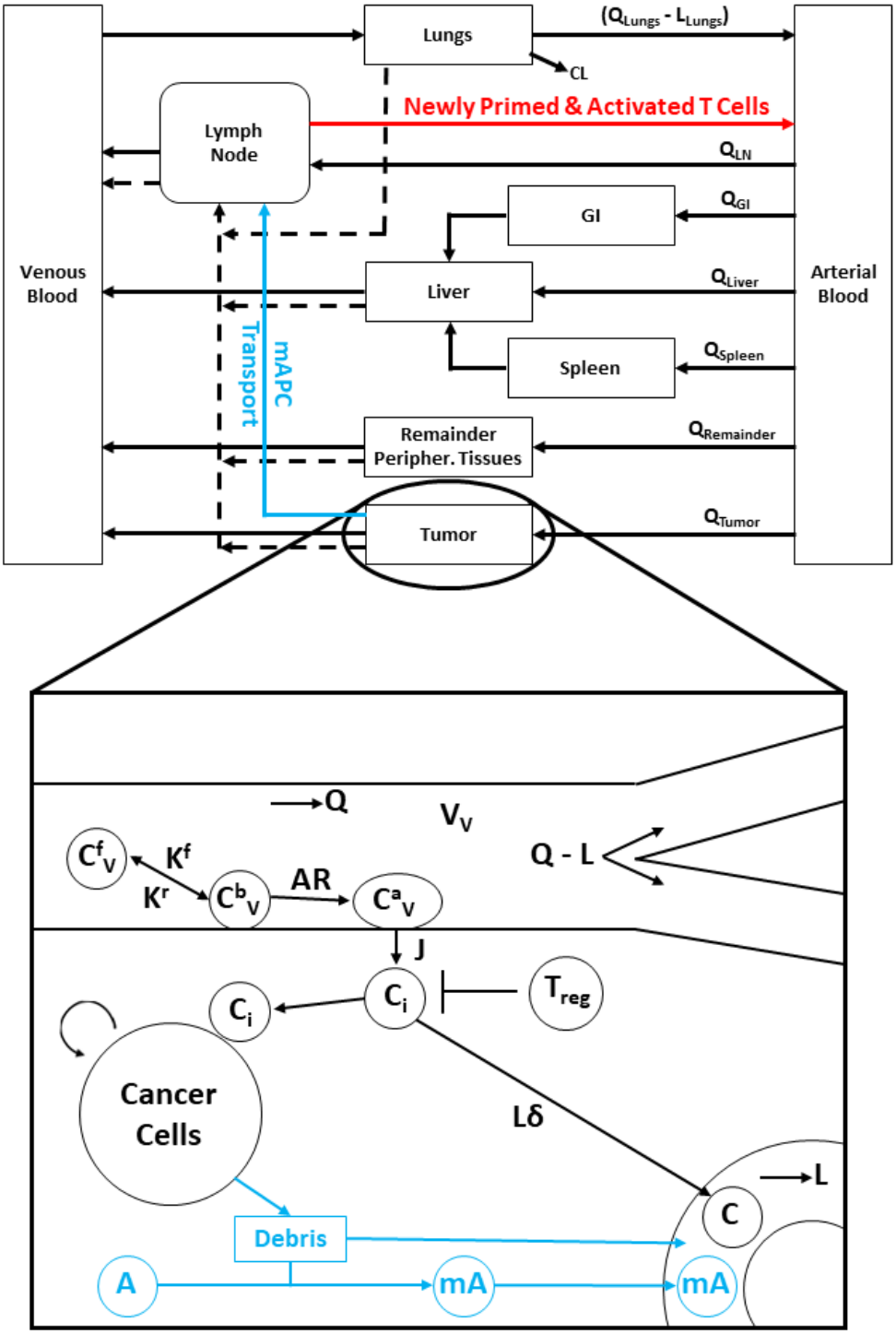

Figure S8. PBPK model cell trafficking used in the QSP model. Model PBPK of Effector T cell (C) trafficking through the tissues in the model via the blood (solid black lines) and lymph (dotted black

lines). Also represented is the trafficking of newly primed and activated Effector T cells from the lymph node to the blood for redistribution (solid red line) the trafficking of mature APCs (solid blue line) to the lymph nodes for priming and activation of naïve T cells to Effector T cells. Cancer Debris also enter the lymph fluid and is brought to the lymph node from the tumor. The bottom panel shows how free Effector cells (C^f_V) in the tumor vasculature are bound the vascular wall (C^b_V), arrested (C^a_V), extravasated (via rate J) into the interstitial space (C_i) to interact with the cancer cells. Regulatory cells (T_{reg}) inhibit the activity of the Effector cells in the tumor and APCs (A) pick up debris to become mAPC (mA). Effector cells can exit the interstitial space (via rate Lδ) and recirculate through the lymphatic system.

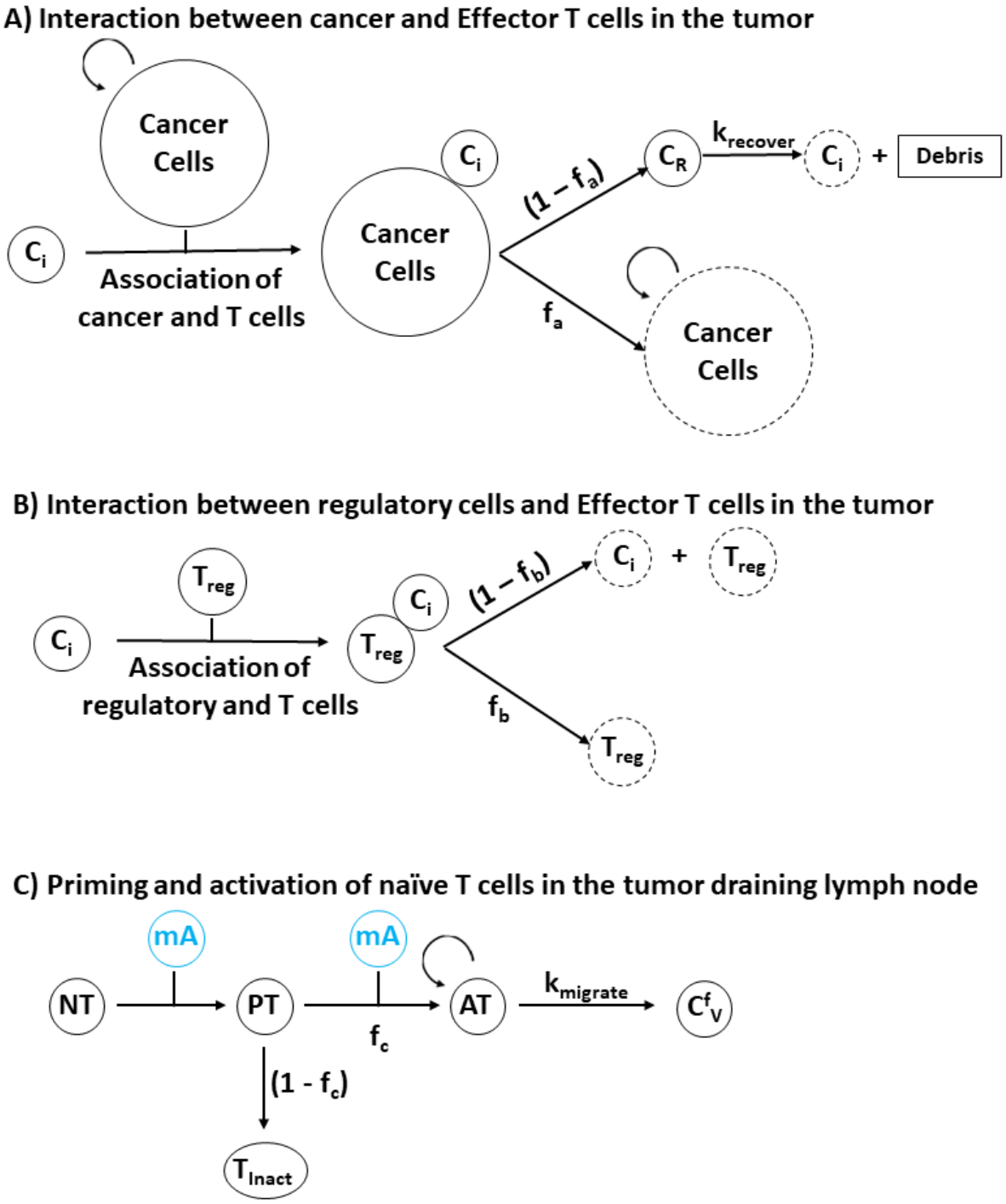

Figure S9. Abstract representation of cell-cell interactions in the model. A) Effector T cells in the interstitial space of the tumor (C_i) interact with cancer cells to form a bound complex (at a rate defined

by the De Pillis-Radunskaya equation described in the methods, equation 1.3). The complex then dissociates with the regeneration of cancer cells and Effector cells relative to the fraction of active checkpoint signaling (f_a). If checkpoint signaling is fully active at inhibiting the Effector cells, for example, then only the cancer cells are regenerated ($f_a = 1$). Alternatively, is antibodies block the signaling to full effect ($f_a = 0$), then only the Effector cells emerge from the bound interaction; along with cancer cell debris that can promote further priming and activation of Effector cells in the lymph nodes. The value of signaling comes out to be between 0 and 1 and is dependent on the checkpoint signaling and interactions with the antibodies that block it. The emerging Effector T cells undergo a recovery delay (C_R) before engaging in interactions with other cancers cells. B) Similarly, as described above, Effector T cells in the tumor interstitial space can interact with regulatory cells (T_{reg}) to form a state variable representing a bound complex. The dissociation of the bound complex determines to what extent the Effector cells are regenerated, which is directly a function of the checkpoint signaling (f_b). C) Mature APCs (mA) interact with naïve and primed T cells (NT and PT, respectively) during two priming stages in the lymph node. Depending on the extent of checkpoint signaling (f_c), primed T cells either become anergic (T_{Inact}) and/or activated T cells (AT); the latter proliferate and become Effector T cells (C^f_V) that migrate out into peripheral circulation.