

Supplemental Table 1: Estimated tumor purity, allele frequency, and independent read depth for all gene mutations classified as either potentially pathogenic or VUS in the metastatic and primary tumor samples.<sup>A</sup>

Sample	Sample Metrics						
		Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy
LN Metastasis	Tumor Purity						
	Computational	Pathology					
	80%	60%					
		ARID1A	5965C>T	R1989*	53.0	585	3
		ATR	2965C>T	R989C	42.0	383	%
		ATRX	3892G>T	E1298*	6.0	343	N/A
		BAP1	901G>A	A301T	52.0	379	3
		CTNNB1	95A>G	D32G	55.0	559	3
		ERBB3	310G>T	V104L	53.0	510	3
		ESR1	1556A>G	N519S	15.0	559	5
		FAM123B	674G>T	R225I	66.0	298	N/A
		LRP1B	628A>C	N210H	48.0	354	3
		MAP2K1	199G>A	D67N	30.0	608	3
		MSH6	2765G>A	R922Q	49.0	515	3
		PIK3CA	263G>A	R88Q	42.0	666	4
		PIK3CA	333G>T	K111N	40.0	596	4
		PIK3CA	1070G>A	R357Q	34.0	350	4
		POLE	1231G>T	V411L	50.0	337	3
		PTEN	389G>A	R130Q	44.0	685	4
		SDHA	223C>T	R75*	25.0	426	3
		SMAD2	962G>A	R321Q	36.0	516	5
		TAF1	3698G>A	R1233Q	71.0	452	N/A
		TP53	637C>T	R213*	81.0	452	3
		XPO1	2246G>A	R749Q	51.0	344	3
		ARID1A	5299G>T	E1767*	26.0	477	3
		ATM	392C>A	S131*	18.0	343	3
		ATRX	1753G>T	E585*	71.0	304	N/A
		BCORL1	3757G>T	E1253*	22.0	427	N/A
		EZH2	736G>T	E246*	43.0	276	2

Sample	Sample Metrics						
	Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy	
LN Metastasis	FAT1	9568G>T	E3190*	24.0	505	3	
	FAT1	2518G>T	E840*	22.0	492	3	
	LRP1B	13750G>T	E4584*	48.0	354	3	
	LRP1B	10282G>T	E3428*	50.0	350	3	
	NOTCH2	1489G>T	E497*	48.0	429	3	
	SPEN	3127G>T	E1043*	23.0	428	3	
	STAG2	3625G>T	E1209*	47.0	414	N/A	
	ABL1	1238A>G	Y413C	54.0	428	3	
	ABL2	3155T>C	V1052A	49.0	571	3	
	ALK	4526C>T	S1509F	26.0	617	3	
	ALK	587C>T	S196L	31.0	438	3	
	ARID1B	4685T>C	L1562P	20.0	844	5	
	ARID2	428G>A	R143H	24.0	270	3	
	ARID2	881G>T	R294I	29.0	586	3	
	ARID2	4446A>C	Q1482H	25.0	576	3	
	ARID2	4712A>G	E1571G	21.0	388	3	
	ATM	3256C>T	R1086C	49.0	504	3	
	ATM	7547T>G	F2516C	8.0	331	3	
	ATR	7573C>T	P2525S	20.0	403	4	
	ATR	7088G>A	R2363Q	17.0	428	4	
	ATR	3113C>A	S1038Y	37.0	378	4	
	AXL	809G>A	G270D	26.0	367	3	
	BCORL1	61C>T	R21C	29.0	490	N/A	
	BCORL1	4313T>G	V1438G	23.0	345	N/A	
	BLM	572G>T	R191I	49.0	461	3	
	BRCA1	4703T>G	I1568S	15.0	441	3	
	BRCA2	2699A>T	N900I	48.0	398	3	
	BRCA2	7241_					
	BRCA2	7242CA>TG	S2414L	27.0	591	3	
	BRD4	2152G>A	E718K	31.0	500	3	
	BRIP1	3516A>C	E1172D	25.0	496	3	
	BRIP1	395C>A	T132N	29.0	455	3	
	BRIP1	237A>C	K79N	8.0	395	3	
	BTK	1574G>A	R525Q	50.0	375	N/A	

Sample	Sample Metrics						
	Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy	
LN Metastasis	C17orf39	637A>C	K213Q	27.0	325	3	
	CARD11	1823G>A	R608H	45.0	249	2	
	CBFB	323T>C	V108A	28.0	387	3	
	CBFB	532T>G	L178V	56.0	387	3	
	CBL	538C>T	R180W	23.0	490	3	
	CD79A	240C>A	F80L	26.0	454	3	
	CDC73	352C>A	L118I	22.0	369	3	
	CHD2	4255a>G	K1419E	5.0	348	3	
	CRKL	832G>A	E278K	26.0	422	3	
	CSF1R	2092G>A	D698N	32.0	288	2	
	CTCF	229A>C	K77Q	55.0	307	3	
	CTNNA1	1178C>A	S393Y	41.0	285	2	
	CUL3	2092G>A	D698N	23.0	523	3	
	CUL3	577T>G	L193V	53.0	406	3	
	DICER1	2119G>A	E707K	5.0	297	2	
	EP300	3600C>A	F1200L	26.0	617	3	
	EPHA3	1375G>T	E459*	42.0	552	4	
	EPHA3	1600T>C	Y534H	41.0	297	4	
	EPHA3	2427T>G	S809R	17.0	643	4	
	EPHA3	2912C>A	A971D	24.0	462	4	
	EPHB1	2608C>T	R870W	44.0	610	4	
	ERG	913A>C	N305H	24.0	441	3	
	EZH2	1983A>C	K661N	33.0	249	2	
	FAM123B	2677A>C	S893R	7.0	382	N/A	
	FAM46C	242T>C	V81A	54.0	493	3	
	FANCC	1643G>A	R548Q	58.0	405	3	
	FANCC	390A>C	E130D	28.0	303	3	
	FANCC	301G>A	E101K	32.0	374	3	
	FANCG	706G>A	A236T	24.0	430	3	
	FANCL	883C>T	R295C	52.0	486	3	
	FAT1	1090C>A	P364T	57.0	802	3	
	FGF23	750C>A	F250L	49.0	314	3	
	FGF3	323C>T	S108L	57.0	516	3	
	FGF6	35C>T	S12F	58.0	304	3	
	FGFR1	34G>A	E12K	52.0	701	5	

Sample	Sample Metrics						
	Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy	
LN Metastasis	FGFR2	1142A>C	Y381S	33.0	533	4	
	FH	1495G>A	E499K	25.0	469	3	
	FLT1	1163A>G	Y388C	29.0	411	3	
	FLT3	2437G>A	A813T	25.0	337	3	
	FLT3	2417C>T	S806L	53.0	235	3	
	FLT3	2127A>T	K709N	28.0	352	3	
	FLT4	3203A>G	Y1068C	41.0	268	2	
	FRS2	455G>A	R152Q	29.0	419	3	
	GABRA6	1127C>A	S376Y	9.0	321	2	
	GNAS	811A>G	T271A	52.0	429	3	
	GNAS	833C>T	P278L	25.0	449	3	
	GNAS	595C>T	R199C	27.0	514	3	
	GPR124	401T>G	L134R	71.0	568	5	
	GSK3B	95A>G	K32R	23.0	537	4	
	HGF	494C>T	S165L	33.0	287	2	
	HGF	107G>T	R36I	24.0	204	2	
	IKZF1	1300G>A	A434T	43.0	224	2	
	INPP4B	1172A>C	E391A	24.0	388	3	
	IRS2	1564G>A	E522K	21.0	480	3	
	JAK1	940G>A	E314K	28.0	520	3	
	JAK3	118C>T	R40C	29.0	368	3	
	KDM5A	1187G>A	R396Q	51.0	367	3	
	KDR	504G>T	K168N	60.0	403	3	
	KDR	281T>G	I94S	7.0	558	3	
	KEL	1307G>A	R436Q	43.0	257	2	
	KEL	1289C>T	A430V	31.0	272	2	
	KLHL6	1804G>A	V602I	42.0	428	4	
	KLHL6	518A>G	N173S	20.0	761	4	
	LRP1B	11042G>A	C3681Y	48.0	273	3	
	LRP1B	4367G>T	G1456V	51.0	395	3	
	LRP1B	1505G>A	R502H	52.0	615	3	
	LRP1B	121G>A	D41N	53.0	432	3	
	LZTR1	1913G>A	R638H	25.0	354	3	
	MAGI2	1370C>T	P457L	36.0	464	2	
	MAP3K1	2816C>G	S939C	60.0	252	3	

Sample	Sample Metrics						
	Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy	
LN Metastasis	MDM4	139T>C	F47L	29.0	339	3	
	MED12	884G>A	R295H	6.0	383	N/A	
	MET	684T>G	F228L	36.0	368	2	
	MITF	1096G>T	E366*	6.0	623	4	
	MLL2	9136G>A	E3046K	52.0	501	3	
	MLL2	1023G>T	E341D	49.0	463	3	
	MLL3	14417G>A	R4806Q	30.0	363	2	
	MLL3	12026G>A	S4009N	30.0	432	2	
	MLL3	5151A>C	K1717N	26.0	377	2	
	MRE11A	1180G>T	D394Y	25.0	495	3	
	MRE11A	764A>C	K255T	7.0	473	3	
	NF1	1319G>A	R440Q	24.0	501	3	
	NFE2L2	1657C>T	R553C	50.0	506	3	
	NFE2L2	1447C>T	R483W	49.0	542	3	
	NOTCH2	5470C>T	R1824C	30.0	222	3	
	NOTCH3	467G>A	R156Q	53.0	391	3	
	NTRK3	1753T>G	F585V	48.0	358	3	
	NTRK3	878G>A	S293N	32.0	316	3	
	PAK3	730T>C	S244P	33.0	414	N/A	
	PALB2	3122A>C	K1041T	5.0	345	3	
	PDK1	1285G>T	D429Y	27.0	381	3	
	PIK3CA	1943T>C	L648S	25.0	179	4	
	PIK3R1	659T>C	I220T	36.0	260	2	
	PLCG2	583G>T	D195Y	50.0	334	3	
	PLCG2	892G>T	E298*	54.0	603	3	
	PLCG2	2180G>A	R727Q	17.0	526	3	
	PMS2	1883G>A	R628Q	34.0	312	2	
	POLE	340C>T	R114*	22.0	556	3	
	PRDM1	1294A>C	N432H	9.0	551	4	
	PREX2	2974A>G	I992V	69.0	626	5	
	PREX2	3886A>C	N1296H	18.0	756	5	
	PRKCI	751C>T	L251F	42.0	595	4	
	PRKDC	9115A>G	T3039A	17.0	399	5	
	PRKDC	2530G>A	E844K	17.0	387	5	
	PRKDC	265T>G	L89V	17.0	524	5	

Sample	Sample Metrics						
	Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy	
LN Metastasis	PRKDC	184G>T	D62Y	51.0	570	5	
	QKI	942T>G	I314M	86.0	651	5	
	RANBP2	3182G>A	S1061N	30.0	646	3	
	RANBP2	8303_ 8306delCAGA	T2768fs*3	24.0	440	3	
	RANBP2	8509A>G	I2837V	27.0	503	3	
	RBM10	1556G>T	G519V	10.0	288	N/A	
	<b>RICTOR</b>	<b>2138C&gt;G</b>	<b>A713G</b>	<b>34.0</b>	<b>346</b>	<b>3</b>	
	ROS1	4906C>A	L1636I	14.0	766	5	
	ROS1	4890T>G	I1630M	16.0	673	5	
	ROS1	3252T>G	I1084M	89.0	781	5	
	ROS1	3218A>C	K1073T	31.0	705	5	
	ROS1	1079G>T	R360I	32.0	609	5	
	RUNX1T1	533G>A	R178K	8.0	589	5	
	SETD2	4198G>T	D1400Y	26.0	450	3	
	SLIT2	3185G>T	C1062F	28.0	396	3	
	SMAD3	108G>T	K36N	16.0	416	3	
	SNCAIP	97C>T	R33*	40.0	415	2	
	SPEN	2438A>C	K813T	27.0	503	3	
	SPTA1	1408C>T	R470C	28.0	370	3	
	SRC	1602G>T	E534D	30.0	359	3	
	STAG2	2118G>T	W706C	27.0	362	N/A	
	STAG2	2797G>A	E933K	24.0	336	N/A	
	STAT4	214T>C	S72P	56.0	412	3	
	TAF1	2990G>A	R997H	70.0	502	N/A	
	TGFBR2	159T>G	F53L	27.0	443	3	
	TOP2A	3438G>T	R1146S	21.0	482	3	
	XPO1	1658G>A	R553H	54.0	445	3	
	ZNF217	2102C>A	S701Y	28.0	577	3	
	Primary Cancer	<b>Tumor Purity</b>					
		<b>Computational</b>	<b>Pathology</b>				
50%		70%					
	ARID1A	5965C>T	R1989*	42.0	610	2	

Sample	Sample Metrics						
	Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy	
Primary Cancer	ATR	2965C>T	R989C	44.0	485	2	
	ATRX	3892G>T	E1298*	37.0	558	2	
	BAP1	901G>A	A301T	9.0	362	2	
	CTCF	145C>T	R49C	4.0	486	2	
	CTNNB1	95A>G	D32G	41.0	654	2	
	ERBB3	310G>T	V104L	39.0	537	2	
	FAM123B	674G>T	R225I	12.0	441	2	
	LRP1B	628A>C	N210H	39.0	527	2	
	MAP2K1	199G>A	D67N	43.0	839	2	
	MSH6	2765G>A	R922Q	6.0	657	2	
	PIK3CA	263G>A	R88Q	41.0	793	2	
	PIK3CA	333G>T	K111N	41.0	720	2	
	PIK3CA	1070G>A	R357Q	41.0	408	2	
	POLE	1231G>T	V411L	40.0	292	2	
	PTEN	389G>A	R130Q	44.0	710	2	
	SMAD2	962G>A	R321Q	41.0	476	2	
	TAF1	3698G>A	R1233Q	8.0	678	2	
	TP53	637C>T	R213*	16.0	541	2	
	XPO1	2246G>A	R749Q	40.0	447	2	
	ARID1A	5299G>T	E1767*	44.0	621	2	
	ATRX	6736G>T	E2246*	33.0	491	2	
	ATRX	1753G>T	E585*	47.0	670	2	
	EZH2	736G>T	E246*	41.0	446	2	
	FAT1	9568G>T	E3190*	41.0	538	2	
	FAT1	2518G>T	E840*	5.0	747	2	
	KIT	124G>T	G42*	33.0	815	2	
	LRP1B	13750G>T	E4584*	40.0	485	2	
	LRP1B	10282G>T	E3428*	6.0	478	2	
	NOTCH2	1489G>T	E497*	8.0	594	2	
	SPTA1	3136C>T	R1046*	32.0	532	2	
	STAG2	3625G>T	E1209*	6.0	490	2	
	ABL1	1238A>G	Y413C	44.0	563	2	
	ABL2	3155T>C	V1052A	7.0	604	2	
	ALK	587C>T	S196L	45.0	453	2	
	ARID2	428G>A	R143H	43.0	329	2	

Sample	Sample Metrics						
	Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy	
Primary Cancer	ARID2	4446A>C	Q1482H	43.0	623	2	
	ATM	3256C>T	R1086C	8.0	623	2	
	ATR	3113C>A	S1038Y	9.0	391	2	
	ATRX	3155A>C	K1052T	7.0	718	2	
	BCORL1	61C>T	R21C	37.0	442	2	
	BCORL1	4808A>G	K1603R	31.0	359	2	
	BLM	572G>T	R191I	9.0	713	2	
	BRCA2	2699A>T	N900I	42.0	662	2	
	BRCA2	7241_ 7242CA>TG	S2414L	44.0	939	2	
	BRD4	2152G>A	E718K	13.0	320	2	
	BTK	1574G>A	R525Q	9.0	454	2	
	CARD11	1823G>A	R608H	52.0	376	2	
	CBFB	532T>G	L178V	45.0	457	2	
	CBL	538C>T	R180W	41.0	573	2	
	CDK12	3728G>T	R1243I	6.0	518	2	
	CHD4	2521G>A	A841T	36.0	428	2	
	CHEK2	1392G>T	K464N	8.0	218	2	
	CRKL	832G>A	E278K	10.0	471	2	
	CSF1R	1660G>A	E554K	32.0	380	2	
	CTCF	229A>C	K77Q	8.0	393	2	
	CTNNA1	210G>T	E70D	7.0	717	2	
	CTNNA1	1178C>A	S393Y	41.0	473	2	
	CUL3	2092G>A	D698N	45.0	615	2	
	CUL3	577T>G	L193V	42.0	450	2	
	EPHA3	1375G>T	E459*	43.0	549	2	
	EPHA3	1600T>C	Y534H	45.0	328	2	
	EPHB1	2608C>T	R870W	47.0	485	2	
	EZH2	1983A>C	K661N	41.0	368	2	
	FAM46C	242T>C	V81A	8.0	468	2	
	FANCC	1643G>A	R548Q	8.0	362	2	
	FANCE	718G>A	E240K	6.0	627	2	
	FANCG	706G>A	A236T	41.0	380	2	
	FANCL	883C>T	R295C	9.0	667	2	
	FAT1	1090C>A	P364T	42.0	890	2	



Sample	Sample Metrics						
	Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy	
Primary Cancer	FGF23	750C>A	F250L	35.0	298	2	
	FGF3	323C>T	S108L	46.0	500	2	
	FGF6	35C>T	S12F	49.0	260	2	
	FH	1495G>A	E499K	9.0	576	2	
	FLT3	2437G>A	A813T	43.0	450	2	
	FLT3	2417C>T	S806L	13.0	454	2	
	FLT4	3203A>G	Y1068C	42.0	365	2	
	FRS2	455G>A	R152Q	47.0	554	2	
	GATA6	457G>A	A153T	37.0	181	2	
	GNAS	811A>G	T271A	9.0	380	2	
	GPR124	401T>G	L134R	48.0	462	2	
	GRIN2A	1548G>T	E516D	25.0	608	2	
	H3F3A	371A>G	D124G	33.0	237	2	
	IKZF1	1300G>A	A434T	9.0	263	2	
	IRF4	850G>A	A284T	41.0	378	2	
	JAK1	2002G>T	E668*	31.0	433	2	
	JAK1	1339G>T	E447*	35.0	422	2	
	JAK2	3182T>G	F1061C	32.0	548	2	
	KDM5A	1187G>A	R396Q	39.0	605	2	
	KDR	504G>T	K168N	6.0	544	2	
	KEL	1307G>A	R436Q	41.0	450	2	
	KEL	1289C>T	A430V	6.0	420	2	
	KLHL6	1804G>A	V602I	11.0	305	2	
	LRP1B	11042G>A	C3681Y	42.0	433	2	
	LRP1B	4247C>A	T1416N	35.0	624	2	
	LRP1B	1505G>A	R502H	40.0	881	2	
	LRP1B	121G>A	D41N	9.0	538	2	
	MAGI2	1370C>T	P457L	44.0	763	2	
	MAP3K1	2816C>G	S939C	49.0	302	2	
	MED12	884G>A	R295H	34.0	496	2	
	MED12	3050G>A	W1017*	26.0	498	2	
	MET	684T>G	F228L	7.0	642	2	
	MLH1	1643A>G	Y548C	33.0	601	2	
	MLL2	9136G>A	E3046K	43.0	602	2	
MLL2	1023G>T	E341D	9.0	451	2		

Sample	Sample Metrics						
	Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy	
Primary Cancer	MLL3	6251A>C	N2084T	8.0	677	2	
	MLL3	1528G>T	E510*	34.0	576	2	
	MLL3	910_911insA	M305fs*28	5.0	2015	2	
	NFE2L2	1657C>T	R553C	44.0	738	2	
	NFE2L2	1447C>T	R483W	41.0	849	2	
	NOTCH2	5470C>T	R1824C	10.0	257	2	
	NOTCH3	467G>A	R156Q	43.0	366	2	
	NTRK1	1525G>T	D509Y	11.0	374	2	
	NTRK3	1753T>G	F585V	38.0	454	2	
	PAK3	730T>C	S244P	38.0	484	2	
	PDGFRA	910A>G	K304E	35.0	644	2	
	PDK1	1285G>T	D429Y	45.0	428	2	
	PIK3CA	184C>A	L62I	5.0	750	2	
	PIK3R1	659T>C	I220T	42.0	518	2	
	PLCG2	583G>T	D195Y	7.0	498	2	
	PLCG2	892G>T	E298*	10.0	535	2	
	PLCG2	2972G>T	R991I	36.0	517	2	
	PMS2	1883G>A	R628Q	44.0	503	2	
	POLE	340C>T	R114*	42.0	667	2	
	PREX2	3886A>C	N1296H	5.0	660	2	
	PRKCI	751C>T	L251F	44.0	601	2	
	PRKDC	9115A>G	T3039A	39.0	342	2	
	QKI	942T>G	I314M	9.0	565	2	
	RANBP2	3182G>A	S1061N	43.0	719	2	
	RANBP2	4493A>C	K1498T	6.0	834	2	
		8303_					
	RANBP2	8306delCAGA	T2768fs*3	37.0	529	2	
	RANBP2	8509A>G	I2837V	7.0	700	2	
	<b>RICTOR</b>	<b>2138C&gt;G</b>	<b>A713G</b>	<b>49.0</b>	<b>488</b>	<b>2</b>	
	ROS1	5027G>T	W1676L	47.0	676	2	
	ROS1	4015G>A	A1339T	38.0	624	2	
	ROS1	3252T>G	I1084M	45.0	801	2	
	ROS1	734G>A	R245K	9.0	580	2	
	RUNX1T1	1625A>C	K542T	33.0	513	2	

Sample	Sample Metrics						
		Gene	CDS Effect	Protein Effect	Allele Frequency (%)	Read Depth	Ploidy
Primary Cancer		SETD2	4198G>T	D1400Y	7.0	595	2
		SETD2	3389A>C	K1130T	37.0	724	2
		SNCAIP	97C>T	R33*	7.0	681	2
		SNCAIP	2579C>A	P860H	8.0	770	2
		SPTA1	1408C>T	R470C	46.0	411	2
		STAG2	2118G>T	W706C	37.0	470	2
		STAT4	214T>C	S72P	43.0	581	2
		TAF1	2990G>A	R997H	53.0	729	2
		TNFAIP3	1784C>T	A595V	45.0	548	2
		XPO1	1658G>A	R553H	41.0	557	2

<sup>A</sup>Potentially pathogenic variants are listed first followed by VUS for each sample. Variants that were also present in germline sequencing are shown highlighted in blue. VUS - variant of unknown significance; CDS - coding DNA sequence; LN - lymph node.

## Supplemental Methods

Data Collection and Analysis of mRNA expression: mRNA expression data of all endometrioid samples were obtained from Broad GDAC firehose (<http://firebrowse.org/?cohort=UCEC>) in the form of RNAseqV2 scaled estimates. Within each sample, median of all genes were set to 1 to eliminate systematic error. CIBERSORT was then used to estimate leukocyte composition of the immune infiltrate in the tumor (23). If CIBERSORT was not confident ( $p \geq 0.05$ ) about the leukocyte composition of a sample, then leukocyte composition of that sample was not used in this study. mRNA expression was then normalized as  $\log_2(1+1023 \times \text{median adjusted scaled estimate})$ . Somatic mutation data and clinical data (including micro-satellite status) were obtained from TCGA (<https://tcga-data.nci.nih.gov/tcga/tcgaDownload.jsp>). All mutation annotation files (as of 30th September, 2015) for endometrioid samples were merged removing duplicate records, and then annotated using Oncotator (<https://www.broadinstitute.org/oncotator/>). Endometrioid samples were classified into 3 groups: (i) POLE (samples with non-synonymous somatic mutation in POLE), (ii) MSI (samples with micro-satellite instability, but no non-synonymous somatic mutation in POLE), (iii) MSS (micro-satellite stable samples, but no non-synonymous somatic mutation in POLE). We compared the expression of ~700 immune genes between the 3 groups (Wilcoxon Rank Sum test followed by Benjamini Hochberg correction for multiple hypothesis testing); 16 genes were differentially expressed between POLE and MSI at  $FDR < 0.25$  and 111 genes were differentially expressed between POLE and MSS at  $FDR < 0.05$ . In the heat map shown in Fig. 2B, the expression levels of each of these differentially expressed genes (119 genes in total) are represented: the 25% of samples with the highest expression levels are shown in red; the 25% of samples with the lowest expression levels are shown in green; and the 50% of samples with intermediate expression levels are shown in black.

Analysis of histological images: High resolution digital images of H&E stained formalin-fixed

paraffin-embedded sections of endometrial cancer from the TCGA dataset were analyzed by a clinical pathologist (HZ) blinded to genomic data. Each image was scored for the presence of lymphocytes on a scale of 1 (minimal) to 3 (robust). Statistical significance of distribution of scores in each category was evaluated by the two-sided Wilcoxon Rank Sum test.