

# SUPPLEMENTAL DATA

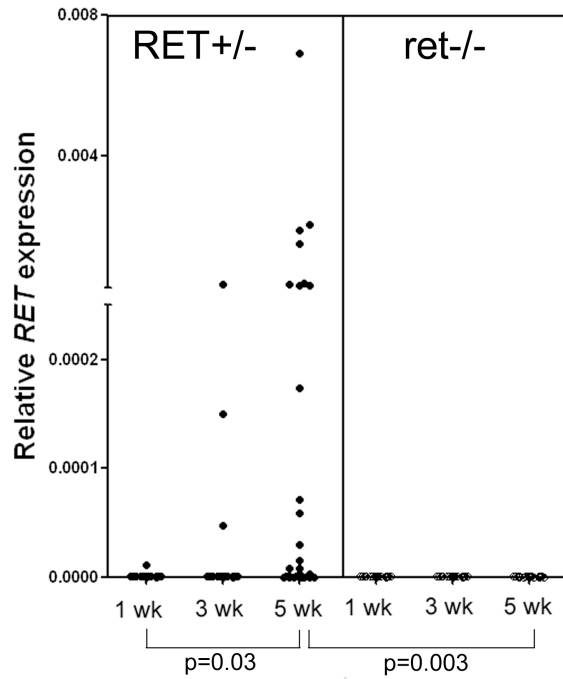
Eyles et al.

**TABLE S1: Percent of conservation:** Each tumor (reference) was compared against every other tumor (tested) from the same or different mouse. The percentage of mutations in the reference tumor that were shared with the tested tumor was averaged for each mouse pair.

		<b>Tested in</b>				
		<b>Mouse 1</b>	<b>Mouse 2</b>	<b>Mouse 3</b>	<b>Mouse 4</b>	<b>Mouse 5</b>
<b>Reference</b>	<b>Mouse 1</b>	34.85	0.00	17.51	1.52	0.00
	<b>Mouse 2</b>	0.00	48.33	0.74	3.89	1.11
	<b>Mouse 3</b>	9.28	0.07	31.49	1.70	0.97
	<b>Mouse 4</b>	5.98	4.38	10.99	17.47	5.07
	<b>Mouse 5</b>	0.00	1.33	8.89	12.78	0.00

**TABLE S2: Tissue origin of tumors**

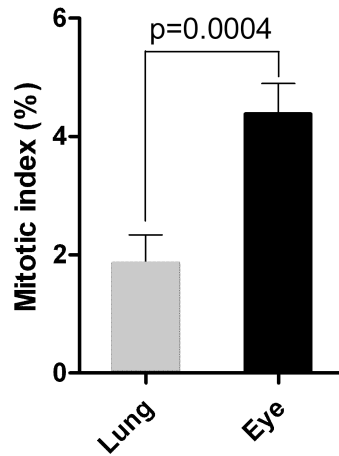
Mouse 1	Mouse 4
LE Left eye	LE Left eye
T1 Right cheek	RE Right eye
T2 Leg muscle	T1 Flank muscle
T3 Neck	T2 Neck
Mouse 2	T3 Right cheek
LE Left eye	T4 Flank muscle
RE Right eye	T5 Tail
T1 Back skin	T6 Peritoneum
T2 Cheek	T7 Reproductive tract
T3 Skin	Mouse 5
T4 Peritoneum	T1 Left cheek
T5 Knee	T2 Left cheek
T6 Shoulder	T3 Dorsal skin
T7 Left ear	T4 Left knee
Mouse 3	T5 Right knee
LE Left eye	T6 Flank muscle
RE Right eye	T7 Neck
T1 Skin	T8 Neck
T2 Ear	T9 Neck
T4 Cheek	T10 Neck
T5 Cheek	T11 Neck
T7 Muscle	T12 Rectum
T8 Neck	T13 Mediastinum
T9 Neck	



## Supplemental Figure S1

### **Supplemental Figure S1: Tumor cell dissemination to internal organs starts at 3 weeks of age.**

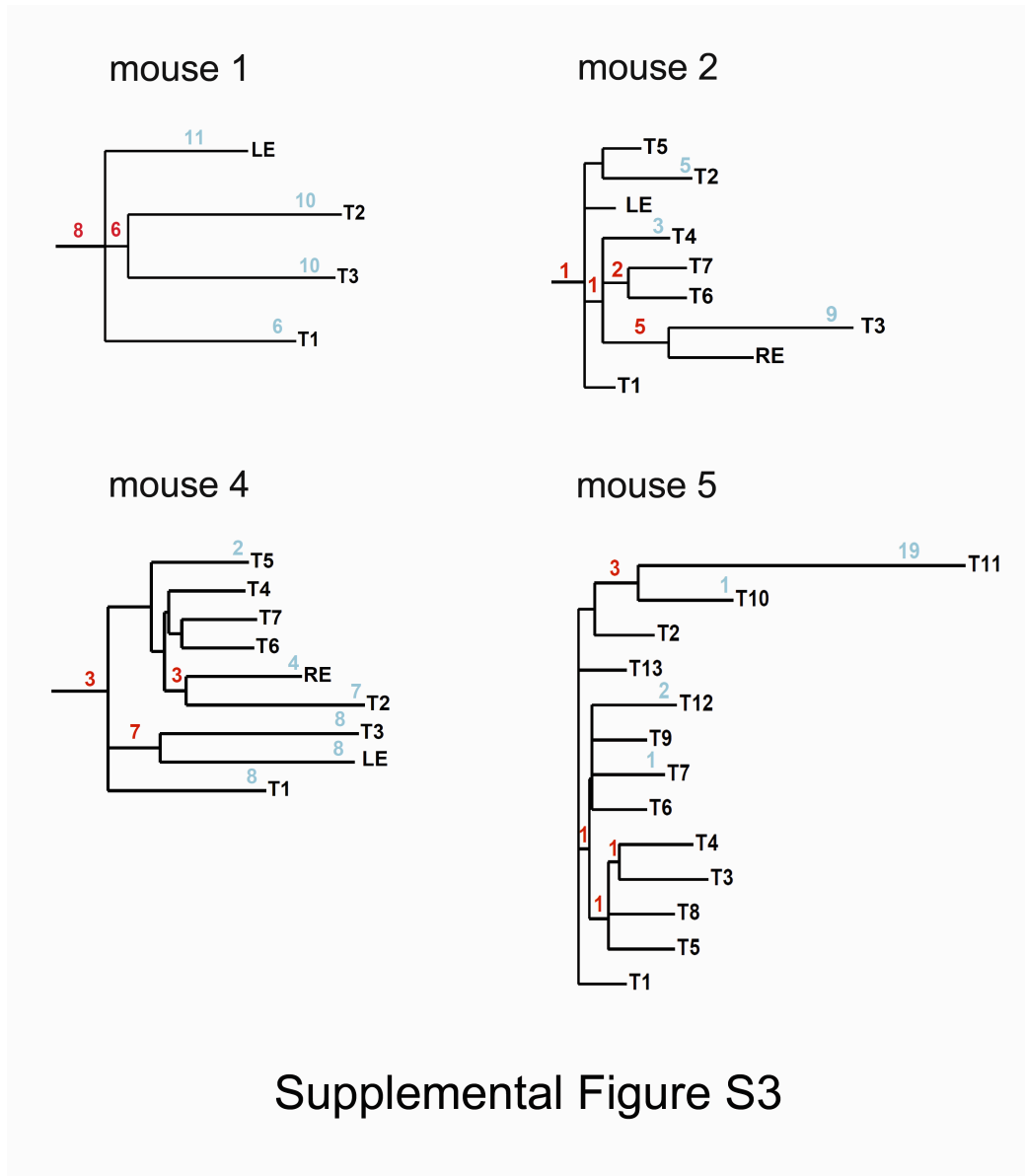
RET expression was measured by qRT-PCR in the lymph nodes, lungs, heart, kidney, liver, stomach, colon, bone marrow, thymus, bladder and small intestine (n = 11 organs per mouse) collected from RET.AAD (RET+/-) mice aged 1 week (n = 3), 3 weeks (n = 3) and 5 weeks (n = 4). Eleven age-matched non-transgenic littermates (ret-/-) were used as controls.



## Supplemental Figure S2

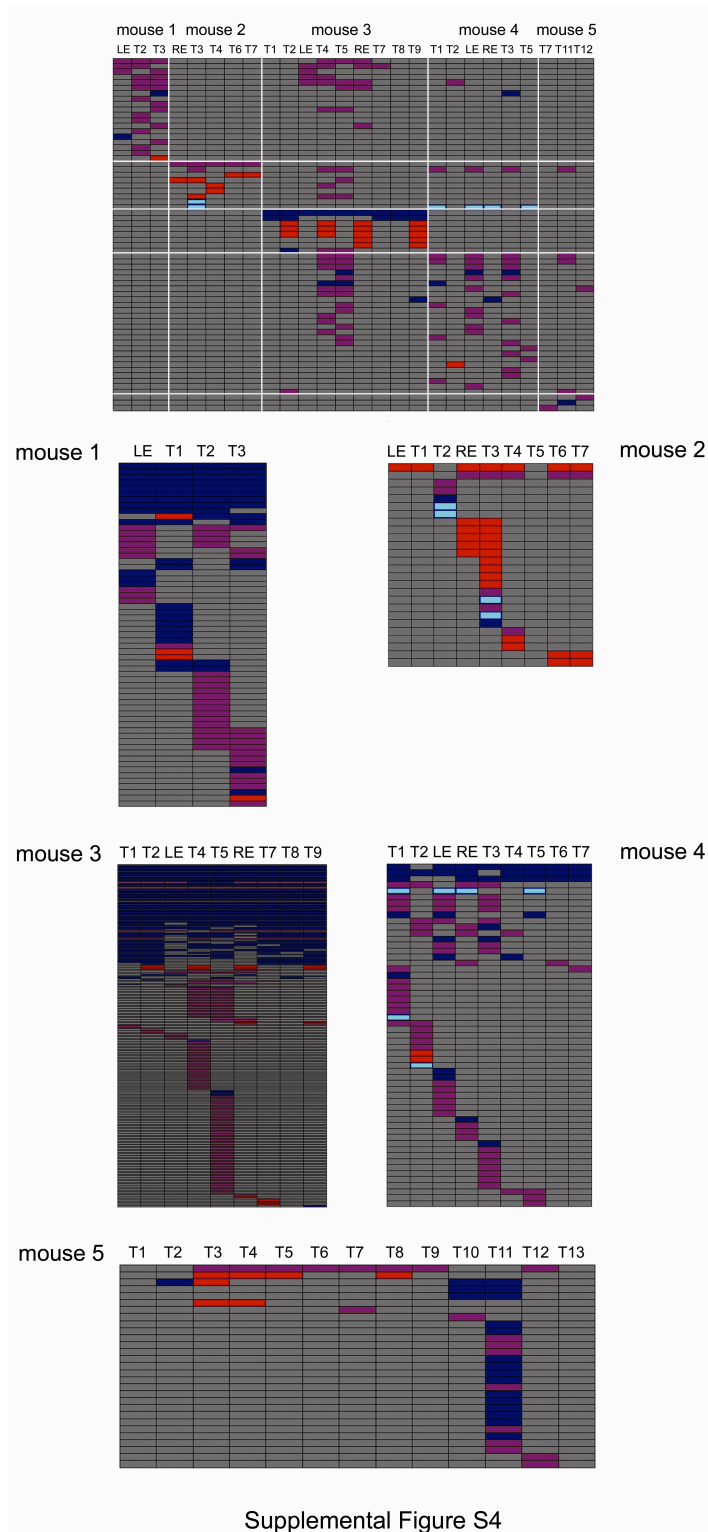
**Supplemental Figure S2: Eye metastases have a higher mitotic index compared to lung tumors.**

Percentage of proliferating tumor cells (S100B+ Ki-67+) in eye and lung tumors. Data are from 12 eyes and 17 lungs from 22 mice, representing a total of 103 tumors. Data represent mean  $\pm$  SEM.



**Supplemental Figure S3: Phylograms of tumors from individual RET.AAD mice.**

The number of mutations conserved along each horizontal branch is indicated in red. The number of mutations unique to each tumor is shown in blue. LE and RE refer to the left and right eye tumor respectively. Tumor tissue origins are given in Supplemental Table S2.



**Supplemental Figure S4:** Genetic alterations identified by comparing the SNP genotypes of each tumor against the tail sample (germline sequence) from the same mouse. Allelic losses and copy number losses are shown in dark and light blue respectively, point mutations and copy number gains are in violet and red, respectively. Top panel shows the heatmap used for cluster analysis in Figure 3A while the other panels show the heatmaps used for individual phylograms shown in Figure 3C and Supplemental Figure S3. Tumor origins are given in Supplemental Table S2.

