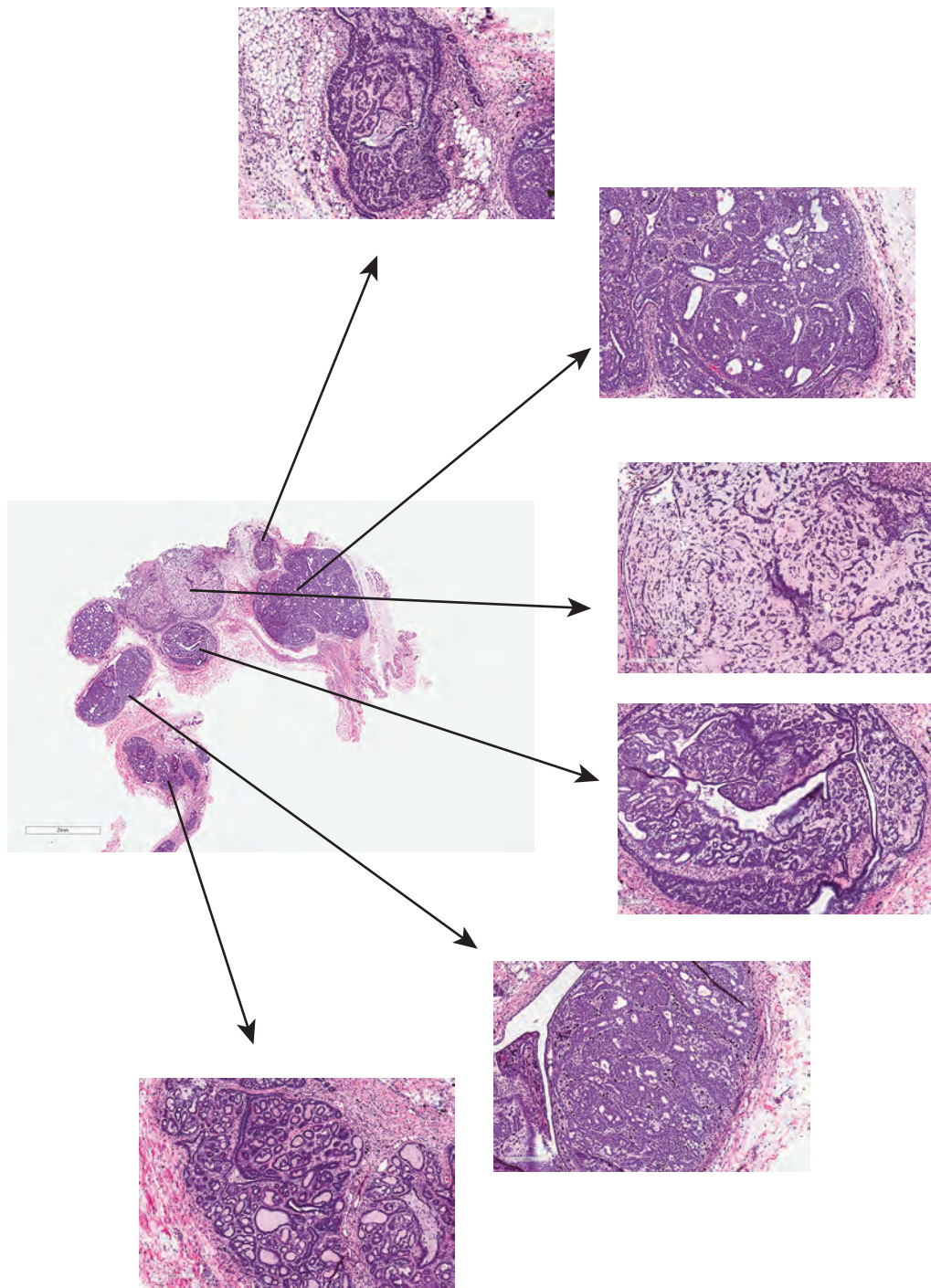
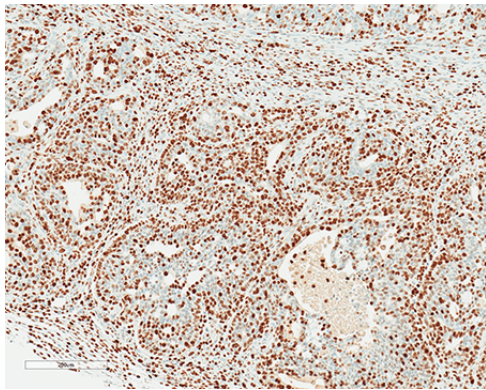


Supplementary Figure 1: Three *Nf1* alleles identified in *Nf1*^{IF-63/PS-11} line. HMA and sequencing identified 3 *NF1* alleles in *Nf1*^{IF-63/PS-11} : a WT allele, an allele with an 11 bp deletion (premature stop), and an allele with a -63 bp deletion. The presence of more than two alleles was confirmed using unique primer sets in two separate labs. The three alleles were transmitted through the *Nf1*^{IF-63/PS-11} germline in F1 and F2 generations and did not segregate in either generation as shown in the HMA profiles of individual F1 and F2 *Nf1*^{IF-63/PS-11} rats.

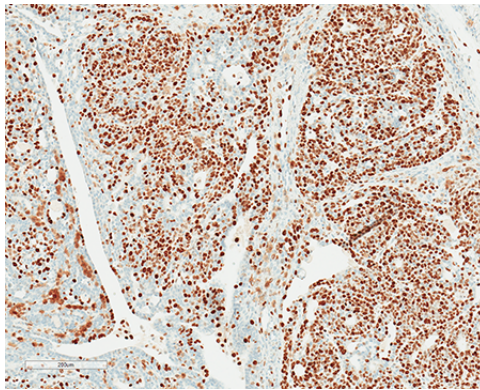


Supplementary Figure 2: Multiple tumors are commonly observed in *Nf1* mammary glands. The level of tumor burden in the mammary pads of several animals was substantial. Shown above is the 4th mammary pad from *rNf1* #413.

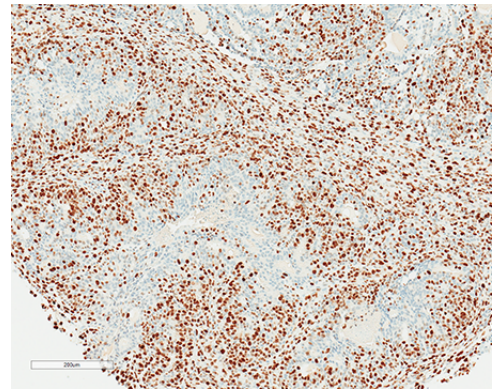
em3 *Nf1*^{PS/+} (#357)



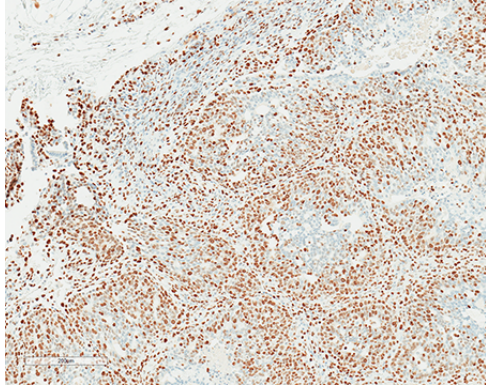
em3 *Nf1*^{PS/+} (#413)



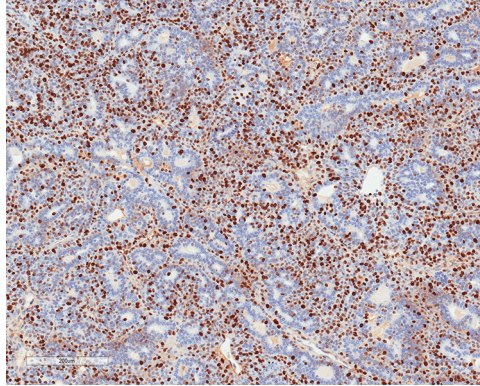
em3 *Nf1*^{PS/+} (#397)



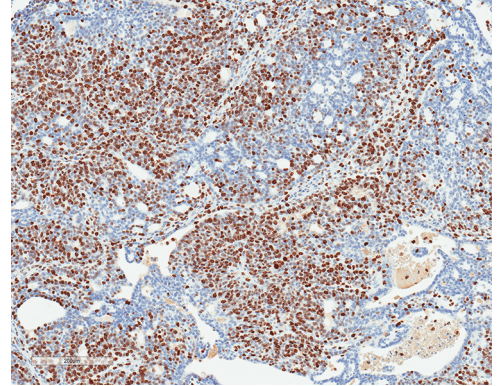
em2 *Nf1*^{IF/+} (#303)



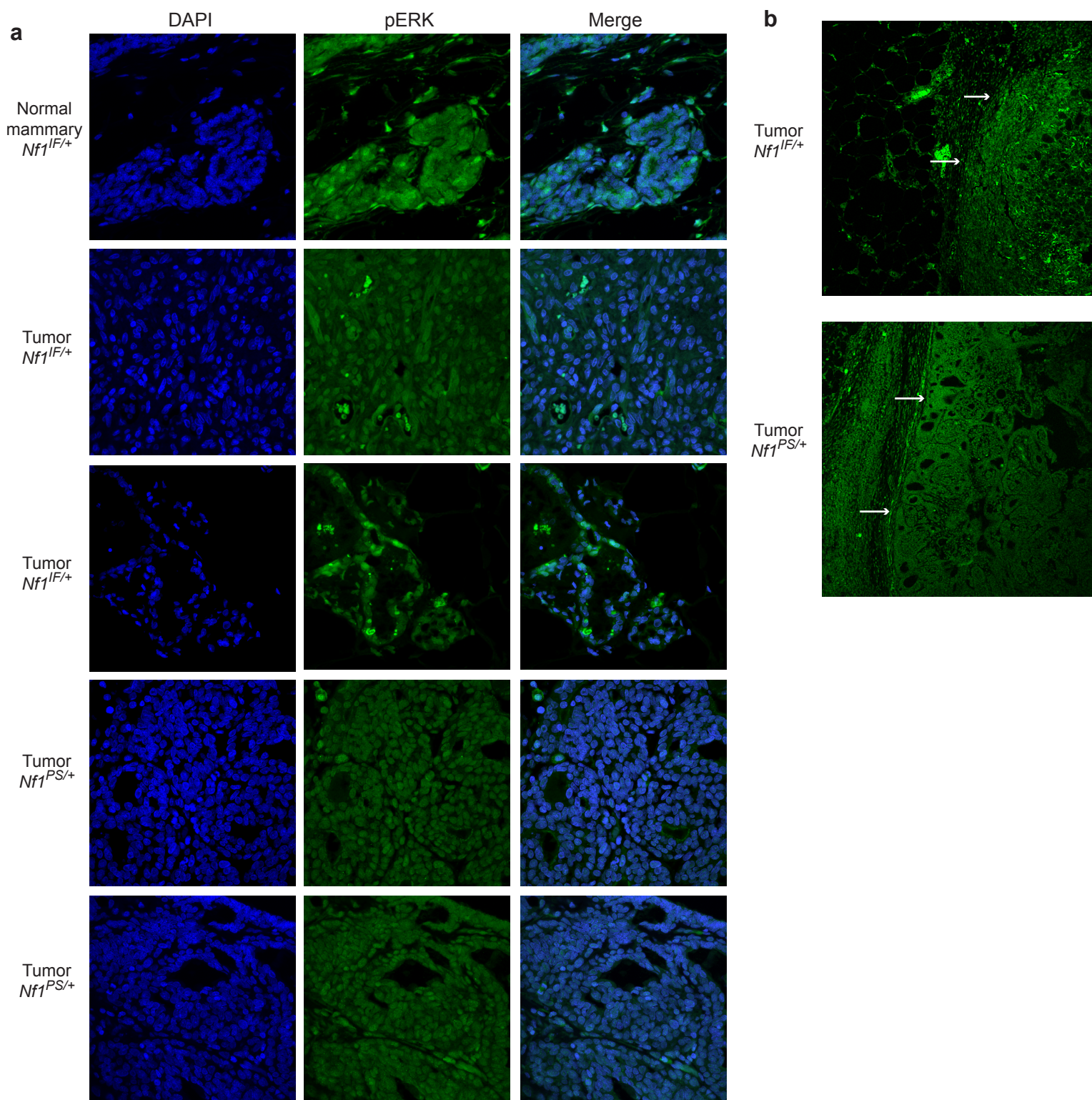
em2 *Nf1*^{IF/+} (#510)



em2 *Nf1*^{IF/+} (#224)

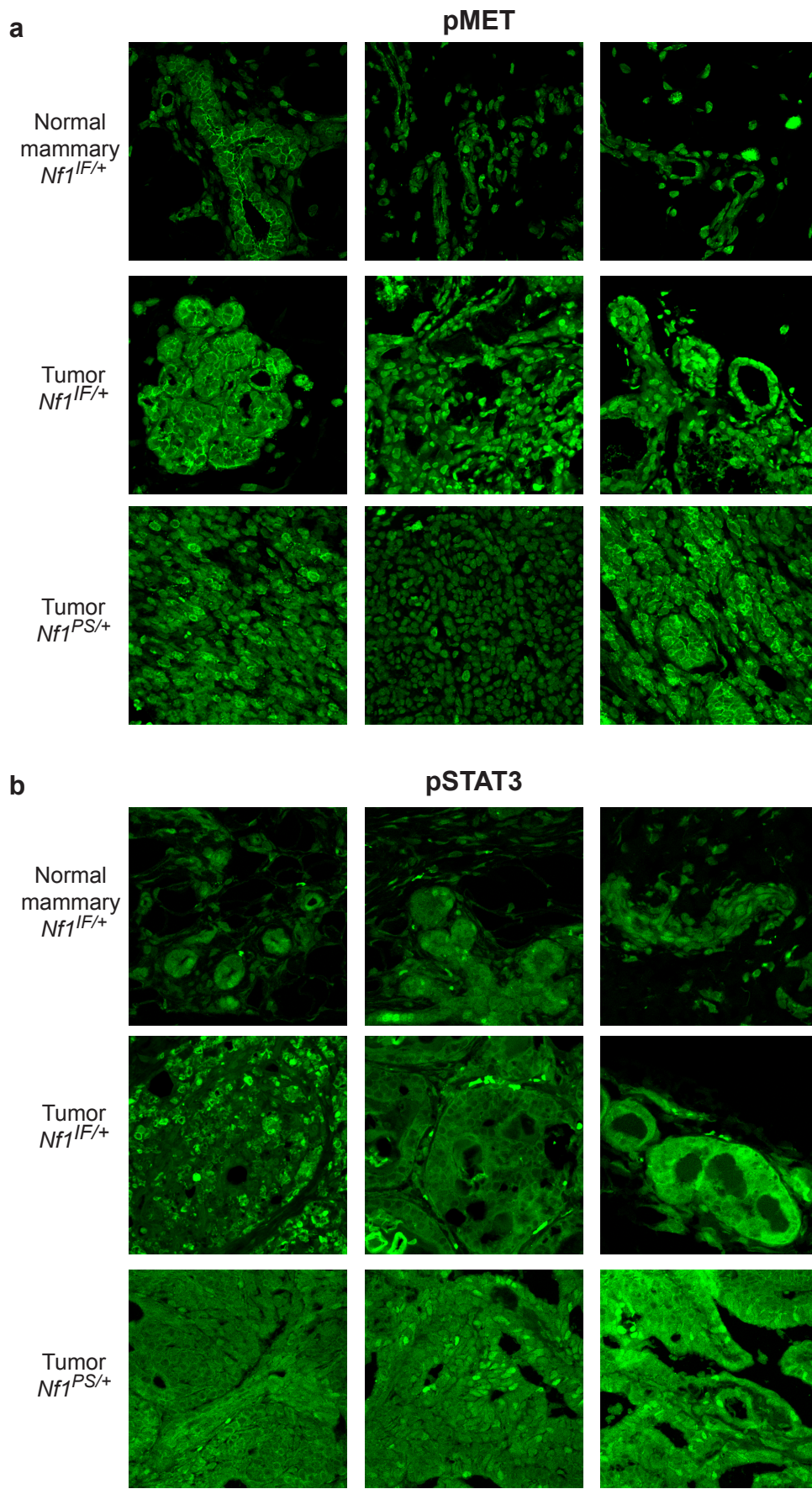


Supplementary Figure 3: Proliferation in *Nf1*^{IF/+} and *Nf1*^{PS/+} tumors. We evaluated Ki67 staining in tumors using the Leica Aperio Nuclear Algorithm and determined there was no significant difference in proliferative staining between *Nf1*^{IF/+} and *Nf1*^{PS/+} tumors. As shown above, Ki67 staining (DAB) was variable among each genotype. Images are shown at 100X magnification.



Supplementary Figure 4: Increased nuclear pERK signal is present in *Nf1*-deficient mammary tumors.

a) Immunofluorescence of pERK (Thr202/Tyr204) was evaluated in a normal mammary gland and mammary adenocarcinomas from *Nf1*^{IF/+} and *Nf1*^{PS/+} rats. In normal tissue, pERK signal was present predominantly in the cytoplasm compared to the nuclear pERK signal present in the tumors. Confocal images are shown at 600X. DAPI was used as a nuclear stain. b) Imaging of tumors at 100X revealed that ERK activation is stronger at the tumor periphery (arrows).



Supplementary Figure 5: Increased pMET and pSTAT3 expression in *Nf1*-deficient mammary tumors. Immunofluorescence of a) pMET (Y1234/35) and b) pSTAT3 (Y705) was evaluated in a normal mammary gland and mammary adenocarcinomas from *Nf1^{IF/+}* and *Nf1^{PS/+}* rats. Confocal images are shown at 600X.

#	Sex	5' CRISPR	3' CRISPR	Tumor Onset (days)	Age of Death (days)	F1	DNA Indels	Line Name
1	M	wt	wt		Alive	NA		
2	M		-57 (wt)	NA	477	Yes	c.2669_2725del	<i>Nf1</i> ^{IF-57/+}
3	M	+1,-8 bp	+4,-10	NA	416	Yes	c.2659_2660insT,2660_2667del,2715_2716insTGTT,2716-2725del c.2669_2725del	<i>Nf1</i> ^{IF-57/PS-8}
4	F		-61 (wt)	53	58	NA		
5	F		IF indel (HMA)	53	63	NA		
6	F		-54	60	77	*		
7	M	+1,-4	-20		Alive	None		
8	F	-11 (wt)	-4		62 [#]	NA		
9	F	+8,-1	-11	29	49	NA		
10	F	-11		51	64	Yes	c.2661_2671del c.2662_2724del	<i>Nf1</i> ^{IF-63/PS-11}
11	M	-57			314	None		
12	F	-6	-10	47	62	*		
13	F	-11	-4	54	198	Yes	c.2661_2671del,2721_2724del c.2669_2722del	<i>Nf1</i> ^{IF-54/PS-11}
14	F	-17		47	68	NA		
15	M		-54					
16	M		-66 (wt)		Alive	NA		
17	M		IF indel (HMA)		Alive	NA		
18	F	-2 (wt)			Alive	NA		
19	F		-66	28	54	NA		
		-11	3sub,2sub					
			+1 (wt)	89	189	NA		

Supplementary Table 1: Summary of G0 animals obtained from CRISPR-Cas9 injections.

Summary of indels resulting from CRISPR-Cas9 injections including tumor onset and survival. The most common base pair alterations at the 5' and 3' CRISPR sites are listed (additional indels that were identified in each G0 animal are listed in Supplemental Table 2). Mutant alleles that resulted in large deletions between 5' and 3' CRISPR target regions are listed in the middle of the 5' and 3' CRISPR columns; "wt" refers to the wildtype allele being observed by sequencing. IF indel (HMA) indicates that indels were identified by HMA but not sequence verified. All females were euthanized due to tumor burden except for #8 that was taken for control tissue (notated with #). DNA indel notations for non-founder animals can be found in Supplementary Table 2. * Euthanized when pregnant due to tumor burden. None = bred but no progeny.

ID	Sequence (5'-3')	5' CRISPR >	3' CRISPR <	Indels (Clones)	Protein	DNA
WT	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCAAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCTGTCAGCAGATTATGGACCGGCTTCTGTCCTTGATGGTG					
	Y S P P M G P V S E R K G S M I S V M S S E G N V D S P V S R F M D R L L S L M V					
1	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCAAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCTGTCAGCAGATTATGGACCGGCTTCTGTCCTTGATGGTG			WT (4)		
	Y S P P M G P V S E R K G S M I S V M S S E G N V D S P V S R F M D R L L S L M V					
2	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCA-----GATTATGGACCGGCTTCTGTCCTTGATGGTG			WT(4);-57(4) 19 aa deletion	In frame deletion	c.2669_2725del
	Y S P P M G P V S E R R F M D R L L S L M V C					
3	TACAGCCCACCTATGGGCCCTGTCA T -----AAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCA TGTT -----GATTATGGACCGGCTTCTGTCCTTGATG GTG			WT(0);+1,-8,+4,-10(3);	Premature stop	c.2659_2660insT,2660_2667del,2715_2716insTGT,2716-2725del
	Y S P P M G P V I K G L *			4 aa* + stop		
	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCA-----GATTATGGACCGGCTTCTGTCCTTGATGGTG			-57(1)	In frame deletion	c.2669_2725del
	Y S P P M G P V S E R R F M D R L L S L M V C			19 aa deletion		
4	TACAGCCCACCTATGGGCCCTGTCAGTGAA-----GATTATGGACCGGCTTCTGTCCTTGATGGTG			WT(2);-61(4) 8 aa* + stop	Premature stop	c.2665_2725del
	Y S P P M G P V S E D L W T G F C P *					
6	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCA-----GCAGATTATGGACCGGCTTCTGTCCTTGATGGTG			WT(0);-54(2) 18 aa deletion	In frame deletion	c.2669_2722del
	Y S P P M G P V S E R S R F M D R L L S L M V					
7	TACAGCCCACCTATGGGCCCTGTCAGTGAAC T ----AGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCC-----GGCTTCTGTCCTTGATGGTG			WT(0);+1,-4,-20(4) 23 aa* + stop	Premature stop	c.2665_2666insT,2666_2669del
	Y S P P M G P V S E L G S M I S V M S S E G N V D S P A S V L D G V *			-66(3)	deletion	c.2661_2726del
	TACAGCCCACCTATGGGCCCTGTCAG-----ATTTATGGACCGGCTTCTGTCCTTGATGGTG			22 aa deletion		
	Y S P P M G P V R F M D R L L S L M V C N H E					
	TACAGCCCACCTATG ACC CTGTCAG-----ATTTATGGACCGGCTTCTGTCCTTGATGGTG			1sub,-66(1) 1 aa* + 22 aa deletion	Missense/In frame deletion	c.2651G>A,2661_2726del
	Y S P P M D P V R F M D R L L S L M V C N H E					
	TACAGCCCACCTATGGGCCCTGTCAG-----GGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCC-----GGCTTCTGTCCTTGATGGTG			-11,-20(1) 9 aa* + stop	Premature stop	c.2661_2671del,2718_2737del
	Y S P P M G P V R V Y D F C N V F *					
8	TACAGCCCACCTATGGGCCCTGTCAG-----GGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCTG----CAGATTATGGACCGGCTTCTG T CTTGATGGTG			WT(3) & -11,-4,1sub (1) 9 aa* + stop	Premature stop	c.2661_2671del,2720_2723del,2747C>T
	Y S P P M G P V R V Y D F C N V F *					
	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCAAAGGG T TATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCTGTCAGCAGATTATGGACCGGCTTCTGTCCTTGATGGTG			1sub(1) 1 aa*	Missense	c.2675C>T
	Y S P P M G P V S E R K G F M I S V M S S E G			-12(1)	deletion	c.2661_2672del
	TACAGCCCACCTATGGGCCCTGTCAG-----GTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCTGTCAGCAGATTATGGACCGGCTTCTGTCCTTGATGGTG			4 aa deletion		
	Y S P P M G P V R S M I S V M S S E G N V D S					
	TACAGCCCACCTATGGGCCCTGTCAG-----GGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCTG----CAGATTATGGACCGGCTTCTGTCCTTGATGGTG			-11,-4(1) 9 aa* + stop	Premature stop	c.2661_2671del,2720_2723del
	Y S P P M G P V R V Y D F C N V F *					
	TACAGCCCACCTATGGGCCCT A TCAG-----GGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCTG----CAGATTATGGACCGGCTTCTGTCCTTGATGGTG			1sub,-11,-4(1) 10 aa* + stop	Premature stop	c.2656G>A,2661_2671del,2720_2723del
	Y S P P M G P I R V Y D F C N V F *					
9	TACAGCCCACCTATGGGCCCTGTCAGTGAACG GTCTATGT -AAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCT-----TATGGACCGGCTTCTGTCCTTGATGGTG			WT(0);+8,-1,-11(2)	Premature stop	c.2666_2667insGTCTATGT,2667del,2719_2729del
	Y S P P M G P V S E R S M *			2 aa* + stop		
10	TACAGCCCACCTATGGGCCCTGTCAG-----GGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTACCTGTCAGCAGATTATGGACCGGCTTCTGTCCTTGATGGTG			WT(1);-11(1) 9 aa* + stop	Premature stop	c.2661_2671del
	Y S P P M G P V R V Y D F C N V F *			-63(2)	deletion	c.2662_2724del
	TACAGCCCACCTATGGGCCCTGTCAGT-----AGATTATGGACCGGCTTCTGTCCTTGATGGTG					

	Y S P P M G P V S R F M D R L L S L M V C N H	21 aa deletion		
11	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCA-----GATTTATGGACCGGCTTCTGTCCTTGATGGTG	WT(0); -57(4)	deletion	c.2669_2725del
	Y S P P M G P V S E R R F M D R L L S L M V C	19 aa deletion		
12	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCA-----GCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	WT(0); -54 (1)	deletion	c.2669_2722del
	Y S P P M G P V S E R S R F M D R L L S L M V	18 aa deletion		
	TACAGCCCACCTATGGGCCCTGTCAGTGAA-----GGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGTCAGCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	-6(1)	deletion	c.2665_2670del
	Y S P P M G P V S E G S M I S V M S S E G N V	2 aa deletion		
	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCAAAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCA-----GATTTATGGACCGGCTTCTGTCCTTGATGGTG	+1, -10(2)	Premature stop	c.2667_2688insC, 2726_2725del
	Y S P P M G P V S E R Q R V Y D F C N V F *	10 aa* + stop		
13	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCA-----GCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	WT(0); -54(1)	deletion	c.2669_2722del
	Y S P P M G P V S E R S R F M D R L L S L M V	18 aa deletion		
	TACAGCCCACCTATGGGCCCTGTCAG-----GGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGT---AGATTTATGGACCGGCTTCTGTCCTTGATGGTG	-11, -4(4)	Premature stop	c.2661_2671del, 2721_2724del
	Y S P P M G P V R V Y D F C N V F *	9 aa* + stop		
14	TACAGCCCACCTATGG-----CCCTGTCAGTGA-----TTTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGTCAGCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	WT(0); -1, -17(1)	Premature stop	c.2651del, 2664_2680del
	Y S P P M A L S V I S V M S S E G N D S P V S R F M D R L L S L M V C N H E K V G	> 33 aa* + stop?		
	TACAGCCCACCTATGGGCCCTGTCAGTGA-----TTTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGTCAGCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	-17(1)	Premature stop	c.2664_2680del
	Y S P P M G P V S D F C N V F *	7 aa* + stop		
	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCA-----GCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	-54(1)	deletion	c.2669_2722del
	Y S P P M G P V S E R S R F M D R L L S L M V	18 aa deletion		
15	TACAGCCCACCTATGGGCCCTGTCAG-----ATTTATGGACCGGCTTCTGTCCTTGATGGTG	WT(3); -66(2)	deletion	c.2661_2726del
	Y S P P M G P V R F M D R L L S L M V C N H E	22 aa deletion		
16	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCAAAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGTCAGCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	WT(3)		
	Y S P P M G P V S E R K G S M I S V M S S E G N V D S P V S R F M D R L L S L M V			
17	TACAGCCCACCTATGGGCCCTGTCAGTGAAC--AAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGTCAGCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	WT(1); -2 (1)	Premature stop	c.2666_2667del
	Y S P P M G P V S E Q R V Y D F C N V F *	10 aa* + stop		
	TACAGCCCACCTATGGGCCCTGTCAG-----ATTTATGGACCGGCTTCTGTCCTTGATGGTG	-66 (1)	deletion	c.2661_2726del
	Y S P P M G P V R F M D R L L S L M V C N H E	22 aa deletion		
	TACGCCCCACCTATGGGCCCTGTCAGTGAA---AAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGTCAGCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	1sub, -3(1)	Premature stop?	c.2638A>G, 2665_2667del
	Y G P P M G P V S E K G S M I S V M S S E G N	< 33 aa* + stop?		
	TACAGCCCACCTATGGGCCCTGTCAGTGAA---AAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGTCAGCAGATTTATGGACCAAGCTTCTGTCCTTGATGGTG	-3, 1sub(1)	In frame deletion/missense	c.2665_2667del, 2738>A
	Y S P P M G P V S E K G S M I S V M S S E G N V D S P V S R F M D Q L L S L M V C	3 aa deletion + 1 aa*		
18	TACAGCCCACCTATGGGCCCTGTCAG-----ATTTATGGACCGGCTTCTGTCCTTGATGGTG	WT(0); -66 (3)	deletion	c.2661_2726del
	Y S P P M G P V R F M D R L L S L M V C N H E	22 aa deletion		
	TACAGCCCACCTATGGGCCCTGTCAG-----GGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGAATGTTGATTTATGGACCGGCTTCTGTCCTTGATGGTG	-11, 3sub, 2sub (1)	Premature stop	c.2661_2671del, 2720T>A, 2721C>A, 2722A>T, 2724C>T, 2725A>T
	Y S P P M G P V R V Y D F C N V F *	9 aa* + stop		
19	TACAGCCCACCTATGGGCCCTGTCAGTGAACGCAAAAGGGTCTATGATTCTGTAATGTCTTCTGAAGGGAATGTTGATTCACCTGTCAAGCAGATTTATGGACCGGCTTCTGTCCTTGATGGTG	WT(1); +1(2)	Premature stop	c.2722_2723insA
	Y S P P M G P V S E R K G S M I S V M S S E G N V D S P V K Q I Y G P A S V L D G V *	12 aa* + stop		

Supplementary Table 2: Detailed sequence analysis of *Nf1* G0 rats. 34 mutant alleles, including 25 unique mutant alleles, were identified by Sanger sequencing. Sequences for all alleles identified in G0 animals are shown.

G0/F0 Animals					
Animal	Sex	Genotype	Age (days)	Tissue/Mammary Pad Description	Pathology
2	M	<i>Nf1</i> ^{IF-57/+}	477	R1 Mammary Fat Pad L4 Mammary Fat Pad R2 Mammary Fat Pad L1 Mammary Fat Pad L4 Mammary Fat Pad R1 Mammary Fat Pad	mammary adenocarcinoma - acinar and mucinous mammary pad - galactorrhea mammary adenocarcinoma - acinar and ductular two mammary adenocarcinomas 1-acinar and ductular 2-secretory acinar mammary pad - galactorrhea mammary pad - galactorrhea
3	M	<i>Nf1</i> ^{IF-57/PS-8}	416	L1 Mammary Fat Pad Right flank L1 Mammary Fat Pad L4 Mammary Fat Pad	mammary adenoma - cystic fibrous histiocytic sarcoma mammary adenocarcinoma with two small intraductal tumors mammary adenoma - cystic
4	F		58	R1 Mammary Fat Pad L4 Mammary Fat Pad R4 Mammary Fat Pad L5/6 Mammary Fat Pad L4 Mammary Fat Pad	mammary adenocarcinoma - acinar mammary adenocarcinoma - acinar and solid mammary adenocarcinoma - acinar and solid mammary adenocarcinoma - acinar and solid mammary adenocarcinoma - acinar and solid
6	F	<i>Nf1</i> ^{IF-54/+}	77	R2 Mammary Fat Pad R5/6 Mammary Fat Pad L2 Mammary Fat Pad L4 Mammary Fat Pad R5/6 Mammary Fat Pad L5/6 Mammary Fat Pad R4 Mammary Fat Pad L4/5 Mammary Pad	mammary adenocarcinoma - acinar mammary adenocarcinoma - acinar mammary adenocarcinoma - acinar mammary hyperplasia, mammary adenocarcinoma - acinar and ductular mammary hyperplasia; mammary adenocarcinoma - acinar, ductular and cystic mild mammary hyperplasia; mammary adenocarcinoma - cystic and papillary mammary adenocarcinoma - ductular moderately severe acinar hyperplasia
10	F	<i>Nf1</i> ^{IF-63/PS-11/+}	64	R4 Mammary Fat Pad R5/6 Mammary Fat Pad R5/6 Mammary Fat Pad L4 Mammary Fat Pad L5/6 Mammary Fat Pad L5/6 Mammary Fat Pad	mammary adenocarcinoma - acinar and solid lactating mammary gland with small acinar adenocarcinoma lactating mammary with adenocarcinoma - acinar and cystic mammary adenocarcinoma - acinar and solid mammary adenocarcinoma - acinar and solid mammary adenocarcinoma - acinar
13	F	<i>Nf1</i> ^{IF-54/PS-11}	198	R4 Mammary Fat Pad L5/6 Mammary Fat Pad L3 Mammary Fat Pad Right Brachial Lymph Node Left Brachial Lymph Node Aortic Lymph Node L4 Mammary Fat Pad	mammary adenocarcinoma - acinar and solid 2 mammary adenocarcinomas - acinar and ductular 2) acinar mammary adenocarcinoma - acinar and ductular large lymph node with hyperplasia large lymph node with hyperplasia lymph node lymph node

rNF1-2 F1 animals					
Folder	Sex	Genotype	Age (days)	Tissue/Mammary Pad Description	Pathology
303	F	<i>Nf1</i> ^{IF-57/+}	62	R4 Mammary Fat Pad R3 Mammary Fat Pad L4 Mammary Fat Pad L4 normal mammary tissue	mammary adenocarcinoma - acinar and solid mammary adenocarcinoma - solid, ductular with stroma slight acinar hyperplasia mild acinar hyperplasia
304	F	<i>Nf1</i> ^{IF-57/+}	89	R4 Mammary Fat Pad L5/6 Mammary Fat Pad L2 Mammary Fat Pad L1 Mammary Fat Pad	mammary adenocarcinoma - acinar and cystic mammary adenocarcinoma - solid, acinar and cystic mammary adenocarcinoma - solid and cystic mammary adenocarcinoma - solid and cystic
366	F	<i>Nf1</i> ^{IF-57/+}	98	L4 Mammary Fat Pad - 1 L4 Mammary Fat Pad - 2 R2 Mammary Fat Pad R4 Mammary Fat Pad - 1 R4 Mammary Fat Pad - 2 L2 Mammary Fat Pad	mammary adenocarcinoma - acinar and ductular mammary adenocarcinoma - acinar and ductular mammary adenocarcinoma - acinar and ductular mammary adenocarcinoma - acinar and ductular mammary adenocarcinoma - cystic and ductular mammary adenoma

rNF1-3 F1 animals					
Folder	Sex	Genotype	Age (days)	Tissue/Mammary Pad Description	Pathology
357	F	<i>Nf1</i> ^{PS-8/+}	84	R5/6 Mammary Fat Pad R1 Mammary Fat Pad L4 Mammary Fat Pad - 2 L4 Mammary Fat Pad - 1 L2 Mammary Fat Pad R4 Mammary Fat Pad R3/R4 Normal Mammary Tissue	mammary adenocarcinoma - mostly solid with some invasion mammary adenocarcinoma - acinar mammary adenocarcinoma - mostly solid with hemorrhage mammary adenocarcinoma - solid mammary adenocarcinoma - acinar and solid mammary adenocarcinoma - acinar and solid small mammary intraductal solid adenocarcinoma
413	F	<i>Nf1</i> ^{PS-8/+}	105	L2 Mammary Fat Pad L4 Mammary Fat Pad - 1 L3 Mammary Fat Pad L4 Mammary Fat Pad - 2 L4 Mammary Fat Pad - 3 L5/6 Mammary Fat Pad R2 Mammary Fat Pad R5/6 Mammary Fat Pad R4 Mammary Fat Pad	mammary adenocarcinoma - acinar mammary adenocarcinoma - acinar and ductular mammary adenocarcinoma - acinar and solid mammary adenocarcinoma - acinar and solid 6 separate mammary tumors, 4 acinar, one adenoma and one with edema solid, acinar, ductular and cystic 5 small mammary acinar tumors in an abscess. mammary adenocarcinoma - ductular, solid and acinar mammary adenocarcinoma - acinar, ductular, cystic

rNF1-10 F1 animals					
Folder	Sex	Genotype	Age (days)	Tissue/Mammary Pad Description	Pathology
246	F	<i>Nf1</i> ^{IF-63/PS-11/+}	96	R2 Mammary Fat Pad L5/6 Mammary Fat Pad - 1 L5/6 Mammary Fat Pad -2 R4 Normal Mammary Tissue	mammary adenocarcinoma - ductular and solid mammary adenocarcinoma - cystic, papillary, solid, and ductal mammary adenocarcinoma - ductular, acinar and cystic mild acinar hyperplasia
252	F	<i>Nf1</i> ^{IF-63/PS-11/+}	183	R4 Mammary Fat Pad L5/6 Mammary Fat Pad L4 Mammary Fat Pad L2 Mammary Fat Pad L2 Mammary Fat Pad	normal mammary gland mammary adenocarcinoma - acinar focal hyperplasia and mammary adenoma mammary adenocarcinoma - solid normal mammary

rNF1-13 F1 animals					
Folder	Sex	Genotype	Age (days)	Tissue/Mammary Pad Description	Pathology
262	F	<i>Nf1</i> ^{PS-11/+}	92	R2 Mammary Fat Pad Normal mammary tissue	mammary adenocarcinoma - solid, ductular with stroma normal mammary tissue
391	F	<i>Nf1</i> ^{PS-11/+}	89	R4 Mammary Fat Pad - 1 R4 Mammary Fat Pad - 2 R4 Mammary Fat Pad - 3 L4 Mammary Fat Pad L2 Mammary Fat Pad R2 Normal Mammary	mammary adenocarcinoma - ductular mammary adenocarcinoma - ductular and solid mammary adenocarcinoma - ductular 3 small mammary adenocarcinomas - acinar mammary adenocarcinoma - acinar and solid normal mammary gland
397	F	<i>Nf1</i> ^{PS-11/+}	118	L2 Mammary Fat Pad L4 Mammary Fat Pad - 2 L5/6 Mammary Fat Pad R5/6 Mammary Fat Pad L4 Mammary Fat Pad - 1 R4 Normal Mammary	mammary adenocarcinoma - solid, acinar and cystic mammary adenocarcinoma - acinar and solid mammary adenocarcinoma - solid mammary adenocarcinoma - solid and acinar mammary adenocarcinoma - ductular mildly hyperplastic mammary gland

Supplementary Table 3: Histopathology of *rNf1* animals

	Shallow Deletion	Diploid	P-value
Sample Size	379	922	
Mean (SD)			
Age at Diagnosis*	55.8 (13)	58.9 (12.2)	< 0.0001
Tumor Size*	29 (20.6)	25 (14.6)	< 0.0001
Median (Q3-Q1)			
NPI [†]	4.07 (5.06-4.03)	4.04 (5.04-3.04)	< 0.0001
Percentages			
Grade [†]			< 0.0001
	1	5.4%	10.7%
	2	27.3%	43.4%
	3	67.3%	45.9%
Stage [†]			0.002
	0	0.4%	1%
	1	28.3%	37.9%
	2	57.2%	53.4%
	3	13.4%	7%
	4	0.7%	0.7%
Subtype [‡]			
Basal	23%	8.4%	< 0.0001
claudin-low	11.9%	13%	0.57
Her2	18.2%	8.1%	< 0.0001
LumA	19%	38%	< 0.0001
LumB	20.8%	23.2%	0.35
Normal	6.9%	9%	0.21
Not Classified	0.3%	0.3%	
Inferred Menopause [‡]			0.0001
Pre-	35.1%	24.6%	
Post-	64.9%	75.4%	
ER [‡]			< 0.0001
Negative	44.1%	21.4%	
Positive	55.9%	78.6%	
Cellularity [†]			< 0.0001
low	7.9%	11.7%	
moderate	31%	41.8%	
high	61.1%	46.5%	

Supplementary Table 4. Clinical and demographic characteristics for patients with shallow deletion *NF1* mutations and diploids. *Differences between shallow deletion and diploid mutations were tested using a t-test. [†]Differences between shallow deletion and diploid mutations were tested using a Wilcox test. [‡] Differences between shallow deletion and diploid mutations were tested using a logistic regression.