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Supplemental Information

FGFR1 Oncogenic Activation Reveals an Alternative Cell of Origin of SCLC in Rb1/p53 Mice

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Supplemental Information

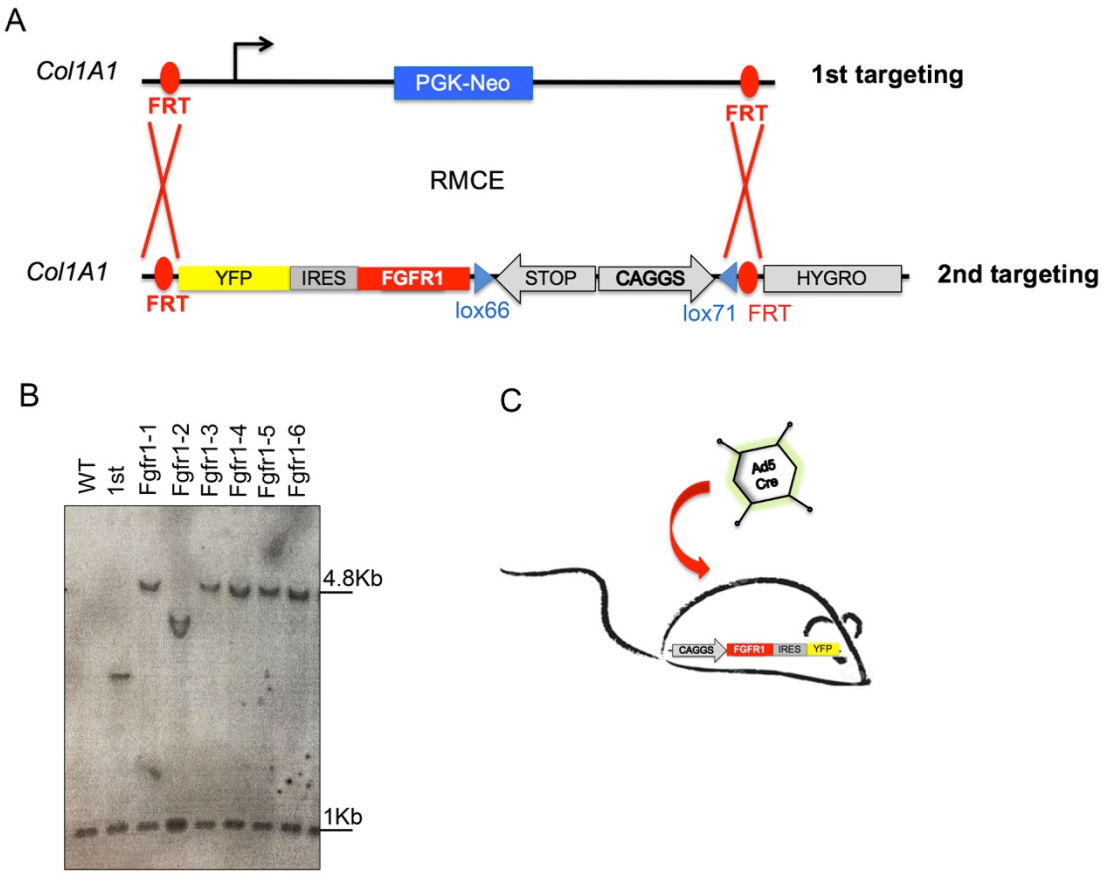


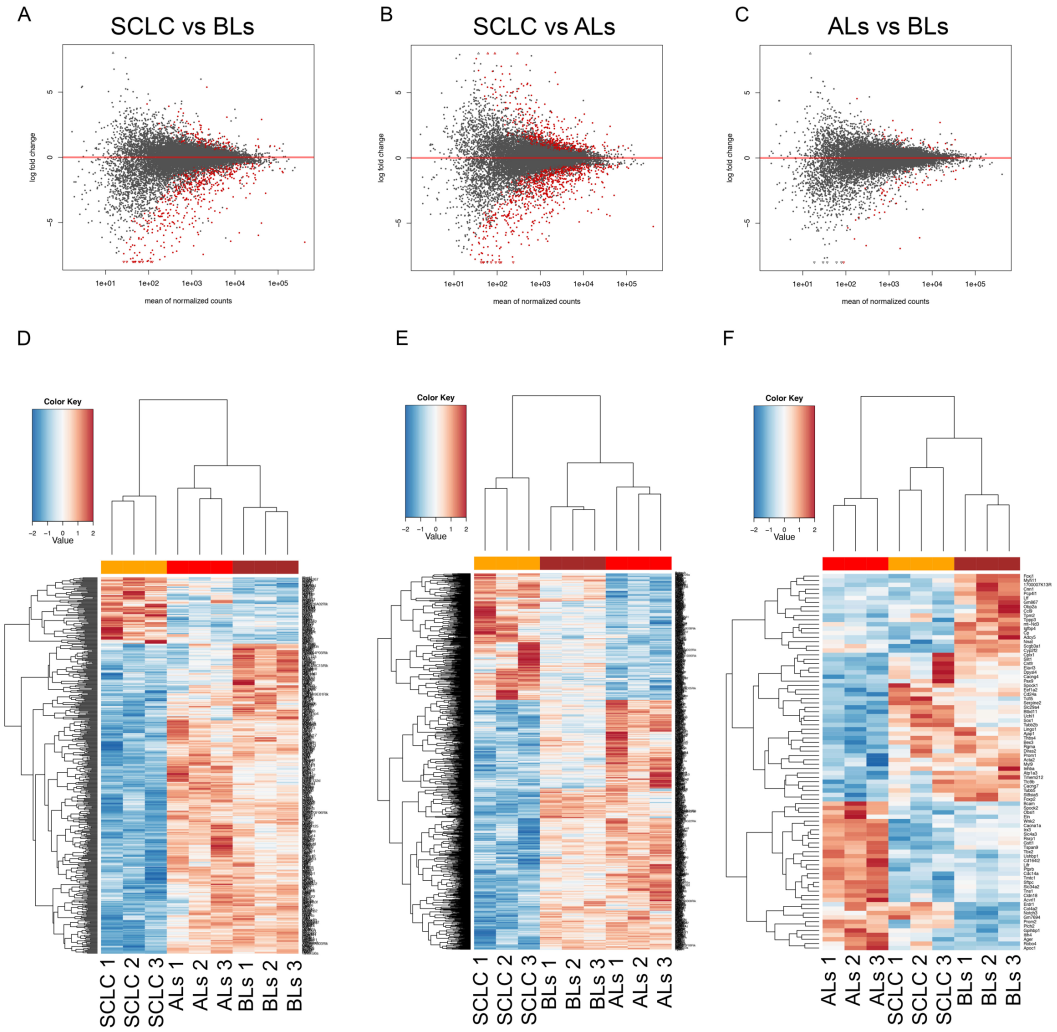
Figure S1. Related to Figure 1

(A) Schematic representation of the Flp-recombinase mediated cassette exchange (RMCE) technology: in the first step a cassette containing PGK-Neomycin flanked by FRT sites was targeted by homologous recombination to the *Col1A1* locus; in the second step, positive ES cell clones were transfected with a plasmid containing LSL-FGFR1^{K656E} followed by YFP and Flp recombinase, which mediated the cassette exchange.

(B) Southern blotting of BglII digested ES cells genomic DNA, hybridized to the *Col1A1* 3' probe, which anneals to a fragment of 1kb in wild-type mice (I line) and to a fragment of 4.9 kb in mice with a floxed allele. 5/6 Fgfr1 ES clones (Line 3 to 8) were heterozygote for the floxed allele. In line 2, an ES cell clone from the first targeting, was loaded as negative control.

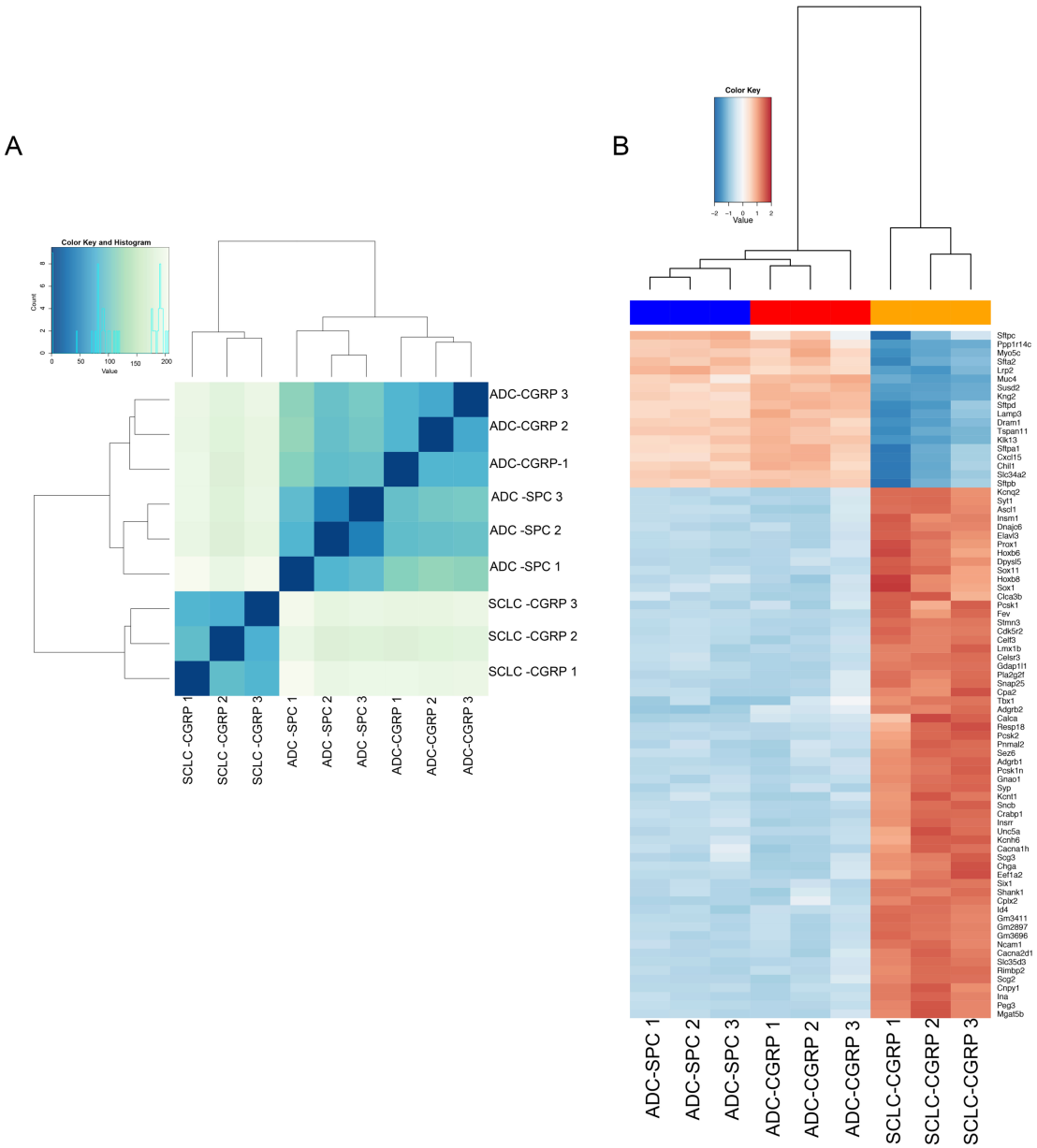
(C) Mice are intratracheally injected with Adenoviruses carrying Cre recombinase in order to activate FGFR1^{K656E} expression in distinctive cell types.

Figure S2. Related to Figure 3



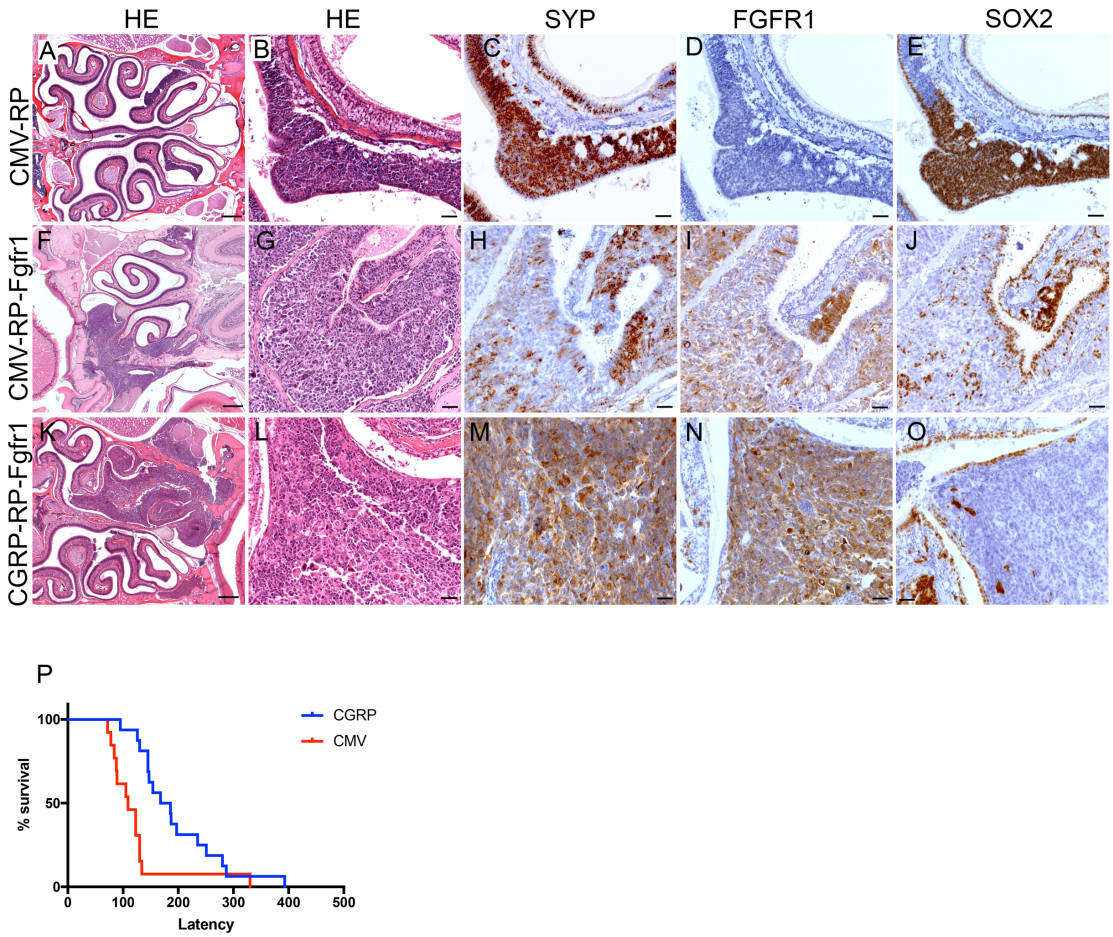
(A-C) MA-plot showing the log 2-fold change vs abundance of normalized gene expression of SCLC vs BLs (A), SCLC vs ALs (B), ALs vs BLs (C). Each point designates a gene; differentially expressed genes are in red. (D-F) Heatmap of significantly (FDR < 0.05) upregulated and downregulated genes in SCLC vs BLs (D), SCLC vs ALs (E), ALs vs BLs (F).

Figure S3. Related to Figure 6



(A) Distance matrix and clustering of samples. Darkest color indicates lowest distance between samples. (B) Heatmap of genes with the highest rotation value for PC1.

Figure S4. Related to Figure 1



(A-T) HE, SYN, FGFR1, SOX2 staining on nasal sections of RP mice (A-E and K-O) and RP-fgfr1 mice (F-J and P-T) injected with either Ad5-CMV-Cre (CMV-RP and CMV-RP-Fgfr1, respectively) or Ad5-CGRP-Cre (CGRP-RP and CGRP-RP-Fgfr1, respectively). Scale bar, 50μm.

(U) Nasal tumor-free survival curve of RP-Fgfr1 mice injected with either Ad5-CGRP-Cre (CGRP) or Ad5-CMV-Cre (CMV).

Table S1. Neoplastic lesions developed by individual RP-Fgfr1 mice injected with Ad5-CMV-Cre. Related to Figure 1.

CMV	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP-Fgfr1	16GFE125	**72	-	-	+	-	+	+
RP-Fgfr1	16GFE050	78	-	-	+	-	-	+
RP-Fgfr1	16GFE051	84	-	-	-	-	-	+
RP-Fgfr1	16GFE067	88	-	-	+	+	-	+
RP-Fgfr1	16GFE068	89	-	-	-	+	-	+
RP-Fgfr1	16GFE077	105	-	-	+	-	-	+
RP-Fgfr1	16GFE148	109	-	-	-	-	-	+
RP-Fgfr1	15GFE229	123	-	-	-	-	-	+
RP-Fgfr1	16GFE160	123	-	-	+	+	+	+
RP-Fgfr1	16GFE096	130	-	-	+	+	+	+
RP-Fgfr1	16GFE163	130	-	-	+	+	+	+
RP-Fgfr1	16GFE074	134	-	-	-	-	-	+
RP-Fgfr1	16GFE080	144	-	-	+	+	+	-
RP-Fgfr1	15GFE255	150	-	-	+	+	+	-
RP-Fgfr1	16GFE098	162	-	-	+	-	+	-
RP-Fgfr1	15GFE286	173	-	-	-	+	+	-
RP-Fgfr1	16GFE135	179	-	-	+	+	+	-
RP-Fgfr1	15GFE285	187	-	-	+	+	+	-
RP-Fgfr1	15GFE291	189	+	-	+	-	+	-
RP-Fgfr1	16GFE150	231	-	-	+	+	+	+
RP-Fgfr1	16GFE042	330	+	-	+	+	-	+
RP-Fgfr1	16GFE062	393	-	-	-	-	-	-
		105,41	0%	0%	58,33%	41,67%	33,33%	***63,63%
		213,8	20%	0%	80%	70%	80%	

*IPD: intrapulmonary dissemination; BL: bronchial lesions; AL: alveolar lesions; ADC: Adenocarcinoma.; NL: nasal lesions.

**Samples depicted in beige indicate mice that died prematurely due to other phenotypes (e.g. nasal tumor) and therefore did not live long enough to develop lung tumors with an expected longer latency such as SCLC. For this reason, we calculated two different penetrance, depicted as well in beige or in white, according to the considered mouse group.

***Nasal tumor are independent from lung tumors and have a much shorter latency, therefore their penetrance is calculated on the total mouse number.

Table S2. Neoplastic lesions developed by individual RP mice injected with Ad5-CMV-Cre. Related to Figure 1

CMV	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP	16GFE092	**123	-	-	+	-	-	+
RP	16GFE109	169	-	-	+	+	-	NA
RP	16GFE110	169	-	-	+	-	-	NA
RP	17GFE042	191	+	+	-	+	-	+
RP	16GFE128	199	+	+	+	+	-	-
RP	16GFE152	208	+	+	+	-	-	-
RP	16GFE154	208	+	+	-	-	-	-
RP	17GFE079	219	+	+	+	+	-	-
RP	16GFE127	223	+	+	-	-	-	-
RP	16GFE023	231	+	+	-	+	-	-
RP	16GFE026	235	+	+	-	-	-	NA
RP	16GFE141	244	+	+	+	+	-	-
RP	16GFE142	244	+	+	+	+	-	-
RP	16GFE144	245	+	+	+	-	-	-
RP	17GFE103	247	+	+	+	-	-	-
RP	16GFE162	249	+	+	-	+	-	-
RP	16GFE032	260	+	+	-	+	-	-
RP	16GFE034	260	+	+	-	+	-	-
RP	17GFE001	266	+	+	+	-	-	+
RP	16GFE035	267	+	+	-	+	-	-
RP	16GFE166	277	+	+	-	-	-	-
RP	17GFE009	298	+	+	+	-	-	-
RP	17GFE041	333	+	+	+	-	-	-
			NA	NA	NA	NA	NA	***15%
		238,27	90%	90%	54,54%	50%	0%	

*IPD: intrapulmonary dissemination; BL: bronchial lesions; AL: alveolar lesions; ADC: Adenocarcinoma.; NL: nasal lesions.

**Samples depicted in beige indicate mice that died prematurely due to other phenotypes (e.g. nasal tumor) and therefore did not live long enough to develop lung tumors with an expected longer latency such as SCLC. For this reason, we calculated two different penetrance, depicted as well in beige or in white, according to the considered mouse group.

***Nasal tumor are independent from lung tumors and have a much shorter latency, therefore their penetrance is calculated on the total mouse number.

Table S3. Neoplastic lesions developed by individual RP-Fgfr1 mice injected with Ad5-CGRP-Cre. Related to Figure 1.

CGRP	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP-Fgfr1	16GFE069	**95	-	-	-	-	-	+
RP-Fgfr1	16GFE149	112	-	-	-	-	-	-
RP-Fgfr1	16GFE070	126	-	-	-	-	-	+
RP-Fgfr1	16GFE095	130	-	-	-	-	-	+
RP-Fgfr1	16GFE168	142	-	-	-	-	-	-
RP-Fgfr1	16GFE170	142	-	-	-	-	-	+
RP-Fgfr1	16GFE169	142	-	-	-	-	-	+
RP-Fgfr1	16GFE171	142	-	-	+	-	-	-
RP-Fgfr1	15GFE252	145	-	-	-	-	-	+
RP-Fgfr1	15GFE253	145	-	-	-	-	-	+
RP-Fgfr1	16GFE081	147	-	-	-	-	-	+
RP-Fgfr1	16GFE112	154	-	-	-	-	-	+
RP-Fgfr1	16GFE103	168	-	-	-	-	-	+
RP-Fgfr1	17GFE046	186	-	-	-	-	-	+
RP-Fgfr1	15GFE284	187	-	-	-	-	-	+
RP-Fgfr1	16GFE145	193	-	-	-	-	-	+
RP-Fgfr1	16GFE147	197	-	-	+	+	+	+
RP-Fgfr1	16GFE007	207	-	-	+	-	-	+
RP-Fgfr1	17GFE094	235	-	-	+	-	+	+
RP-Fgfr1	17GFE099	238	-	-	-	+	-	-
RP-Fgfr1	17GFE006	251	-	-	-	+	-	+
RP-Fgfr1	17GFE013	280	-	-	-	-	-	+
RP-Fgfr1	16GFE033	287	-	-	-	-	+	-
RP-Fgfr1	16GFE040	280	-	-	-	-	-	+
RP-Fgfr1	17GFE155	304	-	-	-	-	+	-
RP-Fgfr1	16GFE047	356	+	+	+	+	+	-
RP-Fgfr1	17GFE198	375	+	+	-	+	+	-
RP-Fgfr1	16GFE057	393	+	+	+	+	-	+
RP-Fgfr1	16ESE019	416	-	-	-	-	+	NA
		135,17	0%	0%	8%	0%	0%	***71,42%
		267,82	17,64%	17,64%	29,41%	35,29%	41,17%	

*IPD: intrapulmonary dissemination; BL: bronchial lesions; AL: alveolar lesions; ADC: Adenocarcinoma.; NL: nasal lesions.

**Samples depicted in beige indicate mice that died prematurely due to other phenotypes (e.g. nasal tumor) and therefore did not live long enough to develop lung tumors with an expected longer latency such as SCLC. For this reason, we calculated two different penetrance, depicted as well in beige or in white, according to the considered mouse group.

***Nasal tumor are independent from lung tumors and have a much shorter latency, therefore their penetrance is calculated on the total mouse number.

Table S4. Neoplastic lesions developed by individual RP mice injected with Ad5-CGRP-Cre. Related to Figure 1.

CGRP	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP	16GFE102	168	-	-	-	-	-	NA
RP	16GFE104	168	-	-	-	-	-	NA
RP	16GFE105	168	-	-	-	-	-	NA
RP	16GFE116	201	-	-	-	-	-	NA
RP	17GFE098	235	+	-	-	+	-	-
RP	16GFE143	245	-	-	-	-	-	-
RP	16GFE164	249	-	-	-	-	+	-
RP	17GFE113	249	-	-	-	-	-	-
RP	17GFE118	259	-	-	-	-	-	-
RP	17GFE131	268	+	-	+	+	-	-
RP	17GFE036	271	+	+	-	-	-	NA
RP	17GFE135	273	+	-	-	-	-	-
RP	17GFE142	284	+	+	-	-	-	-
RP	15ESE030	288	+	+	-	-	-	NA
RP	17GFE005	293	-	+	-	+	-	-
RP	17GFE154	295	+	+	-	-	-	-
RP	15ESE034	307	+	+	-	-	-	NA
RP	15ESE036	311	+	+	-	+	-	NA
RP	16GFE043	343	+	-	-	-	-	NA
RP	17GFE080	369	+	+	-	+	-	-
RP	17GFE137	369	+	-	-	+	-	-
RP	16GFE052	383	+	+	-	-	-	-
RP	16GFE056	393	-	-	-	-	-	-
RP	17GFE217	399	+	+	-	-	-	-
RP	17GFE124	413	+	-	+	-	-	-
RP	17GFE125	413	-	-	-	+	-	-
RP	17GFE126	413	-	-	-	-	-	-
RP	17GFE252	567	-	-	-	-	-	-
RP	17GFE255	598	-	-	-	+	-	-
		316,96	51,72%	34,44%	6,89%	27,58%	3,44%	***0%

*IPD: intrapulmonary dissemination; BL: bronchial lesions; AL: alveolar lesions; ADC: Adenocarcinoma.; NL: nasal lesions.

**Samples depicted in beige indicate mice that died prematurely due to other phenotypes (e.g. nasal tumor) and therefore did not live long enough to develop lung tumors with an expected longer latency such as SCLC. For this reason, we calculated two different penetrance, depicted as well in beige or in white, according to the considered mouse group.

***Nasal tumor are independent from lung tumors and have a much shorter latency, therefore their penetrance is calculated on the total mouse number.

Table S5. Neoplastic lesions developed by individual RP-Fgfr1 mice injected with Ad5-K14-Cre. Related to Figure 4.

K14	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP-Fgfr1	17GFE166	**88	-	-	-	-	-	+
RP-Fgfr1	17GFE171	102	-	-	-	-	-	+
RP-Fgfr1	17GFE188	130	-	-	-	-	-	+
RP-Fgfr1	17GFE191	138	-	-	-	-	-	+
RP-Fgfr1	17GFE202	160	-	-	-	-	-	+
RP-Fgfr1	17GFE216	172	+	+	-	+	-	-
RP-Fgfr1	17GFE224	197	-	-	-	-	-	+
RP-Fgfr1	17GFE225	207	-	-	+	-	+	-
RP-Fgfr1	17GFE283	252	+	+	-	-	-	-
RP-Fgfr1	18GFE003	281	-	-	-	-	-	-
RP-Fgfr1	18GFE008	291	-	-	-	+	-	+
RP-Fgfr1	18GFE049	340	+	+	+	+	+	+
RP-Fgfr1	18GFE055	351	+	+	-	+	+	+
RP-Fgfr1	18GFE060	357	+	+	+	+	-	-
RP-Fgfr1	18GFE070	370	+	+	-	+	+	NA
RP-Fgfr1	18GFE127	466	-	-	-	+	-	NA
RP-Fgfr1	18GFE051	344	-	-	+	-	+	+
		123,6	0%	0%	0%	0%	0%	***66,66%
		302,33	50%	50%	33,33%	58,33%	41,66%	

*IPD: intrapulmonary dissemination; BL: bronchial lesions; AL: alveolar lesions; ADC: Adenocarcinoma.; NL: nasal lesions.

**Samples depicted in beige indicate mice that died prematurely due to other phenotypes (e.g. nasal tumor) and therefore did not live long enough to develop lung tumors with an expected longer latency such as SCLC. For this reason, we calculated two different penetrance, depicted as well in beige or in white, according to the considered mouse group.

***Nasal tumor are independent from lung tumors and have a much shorter latency, therefore their penetrance is calculated on the total mouse number.

Table S6. Neoplastic lesions developed by individual RP mice injected with Ad5-K14-Cre. Related to Figure 4.

K14	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP	17GFE197	**111	-	-	-	-	-	+
RP	17GFE289	253	-	-	-	-	-	-
RP	17GFE328	267	+	+	-	-	-	-
RP	18GFE004	246	-	-	-	-	-	-
RP	18GFE006	251	+	+	-	-	-	-
RP	18GFE045	321	+	+	-	-	-	+
RP	18GFE056	320	+	+	-	+	-	-
RP	18GFE066	334	+	+	+	-	-	NA
RP	18GFE073	340	+	+	-	+	-	NA
RP	18GFE103	414	+	+	-	-	-	NA
RP	18GFE108	435	+	+	-	-	-	NA
RP	18GFE122	459	+	+	-	-	-	NA
RP	18GFE123	466	-	-	-	+	-	NA
RP	18GFE124	466	-	-	-	-	-	NA
RP	18GFE125	431	-	-	-	-	-	NA
RP	18GFE126	431	-	-	-	-	-	NA
			0%	0%	0%	0%	0%	***28,50%
		362,27	60%	60%	6,67%	20%	0%	

*IPD: intrapulmonary dissemination; BL: bronchial lesions; AL: alveolar lesions; ADC: Adenocarcinoma.; NL: nasal lesions.

**Samples depicted in beige indicate mice that died prematurely due to other phenotypes (e.g. nasal tumor) and therefore did not live long enough to develop lung tumors with an expected longer latency such as SCLC. For this reason, we calculated two different penetrance, depicted as well in beige or in white, according to the considered mouse group.

***Nasal tumor are independent from lung tumors and have a much shorter latency, therefore their penetrance is calculated on the total mouse number.

Table S7. Neoplastic lesions developed by individual RP-Fgfr1 mice injected with Ad5-SPC-Cre. Related to Figure 5.

SPC	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP-Fgfr1	16GFE093	125	-	-	-	-	+	+
RP-Fgfr1	17GFE003	142	-	-	-	-	+	-
RP-Fgfr1	16GFE114	144	-	-	-	-	+	-
RP-Fgfr1	16GFE082	147	-	-	-	-	+	-
RP-Fgfr1	16GFE084	150	-	-	-	-	+	-
RP-Fgfr1	16GFE085	151	-	-	-	-	+	-
RP-Fgfr1	16GFE090	151	-	-	-	-	+	-
RP-Fgfr1	16GFE091	151	-	-	+	-	+	-
RP-Fgfr1	16GFE119	153	-	-	-	-	+	NA
RP-Fgfr1	16GFE120	153	-	-	-	-	+	NA
RP-Fgfr1	16GFE099	162	-	-	-	-	+	NA
RP-Fgfr1	17GFE026	168	-	-	-	-	+	-
RP-Fgfr1	16GFE121	173	-	-	-	-	+	NA
RP-Fgfr1	16GFE118	182	-	-	-	-	+	NA
RP-Fgfr1	16GFE129	200	-	-	-	-	+	-
RP-Fgfr1	17GFE057	203	-	-	-	-	+	-
RP-Fgfr1	16GFE153	239	-	-	-	-	+	-
		164,35	0%	0%	5,88%	0%	100%	8,33%

*Besides SCLC, NE neoplastic lesions include IPD: intrapulmonary dissemination, BL: bronchial lesions; AL: alveolar lesions. ADC: Adenocarcinoma. NL: nasal lesions.

Table S8. Neoplastic lesions developed by individual RP mice injected with Ad5-SPC-Cre. Related to Figure 5.

SPC	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP	16GFE107	169	-	-	-	-	-	NA
RP	16GFE108	169	-	-	-	-	-	NA
RP	16GFE111	169	-	-	-	-	-	NA
RP	17GFE070	301	+	+	-	-	-	-
RP	17GFE153	417	-	-	-	-	-	-
RP	17GFE181	333	+	+	-	-	-	+
RP	17GFE187	357	+	+	-	-	-	-
RP	17GFE221	505	+	+	-	-	-	-
RP	17GFE226	434	+	+	-	-	-	-
RP	17GFE260	472	-	-	-	+	-	-
		332,6	50%	50%	0%	10%	0%	14,29%

*Besides SCLC, NE neoplastic lesions include IPD: intrapulmonary dissemination, BL: bronchial lesions; AL: alveolar lesions. ADC: Adenocarcinoma. NL: nasal lesions.

Table S9. Neoplastic lesions developed by individual RP-Fgfr1 mice injected with Ad5-CC10-Cre. Related to Figure 5.

CC10	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP-Fgfr1	17GFE030	253	-	-	-	-	+	NA
RP-Fgfr1	17GFE031	253	-	-	-	-	+	NA
RP-Fgfr1	17GFE032	253	-	-	-	-	-	NA
RP-Fgfr1	17GFE043	268	-	-	-	-	+	-
RP-Fgfr1	17GFE059	279	-	-	-	-	+	-
RP-Fgfr1	17GFE072	290	-	-	-	-	+	-
RP-Fgfr1	17GFE088	310	-	-	-	-	+	-
RP-Fgfr1	17GFE115	330	-	-	-	-	+	-
RP-Fgfr1	17GFE167	399	-	-	-	-	+	+
		292,78	0%	0%	0%	0%	88,89%	16,67%

*Besides SCLC, NE neoplastic lesions include IPD: intrapulmonary dissemination, BL: bronchial lesions; AL: alveolar lesions. ADC: Adenocarcinoma. NL: nasal lesions.

Table S10. Neoplastic lesions developed by individual RP mice injected with Ad5-CC10-Cre. Related to Figure 5.

CC10	PROMAS	DAYS	SCLC	*IPD	*BL	*AL	*ADC	*NL
RP	16GFE146	184	-	-	-	-	-	-
RP	17GFE033	253	-	-	-	-	-	NA
RP	17GFE034	253	-	-	-	-	-	NA
RP	17GFE035	253	-	-	-	-	-	NA
RP	17GFE150	370	+	+	-	-	-	-
RP	17GFE156	380	-	-	-	-	-	-
RP	17GFE247	549	+	-	-	+	-	-
RP	17GFE253	555	-	-	+	-	-	-
RP	17GFE259	555	+	-	-	+	-	-
RP	17GFE262	555	-	-	-	-	-	-
		372,44	30%	10%	10%	20%	0%	0%

*Besides SCLC, NE neoplastic lesions include IPD: intrapulmonary dissemination, BL: bronchial lesions; AL: alveolar lesions. ADC: Adenocarcinoma. NL: nasal lesions.

Table S11. Penetrance of lung lesions according to the targeted cell-of-origin and genotype. Related to Figure 1, 4, 5.

VIRUS	GENOTYPE	MICE #	SCLC	*IPD	*BL	*AL	*ADC	*NL
CMV	RP	22	90%	90%	55%	50%	0%	15%
	RP-Fgfr1	10	20%	0%	80%	70%	80%	64%
CGRP	RP	29	52%	34%	7%	28%	3%	0%
	RP-Fgfr1	17	18%	18%	29%	35%	41%	70%
K14	RP	15	60%	60%	7%	20%	0%	29%
	RP-Fgfr1	12	50%	50%	33%	58%	42%	67%
SPC	RP	10	50%	50%	0%	10%	0%	14%
	RP-Fgfr1	17	**0%	**0%	6%	0%	100%	8%
CC10	RP	10	30%	10%	10%	20%	0%	0%
	RP-Fgfr1	9	**0%	**0%	0%	0%	89%	17%

*IPD: intrapulmonary dissemination; BL: bronchial lesions; AL: alveolar lesions; ADC: Adenocarcinoma.; NL: nasal lesions

** RP-Fgfr1 mice were sacrificed earlier than RP mice, due to the presence of huge lesion of LADC; therefore we cannot exclude a late appearance of SCLC.

Table S12. Latency range of lung tumors in RP mice injected in this study compared to previous publication by Sutherland et al., 2011. Related to Figure 5

Virus	Latency Range	Study
CGRP	268-413	Ferone et al., 2020
CGRP	255-464	Sutherland et al., 2011
SPC	301-505	Ferone et al., 2020
SPC	319-616	Sutherland et al., 2011
CC10	370-555	Ferone et al., 2020
CC10	389-640	Sutherland et al., 2011

Table S13. Comparison across a variety of studies of tumor type and location obtained in *Trp53$^{F/F}$;Rb1$^{F/F}$* mouse models by targeting distinct cell types. Related to Figure 7

Target cells	Genetics	Inducer	Tumor type and location	Reference
NE	*Trp53$^{F/F}$;Rb1$^{F/F}$*	*IT Ad5-CGRP-Cre	SCLC in central lung	Sutherland et al., 2011
CLUB	*Trp53$^{F/F}$;Rb1$^{F/F}$*	IT Ad5-CC10-Cre	Rare ADC in alveolar space	Sutherland et al., 2011
AT2	*Trp53$^{F/F}$;Rb1$^{F/F}$*	IT Ad5-SPC-Cre	SCLC in central lung	Sutherland et al., 2011
All lung	*Trp53$^{F/F}$;Rb1$^{F/F}$*	IN Ad-Cre	SCLC in main airways; *BADJs	Park et al., 2011
CLUB	*Trp53$^{F/F}$;Rb1$^{F/F}$; Scgb1a1-Cre*	constitutive	No tumors	Park et al., 2011
AT2	*Trp53$^{F/F}$;Rb1$^{F/F}$*	*IN Ad-SPC-CreER + *Tam	Rare ADC in alveolar space	Park et al., 2011
AT2	*Trp53$^{F/F}$;Rb1$^{F/F}$;p130$^{F/F}$*	IN Ad-SPC-CreER + Tam	Rare ADC in alveolar space	Park et al., 2011
AT2 and bronchial cells	*Trp53$^{F/F}$;Rb1$^{F/F}$; SPC-rtTA/(tetO)7-Cre*	*Dox	Rare ADC in alveolar space (also without induction by Dox)	Park et al., 2011
All lung cells	*Trp53$^{F/F}$;Rb1$^{F/F}$;p130$^{F/F}$*	IT Ad5-CMV-Cre	SCLC in proximal and distal airways and BADJ	Yang et al., 2018
NE	*Trp53$^{F/F}$;Rb1$^{F/F}$;p130$^{F/F}$*	IT Ad5-CGRP-Cre	Fewer SCLC in proximal airways	Yang et al., 2018

*IT = intratracheal delivery; IN = intranasal delivery; BADJs = bronchioalveolar duct junctions; Tam = Tamoxifen; Dox = Doxycycline