Cancer Bio Course 2025

Session 4: Introduction to cancer biology

Bridge and Engage Scholars

August 27th, 2025

Memorial Sloan Kettering Cancer Center

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Course structure

In-person activities:

- Session 1 – Introduction to course and basic techniques applied in basic cancer research
  - **Explanation of the question under research** - *why on earth did they decide to do this?*
  - **Discussion figure by figure –** *is this paper not as good as authors think?:*
    - What is the point of each figure/panel?
    - Are there any missing experimental conditions?
    - Are results interpretable?
    - Do the results support the conclusions by the authors?
    - Would you have done anything differently?
    - Are there any missing experiments?
    - What are the limitations of the work?
    - What experiments could be done as a follow-up to the paper?
- Session 2 – Paper discussion
- Session 3 – Paper discussion
- Session 4 – Paper discussion

+ Presentations!!

- Session 5 – Guided live research activity


Cancer Cell
Article

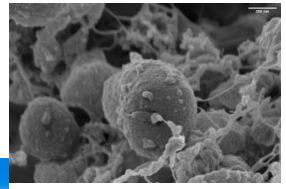
The Genomic Landscape of Endocrine-Resistant Advanced Breast Cancers

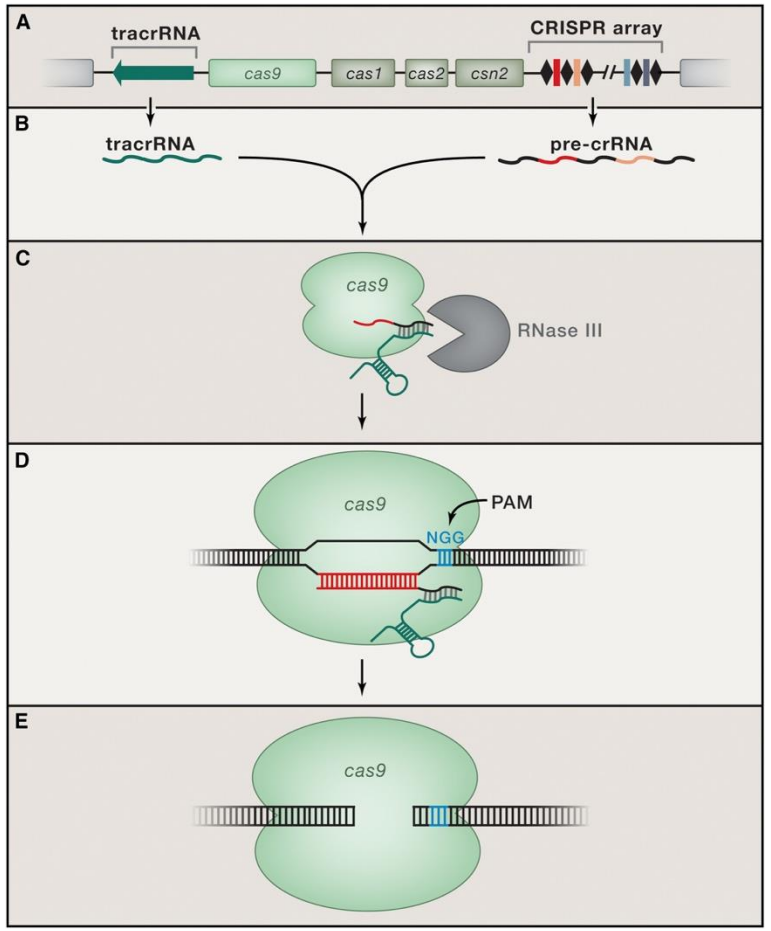

Article

Lung adenocarcinoma promotion by air pollutants

Molecular basis of cancer

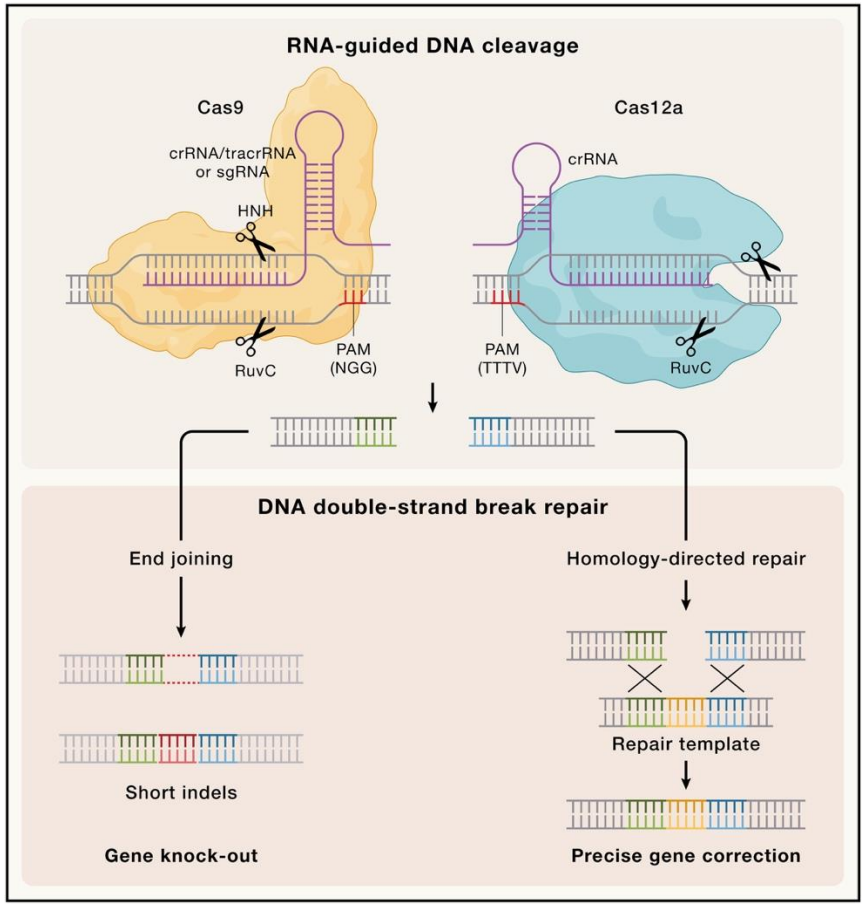
CRISPR-Cas immune system

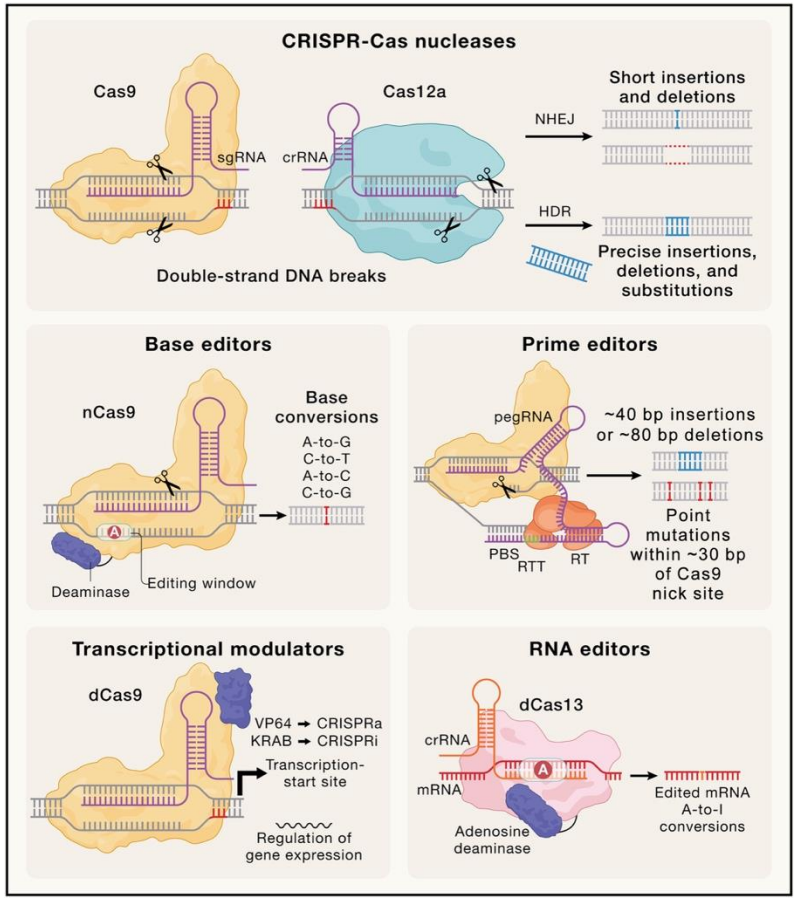




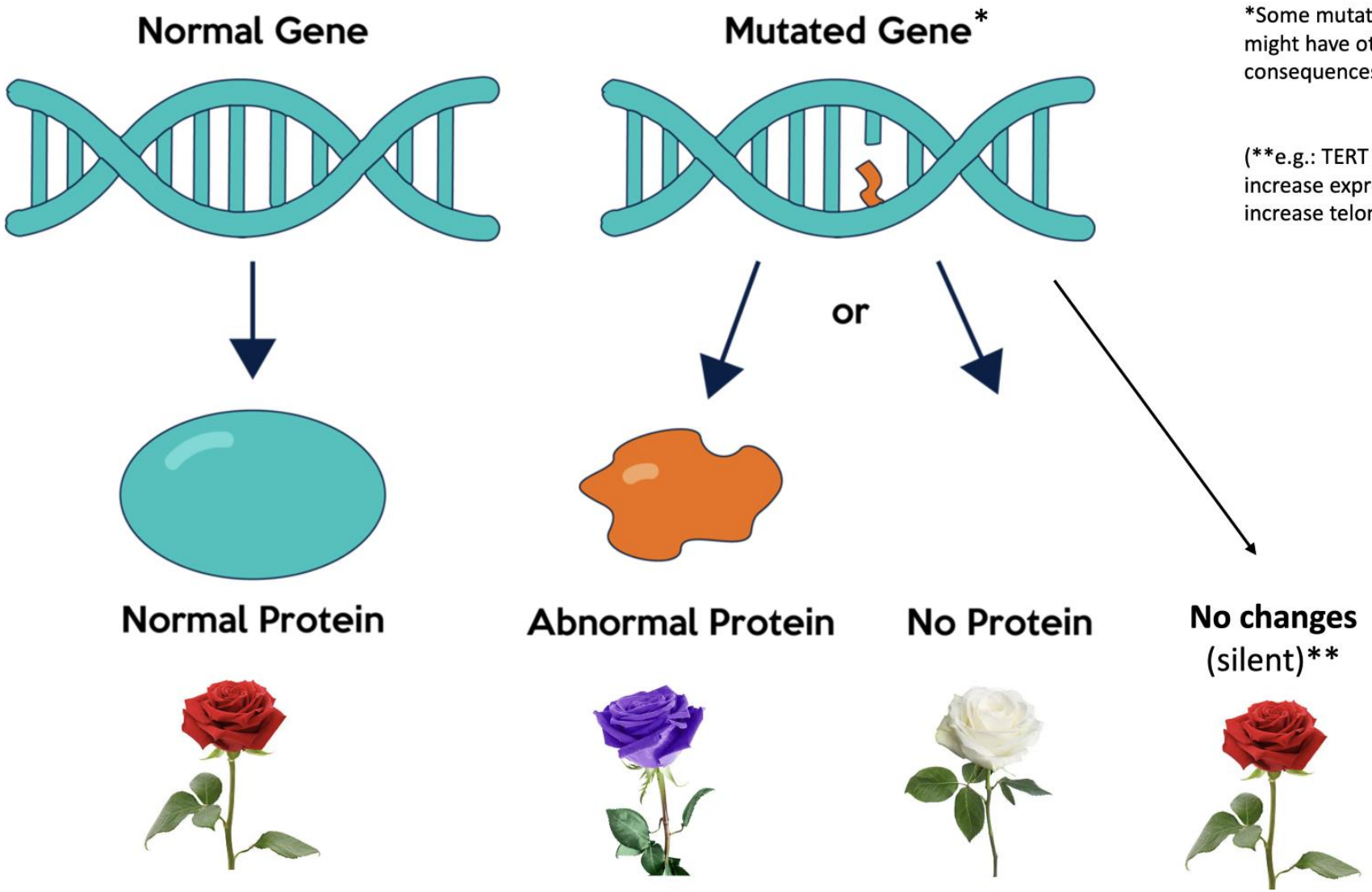
Lander Cell 2016

CRISPR Cas genome editing tools





Mutations in the DNA have functional consequences (or not)



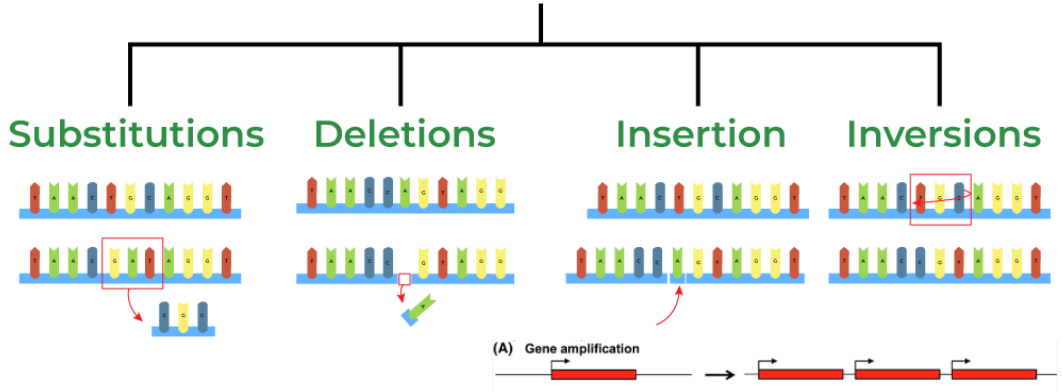
*Some mutations (variants) outside genes might have other non-direct protein coding consequences like altering gene expression.

(**e.g.: TERT promoter mutations lead to increase expression of TERT and ultimately increase telomerase complex function)

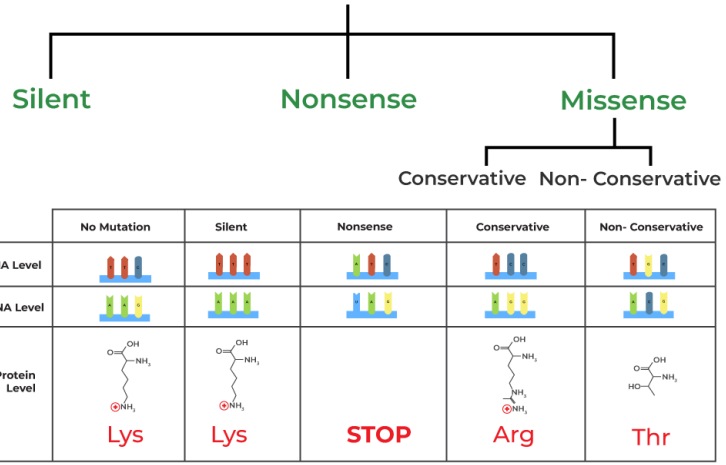
Intro to Cancer Bio 2025 PSV

Cancer 101: Mutations glossary

Types of Mutations
(At the DNA level)



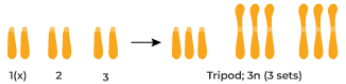
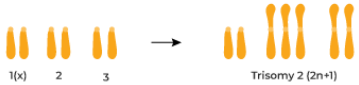
Types of Mutations
(At the Protein level)

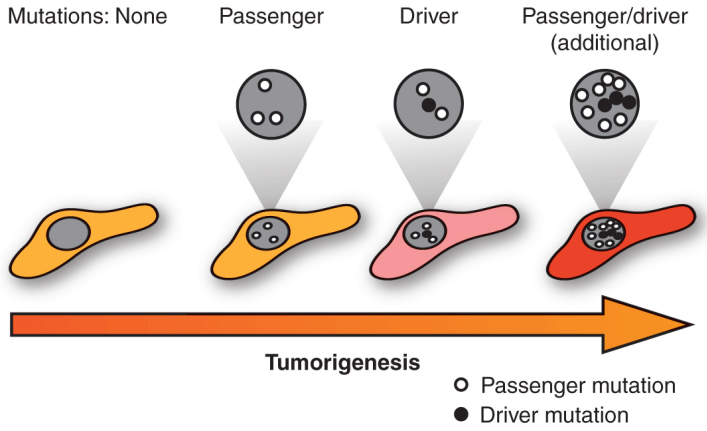


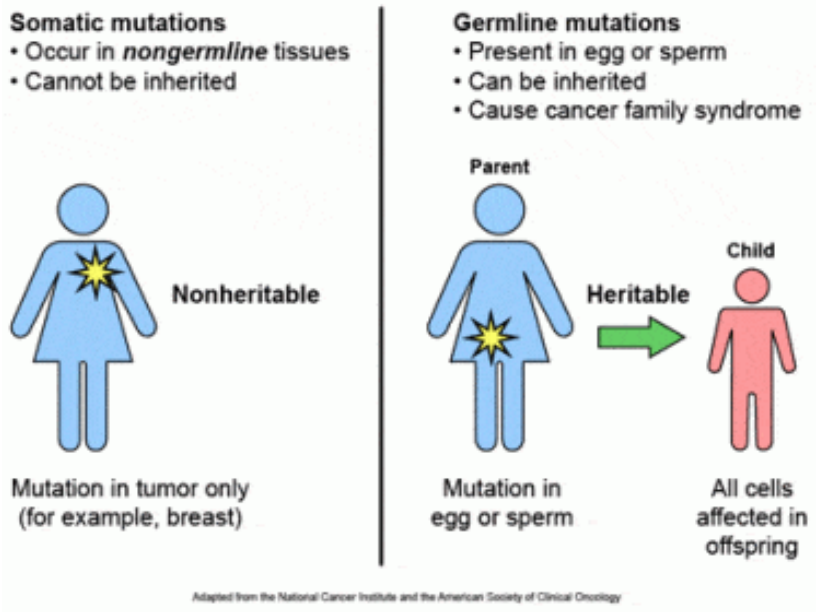
	No Mutation	Silent	Nonsense	Conservative	Non- Conservative
DNA Level					
mRNA Level					
Protein Level	Lys	Lys	STOP	Arg	Thr

Types of Mutations
(At the Chromosomal level)

STRUCTURAL				
Deletion	Duplication	Inversions	Insertions	Translocations
				

NUMERICAL	
Polyploidy	Aneuploidy
	

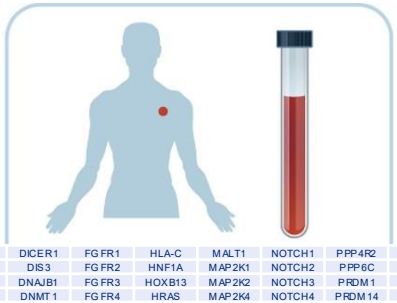


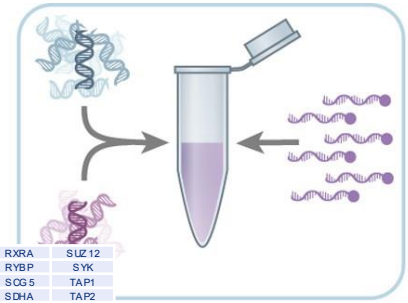


MSK-IMPACT

(Integrated Mutation Profiling of Actionable Cancer Targets

1. Patient consen





Sample preparation

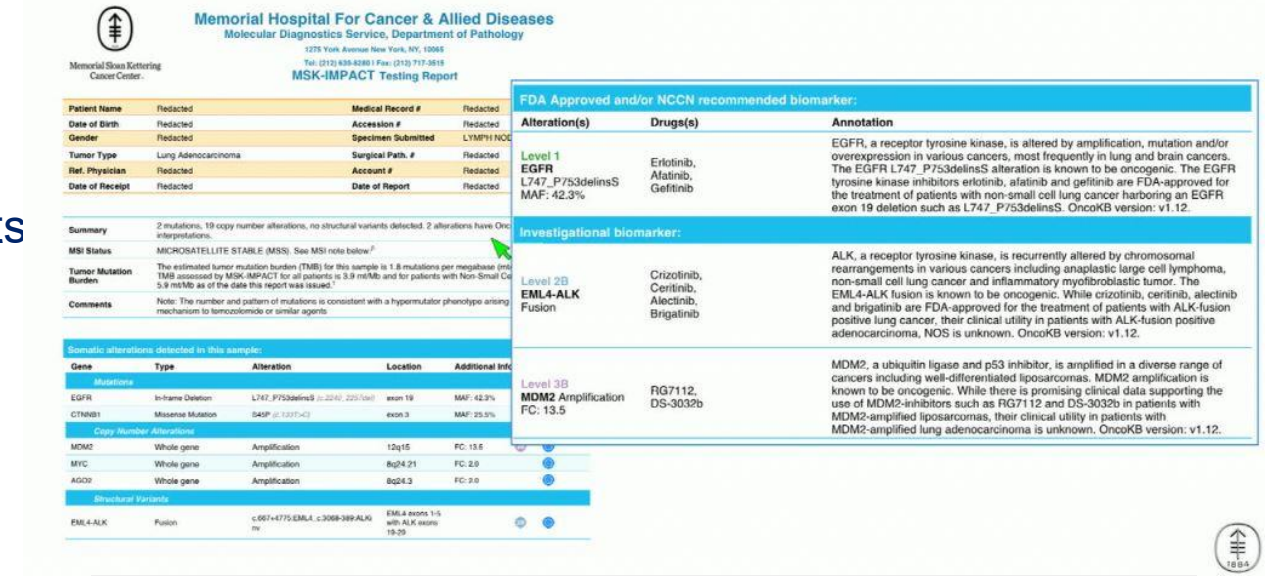
4. Sequencing

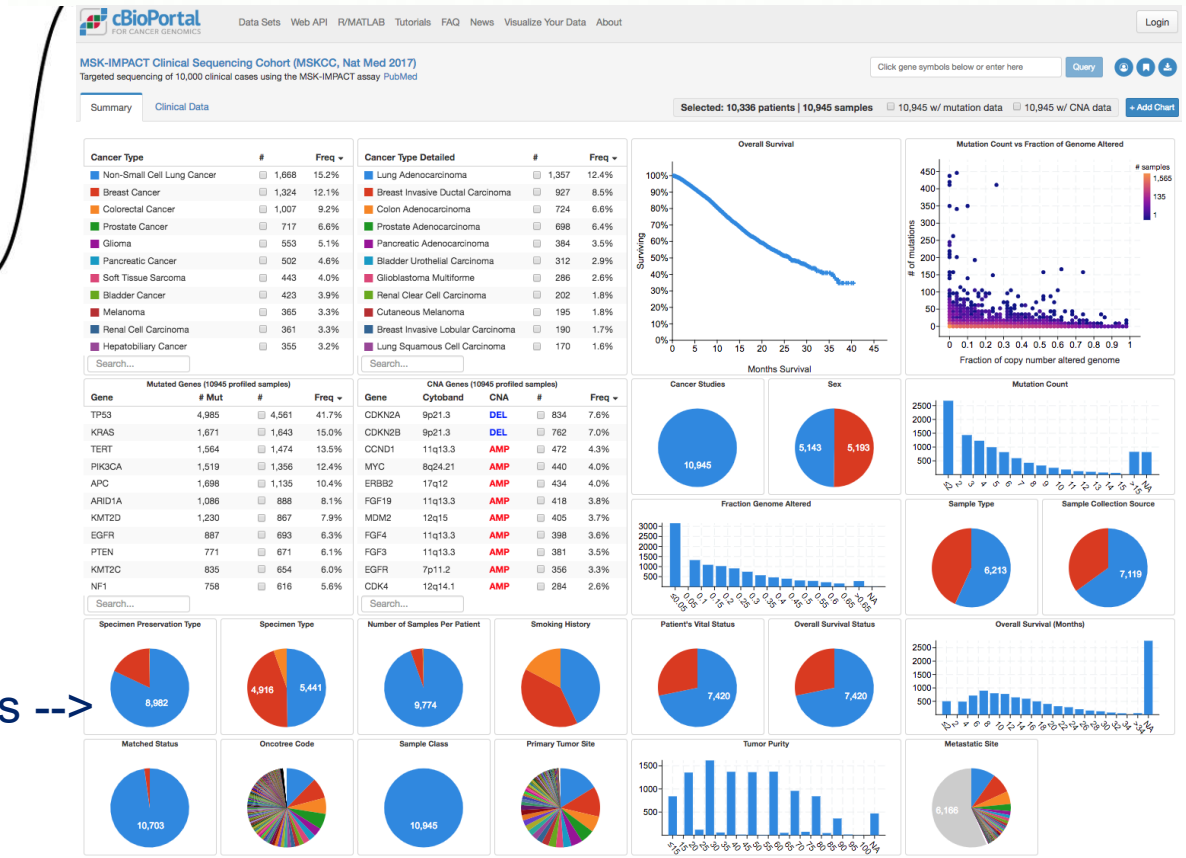
. Case review and sign out

ABL1	CALR	DICER1	FGFR1	HLA-C	MALT1	NOTCH1	PPP4R2	RXRA	SUZ12
ACVR1	CARD11	DIS3	FGFR2	HNF1A	MAP2K1	NOTCH2	PPP6C	RYBP	SYK
AGO1	CARM1	DNAJB1	FGFR3	HOXB13	MAP2K2	NOTCH3	PRDM1	SOG5	TAP1
AGO2	CASP8	DNMT1	FGFR4	HRAS	MAP2K4	NOTCH4	PRDM14	SDHA	TAP2
AKT1	CBFB	DNMT3A	FH	ICOSLG	MAP3K1	NPM1	PREX2	SDHAF2	TBX3
AKT2	CBL	DNMT3B	FLCN	ID3	MAP3K13	NRAS	PRKAR1A	SDHB	TCEB1
AKT3	CCND1	DOT1L	FLT1	IDH1	MAP3K14	NSD1	PRKCI	SDHC	TCF3
ALB	CCND2	DROSHA	FLT3	IDH2	MAPK1	NTHL1	PRKD1	SDHD	TCF7L2
ALK	CCND3	DUSP4	FLT4	IFNGR1	MAPK3	NTRK1	PTCH1	SERPINB3	TEK
ALOX12B	CCNE1	E2F3	FOXA1	IGF1	MAPKAP1	NTRK2	PTEN	SERPINB4	TERT
ANKRD11	CD274	EED	FOXF1	IGF1R	MAX	NTRK3	PTP4A1	SESN1	TET1
APC	CD276	EGFL7	FOXL2	IGF2	MCL1	NUF2	PTPN11	SESN2	TET2
APLNR	CD79A	EGFR	FOXO1	IKBKE	MDC1	NUP93	PTPRD	SESN3	TGFBR1
AR	CD79B	EIF1AX	FOXP1	IKZF1	MDM2	PAK1	PTPRS	SETD2	TGFBR2
ARAF	CDC42	EIF4A2	FUBP1	IL10	MDM4	PAK7	PTPRT	SETDB1	TMEM127
ARHGAP35	CDC73	EIF4E	FYN	IL7R	MED12	PALB2	RAB35	SF3B1	TMPRSS2
ARID1A	CDH1	ELF3	GAB1	INHA	MEF2B	PARK2	RAC1	SH2B3	TNFAIP3
ARID1B	CDK12	EP300	GAB2	INHBA	MEN1	PARP1	RAC2	SH2D1A	TNFRSF14
ARID2	CDK4	EPAS1	GATA1	INPP4A	MET	PAX5	RAD21	SHOC2	TOP1
ARID5B	CDK6	EPCAM	GATA2	INPP4B	MGA	PBRM1	RAD50	SHQ1	TP53
ASXL1	CDK8	EPHA3	GATA3	INPPL1	MITF	PDCD1	RAD51	SLFN11	TP53BP1
ASXL2	CDKN1A	EPHA5	GLI1	INSR	MLH1	PDCD1LG2	RAD51C	SLX4	TP63
ATM	CDKN1B	EPHA7	GNA11	IRF4	MLLT1	PDGFRA	RAD51L1	SMAD2	TRAF2
ATR	CDKN2A	EPHB1	GNAQ	IRS1	MPL	PDGFRB	RAD51L3	SMAD3	TRAF7
ATRX	CDKN2B	ERBB2	GNAS	IRS2	MRE11A	PDPK1	RAD52	SMAD4	TRIP13
ATXN7	CDKN2C	ERBB3	GNB1	JAK1	MSH2	PGBD5	RAD54L	SMARCA2	TSC1
AURKA	CEBPA	ERBB4	GPS2	JAK2	MSH3	PGR	RAF1	SMARCA4	TSC2
AURKB	CENPA	ERCC2	GREM1	JAK3	MSH6	PHF6	RARA	SMARCB1	TSHR
AXIN1	CHEK1	ERCC3	GRIN2A	JUN	MSI1	PHOX2B	RASA1	SMARCD1	U2AF1
AXIN2	CHEK2	ERCC4	GSK3B	KBTBD4	MSI2	PIK3C2G	RB1	SMARCE1	UPF1
AXL	CIC	ERCC5	H3F3A	KDM5A	MST1	PIK3C3	RBM10	SMO	USP8
B2M	CMTR2	ERF	H3F3B	KDM5C	MST1R	PIK3CA	RECQL	SMYD3	VEGFA
BABAM1	CREBBP	ERG	H3F3C	KDM6A	MTAP	PIK3CB	RECQL4	SOCS1	VHL
BAP1	CRKL	ERRFI1	HGF	KDR	MTOR	PIK3CD	REL	SOS1	VTCN1
BARD1	CRLF2	ESR1	HIST1H1C	KEAP1	MUTYH	PIK3CG	REST	SOX17	WHSC1
BBC3	CSDE1	ETAA1	HIST1H2BD	KIT	MYC	PIK3R1	RET	SOX2	WHSC1L1
BCL10	CSF1R	ETV1	HIST1H3A	KLF4	MYCL1	PIK3R2	RFWD2	SOX9	WT1
BCL2	CSF3R	ETV6	HIST1H3B	KLF5	MYCN	PIK3R3	RHEB	SPEN	WWTR1
BCL2L1	CTCF	EZH1	HIST1H3C	KMT2A	MYD88	PIM1	RHOA	SPOP	XIAP
BCL2L11	CTLA4	EZH2	HIST1H3D	KMT2B	MYOD1	PLCG2	RICTOR	SPRED1	XPO1
BCL6	CTNNB1	FAM123B	HIST1H3E	KMT2C	NADK	PLK2	RIT1	SPRTN	XRCC2
BCOR	CTR9	FAM175A	HIST1H3F	KMT2D	NBN	PMAIP1	RNF43	SRC	YAP1
BIRC3	CUL3	FAM46C	HIST1H3G	KMT5A	NCOA3	PMS1	ROS1	SRSF2	YES1
BLM	CXCR4	FAM58A	HIST1H3H	KNSTRN	NCOR1	PMS2	RPS6KA4	STAG2	ZFHX3
BMPR1A	CXORF67	FANCA	HIST1H3I	KRAS	NEGR1	PNRC1	RPS6KB2	STAT3	ZNRF3
BRAF	CYLD	FANCC	HIST1H3J	LATS1	NF1	POLD1	RPTOR	STAT5A	ZRSR2
BRCA1	CYP19A1	FAT1	HIST2H3C	LATS2	NF2	POLE	RRAGC	STAT5B	
BRCA2	CYSLTR2	FBXW7	HIST2H3D	LMO1	NFE2L2	POT1	RRAS	STK11	
BRD4	DAXX	FGF19	HIST3H3	LYN	NFKBIA	PPARG	RRAS2	STK19	
BRIP1	DCUN1D1	FGF3	HLA-A	LZTR1	NKX2-1	PPM1D	RTEL1	STK40	
BTK	DDR2	FGF4	HLA-B	MAD2L2	NKX3-1	PPP2R1A	RUNX1	SUFU	

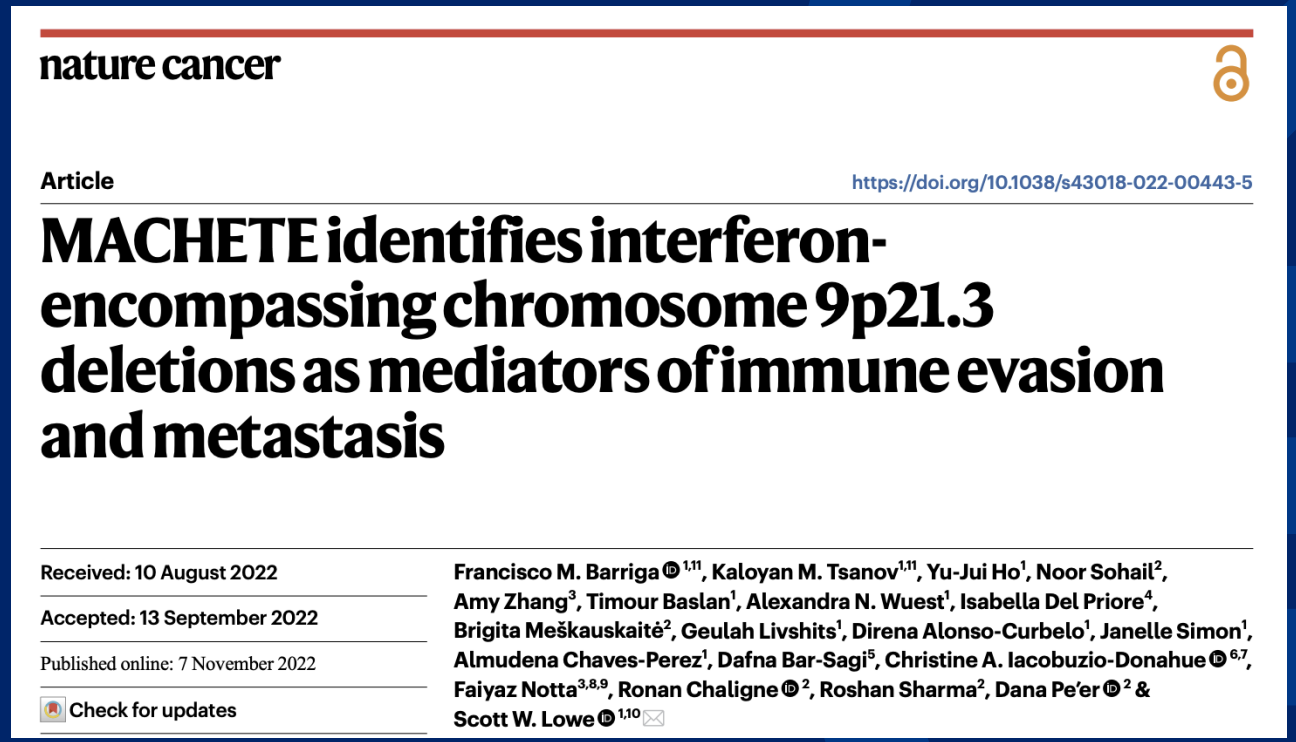
cBioPortal for Cancer Genomics -->

https://www.cbioportal.org





Paper discussion



nature cancer

Article

https://doi.org/10.1038/s43018-022-00443-5

MACHETE identifies interferon-encompassing chromosome 9p21.3 deletions as mediators of immune evasion and metastasis

Received: 10 August 2022

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Check for updates

Francisco M. Barriga[1,11], Kaloyan M. Tsanov[1,11], Yu-Jui Ho[1], Noor Sohail[2], Amy Zhang[3], Timour Baslan[1], Alexandra N. Wuest[1], Isabella Del Priore[4], Brigita Meškauskaitė[2], Geulah Livshits[1], Direna Alonso-Curbelo[1], Janelle Simon[1], Almudena Chaves-Perez[1], Dafna Bar-Sagi[5], Christine A. Iacobuzio-Donahue[6,7], Faiyaz Notta[3,8,9], Ronan Chaligne[2], Roshan Sharma[2], Dana Pe'er[2] & Scott W. Lowe[1,10]

Paper discussion

- **Explanation of the question under research** - *why did they decide to do this?*
- **Discussion figure by figure –** *is this paper not as good as authors think?:*
  - What is the point of each figure/panel?
  - Are there any missing experimental conditions?
  - Are results interpretable?
  - Do the results support the conclusions by the authors?
  - Would you have done anything differently?
  - Are there any missing experiments?
  - What are the limitations of the work?
  - What experiments could be done as a follow-up to the paper?

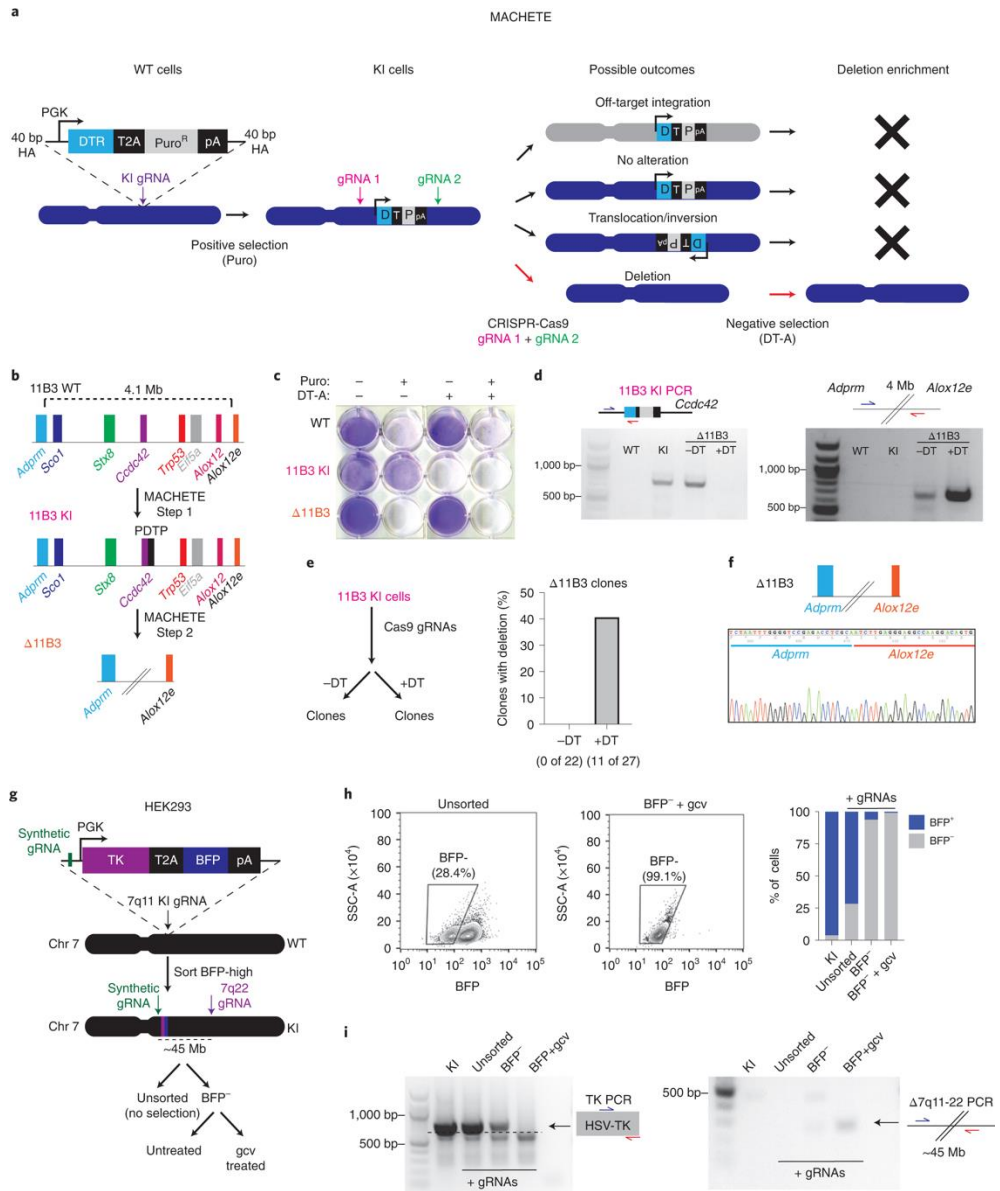
Research Question

- **Explanation of the question under research** - *why did they decide to do this?*

"Most efforts have focused on the characterization of single-nucleotide variants (SNVs), which typically act as ON/OFF switches that affect the output of a single gene. An even larger class of cancer-associated lesions are copy-number alterations (CNAs), which alter the dosage of multiple linked genes… modeling CNAs remains a major challenge that has impeded their functional assessment… Among recurrent CNAs, loss of chromosome 9p21.3 is the most strongly linked to poor prognosis as well as being the most common homozygous deletion across human cancers."

"For the functional study of deletions, CRISPR-Cas9 has been used to engineer these events, yet standard approaches have low efficiency and thus require the isolation and screening of many clonal cell populations. Here, we developed a rapid and flexible approach to engineer megabase-sized deletions. We applied this approach to investigating 9p21.3 deletions in models of pancreatic cancer and melanoma."

Figure 1 and Extended Figure 1



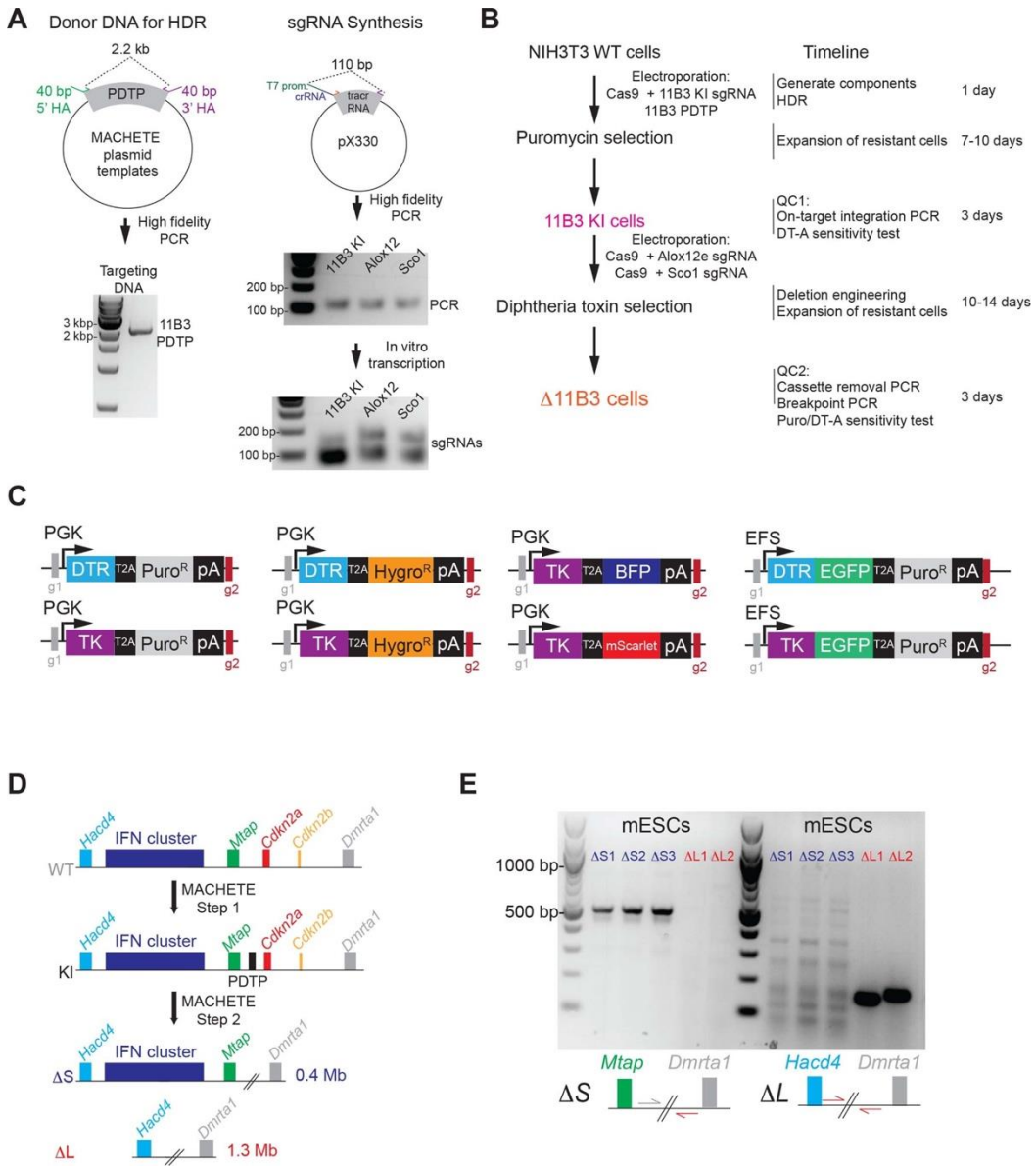
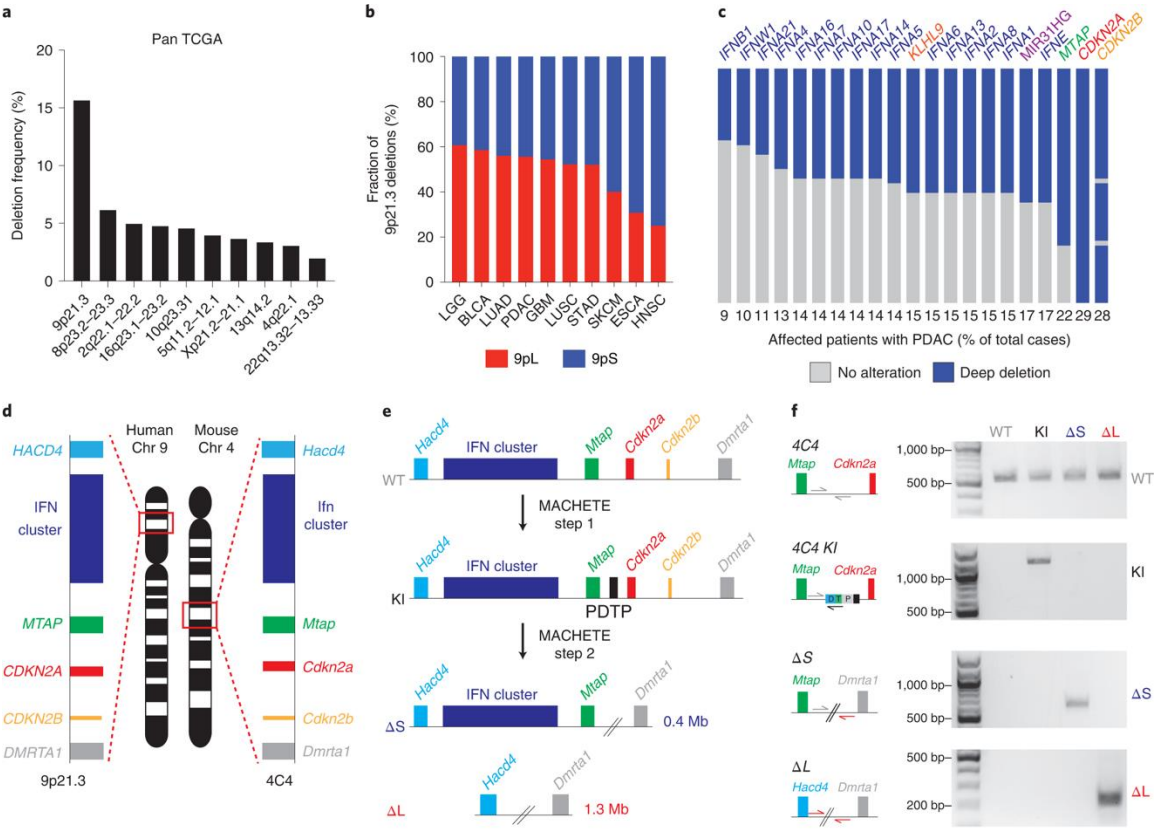
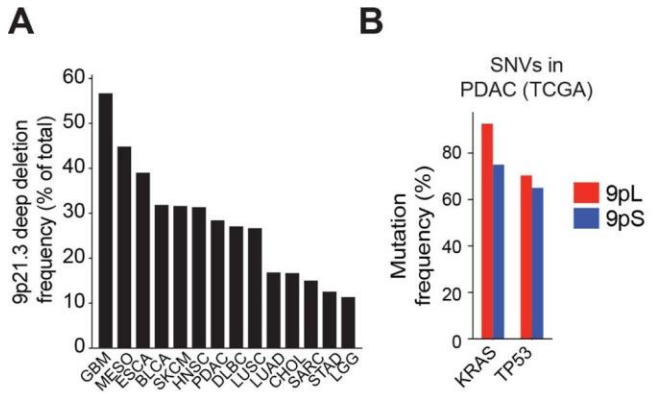
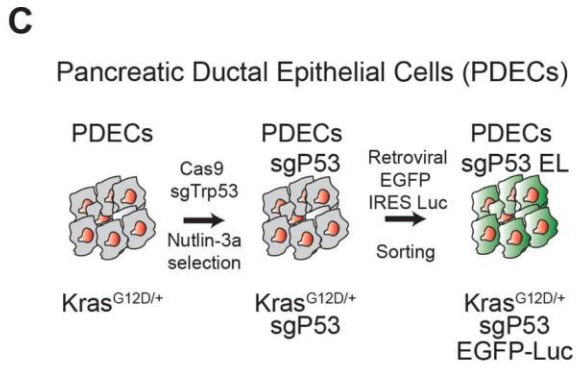
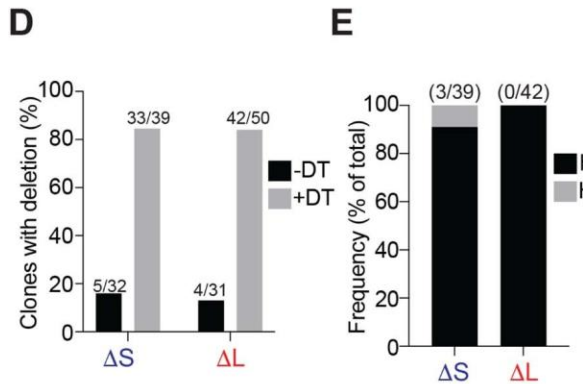


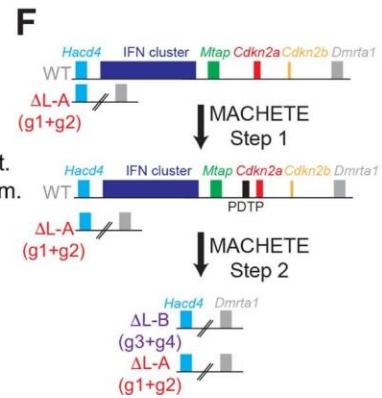
Figure 2 and Extended Figure 2











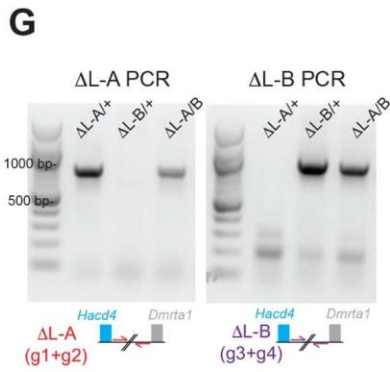


Figure 3

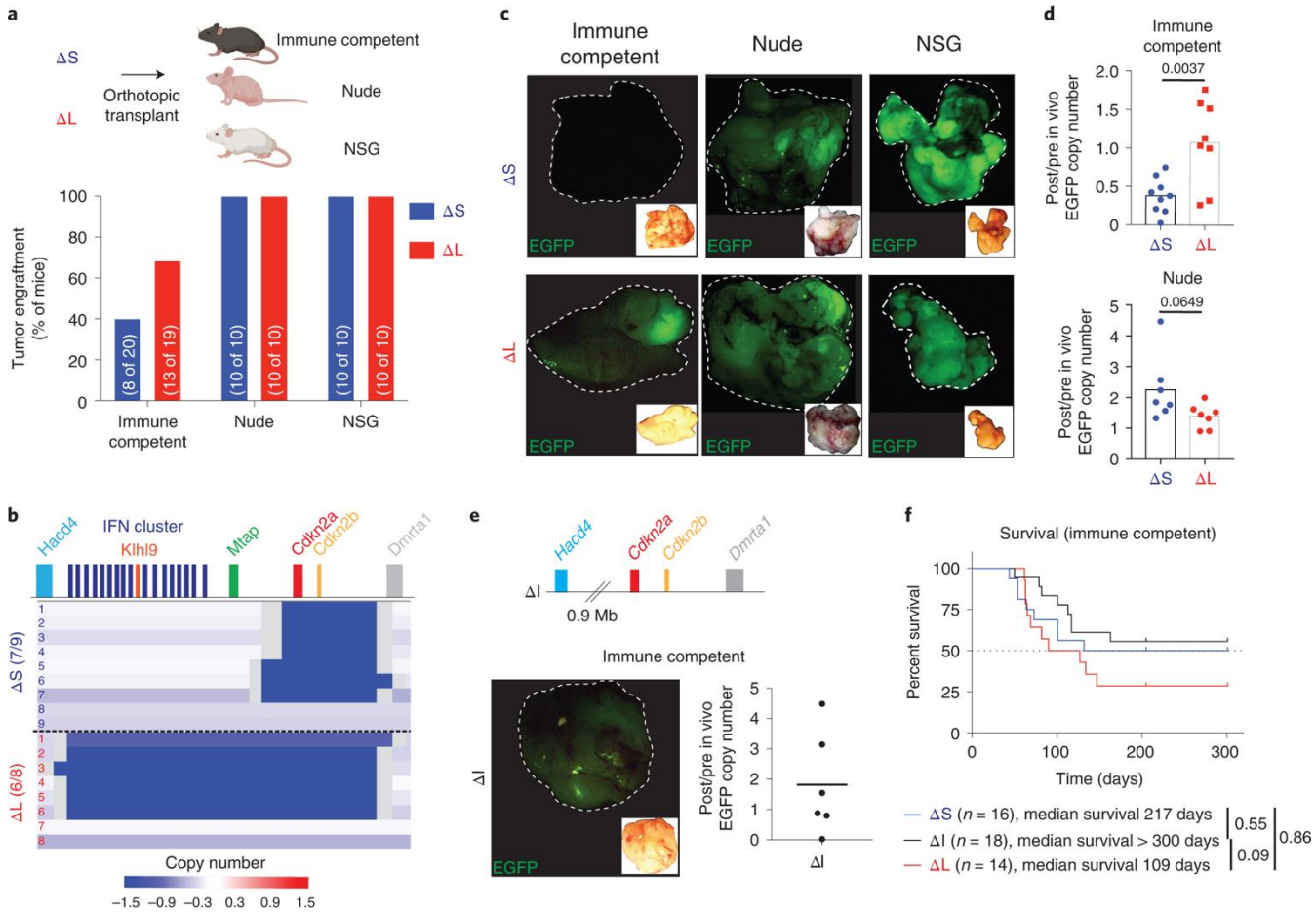
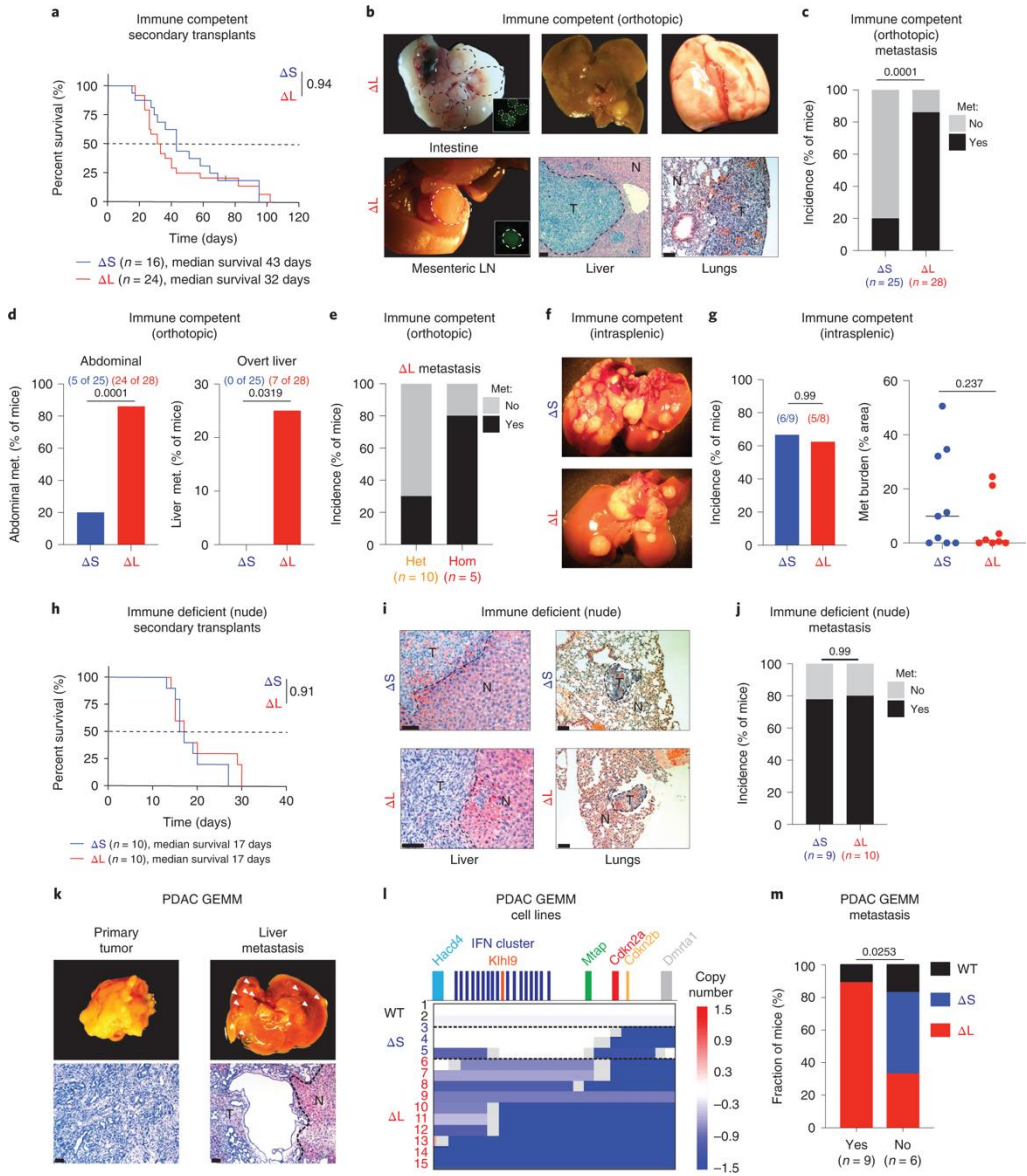
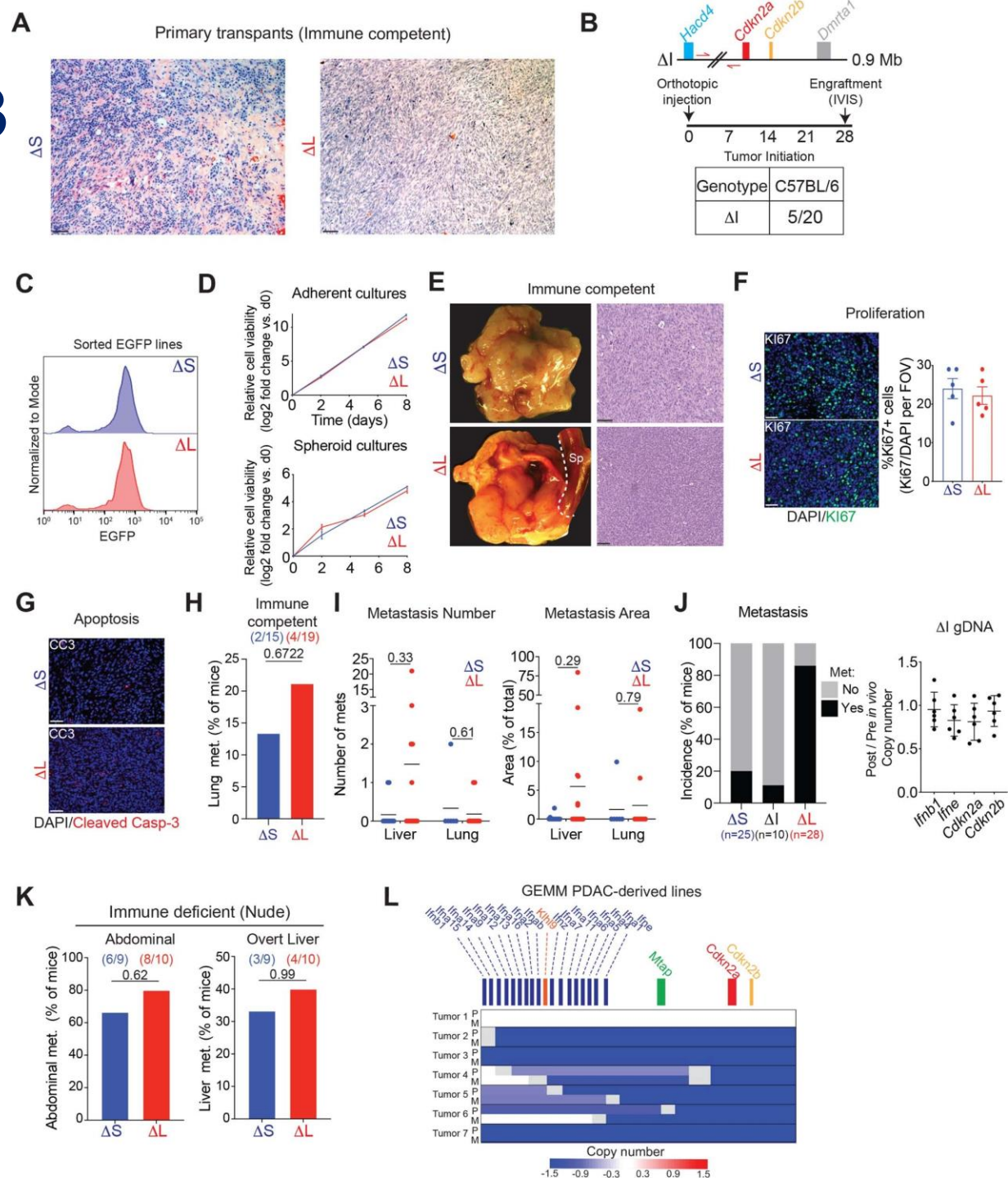
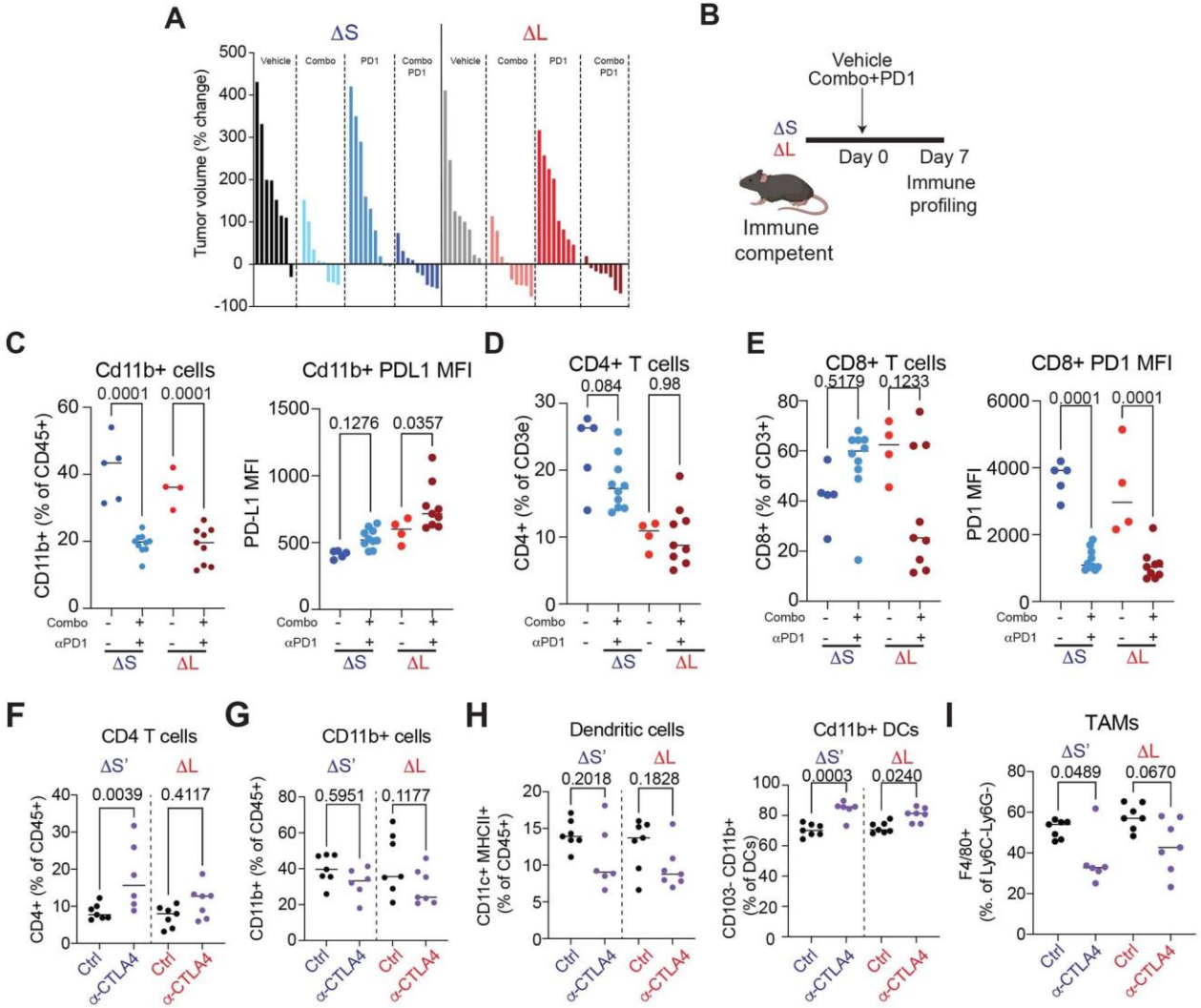

a
ΔS
ΔL
Orthotopic transplant
Immune competent
Nude
NSG
Tumor engraftment (% of mice)
100
80
60
40
20
0
(8 of 20)
(13 of 19)
(10 of 10)
(10 of 10)
(10 of 10)
(10 of 10)
ΔS
ΔL
Immune competent
Nude
NSG
b
Hacd4
IFN cluster
Klhl9
Mtap
Cdkn2a
Cdkn2b
Dmrta1
ΔS (7/9)
ΔL (6/8)
Copy number
−1.5 −0.9 −0.3 0.3 0.9 1.5
c
Immune competent
Nude
NSG
ΔS
ΔL
EGFP
d
Immune competent
0.0037
Post/pre in vivo EGFP copy number
2.0
1.5
1.0
0.5
0
ΔS
ΔL
Nude
0.0649
5
4
3
2
1
0
e
Hacd4
Cdkn2a
Cdkn2b
Dmrta1
ΔI
0.9 Mb
Immune competent
EGFP
Post/pre in vivo EGFP copy number
5
4
3
2
1
0
ΔI
f
Survival (immune competent)
Percent survival
100
75
50
25
0
0
100
200
300
Time (days)
ΔS (n = 16), median survival 217 days
ΔI (n = 18), median survival > 300 days
ΔL (n = 14), median survival 109 days
0.55
0.09
0.86

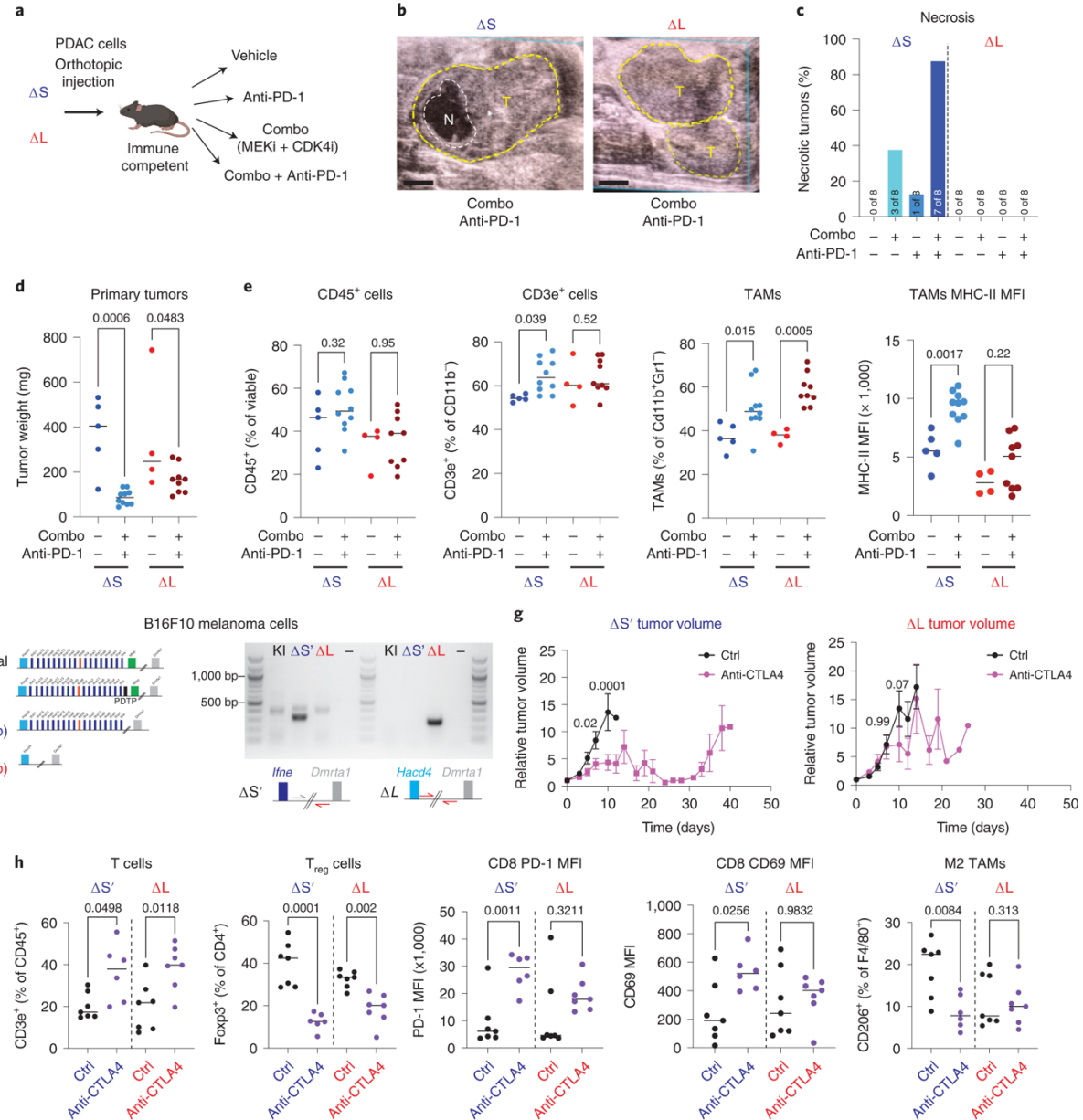
Figure 4 and Extended Figure 3



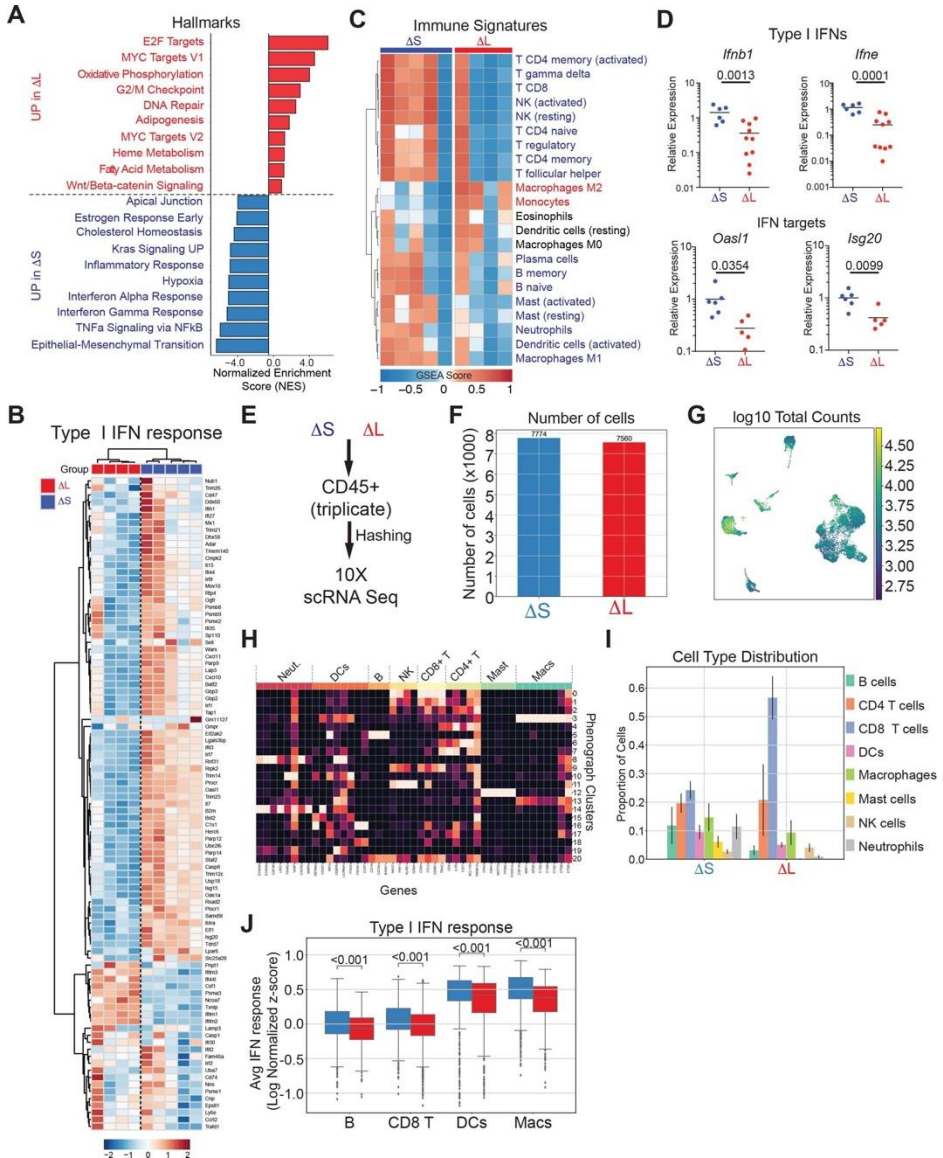


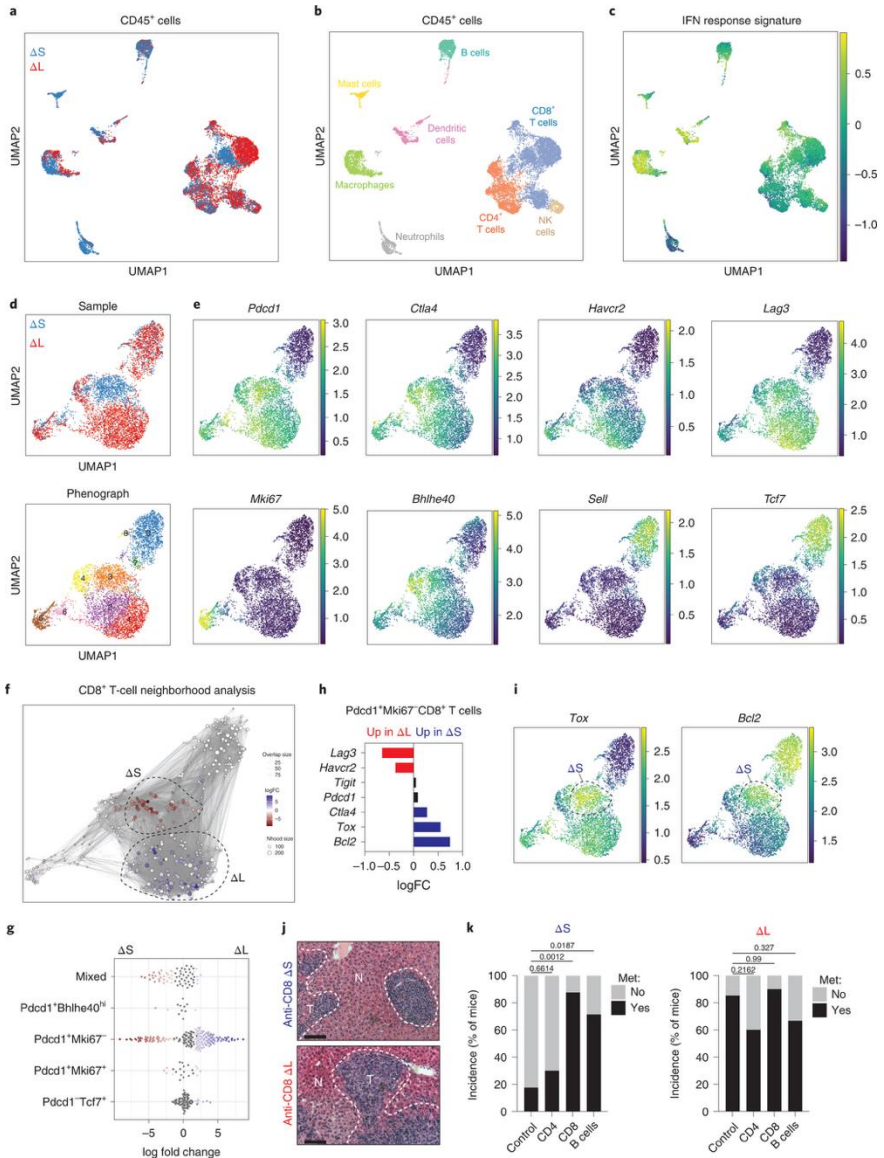
Extended Figure 4 and Figure 5



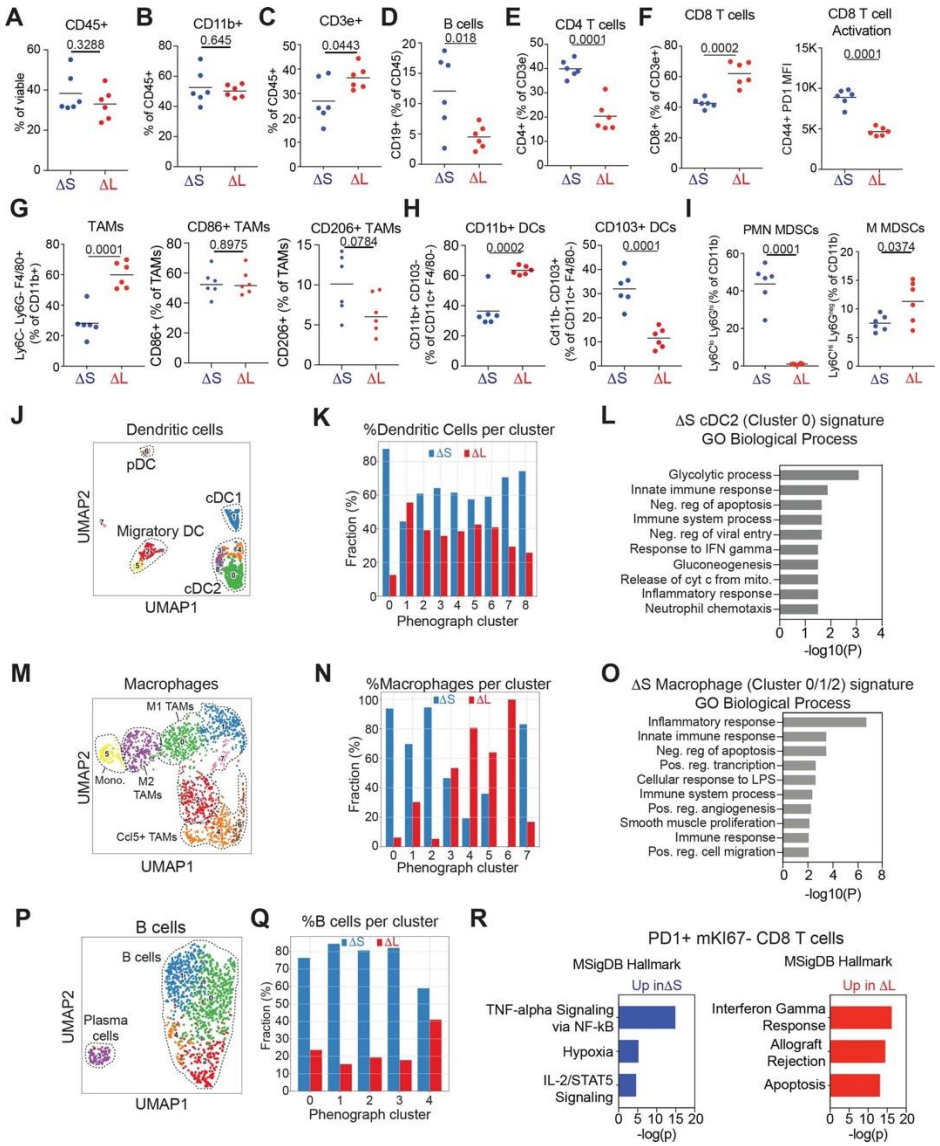


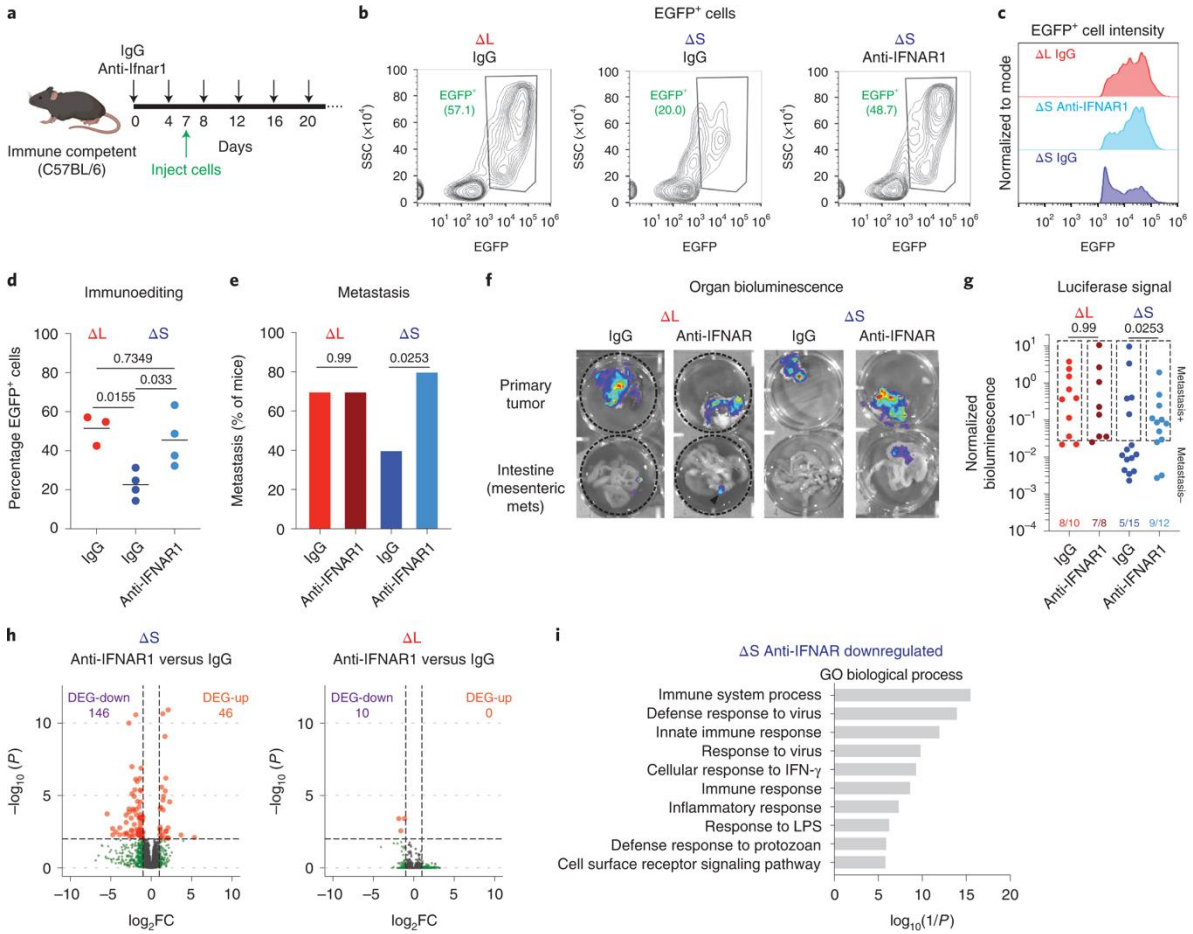
Extended Figure 5 and Figure 6



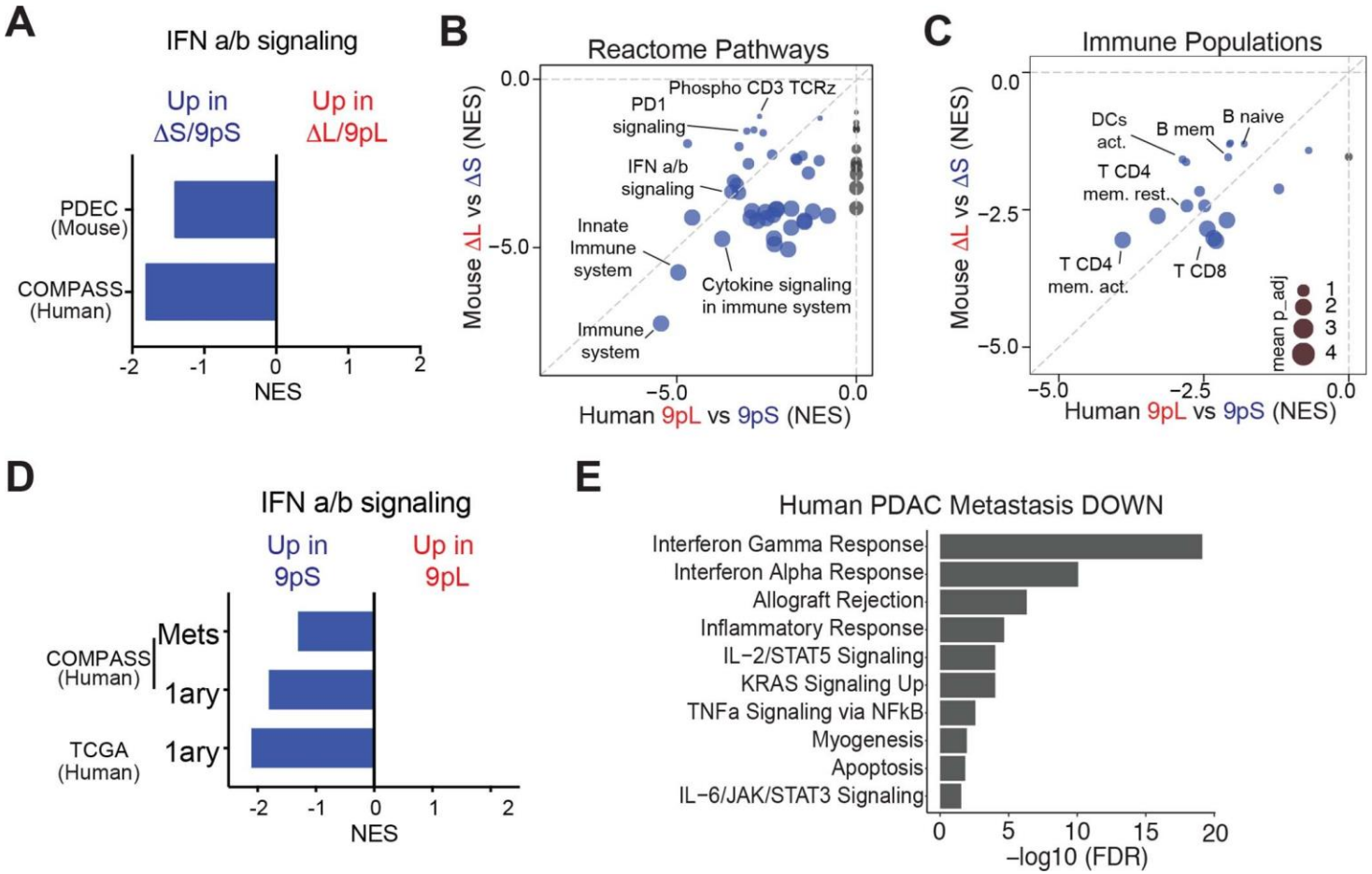


Extended Figure 6 and Figure 7





Extended Figure 7 and Extended Figure 8



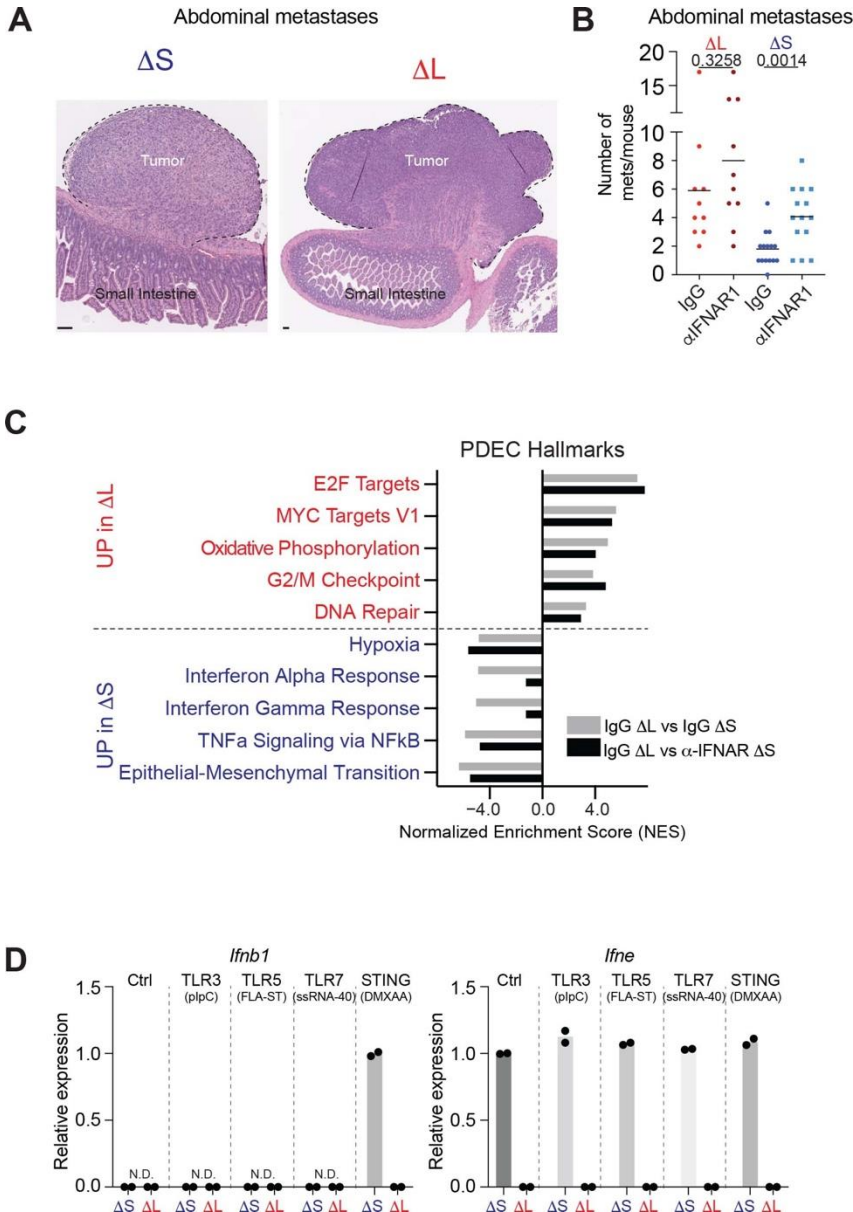
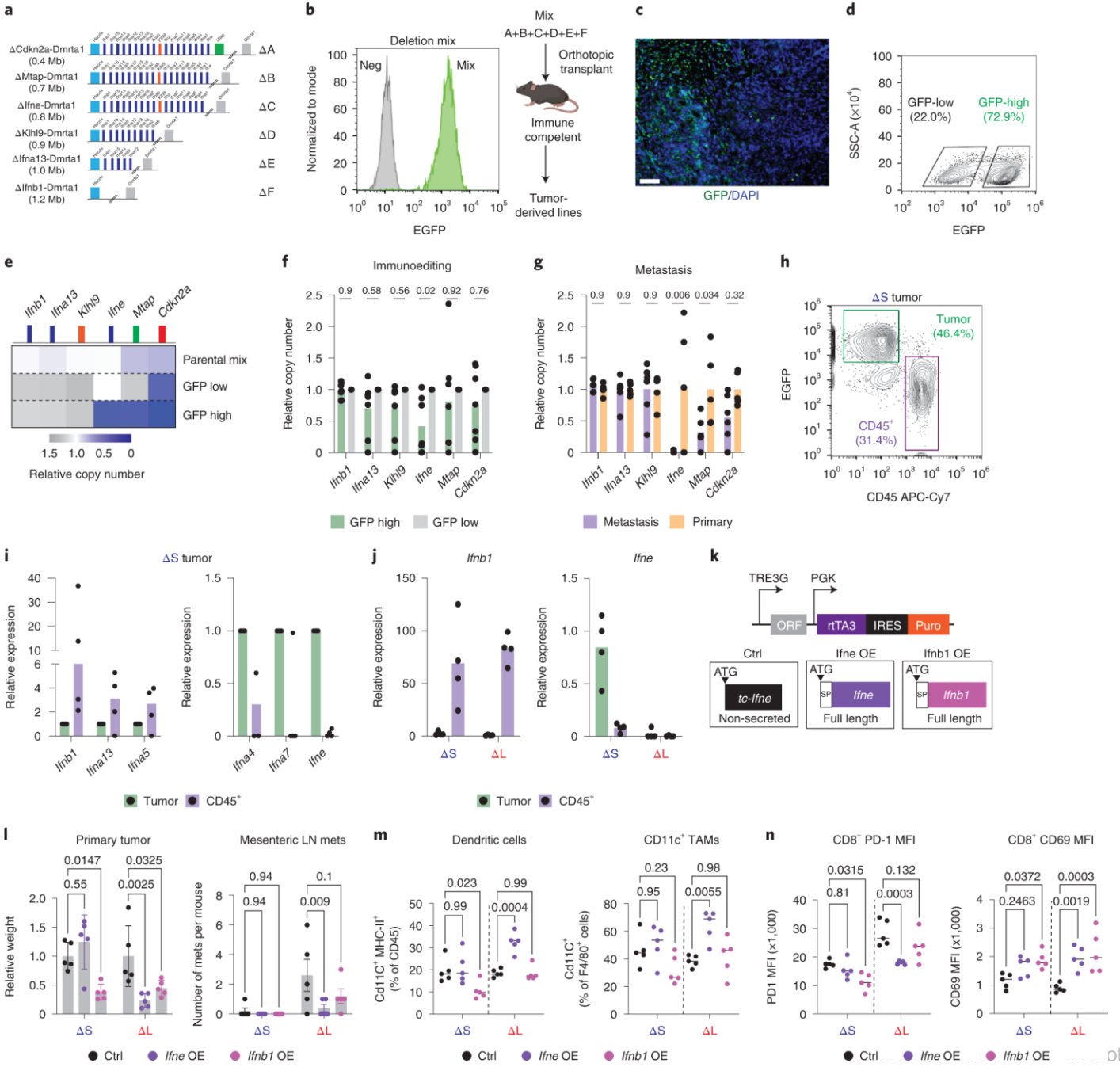
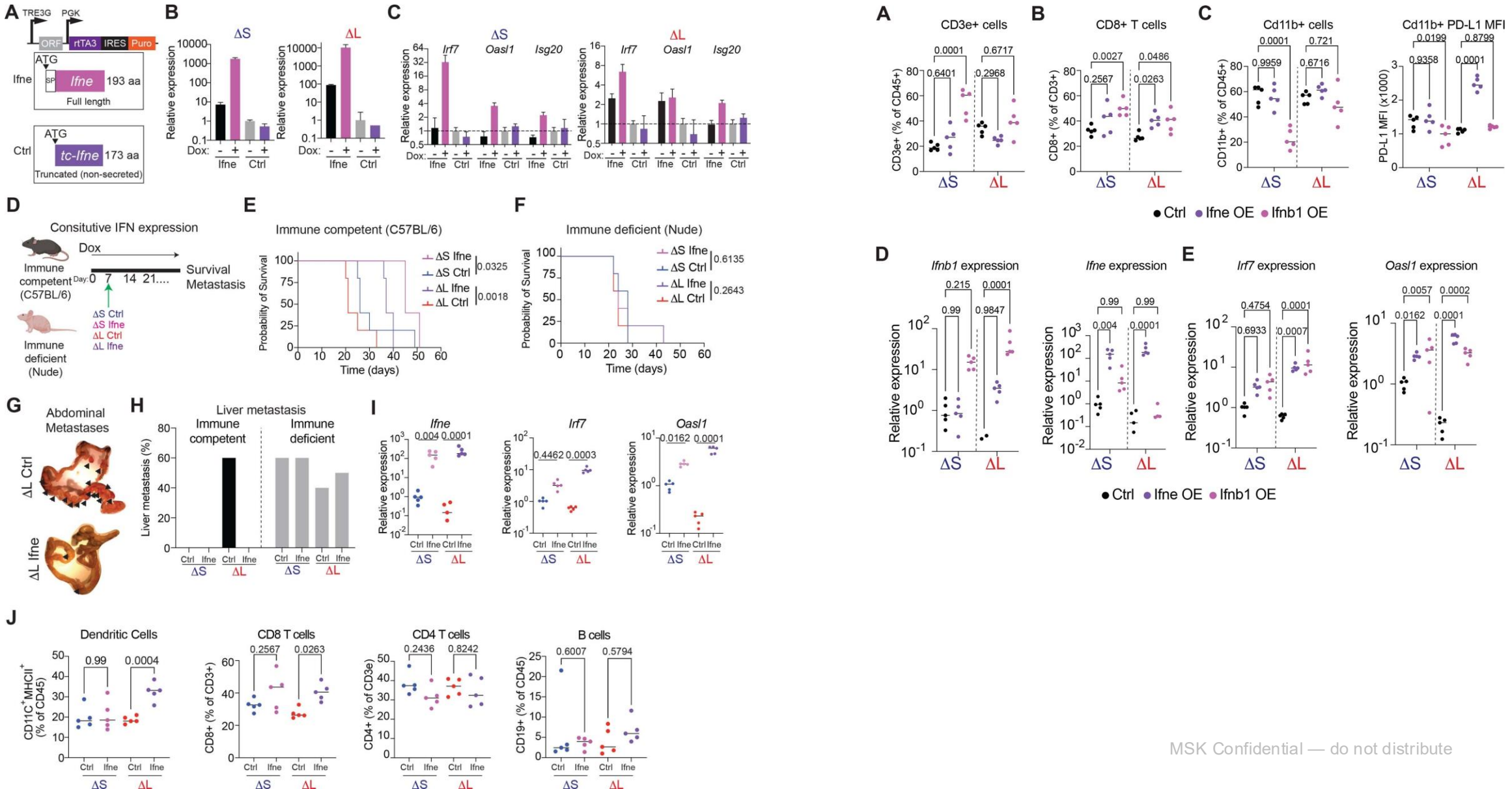


Figure 8


a
ΔCdkn2a-Dmrta1 (0.4 Mb)
ΔMtap-Dmrta1 (0.7 Mb)
ΔIfne-Dmrta1 (0.8 Mb)
ΔKlhl9-Dmrta1 (0.9 Mb)
ΔIfna13-Dmrta1 (1.0 Mb)
ΔIfnb1-Dmrta1 (1.2 Mb)
ΔA
ΔB
ΔC
ΔD
ΔE
ΔF
b
Deletion mix
Neg
Mix
Normalized to mode
EGFP
Mix
A+B+C+D+E+F
Orthotopic transplant
Immune competent
Tumor-derived lines
c
GFP/DAPI
d
GFP-low (22.0%)
GFP-high (72.9%)
SSC-A (×10⁴)
EGFP
e
Ifnb1
Ifna13
Klhl9
Ifne
Mtap
Cdkn2a
Parental mix
GFP low
GFP high
1.5 1.0 0.5 0
Relative copy number
f
Immunoediting
0.9 0.58 0.56 0.02 0.92 0.76
Relative copy number
GFP high
GFP low
g
Metastasis
0.9 0.9 0.9 0.006 0.034 0.32
Metastasis
Primary
h
ΔS tumor
Tumor (46.4%)
CD45⁺ (31.4%)
EGFP
CD45 APC-Cy7
i
ΔS tumor
Relative expression
Ifnb1
Ifna13
Ifna5
Ifna4
Ifna7
Ifne
Tumor
CD45⁺
j
Ifnb1
Ifne
Relative expression
ΔS
ΔL
Tumor
CD45⁺
k
TRE3G
PGK
ORF
rtTA3
IRES
Puro
Ctrl
Ifne OE
Ifnb1 OE
ATG
tc-Ifne
Non-secreted
SP
Ifne
Full length
Ifnb1
Full length
l
Primary tumor
Mesenteric LN mets
Relative weight
Number of mets per mouse
0.0147
0.55
0.0325
0.0025
0.94
0.94
0.1
0.009
ΔS
ΔL
Ctrl
Ifne OE
Ifnb1 OE
m
Dendritic cells
CD11c⁺ TAMs
Cd11C⁺ MHC-II⁺ (% of CD45)
Cd11C⁺ (% of F4/80⁺ cells)
0.023
0.99
0.99
0.0004
0.23
0.95
0.98
0.0055
ΔS
ΔL
Ctrl
Ifne OE
Ifnb1 OE
n
CD8⁺ PD-1 MFI
CD8⁺ CD69 MFI
PD1 MFI (×1,000)
CD69 MFI (×1,000)
0.0315
0.81
0.132
0.0003
0.0372
0.2463
0.0003
0.0019
ΔS
ΔL
Ctrl
Ifne OE
Ifnb1 OE

Extended Figure 9 and Extended Figure 10



Thanks for your attention!

Any questions?


Memorial Sloan Kettering
Cancer Center