Molecular mechanisms and pathobiology of oncogenic fusion transcripts in epithelial tumors

SUPPLEMENTARY MATERIALS

Supplementary Table 1: Examples of oncogenic fusion genes of receptor tyrosine kinases in epithelial tumors. See Supplementary_Table_1

Supplementary Table 2: Examples of oncogenic fusion genes of serine/threonine kinases in epithelial tumors

Fusion gene	Tumor type	Type of rearrangements	Fusion gene domains	Ref
BRAF partners				
KIAA1549	PA (70%), ADG (9.4%)	DEL, TD	N-PK	[52]
SND1	PACC, gastric cancer, SCM, LUAD never smokers	INV	$TN_{(2–3)}$-PK (pancreatic acinar)	[45, 53, 54]
			TN3-RBD-CRD-PK (LUAD)	[52]
PAPSS1	SCM, rectal carcinoma	TR	APS-PK	[53]
TRIM24	Pilocytic astrocytoma	INV	BRM-PK	[53]
FAM131B	Pilocytic astrocytoma	DEL	N-PK	[52, 55]
RNF130	Pilocytic astrocytoma	TR	N-PK	[49]
MKRN1	Pilocytic astrocytoma, anaplastic thyroid cancer	TD	N-PK	[49, 56]
SLC45A3	Prostate cancer	INV	N-CR-PK	[57]
AKAP9	PTC, melanocytic nevi	INV	N-PK	[55, 58]
AGTRAP	Gastric cancer	TR	N-PK	[55]
FCHSD1	Melanocytic nevi	TR	BAR-PK	[56]
RAF1 partners				
SRGAP3	Pilocytic astrocytoma, prostate cancer	TD	N-PK	[57]
ESRP1	Prostate cancer	TR	N-PK	[57]
ATG7	Pancreatic cancer	DEL	N-PK	[55]
BCL6	Anaplastic astrocytoma	INV	N-PK	[55]
NFIA	Pilocytic astrocytoma	TR	N-PK	[59]

N, N-terminal part of the partner protein of chimeric protein.

Supplementary Table 3: Examples of oncogenic fusion genes of transcription factors or regulators

Fusion genes	Tumor types (%)	Type of rearrangements	Refs
TMPRSS2-ERG[#]	PCa (~50%)	DEL, INV	[60–62]
TMPRSS2-ETV1	PCa (5–10%)	TR	[19, 25, 26, 28, 29, 61–63]
TMPRSS2-ETV4	PCa (<5%)	TR	[64]
TMPRSS2-ETV5	PCa (<5%)	TR	[65]
ACSL3-ETV1	PCa	TR	[66]
FLJ35294-ETV1	PCa	TR	[67]
DDX5-ETV4	PCa	INV	[67]
KLK2-ETV4	PCa	TR	[68]
CANT1-ETV4	PCa	INV	[68]
SLC45A3-ERG	PCa	TR	[61]
C15orf21-ETV1	PCa	TR	[61]
HNRPA2B1-ETV1	PCa	DEL	[61]
SLC45A3-ETV1	PCa	TR	[65]
SLC45A3-ETV5	PCa	TR	[61]
HERVK22q11.23	PCa	DEL	[69]
SLC45A3-FLI1	PCa	TR	[69]
PVT1-MYC *PVT1-NDRG1*	Medulloblastoma	Chromothripsis INV	[19, 22, 25, 26, 29, 70]
NFIB-MYB *QKI-MYB* *HMGIC-MYB*	HNACC (86%), ACCB (67%), BACC, SGC (52.9%), ACCSG (28%) Angiocentric glioma (PLGG) (85.7%) Pleomorphic adenoma	TR DEL	[71–76] [77] [71]

Supplementary Table 4: Examples of specific fusion genes of defined tumors

Fusion genes	Tumor types (%)	Type of rearrangement	Ref
EIF3E-RSPO2 *RTPRK-RSPO3*	Colon cancer (0–5%) Colon cancer (5–10%)	DEL INV	[78]
ESRRA-C11orf20	Serous ovarian cancer (15%)	TD	[79]
SLC3A2-NRG1	Invasive mucinous adenocarcinoma of the lung (27%)	TR	[80]
JMJD7-PLA2G4B	HNSCC	RT	[81]
DNAJB1-PRKACA	Fibrolamellar HCC (100%)	DEL	[82]
BRD-NUT	NUT midline carcinoma (66%)	TR	[83]
TFE3-TFEB	Renal cell carcinoma	TR	[84, 85]
MTAP-ANRIL	Melanoma	DEL	[86]
CLDN18-ARHGAP26	Gastric cancer	TR	[87]
RAD51-ATXN7	Colorectal cancer	TR	[88]

Supplementary Table 5: Examples of oncogenic fusions that sensitive or resistant to targeted therapeutics agents. See Supplementary_Table_5

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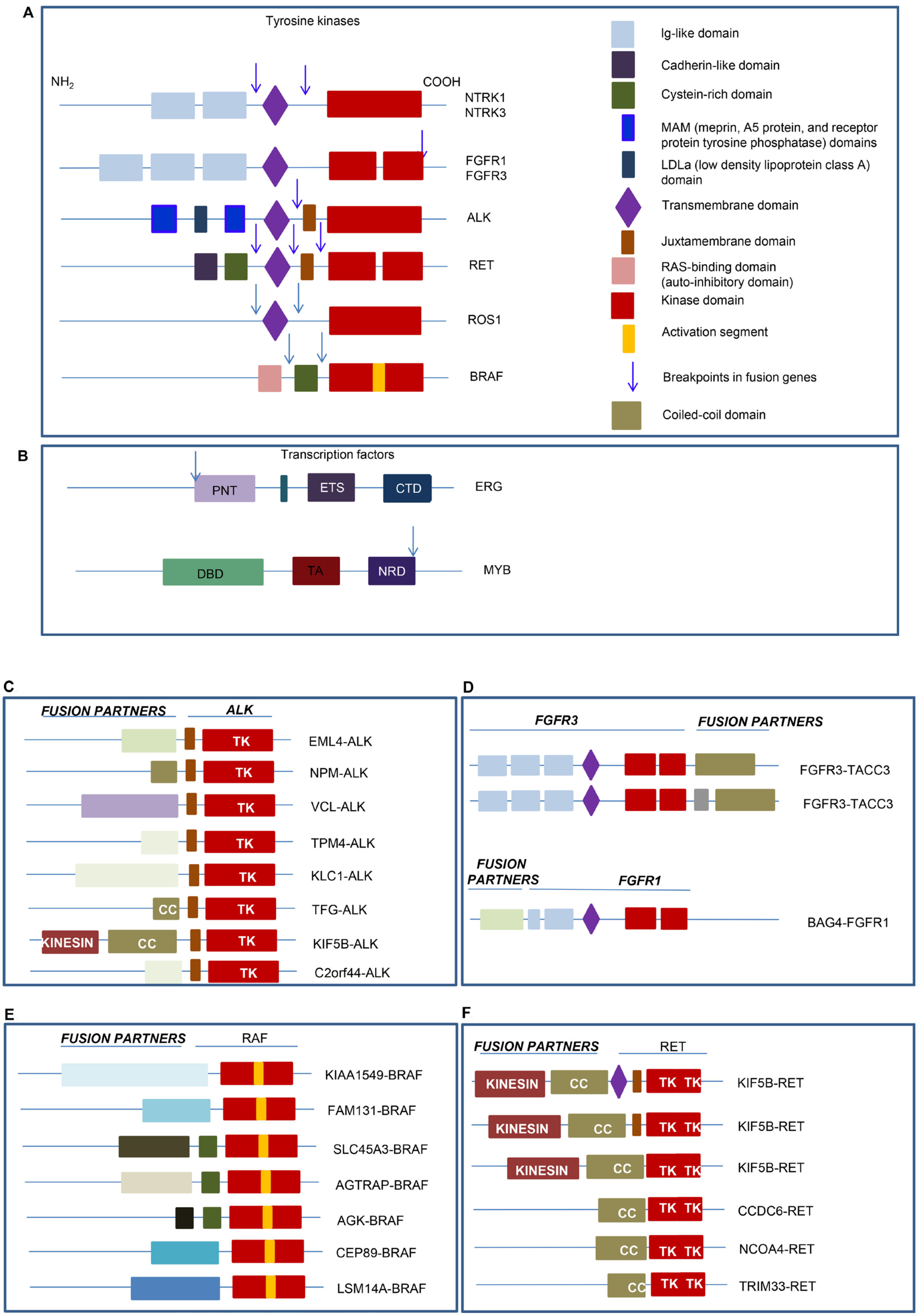
A
Tyrosine kinases
NH2
COOH
NTRK1
NTRK3
FGFR1
FGFR3
ALK
RET
ROS1
BRAF
Ig-like domain
Cadherin-like domain
Cystein-rich domain
MAM (meprin, A5 protein, and receptor protein tyrosine phosphatase) domains
LDLa (low density lipoprotein class A) domain
Transmembrane domain
Juxtamembrane domain
RAS-binding domain (auto-inhibitory domain)
Kinase domain
Activation segment
Breakpoints in fusion genes
Coiled-coil domain
B
Transcription factors
PNT
ETS
CTD
ERG
DBD
TA
NRD
MYB
C
FUSION PARTNERS
ALK
TK
EML4-ALK
NPM-ALK
VCL-ALK
TPM4-ALK
KLC1-ALK
CC
TFG-ALK
KINESIN
KIF5B-ALK
C2orf44-ALK
D
FGFR3
FUSION PARTNERS
FGFR3-TACC3
FGFR3-TACC3
FUSION PARTNERS
FGFR1
BAG4-FGFR1
E
FUSION PARTNERS
RAF
KIAA1549-BRAF
FAM131-BRAF
SLC45A3-BRAF
AGTRAP-BRAF
AGK-BRAF
CEP89-BRAF
LSM14A-BRAF
F
FUSION PARTNERS
RET
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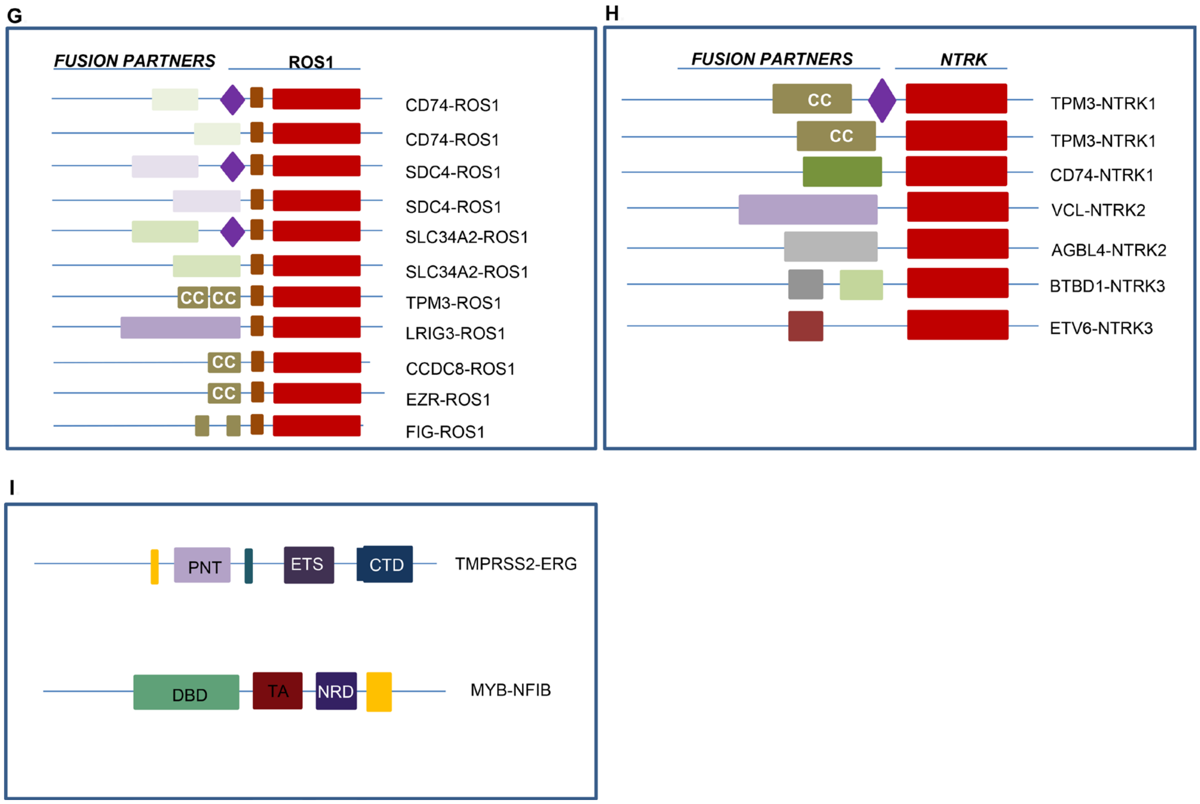
NCOA4-RET
TRIM33-RET



Supplementary Figure 1: Shematic representations of tyrosine kinases (TKs) and transcription factors (TFs), their domains their partners that involve to formation of fusion genes. Breakpoints of (**A**) TKs and (**B**) TFs. ERG protein consists PNT, pointed protein-protein interaction domain; AD, alternative domain; ETS domain that forms a helix-turn-helix DNA-binding domain; CTD, C-terminal transactivation domain. MYB protein consist three functional domains; helix-turn-helix (HTH)-type DNA binding domain (DBD) in N-terminal, trans-activation domain (TAD) and negative regulatory domain (NRD) in C-terminal. (**C**) Some fusion partners of ALK, (**D**) FGFR, (**E**) RAF, (**F**) RET, (**G**) ROS1, (**H**) NTRK, (**I**) ERG and MYB.