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Supplementary information

The actionable transcriptome: a framework for incorporating RNA sequencing into precision oncology

In the format provided by the authors and unedited

Supplementary Information

Supplementary Methods

Actionable Transcriptome List

To generate an 'actionable transcriptome' list, we leveraged our MD Anderson Precision Oncology Decision Support (PODS) actionable gene framework[1-3], which classifies gene actionability according to type of genomic alteration, including copy-number variations (CNVs), in order to provide an initial list of candidate genes to consider for actionability based on RNA expression. This approach identified 115 genes that were actionable based on CNVs at the time of analysis, which we re-evaluated by reviewing current peer-reviewed published literature to determine if data still supports amplification (for oncogenes) or deletion (for tumour-suppressor genes) as predictive of response or resistance to clinically available therapies. We defined clinically available therapies as a therapy that is approved by the FDA for any indication or is available within clinical trials. PODS utilizes a tiered actionability scale to classify genomic alterations from "Yes: Literature based" to "Yes: Inferred", "Potentially", "Unknown", to "No" for treatment with or resistance to specific therapies. Gene CNVs with data supporting a predictive role for particular therapies were classified as "Yes: Literature based" for actionability. Those gene amplifications lacking predictive data but implicated as a target for a clinically available drug that directly binds to and inhibits the gene product were classified as "Potentially" actionable. All others were classified as not actionable. CNVs considered "Yes: Literature based" or "Potentially" actionable were further investigated for peer-reviewed published data demonstrating the predictive value of high RNA expression for oncogenes or low RNA expression for tumour-suppressor genes. These data were reviewed by the PODS advisory team consisting of oncologists, molecular biologists, pathologists and geneticists. Only one gene was determined to have sufficient predictive data regarding RNA expression (*ERBB2*) for classification as "Yes: Literature based" for actionability. Data examined for other genes, if found at all, was deemed premature, and thus high or low RNA expression of these genes was classified as "Potentially" actionable. Both "Yes: Literature based" and "Potentially" actionable genes are included in the actionable transcriptome list.

We also aggregated a list of therapies that could target cell-surface proteins. These include drug-conjugate therapies (antibody–drug, peptide–drug or radioconjugates), monoclonal or bispecific antibodies, chimeric antigen receptors (CAR) cell therapies, and T cell receptor (TCR) cell therapies. To identify drug-conjugate therapies, we computationally searched the definitions of drugs annotated within the PODS knowledgebase and those within US National

Cancer Institute Thesaurus (NCIt) for key words, including “drug conjugate”, “PDC”, “antibody–drug conjugate”, “ADC”, “peptide–drug conjugate”, “radioconjugate”, and “probody drug conjugate”. We additionally retrieved all drugs from the NCIt with the parent concept of “antineoplastic antibody–drug conjugate”, “antineoplastic radiopharmaceutical agent” for our review. To identify bispecific antibodies, we searched definitions of drugs annotated within PODS and found within the NCIt by searching for the word “bispecific” and retrieved all drugs from the NCIt that have the parent concept of “bispecific antibody”. To identify CAR or TCR therapies, we retrieved all drugs from the NCIt with the parent concept of “antineoplastic immune cell” or “antineoplastic immunomodulating agent” and those with one of the following terms found within the PODS or NCIt definition: “TCR”, “CAR”, “T-cell receptor” or “chimeric antigen receptor”. To identify other therapies that are monoclonal antibodies targeting cell-surface proteins, we retrieved all drugs from the NCIt with the parent concept of “antineoplastic antibody” and that mentions a gene name or alias of a gene name with a category of “cell membrane” for its subcellular location within UniProt. PODS members routinely annotate all MD Anderson clinical trials for their biomarker selection criteria. We additionally reviewed the drugs utilized within trials in which protein expression via immunohistochemistry (IHC) is used as a selection criteria. Several published reviews including tables of drug-conjugate therapies were also consulted[4-7]. We then ensured that at least one therapy targeting the gene product is clinically available, as defined above, in order for relative RNA expression (that is, overexpression or underexpression) of the gene to be considered actionable. All genes identified through this process for inclusion in the actionable transcriptome list were classified as “Potentially” actionable.

TCGA RNA Expression Analysis

TCGA Pan-Cancer (PANCAN) gene-expression data were downloaded from UCSC Xena, and log2(TPM + 0.001) transformed values from primary tumour samples were used for all analyses.

Datasets are available at:
https://xenabrowser.net/datapages/?dataset=tcga_RSEM_gene_tpm&host=https%3A%2F%2Ftoil.xenahubs.net&removeHub=https%3A%2F%2Fxena.treehouse.gi.ucsc.edu%3A443

https://xenabrowser.net/datapages/?dataset=tcga_rsem_isoform_tpm&host=https%3A%2F%2Ftoil.xenahubs.net&removeHub=https%3A%2F%2Fxena.treehouse.gi.ucsc.edu%3A443

For each gene evaluated *TACSTD2* (encoding TROP2), *NECTIN4* (nectin-4), *ERBB2* (HER2) and *FOLR1* (folate receptor α), two approaches were taken: (1) pan-cancer percentiles were calculated to classify tumours across all cancer types into four expression categories; and (2)

benchmark tumour types in which antibody–drug conjugates (ADCs) have well-established clinical efficacy were used to define gene-specific RNA-expression quartiles, which were then applied to all tumour types for comparison. Stacked bar plots illustrate the proportion of tumours within each expression category by cancer type, enabling direct comparison of RNA-level target expression prevalence across the TCGA cohort.

Supplementary Tables

Supplementary Table 1 | Biomarker-matched FDA-approved therapies for solid tumours with oncogenic gene fusions

Biomarker	Approved disease	Approved therapies
ALK	Non-small-cell lung carcinoma	Alectinib, brigatinib, ceritinib, crizotinib, lorlatinib, ensartinib
	Inflammatory myofibroblastic tumour	Crizotinib
BRAF	Low-grade gliomas	Tovorafenib
FGFR2	Cholangiocarcinoma	Pemigatinib
	Intrahepatic cholangiocarcinoma	Futibatinib
NRG1	Non-small-cell lung carcinoma	Zenocutuzumab
	Pancreatic adenocarcinoma	
NTRK1/2/3	Solid tumours (histology-agnostic)	Larotrectinib, entrectinib, repotrectinib
RET	Non-small-cell lung carcinoma	Selpercatinib, pralsetinib
	Thyroid carcinoma	Selpercatinib, pralsetinib
	Solid tumour (histology-agnostic)	Selpercatinib
ROS1	Non-small-cell lung carcinoma	Crizotinib, entrectinib, repotrectinib, taletrectinib

Supplementary Table 2 | Actionable transcriptome list based on assessment of copy-number variation actionability

Gene	RNA expression level	Tumour type	Actionable category	Actionable for approved or investigational therapies
ABL1	Increased	Haematological cancers	Treatment	ABL1 inhibitors
ABL2	Increased	Haematological cancers	Treatment	ABL2 inhibitors
AKT1	Increased	Solid tumours	Treatment	AKT or mTOR inhibitors
AKT2	Increased	Solid tumours	Treatment	AKT or mTOR inhibitors
ALK	Increased	Advanced-stage cancers	Treatment	ALK inhibitors
ATM	Decreased	Solid tumours	Treatment	PARP inhibitors
ATR	Decreased	Solid tumours	Treatment	PARP inhibitors
AURKA	Increased	Solid tumours	Treatment	AURKA inhibitors
AURKB	Increased	Solid tumours	Treatment	AURKB inhibitors
AXL	Increased	Solid tumours	Treatment	AXL inhibitors
BARD1	Decreased	Solid tumours	Treatment	PARP inhibitors
BCL2	Increased	Advanced-stage cancers	Treatment	BCL2 inhibitors
BRAF	Increased	Solid tumours	Treatment	MEK, ERK or pan-RAF inhibitors
BRCA1	Decreased	Solid tumours	Treatment	PARP inhibitors or platinum-based chemotherapy
BRCA2	Decreased	Solid tumours	Treatment	PARP inhibitors or platinum-based chemotherapy
BRIP1	Decreased	Solid tumours	Treatment	PARP inhibitors
CCNE1	Increased	Solid tumours	Treatment	CDK2 or WEE1 inhibitors
CCR4	Decreased	Mycosis fungoides, Sezary syndrome	Resistance	Mogamulizumab
CDK12	Decreased	Solid tumours	Treatment	PARP inhibitors
CHEK1	Decreased	Solid tumours	Treatment	PARP inhibitors
CHEK2	Increased	Solid tumours	Treatment	CHK2 inhibitors
	Decreased	Solid tumours	Treatment	PARP inhibitors
CSF1R	Increased	Advanced-stage cancers	Treatment	CSF1R monoclonal antibodies or inhibitors
DDR1	Increased	Solid tumours	Treatment	DDR1 inhibitors
DDR2	Increased	Solid tumours	Treatment	DDR2 inhibitors
DLL3	Increased	Small-cell lung cancer	Treatment	DLL3-Targeted bispecific T-cell engagers
DOT1L	Increased	Solid tumours	Treatment	DOT1L inhibitors
EGFR	Increased	Solid tumours	Treatment	EGFR inhibitors
ERBB2	Increased	Solid tumours	Treatment	HER2, pan-PI3K, and mTOR inhibitors
ERBB3	Increased	Solid tumours	Treatment	HER3 inhibitors
ERBB4	Increased	Solid tumours	Treatment	HER4 inhibitors
FANCA	Decreased	Solid tumours	Treatment	PARP inhibitors
FANCL	Decreased	Solid tumours	Treatment	PARP inhibitors
FAT1	Decreased	Breast carcinoma	Resistance	CDK4/6 inhibitors
FGF10	Increased	Solid tumours	Treatment	FGFR inhibitors
FGF19	Increased	Solid tumours	Treatment	FGFR inhibitors
FGF23	Increased	Solid tumours	Treatment	FGFR inhibitors
FGF3	Increased	Solid tumours	Treatment	FGFR inhibitors
FGF4	Increased	Solid tumours	Treatment	FGFR inhibitors
FGF6	Increased	Solid tumours	Treatment	FGFR inhibitors
FGFR1	Increased	Advanced-stage cancers	Treatment	FGFR1 inhibitors
FGFR2	Increased	Solid tumours	Treatment	FGFR2 inhibitors
FGFR3	Increased	Solid tumours	Treatment	FGFR3 inhibitors
FGFR4	Increased	Solid tumours	Treatment	FGFR4 inhibitors
FLT1	Increased	Solid tumours	Treatment	FLT1 inhibitors
FLT3	Increased	Advanced-stage cancers	Treatment	FLT3 inhibitors
FLT4	Increased	Solid tumours	Treatment	FLT4 inhibitors
JAK1	Increased	Advanced-stage cancers	Treatment	JAK1 inhibitors
JAK2	Increased	Advanced-stage cancers	Treatment	JAK2 inhibitors
JAK3	Increased	Advanced-stage cancers	Treatment	JAK3 inhibitors
KDR	Increased	Solid tumours	Treatment	KDR inhibitors
KIT	Increased	Advanced-stage cancers	Treatment	KIT inhibitors
MAP2K1	Increased	Solid tumours	Treatment	MEK inhibitors
MAP2K2	Increased	Solid tumours	Treatment	MEK inhibitors
MAP2K4	Decreased	Solid tumours	Treatment	MEK inhibitors
MAP3K1	Decreased	Solid tumours	Treatment	MEK inhibitors
MAPK1	Increased	Advanced-stage cancers	Treatment	p38 MAPK1 inhibitors
MDM2	Increased	Solid tumours	Treatment	MDM2 inhibitors or nutlins that inhibit MDM2–p53 interaction

MET	Increased	Solid tumours	Treatment	MET inhibitors
	Increased	Non-small-cell lung cancer	Resistance	EGFR inhibitors
MLH1	Decreased	Solid tumours	Treatment	PD-1 inhibitors
MRE11	Decreased	Solid tumours	Treatment	PD-1 inhibitors
MTAP	Decreased	Solid tumours	Treatment	MAT2A inhibitors
MTOR	Increased	Solid tumours	Treatment	mTOR inhibitors
NBN	Decreased	Solid tumours	Treatment	PARP inhibitors
NF1	Decreased	Solid tumours	Treatment	MEK inhibitors
NF2	Decreased	Solid tumours	Treatment	PI3K pathway inhibitors, mTOR inhibitors, MEK inhibitors, or YAP1/TEAD inhibitors
NPM1	Decreased	Haematological cancers	Treatment	Menin inhibitors
PALB2	Decreased	Solid tumours	Treatment	PARP inhibitors
PDGFRA	Increased	Solid tumours	Treatment	PDGFRA inhibitors
PDGFRB	Increased	Solid tumours	Treatment	PDGFRB inhibitors
PIK3CA	Increased	Solid tumours	Treatment	PI3K, AKT or mTOR inhibitors
PIK3CB	Increased	Solid tumours	Treatment	PIK3CB inhibitors
PIK3CD	Increased	Solid tumours	Treatment	PIK3CD inhibitors
POLE	Decreased	Solid tumours	Treatment	PD-1 inhibitors with or without CTLA4 inhibitors
PTCH1	Decreased	Solid tumours	Treatment	SMO inhibitors
PTEN	Decreased	Solid tumours	Treatment	p110beta, AKT or mTOR inhibitors
RAD50	Decreased	Solid tumours	Treatment	PARP inhibitors
RAD51	Decreased	Solid tumours	Treatment	PARP inhibitors
RAD51B	Decreased	Solid tumours	Treatment	PARP inhibitors
RAD51C	Decreased	Solid tumours	Treatment	PARP inhibitors
RAD51D	Decreased	Solid tumours	Treatment	PARP inhibitors
RAD54L	Decreased	Solid tumours	Treatment	PARP inhibitors
RAF1	Increased	Solid tumours	Treatment	MEK inhibitors
RB1	Decreased	Solid tumours	Resistance	CDK4/6 inhibitors
RET	Increased	Solid tumours	Treatment	RET inhibitors
RICTOR	Increased	Solid tumours	Treatment	AKT or mTORC2 inhibitors
RNF43	Decreased	Solid tumours	Treatment	Porcupine inhibitors
ROS1	Increased	Solid tumours	Treatment	ROS1 inhibitors
SDHA	Decreased	Gastrointestinal stromal tumour	Treatment	Pazopanib, regorafenib, sunitinib, or binimetinib + imatinib
SDHB	Decreased	Gastrointestinal stromal tumour	Treatment	Pazopanib, regorafenib, sunitinib, or binimetinib + imatinib
SDHC	Decreased	Gastrointestinal stromal tumour	Treatment	Pazopanib, regorafenib, sunitinib, or binimetinib + imatinib
SDHD	Decreased	Gastrointestinal stromal tumour	Treatment	Pazopanib, regorafenib, sunitinib, or binimetinib + imatinib
SMARCA1	Decreased	Solid tumours	Treatment	EZH2 inhibitors
SMARCB1	Decreased	Solid tumours	Treatment	EZH2 inhibitors
SMO	Increased	Solid tumours	Treatment	SMO inhibitors
SRC	Increased	Solid tumours	Treatment	SRC inhibitors
STAG2	Decreased	Solid tumours	Treatment	ATR or PARP inhibitors
STK11	Decreased	Solid tumours	Treatment	mTOR inhibitors
SYK	Increased	Advanced-stage cancers	Treatment	SYK inhibitors
TET2	Decreased	Haematological cancers	Treatment	DNA methyltransferase inhibitors
TSC1	Decreased	Solid tumours	Treatment	mTOR inhibitors
TSC2	Decreased	Solid tumours	Treatment	mTOR inhibitors

Supplementary Table 3 | Actionable transcriptome list based on cell-surface proteins that can be targeted with approved or investigational therapies

Target gene	Treatment	Development status*	Tumour types associated with FDA-approved indications
ADGRE2	ADCLEC.syn1	Clinical development	None
ACVRL1	GT90001	Clinical development	None
AFP	Autologous engineered T cell therapy targeting α-fetoprotein (AFP)	Not in active trial	None
	ET140203	Not in active trial	None
AXL	Mecbotamab Vedotin	Clinical development	None
BSG	Licartin	Not in active trial	None
	DS-1471	Clinical development	None
BTN1A1	Nelmastobart	Clinical development	None
BTN3A1	ICT01	Clinical development	None
BTN3A2	ICT01	Clinical development	None
CALR	JNJ-88549968	Clinical development	None
	INCA033989	Clinical development	None
CCKBR	Lu-177-PP-F11N	Clinical development	None
CCR4	Mogamulizumab	FDA approved	Sezary syndrome and mycosis fungoides
CCR7	JBH492	Clinical development	None
CD19	Loncastuximab tesirine	FDA approved	B cell lymphoma
	Blinatumomab	FDA approved	B-ALL
CD200	Samalizumab	Clinical development	None
CD22	Inotuzumab ozogamicin	FDA approved	B-ALL
CD24	ATG-031	Clinical development	None
CD274	Durvalumab	FDA approved	Endometrial cancer, NSCLC, SCLC, biliary tract cancer, bladder cancer, HCC
	Avelumab	FDA approved	Merkel cell carcinoma, urothelial carcinoma, RCC
	Atezolizumab	FDA approved	NSCLC, HCC, melanoma, alveolar soft part sarcoma
	Cosibelimab	FDA approved	Cutaneous squamous cell carcinoma
CD276	Ifinatamab deruxtecan	Clinical development	None
	Vobramitamab duocarmazine	Clinical development	None
	Mirzotamab clezutoclax	Clinical development	None
	I-131-omburtamab	Clinical development	None
	YL201	Clinical development	None
	MGC026	Clinical development	None
	MHB088C	Clinical development	None
	BAT8009	Clinical development	None
	B7H3/CD3-bispecific T cell-engaging molecule TAK-280	Clinical development	None
	XmAb808	Clinical development	None
CD33	Gemtuzumab Ozogamicin	FDA approved	AML
CD37	Naratuximab Emtansine	Not in active trial	None
	Betalutin	Not in active trial	None
	CD37-targeted CAR T cells	Not in active trial	None
	Combination PSB202	Not in active trial	None
CD38	Daratumumab	FDA approved	Multiple myeloma
	Daratumumab and hyaluronidase-fihj	FDA approved	Multiple myeloma, amyloidosis
CD40	Tecaginlimab	Clinical development	None
	Cifurtilimab	Clinical development	None
CD44V6	CD44v6-targeted CAR T cells	Not in active trial	None
CD44v9	AMT-116	Clinical development	None
CD46	FOR46	Clinical development	None
CD47	Simridarlimab	Clinical development	None
	Vislarafusp alfa	Clinical development	None
	6MW3211	Clinical development	None
	BAT7104	Clinical development	None
	HX009	Clinical development	None
	IMM0306	Clinical development	None
	CPO107	Clinical development	None
	PT886	Clinical development	None

	PT886	Clinical development	None
	IMM2520	Clinical development	None
	NI-1801	Clinical development	None
	ISB 1442	Clinical development	None
	LB101	Clinical development	None
	SG1906	Clinical development	None
	PT217	Clinical development	None
	D3L-001	Clinical development	None
	AK132	Clinical development	None
CD5	Autologous CD5-targeted CAR monocytes MT-101	Clinical development	None
CD52	Alemtuzumab	FDA approved	CLL
CD70	Allogeneic IL-15-armoured CD70-targeted CAR-transduced cord blood-derived NK cells	Clinical development	None
	PRO1160	Clinical development	None
	PSMA/CD70-bispecific 4SCAR T cells	Clinical development	None
	GD2/CD70-bispecific 4SCAR T cells	Clinical development	None
	CD19/CD70-bispecific 4SCAR T cells	Clinical development	None
	CD70-targeted CAR T cells	Clinical development	None
CD79B	Polatuzumab vedotin	FDA approved	DLBCL, high-grade B-cell lymphoma
CDH6	Raludotatug deruxtecan	Clinical development	None
	CUSP06	Clinical development	None
CDH17	ARB202	Clinical development	None
	BI 905711	Not in active trial	None
CDH3	AMG 305	Clinical development	None
CEACAM1	CM-24	Clinical development	None
	Cibisatamab	Clinical development	None
CEACAM5	Tusamitamab ravtansine	Clinical development	None
	EBC-129	Clinical development	None
	Autologous CEA-targeted CAR/HLA-A*02-gated inhibitory receptor/*B2M* shRNA-expressing T cells A2B530	Clinical development	None
	BA1202	Clinical development	None
	BGB-B167	Clinical development	None
	Y-90-conjugated monoclonal antibody MN-14	Not in active trial	None
	LM-24C5	Clinical development	None
	IBI3004	Clinical development	None
	TF2	Not in active trial	None
CEACAM6	L-DOS47	Clinical development	None
	Tinurilimab	Not in active trial	None
	EBC-129	Clinical development	None
CLDN18.2	Tecotabart vedotin	Clinical development	None
	Givastomig	Clinical development	None
	AZD0901	Clinical development	None
	PT886	Clinical development	None
	ASP2138	Clinical development	None
	TAC01-CLDN18.2	Clinical development	None
	EO-3021	Clinical development	None
CLDN6	BNT142	Clinical development	None
	TORL-1-23	Clinical development	None
	CLDN6-targeted CAR T cells	Clinical development	None
	DS-9606a	Clinical development	None
	SAIL66	Clinical development	None
	XmAb541	Clinical development	None
CLEC12A	Tepoditamab	Not in active trial	None
	CD371-targeted/YSNVz/IL-18 CAR T cells	Clinical development	None
	ADCLEC.syn1	Clinical development	None
CLU	Sotevtamab	Clinical development	None
CTAG1A	Letetresgene autoleucel	Clinical development	None
	TAEST16001	Clinical development	None
	NY-ESO-1-C259-specific TCR-engineered T cells	Clinical development	None

	Autologous peripheral blood lymphocytes cotransduced with retroviral vectors encoding inducible IL-12 and an anti-NY-ESO-1 TCR	Not in Active Trial	None
	NY-ESO1-specific TCR-transduced autologous CD62L+-derived T cells	Not in Active Trial	None
	Autologous HLA-A2/NY-ESO-1-specific TCR-transduced T cells	Clinical development	None
	Autologous NY-ESO-1-specific TCR/sr39TK lentiviral vector-transduced PBSCs	Not in active trial	None
	Allogeneic IL-15-armoured NY-ESO-1-specific TCR-transduced cord blood-derived NK cells	Clinical development	None
CTAG1B	Letetresgene autoleucel	Clinical development	None
	TAEST16001	Clinical development	None
	NY-ESO-1-C259-specific TCR T cells	Clinical development	None
	IL-12-armoured NY-ESO-1-specific TCR T cells	Not in active trial	None
	NY-ESO1-specific TCR-transduced autologous CD62L+-derived T cells	Not in active trial	None
	Autologous HLA-A2/NY-ESO-1-specific TCR-transduced T cells	Clinical development	None
	Autologous NY-ESO-1 TCR/sr39TK lentiviral vector-transduced PBSCs	Not in active trial	None
	Allogeneic IL-15-armoured NY-ESO-1-specific TCR-transduced cord blood-derived NK cells	Clinical development	None
CTGF	Pamrevlumab	Clinical development	None
CXCL8	Adakitug	Clinical development	None
CXCR4	Pb-212-pentixather	Clinical development	None
DDR1	PRTH-101	Clinical development	None
DKK1	JS015	Clinical development	None
DLK1	ADC TORL-4-500	Clinical development	None
	ADCT-701	Clinical development	None
DLL3	Tarlatamab	FDA approved	SCLC
DLL4	Navicixizumab	Clinical development	None
	CTX-009	Clinical development	None
EGFR	Cetuximab	FDA approved	CRC, HNSCC
	Panitumumab	FDA approved	CRC
	Amivantamab	FDA approved	NSCLC
ENG	Carotuximab	Clinical development	None
ENPP3	AGS-16M8F	Not in active trial	None
	XmAb819	Clinical development	None
	JNJ-87890387	Clinical development	None
EPCAM	M701	Clinical development	None
	A-337	Clinical development	None
	Catumaxomab	Clinical development	None
	CX-2051	Clinical development	None
	BA3182	Clinical development	None
	BNT314	Clinical development	None
	AM-928	Clinical development	None
EPHA2	BT5528	Clinical development	None
EPHA5	MBRC-101	Clinical development	None
ERBB2	Trastuzumab deruxtecan	FDA approved	Solid tumours (HER2 IHC 3+)
	Pertuzumab	FDA approved	Breast cancer
	Trastuzumab	FDA approved	Breast cancer, gastric cancer, GEJ adenocarcinoma
	Trastuzumab emtansine	FDA approved	Breast cancer
	Trastuzumab/hyaluronidase-oysk	FDA approved	Breast cancer
	Hyaluronidase-zzxf/pertuzumab/trastuzumab	FDA approved	Breast cancer
ERBB3	Zenocutuzumab	FDA approved	NSCLC, pancreatic adenocarcinoma
F3	Tisotumab vedotin	FDA approved	Cervical cancer
FAP	RO7122290	Clinical development	None
	Lu-177-FAP-2286	Clinical development	None
	Ga-68-FAP-2286	Clinical development	None
	FAP-specific CD8-positive T cells	Not in active trial	None
	Lu-177-PNT6555	Clinical development	None
	BI 765179	Clinical development	None

FCRL5	Cevostamab	Clinical development	None
FGF23	Burosumab	FDA approved	Non-cancer indication
FGFR2	Bemarituzumab	Clinical development	None
FLT3	CLN-049	Clinical development	None
	SENTI-202	Clinical development	None
FOLH1	Nezastomig	Clinical development	None
	Voxalatamab	Not in active trial	None
	REGN4336	Clinical development	None
	Lu-177 PNT2002	Clinical development	None
	CBP-1018	Clinical development	None
	ARX517	Clinical development	None
	Rosopatamab tetraxetan	Clinical development	None
	Lu-177-rosopatamab tetraxetan	Clinical development	None
	Lu-177-PSMA-I&T	Clinical development	None
	ABBV-969	Clinical development	None
	Ac-225-PSMA-trillium	Clinical development	None
	Lu-177-capromab	Not in active trial	None
	PSMA/CD70-bispecific 4SCAR T cells	Clinical development	None
	LAVA-1207	Clinical development	None
	Autologous GD2/PSMA-bispecific 4SCAR T cells	Clinical development	None
	JNJ-87189401	Clinical development	None
	JANX007	Clinical development	None
FOLR1	Mirvetuximab soravtansine	FDA approved	Ovarian, fallopian tube or primary peritoneal cancer
GD2	GD2/CD56-bispecific 4SCAR T cells	Clinical development	None
	GD2/CD70-bispecific 4SCAR T cells	Clinical development	None
	Autologous GD2/PSMA-bispecific 4SCAR T cells	Clinical development	None
GDF15	Visugromab	Clinical development	None
GJA1	ALMB-0168	Clinical development	None
GPC2	Autologous GPC2-targeted CAR T cells	Clinical development	None
GPC3	ERY974	Clinical development	None
	TAK-102	Clinical development	None
	ECT204	Clinical development	None
	CM350	Clinical development	None
	Codrituzumab	Clinical development	None
	BOXR1030	Clinical development	None
	AZD5851	Clinical development	None
GPRC5D	Talquetamab	Clinical development	None
	Forimtamig	Clinical development	None
	LBL-034	Clinical development	None
GUCY2C	GUCY2C-targeted CAR T cells	Clinical development	None
IGF1	Xentuzumab	Clinical development	None
IGF1R	Ac-225-FPI-1434	Clinical development	None
IGF2	Xentuzumab	Clinical development	None
IL13RA2	YYB-103	Not in active trial	None
IL2RA	Y-90-basiliximab	Clinical development	None
IL3RA	Vibecotamab	Clinical development	None
	Pivekimab sunirine	Clinical development	None
	Flotetuzumab	Clinical development	None
	UCART123	Clinical development	None
	SAR443579	Clinical development	None
	VIP943	Clinical development	None
	CD123/CD3-bispecific DART molecule MGD024	Clinical development	None
	AFM28	Clinical development	None
IL1RAP	Nidanilimab	Clinical development	None
IL6	Siltuximab	FDA approved	Castleman disease
ITGA5	Lu-177-FF58	Clinical development	None
ITGAV	Lu-177-FF58	Clinical development	None
ITGB3	Lu-177-AB-3PRGD2	Clinical development	None
	Internalized-arginylglycylaspartic acid cyclic peptide	Clinical development	None
	Lu-177-DOTA-ABM-5G	Clinical development	None
	VIP236	Clinical development	None

ITGB1	OS2966	Not in active trial	None
ITGB3	Lu-177-AB-3PRGD2	Clinical development	None
ITGB6	SGN-B6A	Clinical development	None
	Lu-177-DOTA-ABM-5G	Clinical development	None
	Sigvotatug vedotin	Clinical development	None
KAAG1	Olintatug tesirine	Clinical development	None
KDR	Ramucirumab	FDA approved	Gastric cancer, GEJ adenocarcinoma, HCC, NSCLC, CRC
KIR3DL2	Lacutamab	Clinical development	None
KIT	Briquilimab	Clinical development	None
KLK2	JNJ-75229414	Clinical development	None
	JNJ-78278343	Clinical development	None
LAIR1	NGM438	Clinical development	None
	NC525	Clinical development	None
LGR5	MCLA-158	Clinical development	None
LIF	Falbikitug	Clinical development	None
LILRB1	ADA-011	Clinical development	None
LILRB2	ADA-011	Clinical development	None
	CDX-585	Clinical development	None
LILRB3	ADA-011	Clinical development	None
LILRB4	IO-202	Clinical development	None
	NGM831	Clinical development	None
	SG2918	Clinical development	None
LRP1	Paclitaxel trevatide	Clinical development	None
LY75	OBT076	Clinical development	None
	Oberotatug ravtansine	Clinical development	None
MAGEA1	TSC-204-A0201	Clinical development	None
	TSC-204-C0702	Clinical development	None
MAGEA3	KITE-718	Clinical development	None
	Autologous HLA-DP0401/0402-restricted MAGE-A3-reactive TCR-transduced T cells	Not in active trial	None
MAGEA4	Afamitresgene autoleucel	FDA approved	Synovial sarcoma
MAGEA6	KITE-718	Clinical development	None
MAGEC2	Autologous MAGE-C2-specific HLA-A2-restricted TCR T cells	Clinical development	None
MET	Amivantamab	FDA approved	NSCLC
	Telisotuzumab vedotin	FDA approved	NSCLC
MICA	CLN-619	Clinical development	None
	KD-496	Clinical development	None
MICB	CLN-619	Clinical development	None
	KD-496	Clinical development	None
MLANA	Autologous anti-MART-1 F5 TCR-engineered peripheral blood lymphocytes	Not in active trial	None
MMP2	Chlorotoxin (EQ)-CD28-CD3ζ-CD19t CAR T cells	Clinical development	None
MS4A1	Rituximab	FDA approved	Non-Hodgkin lymphoma, CLL
	Mosunetuzumab	FDA approved	FL
	Rituximab and human hyaluronidase	FDA approved	FL, DLBCL, CLL
	Glofitamab	FDA approved	DLBCL NOS, LBCL arising from FL
	Epcoritamab	FDA approved	DLBCL, high-grade B cell lymphoma, FL
	Obinutuzumab	FDA approved	FL, CLL
MSLN	Gavocabtagene autoleucel	Clinical development	None
	Misitatug blivedotin	Clinical development	None
	FH-TCR TMSLN	Clinical development	None
	Anetumab ravtansine	Clinical development	None
	SynKIR-110	Clinical development	None
	NI-1801	Clinical development	None
	TC-510	Clinical development	None
	AMG 305	Clinical development	None
MUC1	Tifcemalimab	Clinical development	None
	M1231	Not in active trial	None
	DS-3939a	Clinical development	None
	Gatipotuzumab	Not in active trial	None
MUC16	Ubamatamab	Clinical development	None

	REGN5668	Clinical development	None
	LBL-033	Clinical development	None
MYO1G	TSC-101	Clinical development	None
NCAM1	GD2/CD56-bispecific 4SCAR T cells	Clinical development	None
NCR3LG1	BI 765049	Clinical development	None
NECTIN4	Enfortumab vedotin	FDA approved	Urothelial cancer
NRP1	CEND-1	Clinical development	None
NT5E	Dalutrafusp alfa	Clinical development	None
	AK131	Clinical development	None
NTN1	NP137	Clinical development	None
NTSR1	Lu-177-zalsenertant tetraxetan	Not in active trial	None
PDCD1LG2	IMGS-001	Clinical development	None
PDGFRA	Olaratumab	FDA approved	Soft tissue sarcoma
PLEC	Ibentatug	Not in active trial	None
PMEL	Tebentafusp	FDA approved	Uveal melanoma
PRAME	IMC-F106C	Clinical development	None
	IMA203CD8	Clinical development	None
PTK7	Cofetuzumab pelidotin	Clinical development	None
PTPRC	BC8-B10	Clinical development	None
	Iomab B	Clinical development	None
	Y-90-conjugated anti-CD45 monoclonal antibody BC8	Not in active trial	None
PVR	NTX-1088	Clinical development	None
PVRIG	COM701	Clinical development	None
	GSK4381562	Clinical development	None
	SIM0348	Clinical development	None
	PM1009	Clinical development	None
	NM1F	Clinical development	None
RAET1E	KD-496	Clinical development	None
RAET1G	KD-496	Clinical development	None
RAET1L	KD-496	Clinical development	None
ROBO1	ROBO1-targeted BiCAR NKT cells	Not in active trial	None
ROR1	Zilovertamab vedotin	Clinical development	None
	CS5001	Clinical development	None
	NVG-111	Clinical development	None
	Nebratamig	Clinical development	None
	EMB-07	Clinical development	None
ROR2	Ozuriftamab vedotin	Clinical development	None
	CCT301-59	Not in active trial	None
SEMA4D	Pepinemab	Clinical development	None
SEZ6	ABBV-706	Clinical development	None
SIGLEC15	NC318	Clinical development	None
	Aldastotug	Clinical development	None
SLAMF7	Elotuzumab	FDA approved	Multiple myeloma
SLC34A2	Upinitatug rilsodotin	Clinical development	None
SLC39A6	Ladiratuzumab vedotin	Clinical development	None
	BRY812	Clinical development	None
SLC3A2	IGN523	Not in active trial	None
SORT1	Sudocetaxel zendusortide	Clinical development	None
STAB1	Bexmarilimab	Clinical development	None
STEAP1	Xaluritamig	Clinical development	None
	ABBV-969	Clinical development	None
	Anti-STEAP1 CAR T cells	Clinical development	None
TACSTD2	Sacituzumab govitecan	FDA approved	Breast cancer
	Datopotamab deruxtecan	FDA approved	Breast cancer, NSCLC
TGFB1	Dalutrafusp alfa	Clinical development	None
	Y101D	Clinical development	None
	LBL-015	Clinical development	None
	Fusion protein ZGGS18	Clinical development	None
	DR30206	Clinical development	None
TGFB2	Dalutrafusp alfa	Clinical development	None
	Y101D	Clinical development	None
	LBL-015	Clinical development	None

	Fusion protein ZGGS18	Clinical development	None
	DR30206	Clinical development	None
TGFB3	Dalutrafusp alfa	Clinical development	None
	Y101D	Clinical development	None
	LBL-015	Clinical development	None
	Fusion protein ZGGS18	Clinical development	None
	DR30206	Clinical development	None
TMEFF2	JNJ-70218902	Clinical development	None
TNFRSF10B	Ozekibart	Clinical development	None
	Aplitabart	Clinical development	None
	IBI3004	Clinical development	None
TNFRSF13C	Ianalumab	Clinical development	None
	Autologous BAFFR-targeting CAR T cells	Clinical development	None
	ESG206	Clinical development	None
TNFRSF17	Elranatamab	FDA approved	Multiple myeloma
	Teclistamab	FDA approved	Multiple myeloma
TNFRSF8	Brentuximab vedotin	FDA approved	Mycosis fungoides
TNFSF11	Denosumab	FDA approved	ALCL, PTCL, cHL, LBCL
TNFSF13B	Zigakibart	Clinical development	None
TPBG	SYD1875	Not in active trial	None
	ALG.APV-527	Clinical development	None
TRPV6	CBP-1008	Clinical development	None
	CBP-1019	Clinical development	None
ULBP1	KD-496	Clinical development	None
ULBP2	KD-496	Clinical development	None
ULBP3	KD-496	Clinical development	None
VEGFA	Navicixizumab	Clinical development	None
	hPV19	Not in active trial	None
	CTX-009	Clinical development	None
	Faricimab	Clinical development	None
	AK112	Clinical development	None
	Ivonescimab	Clinical development	None
	BNT327	Clinical development	None
	Fusion protein ZGGS18	Clinical development	None
	JS207	Clinical development	None
	TAVO412	Clinical development	None
	DR30206	Clinical development	None
VEGFB	hPV19	Not in active trial	None
	TAVO412	Clinical development	None
VEGFC	hPV19	Not in active trial	None
	VGX-100	Not in active trial	None
	TAVO412	Clinical development	None
VEGFD	hPV19	Not in active trial	None
	TAVO412	Clinical development	None
VIM	Pritumumab	Not in active trial	None
VTCN1	AZD8205	Clinical development	None
	SGN-B7H4V	Clinical development	None
	CLN-418	Clinical development	None
	Emiltatug ledadotin	Clinical development	None
	Puxitatug samrotecan	Clinical development	None
	GEN1047	Clinical development	None

*Development status as determined in October of 2024. Ac-225, actinium-225; ALCL, anaplastic large cell lymphoma; AML, acute myeloid leukaemia; B-ALL, B cell precursor acute lymphoblastic leukaemia; BiCAR, bispecific chimeric antigen receptor; CAR, chimeric antigen receptor; cHL, classical Hodgkin lymphoma; CLL, chronic lymphocytic leukaemia; CRC, colorectal cancer; DLBCL, diffuse large B cell lymphoma; FL, follicular lymphoma; Ga-68, gallium-68; GEJ, gastroesophageal junction; HCC, hepatocellular carcinoma; HNSCC, head and neck squamous cell carcinoma; I-131, iodine-131; IHC, immunohistochemistry; LBCL, large B cell lymphoma; Lu-177, lutetium-177; NK, natural killer; NKT, natural killer T; NOS, not otherwise specified; NSCLC, non-small-cell lung cancer; Pb-212, lead-212; PBSC, peripheral blood stem cells; PTCL, peripheral T cell lymphoma; RCC, renal cell carcinoma; SCLC, small-cell lung cancer; TCR, T cell receptor; Y-90, yttrium-90.

Supplementary Table 4 | Commercial RNA-seq providers

Biomarker	Providers	Panels	Links
RNA expression	BostonGene	Tumor Portrait	https://bostongene.com/providers/tumor-portrait
	Caris Life Sciences	MI Profile™ Comprehensive Testing	https://www.carislifesciences.com/products-and-services/molecular-profiling/tissue-profiling/ (https://www.carislifesciences.com/wp-content/uploads/2024/05/TN0713-v2-Profile-Menu-Tissue-Blood_Singles.pdf)
	Columbia University	Cancer Whole Exome Sequencing with Transcriptome	https://www.pathology.columbia.edu/diagnostic-specialties/personalized-genomic-medicine/oncology-testing/cancer-whole-exome-sequencing-transcriptome
	Genomic Testing Cooperative	Solid Tumor Profile Plus; Hematology Profile Plus	https://genomictestingcooperative.com/genomic-tests/solid-tumor-profile-plus/; https://genomictestingcooperative.com/genomic-tests/gtc-hematology-profile-plus/
	OmniSeq	OmniSeq INSIGHT	https://oncology.labcorp.com/cancer-care-team/test-menu/omniseq-insight
	Strata Oncology	Strata Select™	https://strataoncology.com/strata-select/
	Tempus	Tempus RNA (research only)	
	University of Michigan	Mi-OncoSeq (OncoSeq V6a)	https://www.pathology.med.umich.edu/mctp/mi-oncoseq-study; https://www.pathology.med.umich.edu/static/apps/cms/ckfinder/userfiles/388/files/OncoSeq-Test-Definition-V6a.pdf; [PMID:22133722]
Fusion variants	Boston Children's hospital	Hematologic Malignancy Fusion Panel	https://www.childrenshospital.org/departments/pathology-department/molecular-pathology-lampp/test-menu
	BostonGene	Tumor Portrait	https://bostongene.com/providers/tumor-portrait
	Caris Life Sciences	MI Profile™ Comprehensive Testing	https://www.carislifesciences.com/products-and-services/molecular-profiling/tissue-profiling/ (https://www.carislifesciences.com/wp-content/uploads/2024/05/TN0713-v2-Profile-Menu-Tissue-Blood_Singles.pdf)
	Children's hospital of Philadelphia	Cancer Gene-fusion Panel	https://www.testmenu.com/chop/Tests/785504
	Cleveland clinic	Solid Tumor Gene Fusion Next-Generation Sequencing Panel	https://clevelandcliniclabs.com/solid-tumor-gene-fusion-next-generation-sequencing-panel/
	Columbia University	Columbia Targeted Fusion Panel	https://www.pathology.columbia.edu/diagnostic-specialties/personalized-genomic-medicine/oncology-testing/columbia-targeted-fusion-panel-ctfp
	Cornell University	TruSight Oncology 500 Assay	https://clinicalgenomics.weill.cornell.edu/testing-portfolio/trusight-oncology-500-assay
	Exact Science	OncoExTra®	https://precisiononcology.exactsciences.com/healthcare-providers/therapy-selection/advanced-solid-tumors/oncoextra/clinical-utility
	Genomic Testing Cooperative	Solid Tumor Profile Plus; Hematology Profile Plus	https://genomictestingcooperative.com/genomic-tests/solid-tumor-profile-plus/; https://genomictestingcooperative.com/genomic-tests/gtc-hematology-profile-plus/
	Massachusetts general hospital	Fusion Assays (NGS)	https://www.massgeneral.org/pathology/services/center-for-integrated-diagnostics
	Mayo Clinic	MayoComplete Comprehensive Sarcoma Panel	https://www.mayocliniclabs.com/test-catalog/overview/616492
	Nationwide Children's hospital	Hematologic Cancer Fusion; Solid tumor fusion analysis	https://www.testmenu.com/nationwidechildrens/Tests/1206770; https://www.testmenu.com/nationwidechildrens/Tests/1206768
	Natera	Altera™ Comprehensive Genomic Profiling	https://www.natera.com/oncology/signatera-advanced-cancer-detection/clinicians/altera/
	NeoGenomics	NTRK NGS Fusion Panel; NTRK & RET NGS Fusion Panel; Lung NGS Fusion Panel	https://neogenomics.com/test-menu/ntrk-ngs-fusion-panel; https://neogenomics.com/test-menu/ntrk-ret-ngs-fusion-panel; https://neogenomics.com/test-menu/lung-ngs-fusion-panel-complete-or-limited
	Oregon Health & Science University	The GeneTrails® Comprehensive Solid Tumor Panel (CSTP)	https://knightdxlabs.ohsu.edu/home/test-details?id=GeneTrails+Comprehensive+Solid+Tumor+Panel
	Personalis	NeXT Dx	https://www.personalis.com/for-clinicians/next-dx/
	Stanford Medicine	Fusion-STAMP	https://stanfordlab.com/test-details/f/FSTAMP.html
	Tempus	TEMPUS xR	https://www.tempus.com/life-sciences/tempus-xr/

	University of Pennsylvania	Fusion Transcript Panel	https://www.pennmedicine.org/departments-and-centers/center-for-personalized-diagnostics/gene-panels
	University of California, Los Angeles	Solid Tumor Fusion Gene Panel	https://www.testmenu.com/UCLA/Tests/1165250
	University of California, San Francisco	RNA Fusions Heme Panel	https://genomics.ucsf.edu/content/rna-fusions-heme-panel-blood; https://genomics.ucsf.edu/content/rna-fusions-heme-panel-non-blood
	University of Chicago	RNA Gene Fusion Next Generation Sequencing Assay	https://uchicagomedlabs.testcatalog.org/show/FUSNCS-
	University of Michigan	Mi-OncoSeq (OncoSeq V6a)	https://www.pathology.med.umich.edu/mctp/mi-oncoseq-study; https://www.pathology.med.umich.edu/static/apps/cms/ckfinder/userfiles/388/files/OncoSeq-Test-Definition-V6a.pdf; PMID:22133722
	University of Texas MD Anderson Cancer Center	Solid Tumor Genomic Assay 2018 - RNA (Fusions)	[PMID:35241495] Supplementary data. jitc-2021-004371supp003.pdf
	University of Washington	FusionPlex® Pan-Heme Panel	http://uwcpdx.org/fusionplex-pan-heme-panel/
	UT Southwestern medical center	1385-Gene Pan-Cancer Mutation Test	https://www.utsouthwestern.edu/education/medical-school/departments/pathology/services/once-upon-a-time/doclib/comprehensive-pan-cancer-next-generation-sequencing-sample-report.pdf
	Variantyx	OncoAlly™ Solid Tumor Analysis	https://www.variantyx.com/products-services/oncoally-solid-tumor/
	VCU Health	Oncogenomic Solid tumor V2	https://pathcat.vcu.edu/Tests/Details/1230133668

Current as of July, 2024. RNA-seq, RNA sequencing.

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