The new CTA set

What survives, what fails, and what deserves another look

Retained CTA candidates	Neither	Excluded / Unsafe
399	561	1,580

The report covers all 2,540 mapped CTA nominations. CTA means a research-screen pass, Unsafe means exclusion from targeting and inclusion in the forbidden background, and Neither means neither selected nor added to that background. No category constitutes clinical clearance.

The latest change excludes any observed RNA >30 TPM or >30 nTPM outside explicitly mapped Reproductive/Disposable contexts. It removes 37 previously retained CTAs and 253 previous Neither genes across the full canonical universe. Existing stricter RNA and protein rules remain.

MAGEA3 and ROPN1 are the two new clinical/requested benchmark losses. CT55 stays retained. CTAG2 stays Variable; FOXR2 stays under antibody review. The review questions and exact reasons are preserved rather than waived for familiar targets.

New literature review flags 37 retained genes for normal-tissue conflicts. ABCC11 and MAGEC2 warrant urgent protein-evidence review before target use. These flags are shown beside the frozen decisions; they are not silently treated as clean passes.

How to use this report

Question	Where to look
Which genes made it?	Retained catalog: all 399; retained.csv for full evidence.
Which could be reconsidered?	Priority follow-up and boundary sections; Neither catalog (561) and excluded catalog (1,580).
How often are they expressed in cancer?	Cancer occurrence heatmap and tables; complete RNA/IHC cohort exports.
Which have benefit or toxicity evidence?	Primary clinical literature and 30 clinical-target entries; registration is not an outcome.
What is known about their biology?	Every gene has a UniProt annotation or an explicit mapping/function gap; source-linked full text is in all-genes.csv.gz.

Search all genes, evidence and sources online

The current rules

Admission and normal counterevidence are separate. A nomination needs reproductive RNA >=5 nTPM, reliable positive reproductive protein, or cited reproductive plus tumor/recognition support. Good positive protein evidence can satisfy admission below 5 nTPM. None of these bypass normal-expression gates.

Tissue category	RNA ceilings, nTPM	Selectivity minima
Vital	2 / 4 / 6 / 12	80 / 75 / 70 / 65%
Protected	6 / 8 / 12 / 24	75 / 70 / 65 / 60%
Manageable	10 / 20 / 30 / 60	70 / 65 / 60 / 55%

Order: missing/uncertain, Approved-negative, Supported-negative, Enhanced-negative. Relaxation requires complete local negative IHC and a reliable reproductive positive control. Any accepted positive normal IHC, including Low, excludes. Uncertain/cross-reactive antibodies are handled separately.

For each bulk tissue, require N <= C, N <= R(1-s)/s + 0.1, and N < R. R is the maximum reproductive RNA, N the tissue RNA, C its ceiling and s its selectivity minimum. The fixed 0.1 nTPM allowance is not a fitted uncertainty interval. The new >30 rule independently caps every audited individual/cluster observation, regardless of enrichment or IHC.

Normal-cell and immune data also trigger review at lower values: source-specific rules inspect clusters, DICE distributions, immune summaries, corneal CP10K and primary antibody conflicts. These can produce Neither even when the bulk RNA/IHC grid passes. CP10K is never compared numerically with TPM/nTPM.

Reproductive and Disposable contexts are permitted by this research policy. Immune cells sampled inside those organs retain their immune identity. Unresolved anatomy does not establish permission. Human thresholds have not been validated for dogs or mice.

Genes and proteins are different scopes

Scope	CTA	Unsafe	Neither
Mapped CTA nominations	399	1,580	561
Canonical human genes	399	17,699	1,999
Complete unique proteins	723	126,384	2,878

Exact shared sequences use Unsafe > Neither > CTA. An additional 391 noncanonical reference loci have high-RNA exclusions. Gene expression does not establish which isoform is expressed; full-protein disjointness does not make their k-mers disjoint.

Where candidates leave the funnel

Counts below are mutually exclusive final reason labels, not the number of every failing measurement. A gene can have several counterevidence findings even though it has one final label.

Result	Principal reason	Genes
Neither	Antibody evidence unresolved	199
Neither	Cell / immune RNA conflict	70
Neither	Weak affirmative reproductive evidence	191
Neither	Other screening requirements	59
Neither	Insufficient reproductive enrichment	10
Neither	Coverage / identity gap	31
Neither	Vital donor zero/high pattern	1
Unsafe	New high normal RNA rule	125
Unsafe	Published normal-cell protein	3
Unsafe	Positive normal IHC	845
Unsafe	Bulk RNA above applicable ceiling	606
Unsafe	Reviewed safety hold	1

Neither is not a safe reserve list. Low means insufficient target evidence; Cellular and Antibody mean unresolved conflicts. The maximum audited non-permitted values remaining anywhere in canonical Neither are 29.9398 TPM and 30 nTPM. Missing measurements remain missing.

Cancer occurrence: the measured landscape



HPA v25.1-1 TCGA cohorts; RNA >=5 native pTPM. Gray cells are missing exact-ID coverage, not negatives. Label colors show CTA (teal), Neither (amber) and Unsafe (red). Full tables include both TCGA and independent validation cohorts and thresholds 0.1, 1, 2 and 5 pTPM.

This does not estimate prevalence in all patients with cancer: cohorts differ in histology, stage, sampling and selection. A bulk tumor signal can arise in tumor-associated normal cells. Closely related genes may share sequence and antibody recognition. Gene-level expression cannot prove target-peptide presentation.

Cancer occurrence for key targets

Gene / result	Highest ranked RNA cohorts (>=5 pTPM)	Cancer IHC Medium/High
CT55 CTA	Skin Cuteneous Melanoma (TCGA): 5/99 (5.1%); Lung Squamous Cell Carcinoma (TCGA): 20/489 (4.1%); Stomach Adenocarcinoma (TCGA): 14/346 (4.0%)	No exact-ID IHC coverage in the HPA cancer snapshot
CT83 CTA	Stomach Adenocarcinoma (TCGA): 174/346 (50.3%); Lung Adenocarcinoma (validation): 49/105 (46.7%); Lung Adenocarcinoma (TCGA): 213/497 (42.9%)	No exact-ID IHC coverage in the HPA cancer snapshot
CTAG1A CTA	Bladder Urothelial Carcinoma (TCGA): 24/169 (14.2%); Lung Squamous Cell Carcinoma (TCGA): 67/489 (13.7%); Ovary Serous Cystadenocarcinoma (TCGA): 40/349 (11.5%)	testis cancer: 2/12 (16.7%); melanoma: 1/11 (9.1%)
CTAG1B CTA	Bladder Urothelial Carcinoma (TCGA): 16/169 (9.5%); Lung Squamous Cell Carcinoma (TCGA): 46/489 (9.4%); Lung Squamous Cell Carcinoma (validation): 6/68 (8.8%)	testis cancer: 3/12 (25.0%); ovarian cancer: 1/11 (9.1%)
CTAG2 Neither	Testicular Germ Cell Tumor (TCGA): 35/133 (26.3%); Skin Cuteneous Melanoma (TCGA): 25/99 (25.3%); Bladder Urothelial Carcinoma (TCGA): 39/169 (23.1%)	colorectal cancer: 5/11 (45.5%); lung cancer: 4/12 (33.3%)
FOXR2 Neither	Testicular Germ Cell Tumor (TCGA): 8/133 (6.0%); Skin Cuteneous Melanoma (TCGA): 2/99 (2.0%); Uterine Corpus Endometrial Carcinoma (TCGA): 2/176 (1.1%)	melanoma: 3/8 (37.5%); endometrial cancer: 4/11 (36.4%)
MAGEA3 Unsafe	Skin Cuteneous Melanoma (TCGA): 55/99 (55.6%); Lung Squamous Cell Carcinoma (TCGA): 223/489 (45.6%); Bladder Urothelial Carcinoma (TCGA): 68/169 (40.2%)	No exact-ID IHC coverage in the HPA cancer snapshot
MAGEA4 CTA	Lung Squamous Cell Carcinoma (TCGA): 270/489 (55.2%); Lung Squamous Cell Carcinoma (validation): 36/68 (52.9%); Head and Neck Squamous Cell Carcinoma (TCGA): 181/492 (36.8%)	testis cancer: 5/12 (41.7%); skin cancer: 4/12 (33.3%)
PRAME CTA	Skin Cuteneous Melanoma (TCGA): 94/99 (94.9%); Uterine Corpus Endometrial Carcinoma (TCGA): 165/176 (93.8%); Ovary Serous Cystadenocarcinoma (validation): 72/81 (88.9%)	melanoma: 1/12 (8.3%); breast cancer: 0/11 (0.0%)
ROPN1 Unsafe	Skin Cuteneous Melanoma (TCGA): 81/99 (81.8%); Breast Invasive Carcinoma (validation): 15/50 (30.0%); Breast Invasive Carcinoma (TCGA): 160/1022 (15.7%)	colorectal cancer: 2/11 (18.2%); liver cancer: 1/9 (11.1%)
XAGE1A CTA	Lung Adenocarcinoma (validation): 81/105 (77.1%); Lung Adenocarcinoma (TCGA): 357/497 (71.8%); Testicular Germ Cell Tumor (TCGA): 55/133 (41.4%)	No exact-ID IHC coverage in the HPA cancer snapshot
XAGE1B CTA	Lung Adenocarcinoma (validation): 71/105 (67.6%); Lung Adenocarcinoma (TCGA): 314/497 (63.2%); Liver Hepatocellular Carcinoma (TCGA): 82/362 (22.7%)	No exact-ID IHC coverage in the HPA cancer snapshot

RNA and IHC are unpaired. Small cancer IHC groups (often about 8-12 patients) do not calibrate antibody sensitivity. The aggregate download lacks antibody identity and reliability; discordance should prompt assay review rather than numerical averaging. Synovial sarcoma trial enrichment is not represented by a dedicated HPA RNA cohort here.

Retained genes with notable normal RNA

These are the 15 retained genes with the largest audited non-permitted nTPM values. Native TPM is shown separately in the downloadable table. Single-cell nTPM is not directly comparable to bulk-tissue nTPM; the source and cell identity matter. A retained label does not mean no normal expression.

Gene	Highest normal observation	Reproductive bulk nTPM
TEX14	29.7 nTPM; breast/macrophages; hpa_single_cell_tissue; vital	26.2
MORC1	28.5 nTPM; pbmc/platelets; hpa_single_cell_tissue; vital	15.5
KIAA1210	27.7 nTPM; prostate/t-cells; hpa_single_cell_tissue; vital	40.8
KLF17	27.4 nTPM; unsited/Oligodendrocyte precursor cells; hpa_single_cell; unresolved	8.1
YBX2	27 nTPM; colon/distal enterocytes; hpa_single_cell_tissue; protected	536
CGB3	25.9 nTPM; pancreas/mixed cell types; hpa_single_cell_tissue; vital	9.5
C10orf62	24.8 nTPM; testis/macrophages; hpa_single_cell_tissue; vital	270
MEIOB	24.2 nTPM; placenta/mixed immune cells; hpa_single_cell_tissue; vital	26.5
TEX15	24 nTPM; brain/inhibitory neurons; hpa_single_cell_tissue; vital	11.8
TMEM210	21.6 nTPM; pbmc/dendritic cells; hpa_single_cell_tissue; vital	14.4
CAPZA3	21.1 nTPM; testis/macrophages; hpa_single_cell_tissue; vital	178
LDHC	20.5 nTPM; testis/macrophages; hpa_single_cell_tissue; vital	257
PSG1	20.4 nTPM; placenta/mixed immune cells; hpa_single_cell_tissue; vital	253
PDCL2	20.4 nTPM; brain/inhibitory neurons; hpa_single_cell_tissue; vital	63.3
PRAME	20.3 nTPM; colon/undifferentiated cells; hpa_single_cell_tissue; protected	102

Examples near 30 are TEX14 (breast macrophages), MORC1 (PBMC platelets), and KIAA1210. Immune cells inside breast are not granted reproductive permission. These findings warrant source/identity/protein follow-up; the present report does not change their frozen decisions.

Retained does not resolve these literature conflicts

The new UniProt review was screened manually for positive normal-tissue assertions, excluding sentences that merely mention cancer or negative expression. These are follow-up flags, not automatic rule changes. ABCC11 and MAGEC2 have primary normal neural protein reports and deserve urgent adjudication. Other entries are RNA-, isoform- or context-dependent and need their original assays checked.

Gene(s)	Priority / reported conflict
YBX2	Normal protein review: Published staining includes vascular smooth muscle in pulmonary artery, myocardium and skeletal muscle, plus adrenal cortical cells.
SLC22A14	Normal RNA review: UniProt describes ubiquitous expression based on historical human tissue work, despite strong reproductive enrichment in current bulk data.
SUN5	Conflicting tissue studies: UniProt explicitly records conflicting reports of widespread versus testis-specific expression.
WFDC6	Normal RNA review: UniProt describes ubiquitous expression with high levels in trachea as well as epididymis and testis.
ABCC11	Urgent protein review: Published human brain immunoblotting and axonal immunofluorescence conflict with a reproductive-restricted target label.
MAGEC2	Urgent protein review: A 2003 study reported cerebellar Purkinje-cell staining with the TC-1 polyclonal anti-HCA587 reagent.
PATE2	Isoform review: UniProt assigns normal male/female brain expression to isoform 2, while reproductive expression includes both forms.
TPTE2	Isoform review: Primary work describes TPIP splice variants in brain and stomach as well as testis.
EQTN	Isoform review: UniProt reports low skin and blood expression for isoform 2, distinct from the highly testicular isoform 1.
ACTL8	Normal RNA review: Curated tissue annotation describes strong testis and pancreas expression.
FAM170A	Normal RNA review: UniProt reports strong testis and brain expression and weaker expression in several other organs.
FKBP6	Normal RNA review: UniProt describes detection across all tissues examined, including heart, muscle, liver and kidney.
GOLGA6A	Normal RNA review: Curated tissue annotation reports intermediate pancreas and lymph-node expression and lower expression in other organs.
HORMAD2	Low normal expression review: Curated annotation reports lower expression in liver, brain and kidney.
PRAME	Low normal expression review: UniProt records detection in kidney, brain and skin samples; current source-native normal RNA remains below the new 30 ceiling.
MAGEA11	Normal RNA review: Curated tissue annotation includes adrenal tissue alongside reproductive organs.

Gene(s)	Priority / reported conflict
CT47A1, CT47A2, CT47A3, CT47A4, CT47A5, CT47A6, CT47A7, CT47A8, CT47A9, CT47A10, CT47A11, CT47A12	Shared-locus review: One shared UniProt entry describes very low brain expression for this family.
ACTRT1	Normal compartment review: Curated tissue annotation includes normal epidermal layers, sweat glands and follicles.
CCDC158	Normal RNA review: Curated tissue annotation includes kidney as well as testis.
LGALS13	Normal compartment review: Curated annotation includes adult urinary bladder and spleen, in addition to placental and fetal tissues.
PASD1	Context review: An older study reported histologically normal tissues from patients with lung and small-intestinal cancers.
RNF148	Low normal expression review: Curated annotation reports slight pancreatic expression.
SLCO6A1	Low normal expression review: Curated annotation reports weak adult brain and spleen expression, separately from fetal brain.
SSX2, SSX2B	Low normal expression review: Curated tissue annotation reports low thyroid expression; SSX2 and SSX2B share the UniProt entry.
SSX1	Low normal expression review: Curated tissue annotation reports low thyroid expression.

Full citations and evidence required for each review are in retained-literature-conflicts.csv and in the relevant gene entries. No change to the 399-gene frozen set or forbidden sequences is implied by this reporting layer.

Priority reconsideration queue

Priority reflects prior biological/clinical interest and a specific resolvable question, not a numerical claim of safety. A positive result on one follow-up does not waive the remaining gates.

Gene / result	Question and evidence needed
ACRBP Unsafe / High RNA	Does the broad immune and platelet RNA represent endogenous ACRBP expression? Resolve normal-cell RNA identity and reliable local protein evidence before changing the general exclusion.
BRDT Neither / Cellular	Does the Monaco-only borderline signal reflect genuine immune expression? Reconcile Monaco CD8/basophil RNA with the much lower DICE values and obtain relevant protein evidence.
CTAG2 Neither / Variable	When and why do some normal heart specimens contain CTAG2 RNA? Resolve donor variability and obtain paired RNA/protein information from the implicated cardiac context.
CTAGE1 Neither / Antibody	Can the uncertain primary-antibody normal staining be resolved? Use independently validated protein evidence to adjudicate primary staining conflicts.
DAZL Neither / Cellular	Is the naive-B-cell RNA translated in normal B cells? Review gene-specific mapping and reliable protein evidence in naive B cells.
FOXR2 Neither / Antibody	Which primary antibody staining is specific to FOXR2? Resolve discordance between HPA034487 and HPA057358 using independently validated protein evidence.
GAGE12F Unsafe / High RNA	Is the immune signal correctly assigned within the GAGE family? Review uniquely assigning reads and exact gene/protein identity before reconsidering local expression.
HORMAD1 Neither / Cellular	Why is RNA repeatedly detected in monocytes and naive B cells despite reproductive-positive curated IHC? Review gene-specific read mapping and obtain reliable protein evidence in the implicated immune populations.
MAGEA3 Unsafe / High RNA	Is the colonic undifferentiated-cell RNA correctly attributed and endogenous? Resolve the pinned high normal-cell signal and exact locus/protein identity before reconsideration.
PAGE2B Unsafe / High RNA	Are borderline DICE B-cell RNA and other cell-context signals genuine? Review exact loci and source-specific normal-cell signals; reliable protein evidence must address implicated cells.
ROPN1 Unsafe / High RNA	Is the salivary serous-cell RNA above 30 nTPM a genuine local signal? Review the underlying cluster and gene-specific reads with reliable local protein evidence before reconsideration.
TDRD1 Neither / Cellular	Are the few activated-CD4 values and Monaco plasmacytoid-DC summary reproducible? Resolve the borderline immune RNA with source-specific read review and reliable local protein evidence.
TEX101 Unsafe / High RNA	What explains high basophil RNA in HPA and Monaco? Resolve basophil RNA identity and local protein evidence before reconsideration.
TRIP13 Unsafe / High RNA	Does its broader normal-cell expression permit a reproductive-restricted classification? Resolve the documented non-permitted cell expression before any reproductive-restricted designation.
ZNF730 Neither / Cellular	Does the full normal-cell distribution support reproductive restriction? Review diffuse RNA and missing reliable protein evidence rather than selecting the largest reproductive value.

For CTAG2, pinned heart RNA donors are 13.5, 0, 0 and 7.1 nTPM; negative heart IHC comes from different specimens. Both nonzero donors fail the existing local rules. The expanded 24.9 nTPM maximum is from

another normal context and does not replace the heart evidence. FOXR2's normal bulk RNA is low, but uncertain antibody staining still requires adjudication.

Which exclusions sit near an arbitrary cutoff?

These transparent review bands are descriptive: within 10% above the new 30 ceiling, or all failed bulk numeric comparisons within 20% of their limits. They are not new acceptance thresholds. RNA-only does not mean clinically safe, and many genes still have additional holds.

Gene	Result	Boundary flag
ACRV1	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
ACTRT3	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
ADAD2	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
AHRR	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
AKAP3	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
APLF	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
BOD1L2	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
C12orf54	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
C18orf54	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
C2CD6	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
C9orf153	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
CATSPERG	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
CCDC15	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
CDRT15L2	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
CFAP144P1	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
CGB8	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
CMTM1	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue

Gene	Result	Boundary flag
COX6B2	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
EDDM3A	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
EPHA6	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
EPPIN	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
ERVFRD-1	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
ETV2	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
FAM209B	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
FNDC7	Neither / Selectivity	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
GAGE12J	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
GGTLC2	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
HMHB1	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
KRT72	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
KRTAP10-1	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
LY6K	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
NXF2B	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
OR3A1	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
OR6C2	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
PAPOLB	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
PLAC8L1	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue

Gene	Result	Boundary flag
PSG5	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
ROPN1	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
SDK2	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
SLC9C1	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
SPATA4	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
SPMIP5	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review
TKTL1	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
TMEM31	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
TSACC	Unsafe / RNA	Failed bulk numeric comparisons are within 20% of their cutoffs; not an automatic rescue
WDR64	Unsafe / High RNA	All audited maxima are within 10% above 30; other gates still require review

What the clinical literature actually supports

This is a targeted primary-source review, not a systematic review of all 2,540 genes. Outcomes below retain the study/product context. Trials with multiple antigens cannot attribute benefit to every component. Reported CRS, conditioning-related cytopenias and receptor cross-reactivity are distinct from demonstrated on-target injury to normal tissue.

YBX2 | Normal protein conflict

Normal-tissue staining included vascular smooth muscle and adrenal cortical cells. Specimens included non-tumor surgical regions and autopsies. Reconcile antibody specificity and tissue context before accepting reproductive restriction; the report did not test therapeutic toxicity.

dbpC/contrin (YBX2) normal-tissue and tumor staining, 2006

ABCC11 | Normal protein conflict

Human brain immunoblotting and axonal immunofluorescence support neural ABCC11 protein. This is a priority conflict with its current retained classification, requiring normal-protein adjudication before target use; clinical injury was not tested.

ABCC11 axonal localization, Neuroscience 2006

MAGEC2 | Normal protein conflict

The TC-1 polyclonal reagent stained normal cerebellar Purkinje cells. This priority conflict requires antibody/paralog specificity review; neither the current retained label nor historical staining alone establishes clinical safety or injury.

HCA587/MAGEC2 normal and cancer protein staining, 2003

MAGEA4 | Approved product

Selected synovial sarcoma patients aged 12+: 60/137 responses (43.8%), median response duration 5.3 months. CRS 72% (2% grade >=3), ICANS 4%, grade >=3 infections 12%. Product-specific evidence; not blanket MAGEA4 safety.

FDA TECELRA label, revised June 2026

PRAME | Clinical outcomes

Confirmed responses: 11/38 (28.9%); unconfirmed-plus-confirmed: 21/40 (52.5%). Severe CRS: 2/41. No severe neurotoxicity or treatment-related deaths reported. This does not establish safety of other PRAME-directed products or rule out rare adrenal injury.

IMA203 phase 1, Nature Medicine 2025

CTAG1A / CTAG1B | Clinical outcomes

Objective responses in 11/18 synovial sarcomas and 11/20 melanomas. HLA- and antigen-selected, uncontrolled cohort; shared NY-ESO-1 protein attribution does not distinguish CTAG1A from CTAG1B.

Robbins et al., NY-ESO-1 TCR follow-up, 2015

CTAG1A / CTAG1B / CTAG2 | Clinical outcomes

One durable response among 18 treated patients; cytopenias and CRS were common, without fatal treatment-related serious adverse events. Recognition includes a shared NY-ESO-1/LAGE-1A epitope; this is not proof of all-isoform CTAG2 safety.

Lete-cel NSCLC pilot studies, 2025

CTAG1A / CTAG1B / CTAG2 | Clinical outcomes

Responses: 2/10 and 4/10 across two cohorts. A potentially related fatal cardiac arrest occurred on day 161 amid substantial competing illness/treatment. It does not establish CTAG2-mediated myocardial injury; the independent donor-expression hold remains.

Lete-cel myxoid/round-cell liposarcoma pilot, 2025

MAGEA3 | Clinical safety signal

Two fatal cardiac events followed affinity-enhanced MAGE-A3 TCR treatment. Cross-recognition of unrelated cardiac titin explains the hazard; it does not demonstrate native MAGEA3 expression in heart.

Linette et al., cardiovascular toxicity and titin cross-reactivity, 2013

MAGEA3 / MAGEA12 | Clinical safety signal

Five of nine patients had tumor regression; three developed neurological toxicity and two died. The receptor cross-recognized MAGE-A12, with brain RNA evidence; pan-MAGE neuronal staining did not uniquely establish the causal paralog.

Morgan et al., anti-MAGE-A3 neurological toxicity, 2013

MAGEA3 | Negative randomized trial

MAGE-A3 vaccination did not improve disease-free survival after NSCLC resection (hazard ratio 1.02; 95% CI 0.89-1.18). Trial nomination is therefore not evidence of benefit.

MAGRIT randomized phase 3 trial, 2016

MAGEA10 | Clinical outcomes

Eleven treated; one partial response after repeat infusion, followed by aplastic anemia and death. CRS occurred in three patients. Investigators found no evidence of off-target binding or alloreactivity; conditioning and cell-therapy risks remain.

ADP-A2M10 NSCLC phase 1, 2022

MAGEA10 | Clinical outcomes

Ten treated; no objective responses, four stable diseases. Two CRS events resolved. Small cohorts cannot establish absence of rare target-mediated toxicity.

ADP-A2M10 head/neck, melanoma and urothelial phase 1, 2022

CLDN6 | Clinical outcomes

Initial report: 7/21 unconfirmed responses (33%); CRS 10/22, including one grade 3 event; one grade 1 ICANS. Oncofetal surface-target experience does not validate unrestricted targeting of all developmental tissues.

BNT211-01 initial phase 1 report, 2023

Biological promise is a separate question

CT83 | Human tumor recognition

KK-LC-1 recognition was found in therapeutic TIL associated with complete cervical-cancer regression. Mixed antigen-specific TIL cannot isolate CT83-specific efficacy or safety.

Landscape of immunogenic antigens in successful cervical-cancer TIL therapy, 2017

CT55 | Human tumor recognition

Human antigen-specific CTLs recognized patient-derived CML stem/progenitor cells. Endogenous immune associations after imatinib cessation support interest, but are not an interventional efficacy or safety trial.

CXorf48 as a CML stem-cell immune target, 2017

FOXR2 | Cancer mechanism

Activation occurred in 8% of individual tumors across 70% of cancer types; experimental work supports ETS-circuit-driven growth. Testis restriction supports reconsideration, but the antibody conflict still needs resolution. No therapeutic outcome is established here.

FOXR2 is an epigenetically regulated pan-cancer oncogene, 2022

ABCB5 | Normal function

Normal limbal stem-cell expression and corneal-regeneration function contradict reproductive restriction. Tumor association does not erase the normal eye compartment.

ABCB5 identifies limbal stem cells and supports corneal maintenance, 2014

IL5 | Normal function

IL-5 is produced by normal activated immune cells. Baseline tissue silence cannot establish reproductive restriction; neutralizing a secreted cytokine is different from destroying every cell that produces it.

Human IL-5-producing T-helper-cell biology, 2012

IL13 | Normal function

Activated nonmalignant T cells produce IL-13. State-dependent cytokine expression defeats a reproductive-restricted label even if resting bulk-tissue RNA is low.

Normal human T-cell IL-13 expression, 1996

PAPPA | Normal function

Activated human coronary vascular cells can produce PAPP-A. Placental association does not imply exclusive reproductive expression.

Regulation of PAPP-A in human coronary vascular cells, 2007

SPAG9 | Tumor expression and immunity

Ovarian-cancer expression and patient antibody responses establish interest, not reproductive exclusivity. Current normal RNA and protein counterevidence supports exclusion.

SPAG9 in epithelial ovarian cancer, 2007

BAGE | Human tumor recognition

Original human CTL recognition supports historical antigen status. Contemporary locus identity and missing matched expression measurements remain unresolved; a related BAGE paralog cannot be substituted.

BAGE antigen recognized by human melanoma-reactive CTLs, 1995

All clinical-target intake records

The 30 curated trial/therapy-linked genes are shown whether retained or excluded. A registry entry is a traceable nomination, not a demonstrated response, approved use, current recruitment status or absence of toxicity.

Gene	Current decision	Evidence recorded
AKAP4	CTA / Pass	Trial registration only
BIRC5	Unsafe / Protein	Trial registration only
CLDN6	Unsafe / High RNA	Clinical outcomes
CT83	CTA / Pass	Human tumor recognition
CTAG1A	CTA / Pass	Clinical outcomes
CTAG1B	CTA / Pass	Clinical outcomes
CTAG2	Neither / Variable	Clinical outcomes
DEPDC1	Unsafe / Protein	Trial registration only
IGF2BP3	Unsafe / Protein	Clinical publication
KIF20A	Unsafe / Protein	Trial registration only
KIF20B	Unsafe / Protein	Trial registration only
LY6K	Unsafe / RNA	Trial registration only
MAGEA1	CTA / Pass	Trial registration only
MAGEA10	CTA / Pass	Clinical outcomes
MAGEA12	Unsafe / Safety	Clinical safety signal
MAGEA3	Unsafe / High RNA	Clinical safety signal | Negative randomized trial
MAGEA4	CTA / Pass	Approved product
MAGEC1	CTA / Pass	Trial registration only
MAGEC2	CTA / Pass	Normal protein conflict
NUF2	Unsafe / RNA	Clinical publication
PRAME	CTA / Pass	Clinical outcomes
PTTG1	Unsafe / Protein	Trial registration only
ROPN1	Unsafe / High RNA	Clinical family label; locus unresolved
ROPN1B	Unsafe / RNA	Clinical family label; locus unresolved

Gene	Current decision	Evidence recorded
SPA17	Unsafe / Protein	Trial registration only
SPAG9	Unsafe / Protein	Tumor expression and immunity
SPANXB1	CTA / Pass	Trial registration only
SSX2	CTA / Pass	Trial registration only
TTK	Unsafe / Protein	Trial registration only
XAGE1B	CTA / Pass	Trial registration only

Coverage, gaps and interpretation

Evidence layer	Genes covered / 2,540
UniProt exact-ID genes	2,505
UniProt function genes	1,873
Cancer RNA genes	2,529
Cancer IHC genes	1,671
Targeted literature review genes	19
Trial-linked genes	30
Boundary-flagged genes	55
Retained genes with literature conflicts	37

UniProt annotation is available through an exact Ensembl cross-reference for 2,505 genes, but only 1,873 have a function annotation. No function annotation is not evidence of no function. Shared UniProt records remain flagged. Cancer mechanisms and normal physiological roles are reproduced as curated assertions, preserving 'may' and 'by similarity' qualifiers.

BAGE and GAGE2B remain in intake but outside the 2,540 mapped-gene denominator. Their historical antigen identities and absent matched reference/HPA rows need explicit locus/sequence resolution. No paralog or zero expression is substituted. SPAG9 is mapped and excluded for clear normal RNA/protein expression.

Earlier Unsafe genes were not all re-audited against every expanded normal source. A blank normal maximum for these genes is an audit-coverage gap, not a negative result. Source cohorts overlap (HPA summaries can contain the same DICE/immune data); repetitions are not independent biological validation.

The current tissue permission policy is a research selection assumption, not a clinical statement that reproductive or disposable-tissue injury is harmless. Pregnancy- and fertility-specific subsets require their separate anatomy definitions. Neither absence of toxicity in a small trial nor negative IHC proves universal safety.

Reproduce and inspect

```
python scripts/build_cta_atlas.py
python scripts/render_cta_atlas.py
```

```
from oncoref import protein_annotations, reference_data
protein_annotations.gene_annotations(['ENSG00000147381'])
reference_data.provenance('uniprot_reviewed_human')
```

Shared sources are checksum pinned: HPA normal v23; HPA cancer v25.1-1; UniProt 2026_03. The report adds evidence and navigation without changing policy 2026-10-24.1. Human data and thresholds are not automatically transferred across species.

Source provenance and checksums | Merged policy review PR #619 | Pinned protein assets