CURRENT SELECTION

Human and dog CTA evidence

701 human CTA proteins

747 loci / 18,062 Unsafe / 453 Other

647 unassigned; dog selection remains unassessed

Sources, expression profiles, single-cutoff filtering and measured tissue evidence.

Safety, cancer and Reproductive evidence

Assessment	Question	Current rule
Safety	Concerning normal expression?	Absolute RNA / IHC and clinical rules
Cancer expression	Expressed in a measured cancer?	One sample >0 TPM/pTPM or reviewed tumor protein
Reproductive evidence	Expression in a qualifying branch?	Bulk/cell RNA ≥5, reliable reproductive protein, or embryonic RNA
Coverage	Are required panels measured?	All GTEx core contexts and existing HPA panels

Only safety establishes Unsafe. Missing core data remain unassigned. RNA is not a direct protein measurement.

Diffuse expression is an identity question

Term	Meaning
N	HPA v23 normal-tissue nTPM
R	Highest Reproductive nTPM in HPA v23 (adult/placental)
N / (N + R)	Average across 29 organs / 38 contexts; thymus excluded
Active boundary	Average >10%, with a supported positive R and complete comparison

MTCP1 is Other:Diffuse at 24.53%. Thymus is excluded. Embryonic concentration remains unassessed.

A fixed GTEx core for every protein

Requirement	Interpretation
GTEx v11: 52 bulk contexts	Same contexts for every protein; measured zero counts
All member loci measured	Missing identities are not replaced by paralogs
Missing core coverage	Blocks CTA; unassigned unless independent Unsafe evidence
Optional DICE / cornea	Missing coverage allowed; observed safety evidence counts

GTEx does not cover every organ, fetal stage or rare cell. Existing HPA cell / immune coverage requirements also apply.

ZNF730: panel composition matters

Calculation	HPA v23	GTEx v11
Reproductive reference (testis)	4.9 nTPM	4.91414 TPM
Full source panel	9.53%: 29 anatomy units	1.65%: 23 anatomy units
Same 20 anatomy units	6.36%	1.71%

Thymus is Permissive: excluded from both sides of the score

Thymus exclusion changes HPA 10.34% → 9.53%. Independent safety evidence keeps ZNF730 Unsafe.

Published candidate lists

Paper	Proteins	CTA	Unsafe	Other	Unassigned
da Silva et al. (2017)	1,017	475	406	88	48
Wang et al. (2016)	988	322	641	14	11
Chang et al. (2019)	985	332	639	3	11
Gong et al. (2021)	729	399	306	14	10
Bruggeman et al. (2018)	692	24	663	0	5
Jamin et al. (2021)	469	39	427	1	2
Loriot et al. (2025)	202	99	101	0	2
Carter et al. (2023)	103	65	37	0	1
Hirbo et al. (2015)	78	13	64	0	1
Seager et al. (2024)	15	12	2	0	1
Sasaroli et al. (2011)	13	0	13	0	0
Garg et al. (2007)	5	3	2	0	0

Union: 2,514 proteins / 2,570 loci. 565 selected proteins have an annotation; 136 do not.

Broader published nominations

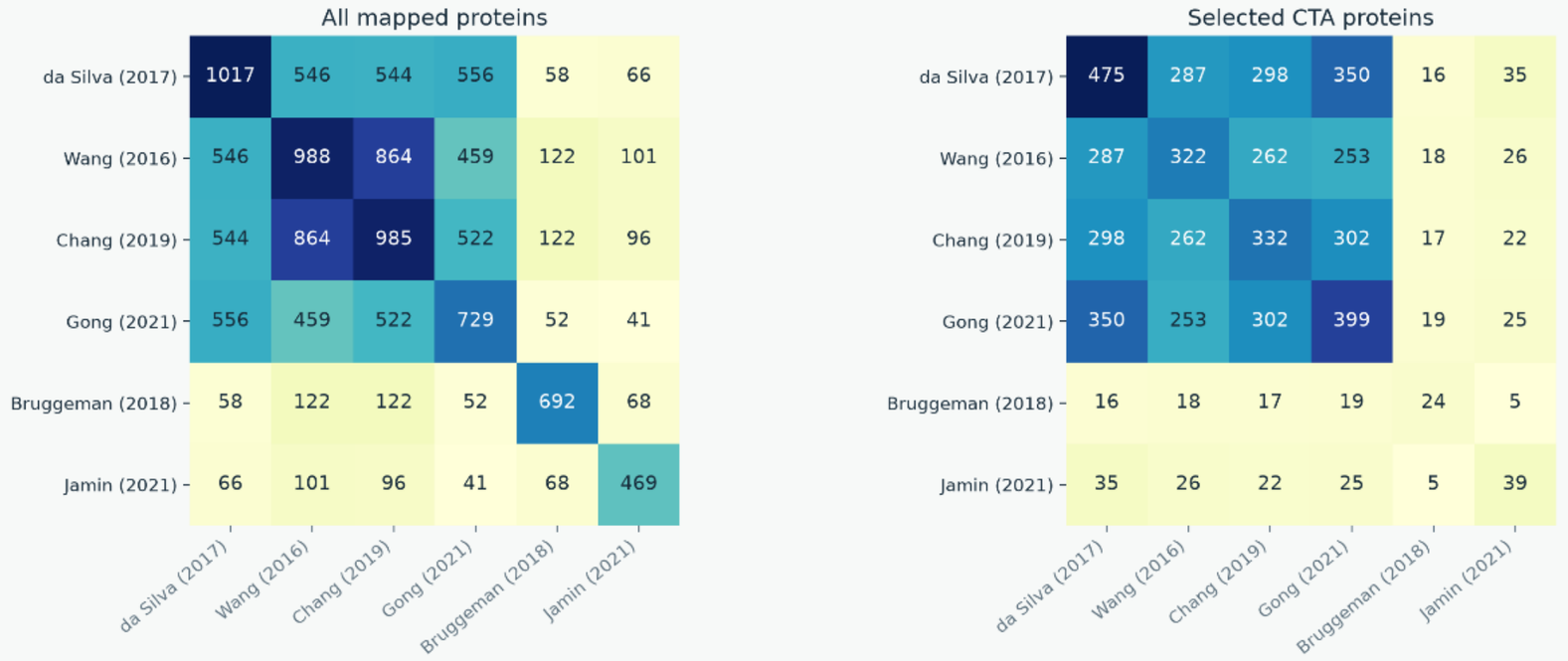
Paper	Published scope	Identity accounting
Sasaroli et al. (2011)	13 detailed tumor-vascular candidates	13 matched genes
Hirbo et al. (2015)	86 placenta-enriched genes, including 30 fast-evolving	82 matched, 4 unresolved
Compact source view	Bai, Boël and Bradley covered by larger sets	All memberships retained
Garg et al. (2007)	Still uniquely contributes SPAG9	Retained in main view

Vascular and placental nominations retain their scope. Paper membership never bypasses the quantitative funnel.

Overlap between published lists

Overlap between published lists

The six largest mapped paper sets; full pairwise tables are downloadable



Diagonal cells give each paper's set size. Off-diagonal cells count shared proteins, not independent validation studies. Citations and original source-table IDs remain linked in the source inventory.

Reproductive evidence: measured branches

Qualifying route	Entrants	Final CTA
Adult/placental evidence only	4,686	470
Embryonic-only evidence	459	92
Both measured routes	12,546	139

RNA and reliable reproductive IHC establish association

Entrants count positive expression before the other admission gates. Reproductive presence and profile concentration are separate questions.

Normal and cancer measurement sources

Evidence	Source	Quantity
Normal / reproductive bulk	HPA v23 consensus / brain + GTEx v11	nTPM / TPM
Normal tissue cells	HPA v23 clusters, at least 20 reads	nTPM
Immune cells	HPA v23 / Monaco / original DICE	Native nTPM / TPM
Adult cornea	Collin et al., GSE155683	CP10K
Normal protein	HPA v23 + curated external IHC	Staining / reagent confidence
Cancer	132 compatible OncoRef cohort views + HPA	TPM / protein-coding TPM
Developmental	Tyser gastrulation + Petropoulos preimplantation	Stage / lineage mean TPM

DICE and corneal coverage are optional. Measured counterevidence still contributes.

RNA cutoffs

Ceiling	Missing / unusable	Approved –	Supported –	Enhanced –
Vital	4	8	16	32
Protected	8	16	32	64
Manageable	16	32	64	128

One boundary: above-cutoff Vital / Protected is Unsafe

Manageable excess blocks CTA. Bowel epithelium and identified fibroblasts use Manageable. Equality passes.

Clinical evidence adjusts RNA ceilings

With clinical credit	Missing / unusable	Approved –	Supported –	Enhanced –
Vital	8	16	32	32
Protected	16	32	64	64
Manageable	32	64	128	128

IHC grades stay unchanged. Trials do not stack.

Protein and clinical-injury exclusions remain. This is protein-profile credit with tested epitope limitations, not clinical clearance.

Serious events and antigen specificity

Targeted CTA epitope	Important event	Specificity attribution
MAGE-A3 / a3a	Two fatal cardiac injuries	Titin cross-recognition implicated
MAGE-A3/A9 / NCI receptor	Three neurological cases; two deaths	MAGE-A12 brain recognition implicated
NY-ESO-1 / LAGE-1A, c259	Late cardiac death; two GBS cases	Peptide-specific mechanism not established
NY-ESO-1 / TBI-1301	Grade 3 lung injury	Unresolved; no credit for this product
MAGE-A4 / afami-cel	Aplasia and stroke deaths in phase 1	No demonstrated antigen-specific mechanism
MAGE-A10 / ADP-A2M10	Grade 4 CRS; fatal aplasia after repeat treatment	Conditioning favored for marrow injury

Clinical trial and SAE review. Seriousness differs from severity; this is a selected summary, not a pooled event rate.

Other records one unmet identity gate

Reason	Meaning	Proteins
Nonreproductive	No qualifying reproductive / placental / embryonic evidence	448
Reproductive	Reproductive presence qualifies; cancer presence does not	0
Diffuse	Presence requirements pass; reproductive concentration fails	5

Normal RNA level, tumor support and Disposable expression are separate attributes.

Evidence attributes stay independent

Question	Fields / interpretation
How high in cancer?	Native TPM / HPA pTPM maxima; two identified tumors >=10 TPM is a support flag
How high in adult normal?	Separate nTPM / TPM / CP10K summaries; raw unsupported observations remain visible
Adult Disposable pattern?	Permitted adult expression with low measured adult expression elsewhere
Developmental expression?	Separate lineage RNA and measured-stage coverage; never changes adult tissue permission

cta_selection.profiles() exposes these fields. Low / Weak / Normal are no longer competing classes.

Reproductive cell evidence

Route	Positive evidence	Additional requirements
Identified lineage	≥5 nTPM with ≥20 reads	Mapped reproductive lineage; all protein loci measured
Indirect site	Generic/immune cell in reproductive tissue	Complete outside cluster panel; every value <5 nTPM; no normal-induction conflict
Examples	CAGE1 208.9; PRDM9 61.8; FOXR2 5.2 nTPM	Spermatids / spermatocytes / spermatogonia
Counterexample	IFNA2 and IFNA14 in breast macrophages	Reviewed normal immune protein → Unsafe

Indirect support identifies the sample site, not the producing cell. Normal and bulk-concentration gates still apply.

Reviewed normal-cell knowledge

Evidence	Consequence
Established normal production	Vital/Protected protein or localized RNA plus orthogonal cell function can establish Unsafe
Unresolved normal findings	Sparse RNA, uncertain species/stage or isoforms remain review holds
Reproductive protein	Supplies presence below the RNA floor; safety and concentration still apply
Search and curation	All 611 baseline Other genes searched; accepted findings remain separate from search leads

Rare normal cells and activation states count. Expression exclusions do not assert clinical injury.

High tumor expression does not establish CTA identity

Protein	Cancer TPM	Adult atlas nTPM	Current reasoning
DBX1	297.5	0.8; thymic T cells	No qualifying reproductive evidence
OR2B2	246.3	0.5; pons	No qualifying reproductive evidence
KRTAP20-2	147.6	1.4; skin	Skin expression; reproductive identity unestablished
OR10A4	138.0	1.9; basal ganglia	Normal nasal RNA: review hold

Disposable describes allowed adult tissues. Developmental expression is a separate measurement.

Other accumulates as identity gates fail

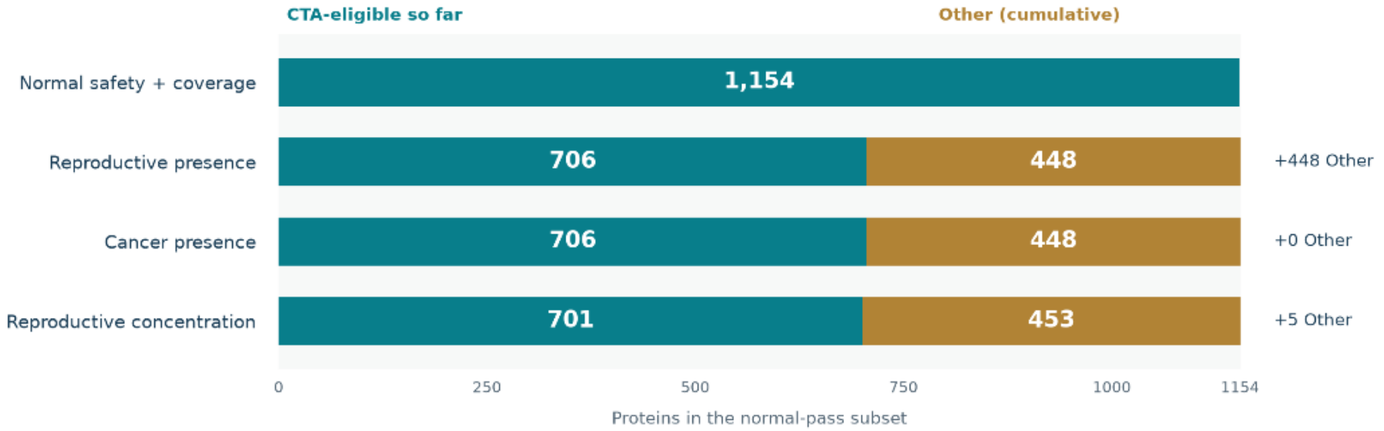
Where proteins become CTA or Other

OncoRef 1.27.0 | 19,863 representative proteins | Normal assessment first

701	18,062	453	647
CTA	Unsafe	Other	Unassessed

Follow the 1,154 proteins that pass normal safety and coverage

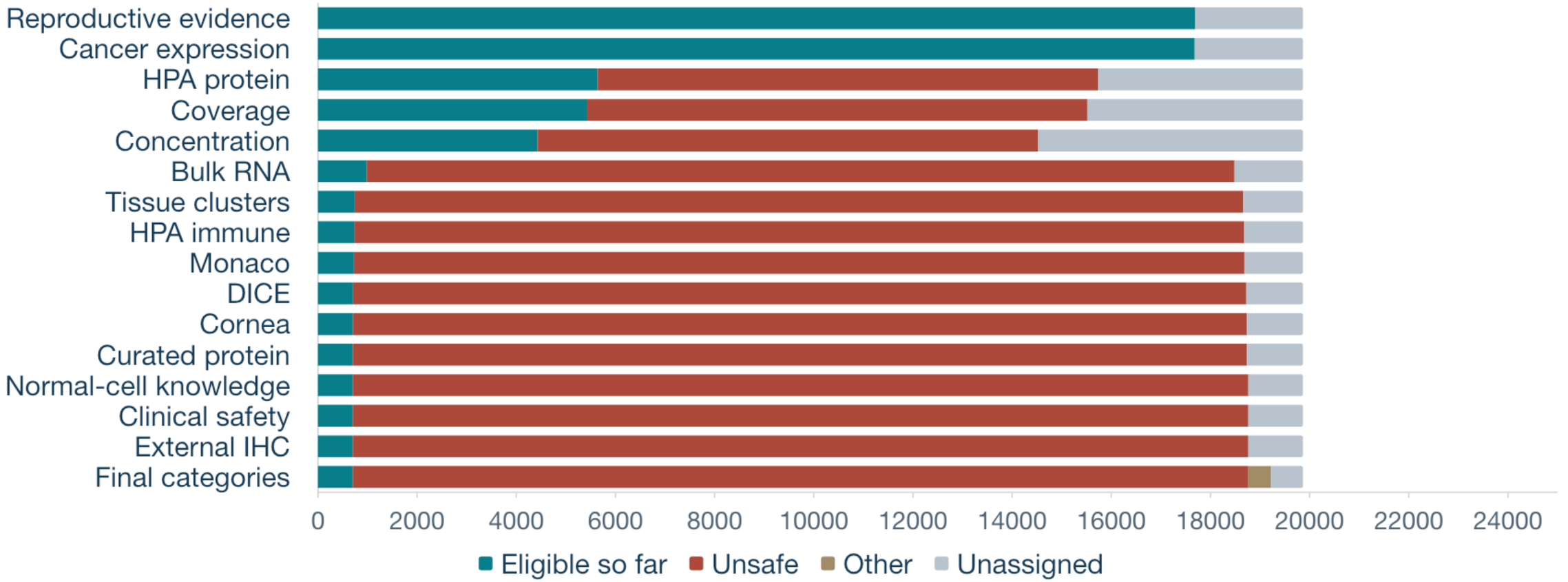
18,062 Unsafe and 647 Unassessed remain outside this candidate track at every stage below.



448 lack qualifying reproductive evidence; 5 additional proteins fail concentration.

Cancer presence moves 0 additional proteins into Other; 706 remain eligible.
Reproductive includes placental and embryonic/fetal contexts. Other requires a complete, passing normal screen.
The figure changes display order only; all final categories exactly match the released classification.

Every filtering layer can contribute



Final: 701 CTA / 18,062 Unsafe / 453 Other / 647 unassigned.

Removals at each filter

Layer	First removals	Eligible	Unsafe
Association	2,172	17,691	0
Cancer expression	9	17,682	0
HPA normal protein	12,044	5,638	10,094
Required RNA coverage	212	5,426	10,094
Reproductive concentration	997	4,429	10,094
Normal bulk	3,445	984	17,500
HPA tissue clusters	238	746	17,914
HPA immune	12	734	17,944
Monaco immune	7	727	17,961
DICE immune	19	708	18,016
Adult cornea	3	705	18,028
Accepted normal-protein evidence	3	702	18,030
Reviewed normal-cell knowledge	0	702	18,061
Clinical safety exclusion	1	701	18,062
External validated normal protein	0	701	18,062
CTA and Other assignments	0	701	18,062

Sequential removals overlap. Final categories use every applicable evidence layer.

IHC matching to measured RNA compartments

Context	Evidence and current ceiling
PRAME colon epithelial cells	20.3 nTPM / 96 reads; Enhanced-negative glandular IHC; Manageable 128
PRAME adrenal bulk	3.6 nTPM; incomplete IHC coverage; Vital 4 → 8 with IMA203 credit
CTAG2 bronchial basal cells	24.9 nTPM / 58 reads; Enhanced-negative respiratory IHC; Vital 32
Unrelated cells in the same tissue	No negative-IHC credit without exact or declared compartment coverage

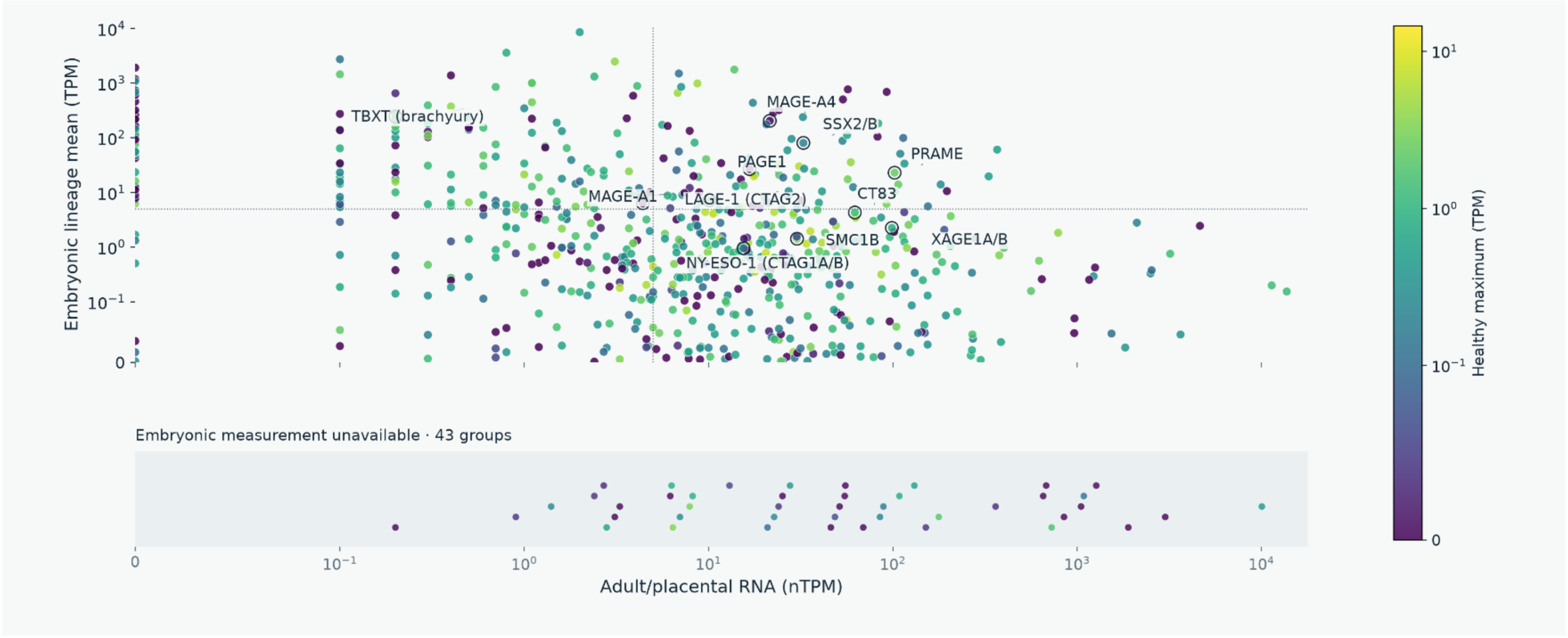
PRAME and CTAG2 pass this policy. Parent-compartment sensitivity and PRAME's Low adrenal protein remain explicit limitations.

Selected CTA: adult/placental versus embryonic RNA



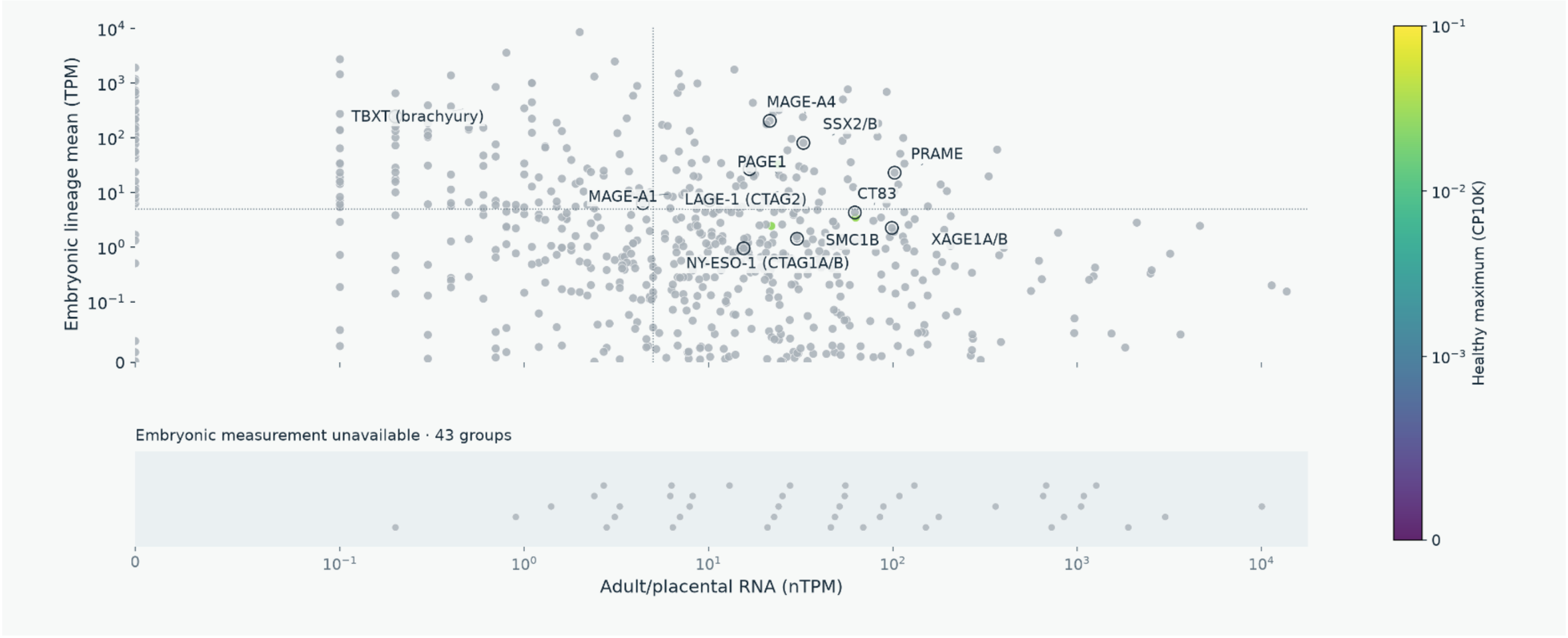
Gray: healthy measurement unavailable. The lower band has no embryonic-expression value.

Selected CTA: healthy RNA in TPM



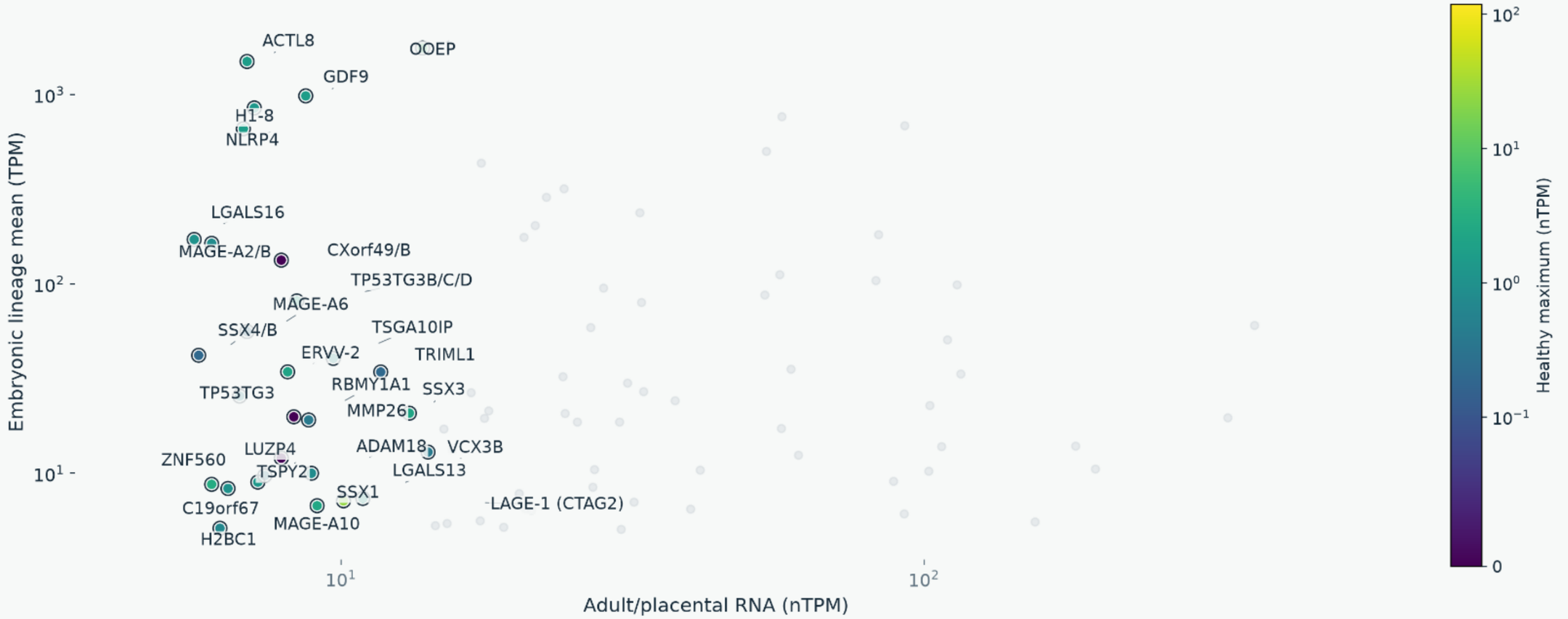
Gray: healthy measurement unavailable. The lower band has no embryonic-expression value.

Selected CTA: normal corneal RNA

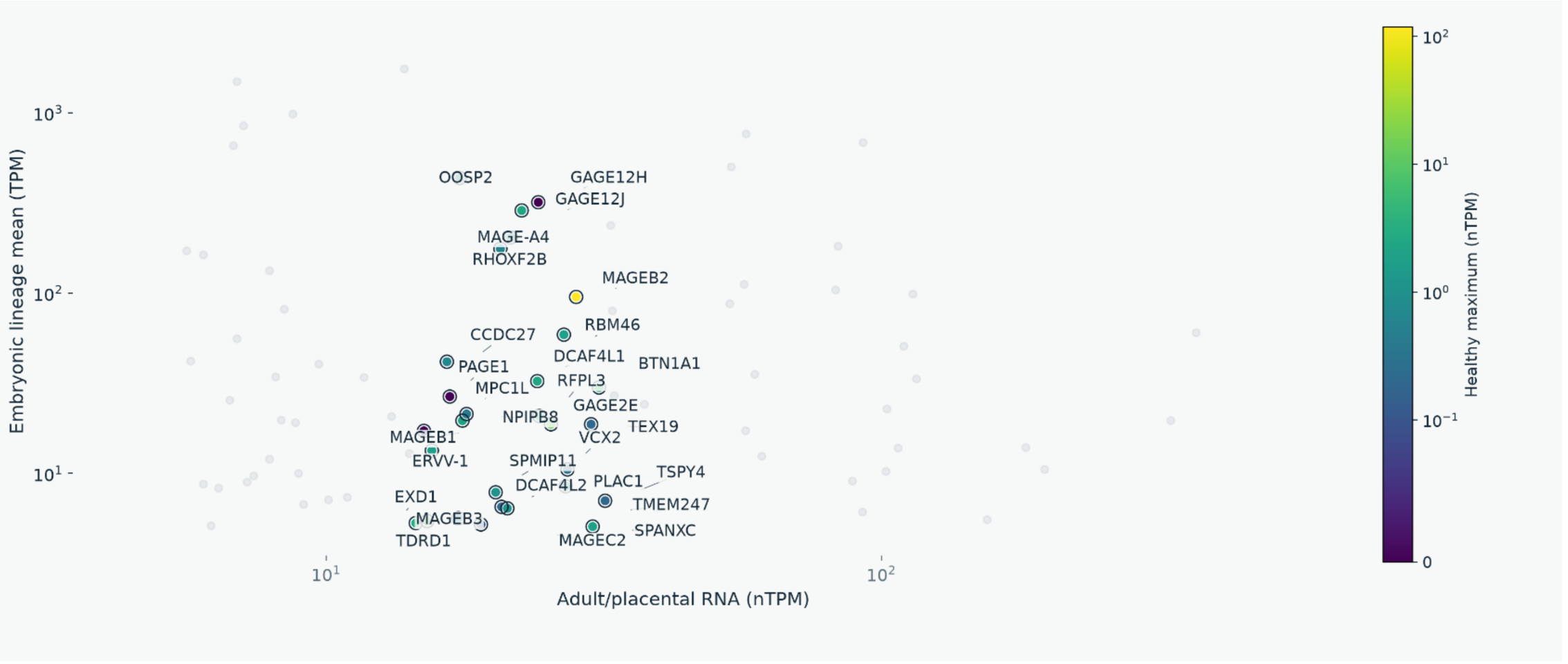


Gray: healthy measurement unavailable. The lower band has no embryonic-expression value.

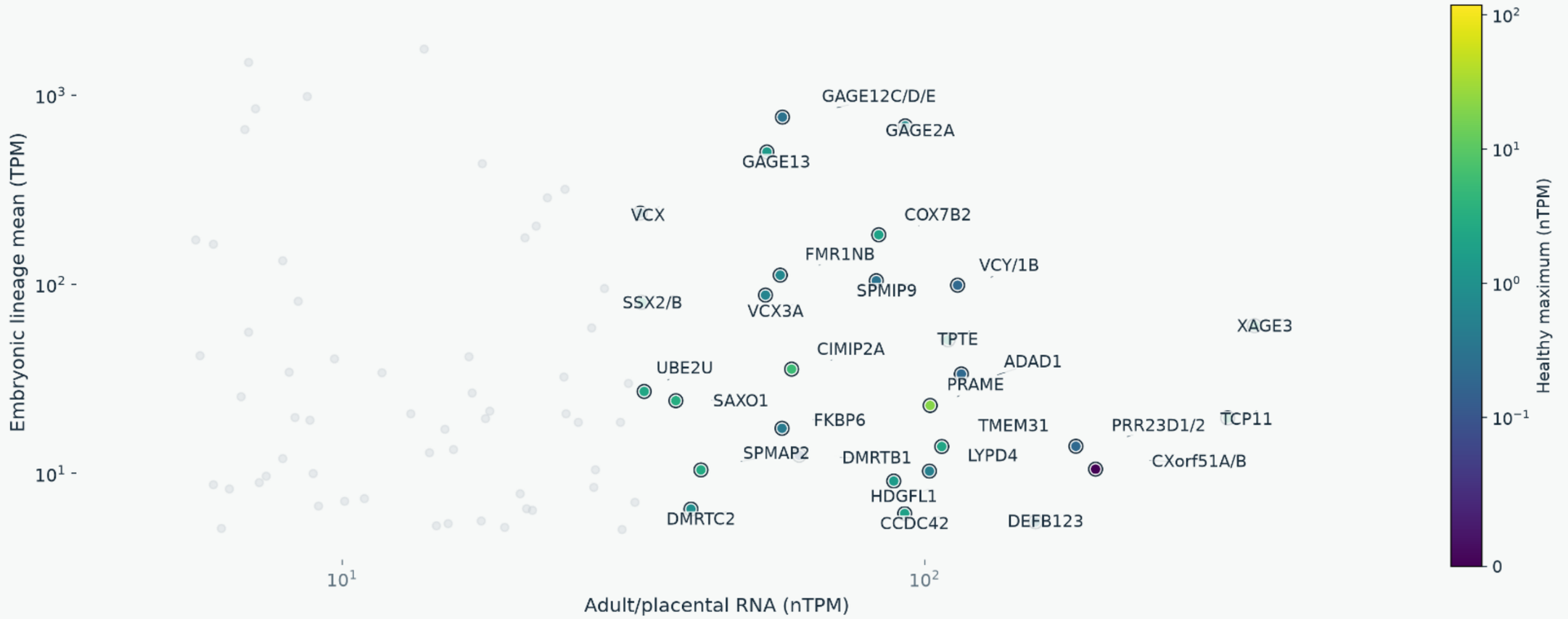
High adult/placental and embryonic RNA: labels 1 of 3



High adult/placental and embryonic RNA: labels 2 of 3



High adult/placental and embryonic RNA: labels 3 of 3



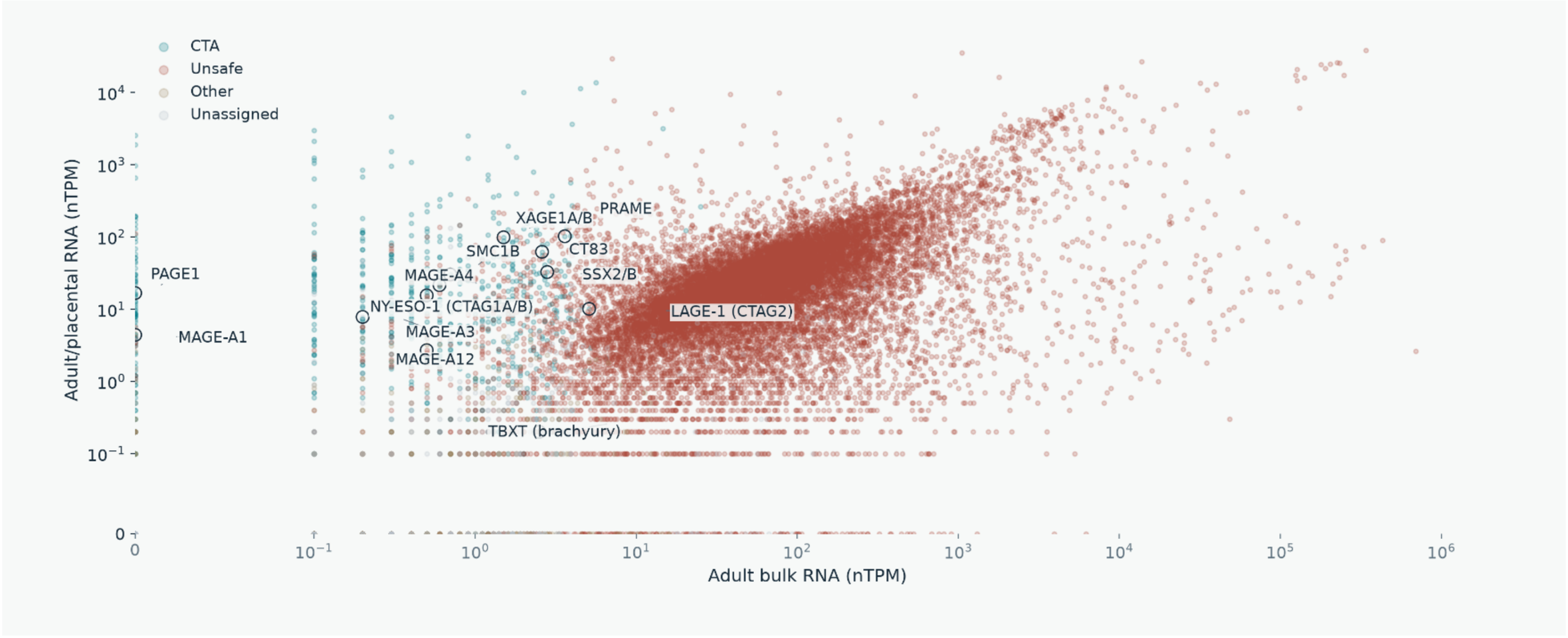
Complementary embryonic measurements

Source	Measured cells / embryos	Developmental scope
Tyser et al. (2021)	1,195 cells / 1 embryo	Gastrulation, Carnegie stage 7
Petropoulos et al. (2016)	1,519 cells / 88 embryos	Preimplantation, days 3–7
Recovered coverage	683 of 1,006 earlier missing groups	Measured TPM, including familiar CTAs

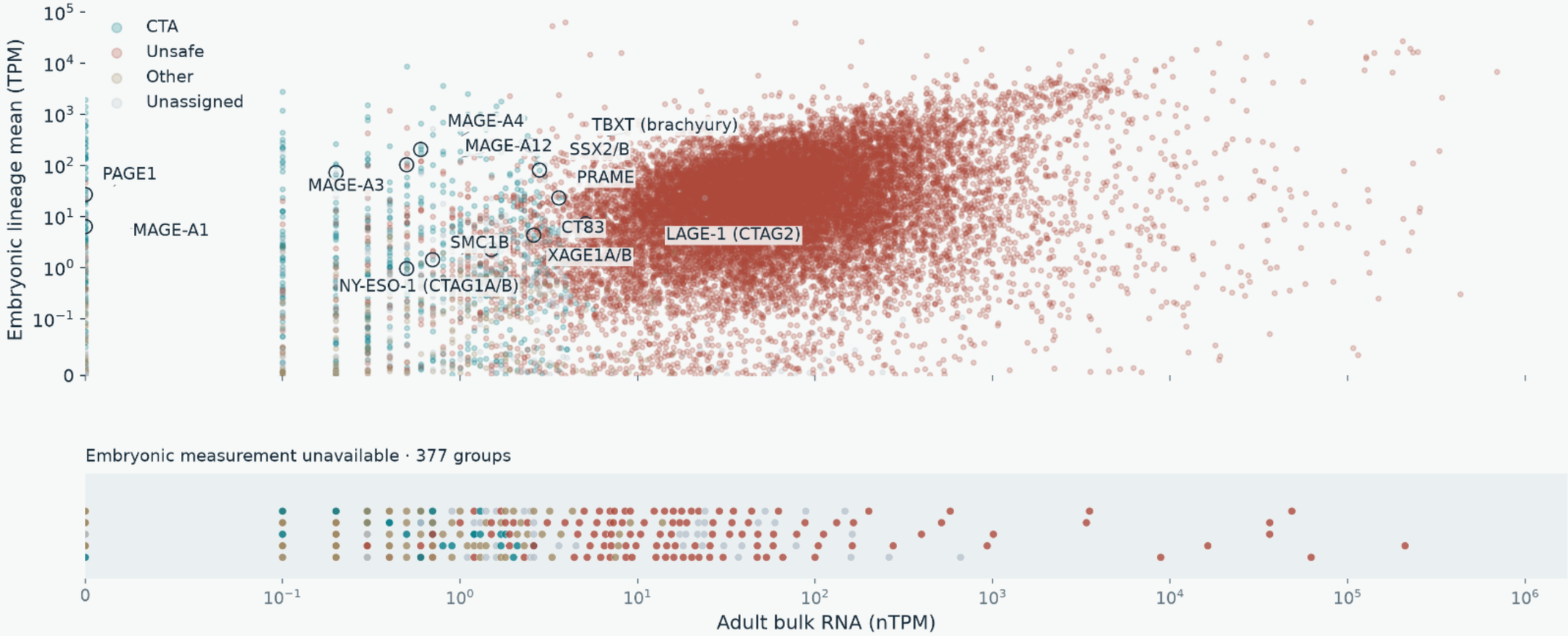
PRAME, MAGE-A4, CTAG1A/B, XAGE1A/B and CT83 now have TPM rows

Each source keeps its own stages. Neither atlas covers all fetal or pediatric development.

Widely studied antigens: adult/placental RNA



Widely studied antigens: embryonic RNA



Assessment status is separate from category

API status	Meaning	Human proteins
screened	Candidate, Unsafe or Other assigned	19,216
incomplete_evidence	Unassigned with missing coverage or unresolved evidence	475
normal_evidence_hold	Required normal coverage passes; a normal-screen hold remains	172
unassessed	No species-specific selection policy applied	0

Other requires a complete, resolved normal screen. Unassigned does not mean Unsafe or low expression.

Which sources have incomplete evidence

Source or unresolved evidence	Proteins
HPA v23 consensus bulk	374
Combined normal bulk: HPA consensus + HPA brain + direct GTEx	366
HPA v23 tissue-cell clusters	335
HPA v23 immune cells	304
Monaco immune cells via HPA v23	304
Required GTEx v11 bulk panel (52 contexts)	413
Combined Tyser + Petropoulos TPM	86
No tumor measurement: OncoRef + HPA	34
Measured tumor, incomplete group profile	3
HPA v23 Uncertain normal-tissue IHC	28

Overlapping gaps within 475 unassigned proteins. DICE and corneal coverage are optional.

Dog evidence and integration gaps

Layer	Available evidence / remaining gap
Nominations	5 + 10 – 1 shared = 14 native nominations
Identity	13 unique mappings; one ambiguous MAGE-family assay
Normal / developmental RNA	Bgee TPM and BarkBase TMM-CPM need reference reconciliation
Tumor RNA	GSE304066 count/FPKM and reference conflicts remain unresolved
Normal protein	Limited study IHC; Pfizer pooled iBAQ is not cell-resolved IHC
Selection	All 14 unassigned / unassessed; no canine quantitative policy

Human thresholds, antibody grades and normal-tissue absence never transfer by orthology.

Curated oncofetal sources

Source	Scope and integration status
Tyser + Petropoulos	Current gastrulation and preimplantation TPM sources
Shaw et al. (2024)	157 cancer-specific targets; six oncofetal annotations. Exon-specific scope retained
TRIM71 liver study (2024)	Liver oncofetal signature; requires identity and measurement ingestion
Cardoso-Moreira et al. (2019)	Developmental organ trajectories with child/adult comparisons; not integrated

Published nominations need independent normal/tumor filtering and postnatal coverage.

Common API with native evidence underneath

```
results = cta_selection.results(species="human")
audit = cta_selection.audit(species="human")
audit.sources    audit.overlaps    audit.funnel
audit.explain("PRAME")
```

Field	Meaning
category	CTA / Unsafe / Other; classification gives the named category
assessment_status	Screened, incomplete evidence, normal hold, or unassessed
classification / subtype	One categorical label; Other subtype always populated

Source-specific native units, tissue/cell context, confidence and coverage remain inspectable.

Every source resolves to a concrete version

```
catalog.ensure("gtex_tissue_rna")              # v11
catalog.ensure("gtex_tissue_rna", version="v10")
catalog.provenance("gtex_tissue_rna", "v11")
```

Shared choice	Source-specific meaning
Default / latest	Newest registered release; saved runs keep explicit pins
Concrete version	GTEx v11; HPA v25.1; a study snapshot or OncoRef build
Provenance	Version, content checksum, native unit, annotation and pipeline
Species	The same selector applies to native dog and mouse assets

This analysis pins GTEx v11 and HPA v23 normal panels. A newer public default does not rewrite it.