CURRENT SELECTION

Human and dog CTA evidence

522 human CTA proteins

558 loci / 18,031 Unsafe / 20 Neither

1,290 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 ≥2 TPM or pTPM
Reproductive evidence	Expression in a qualifying branch?	Adult/placental ≥5 nTPM or supported embryonic ≥5 TPM
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 R ≥5 and a complete comparison

MTCP1 moves to Neither: 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	Neither	Unassigned
da Silva et al. (2017)	1,017	372	401	1	243
Wang et al. (2016)	988	264	640	1	83
Chang et al. (2019)	985	285	639	0	61
Gong et al. (2021)	729	337	306	0	86
Bruggeman et al. (2018)	692	23	663	0	6
Jamin et al. (2021)	469	34	427	0	8
Loriot et al. (2025)	202	81	101	0	20
Carter et al. (2023)	103	57	37	0	9
Hirbo et al. (2015)	78	12	64	0	2
Seager et al. (2024)	15	11	2	0	2
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. 434 selected proteins have an annotation; 88 do not.

Broader published nominations

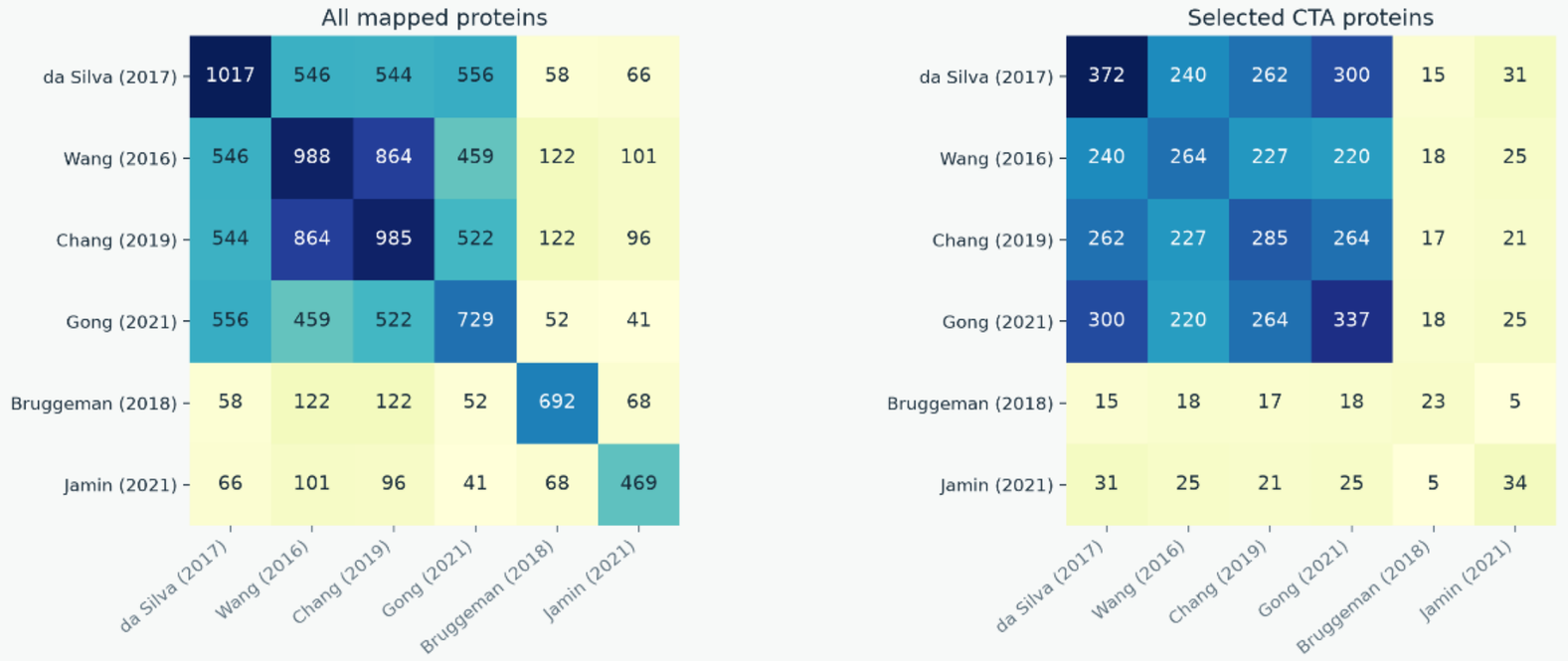
Paper	Published scope	Identity accounting
Sasaroli et al. (2011)	13 detailed tumor-vascular candidates	13 matched genes
Hirbo et al. (2015)	86 placenta-enriched genes, including 30 fast-evolving	82 matched, 4 unresolved
Compact source view	Bai, Boël and Bradley covered by larger sets	All memberships 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	2,322	291
Embryonic-only evidence	2,095	154
Both measured routes	10,910	77

Whole-reference RNA measurements create this set

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

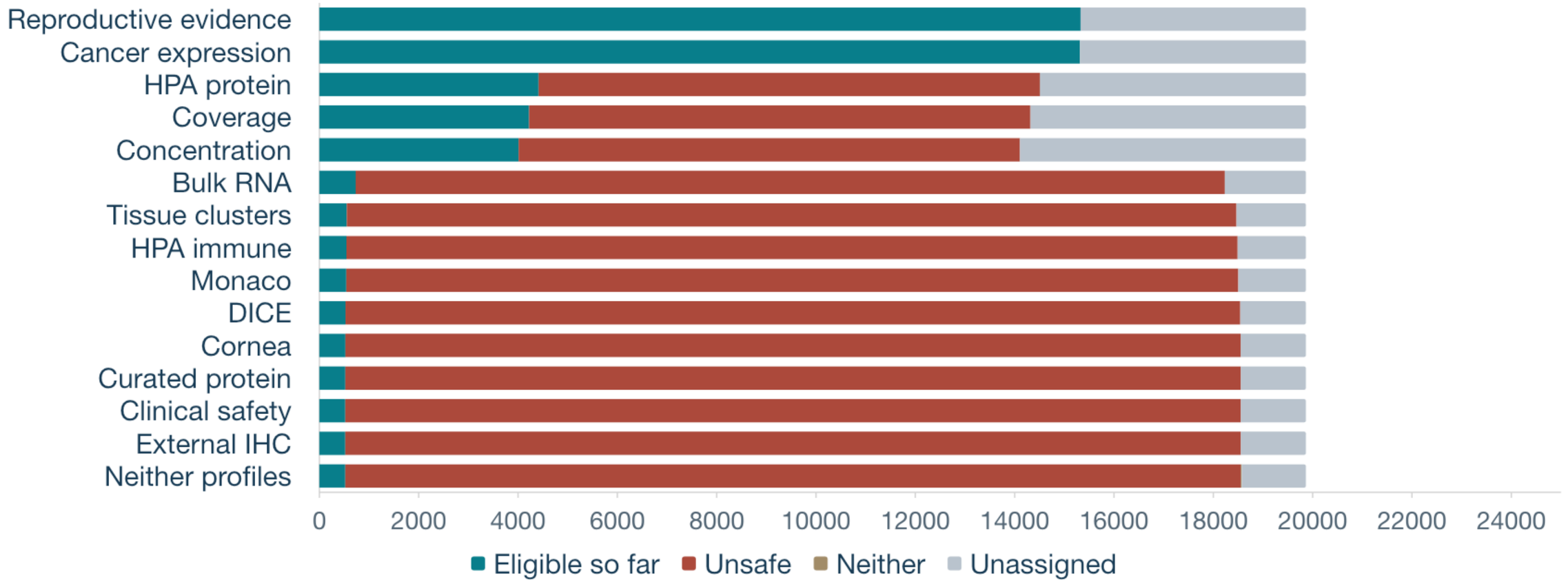
Clinical trial and SAE review. Seriousness differs from severity; this is a selected summary, not a pooled event rate.

Neither describes a measured profile

Profile	Required evidence	Proteins
Low expression	RNA below 2 across measured normal / reproductive / embryonic / tumor panels; no detected protein	9
Diffuse Manageable	No association route; RNA ≥2 in at least two Manageable tissue concepts; no Vital / Protected exclusion	10
Diffuse Reproductive	HPA score >10%; no qualifying route left; normal safety passes	1

All require complete normal RNA coverage and resolved evidence. Other failures remain unassigned.

Every filtering layer can contribute



Final: 522 CTA / 18,031 Unsafe / 20 Neither / 1,290 unassigned.

Removals at each filter

Layer	First removals	Eligible	Unsafe
Association	4,536	15,327	0
Tumor sample ≥2 TPM/pTPM	13	15,314	0
HPA normal protein	10,900	4,414	10,094
Required RNA coverage	191	4,223	10,094
Reproductive concentration	211	4,012	10,094
Normal bulk	3,281	731	17,500
HPA tissue clusters	179	552	17,914
HPA immune	7	545	17,944
Monaco immune	3	542	17,961
DICE immune	15	527	18,016
Adult cornea	3	524	18,028
Accepted normal-protein evidence	1	523	18,030
Clinical safety exclusion	1	522	18,031
External validated normal protein	0	522	18,031
Neither expression profiles	0	522	18,031

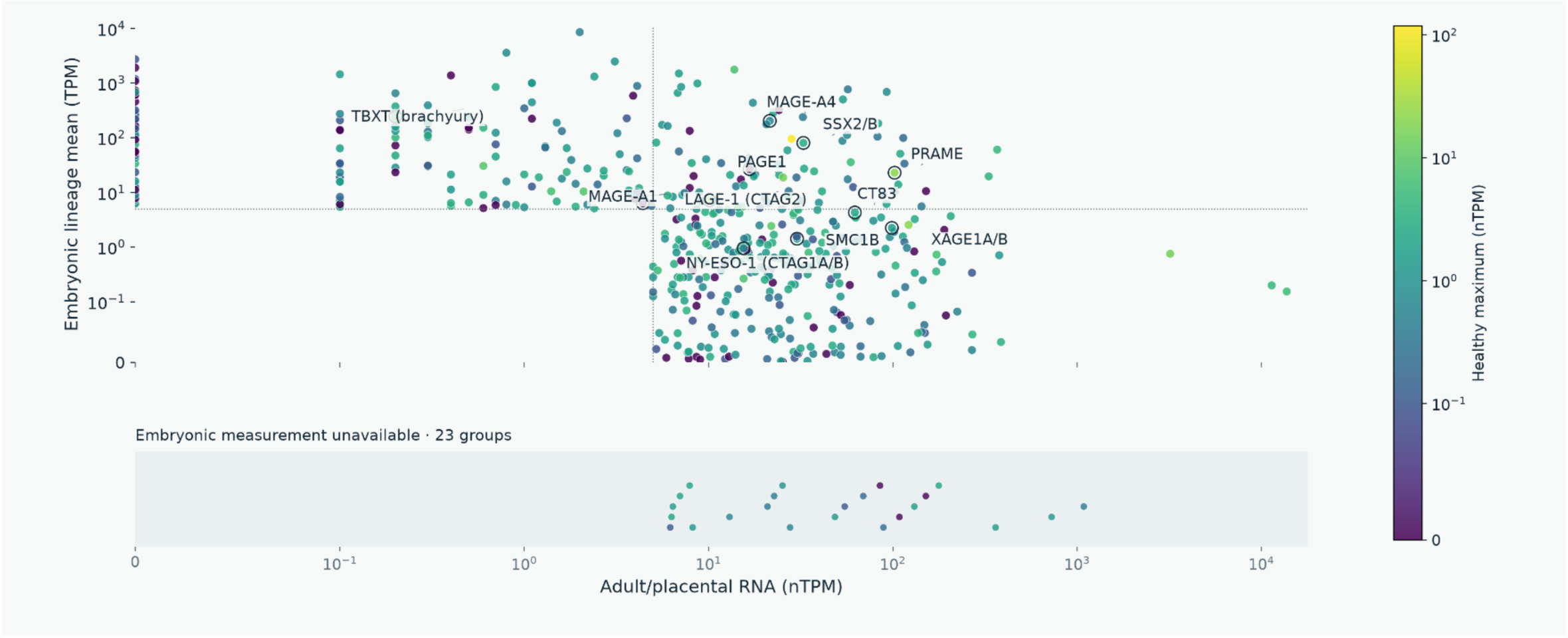
Only MTCP1 changes category; other concentration failures also fail other gates.

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

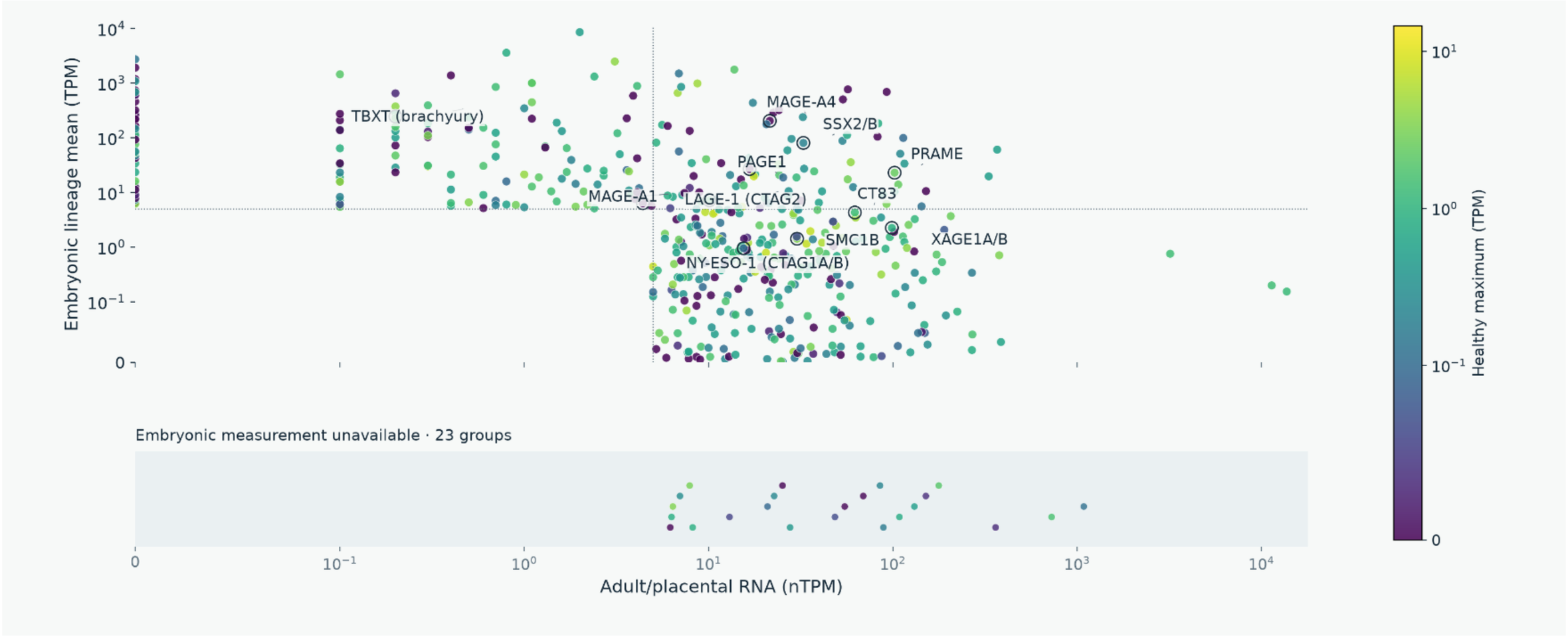
PRAME and CTAG2 pass this policy. Parent-compartment sensitivity and PRAME's Low adrenal protein remain explicit limitations.

Selected CTA: adult/placental versus embryonic RNA



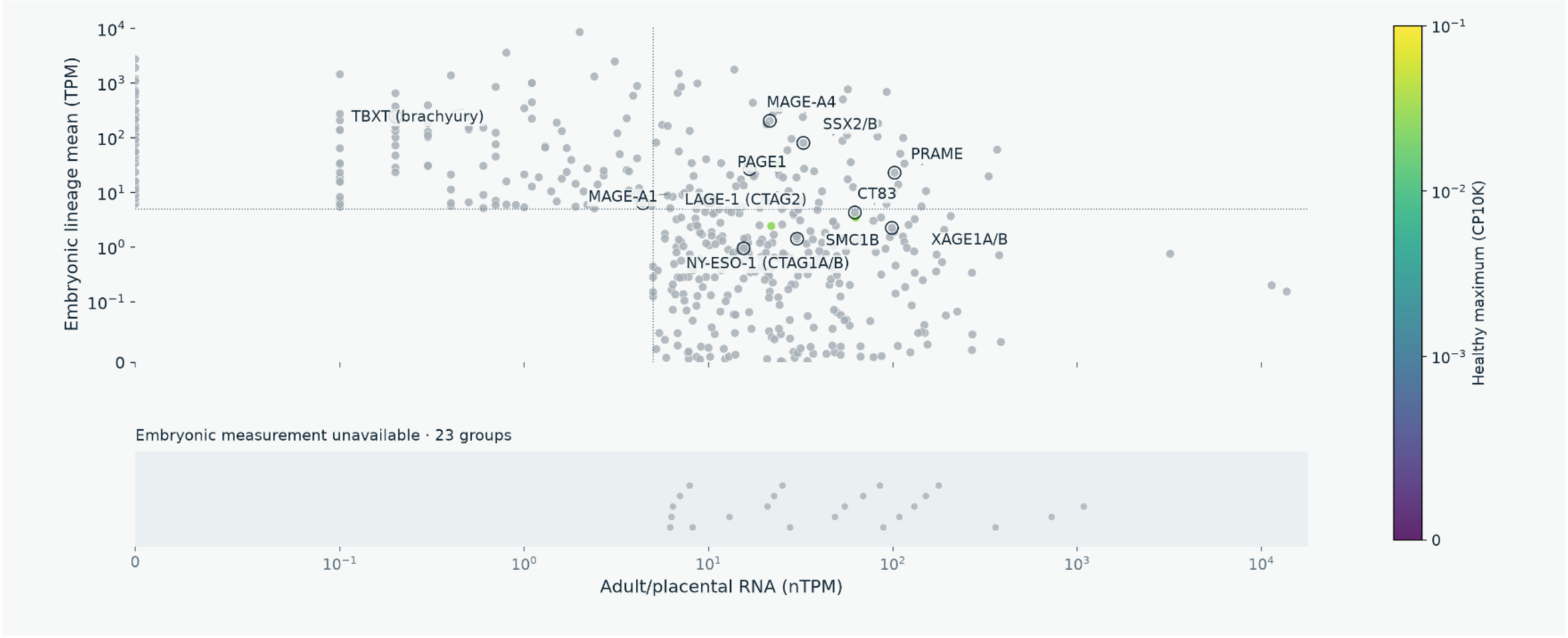
Gray: healthy measurement unavailable. The lower band has no embryonic-expression value.

Selected CTA: healthy RNA in TPM



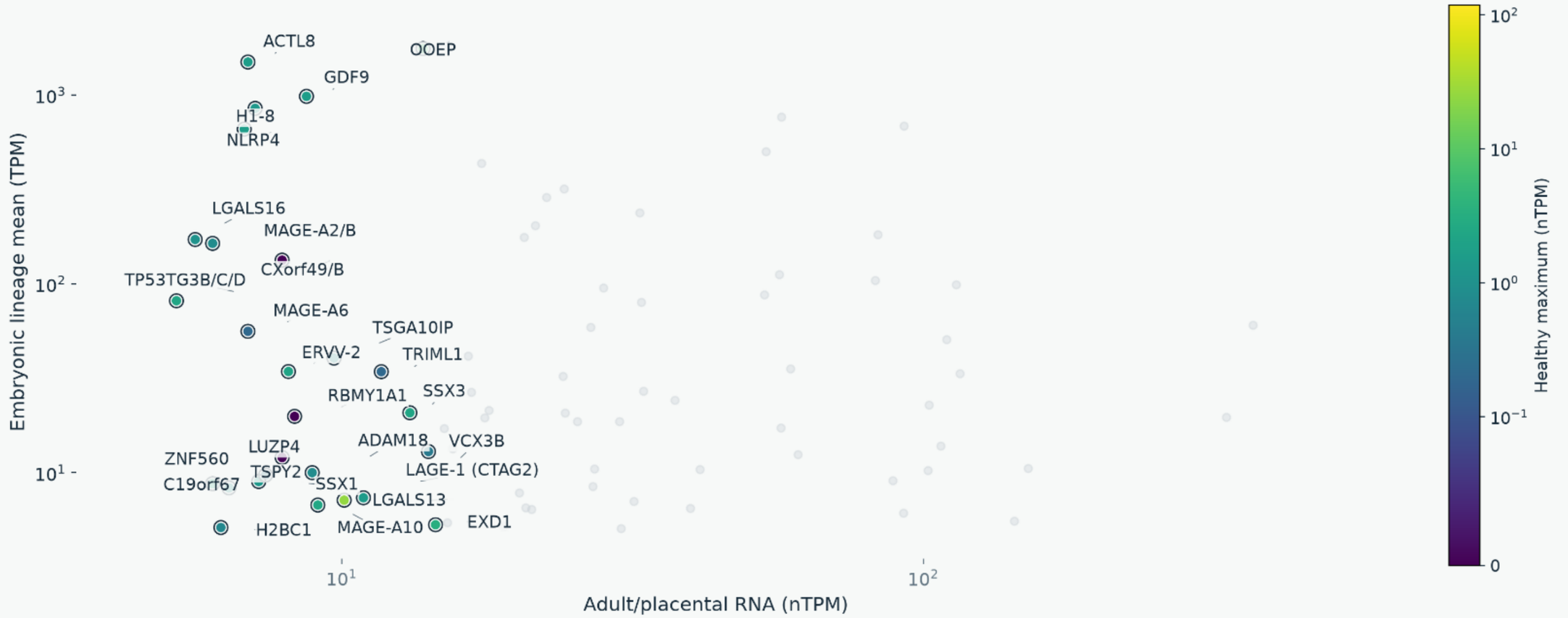
Gray: healthy measurement unavailable. The lower band has no embryonic-expression value.

Selected CTA: normal corneal RNA

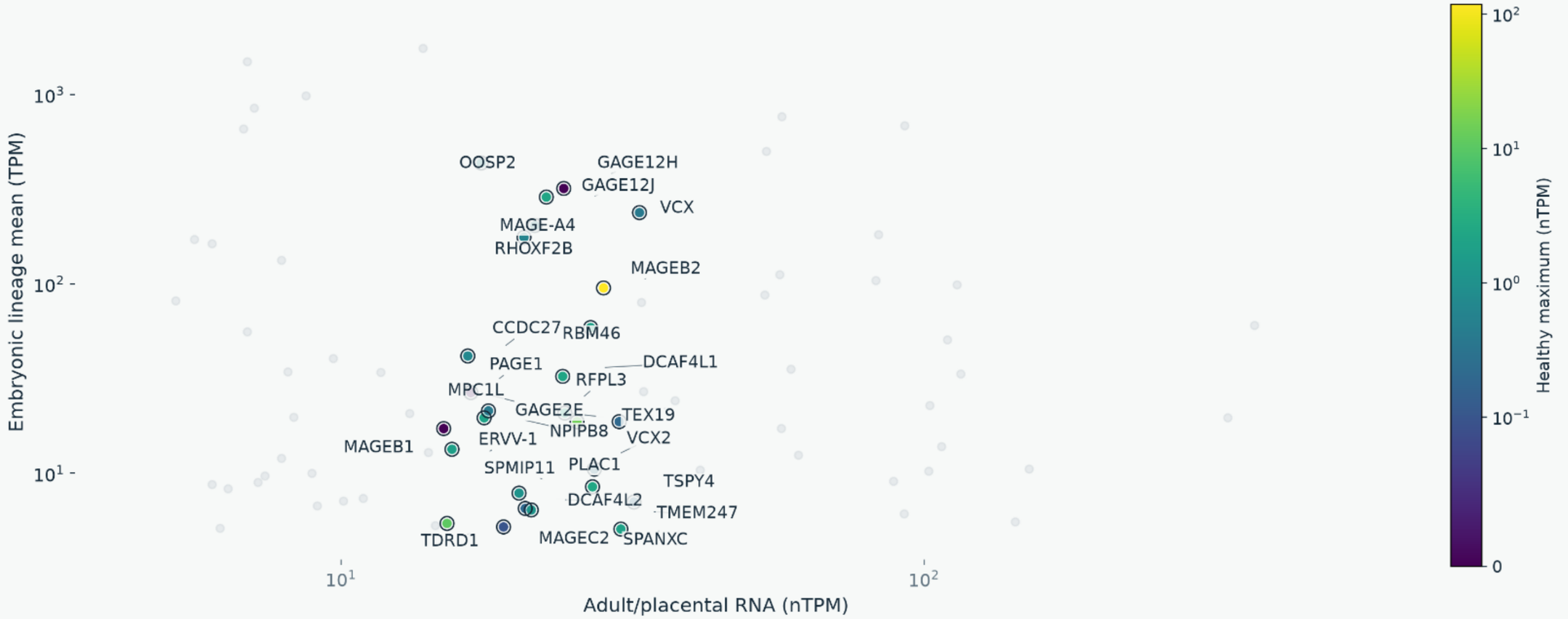


Gray: healthy measurement unavailable. The lower band has no embryonic-expression value.

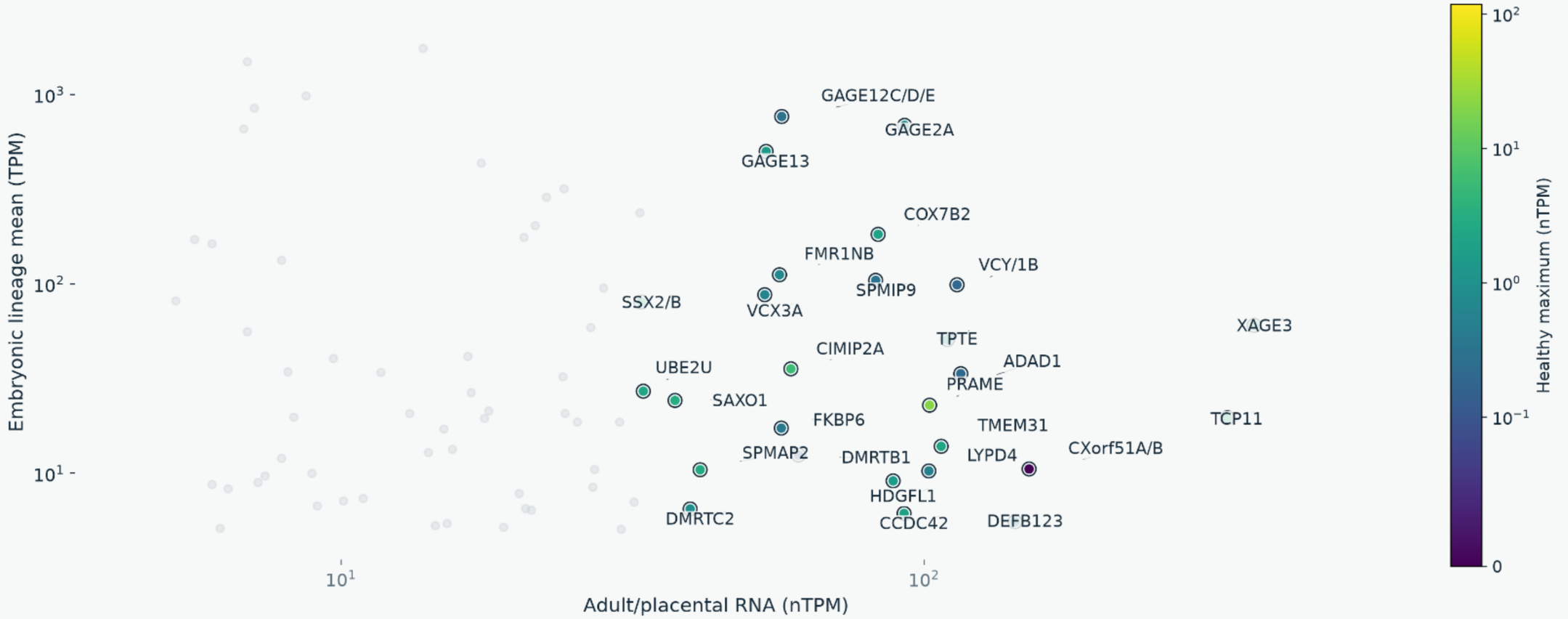
High adult/placental and embryonic RNA: labels 1 of 3



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



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



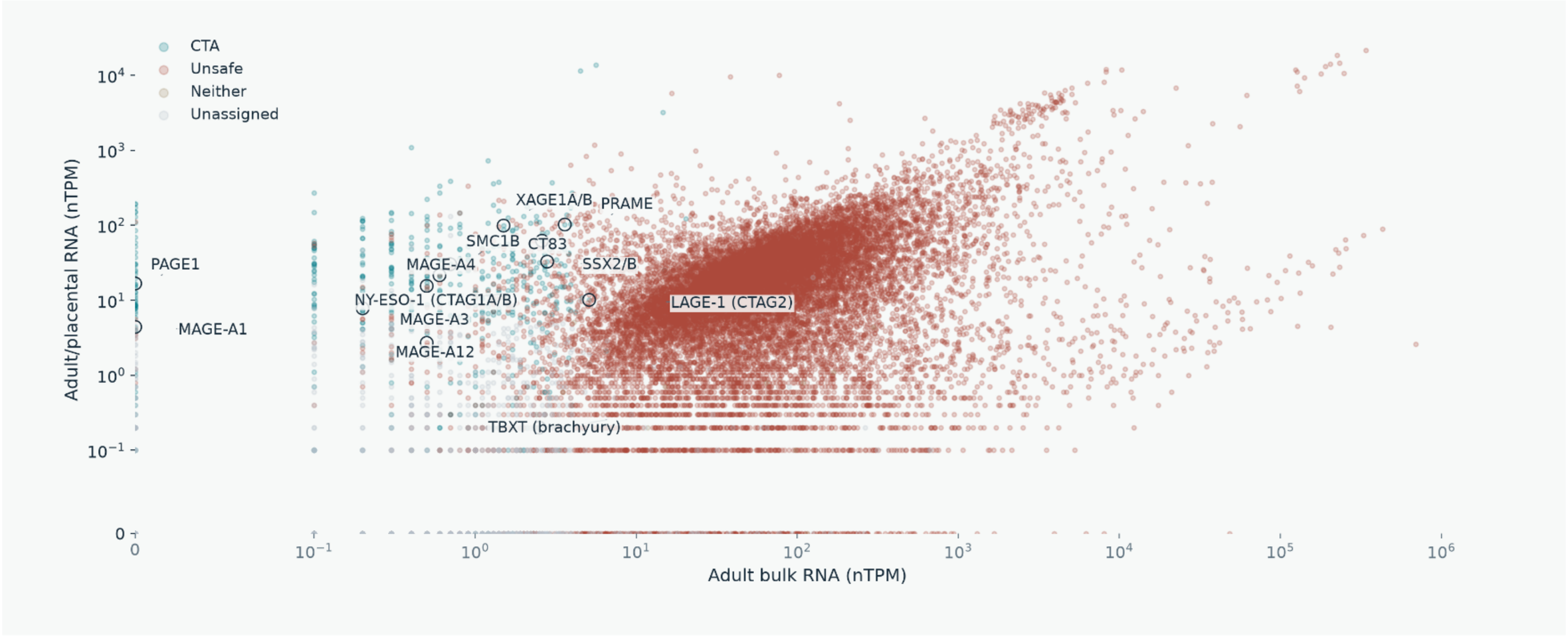
Complementary embryonic measurements

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

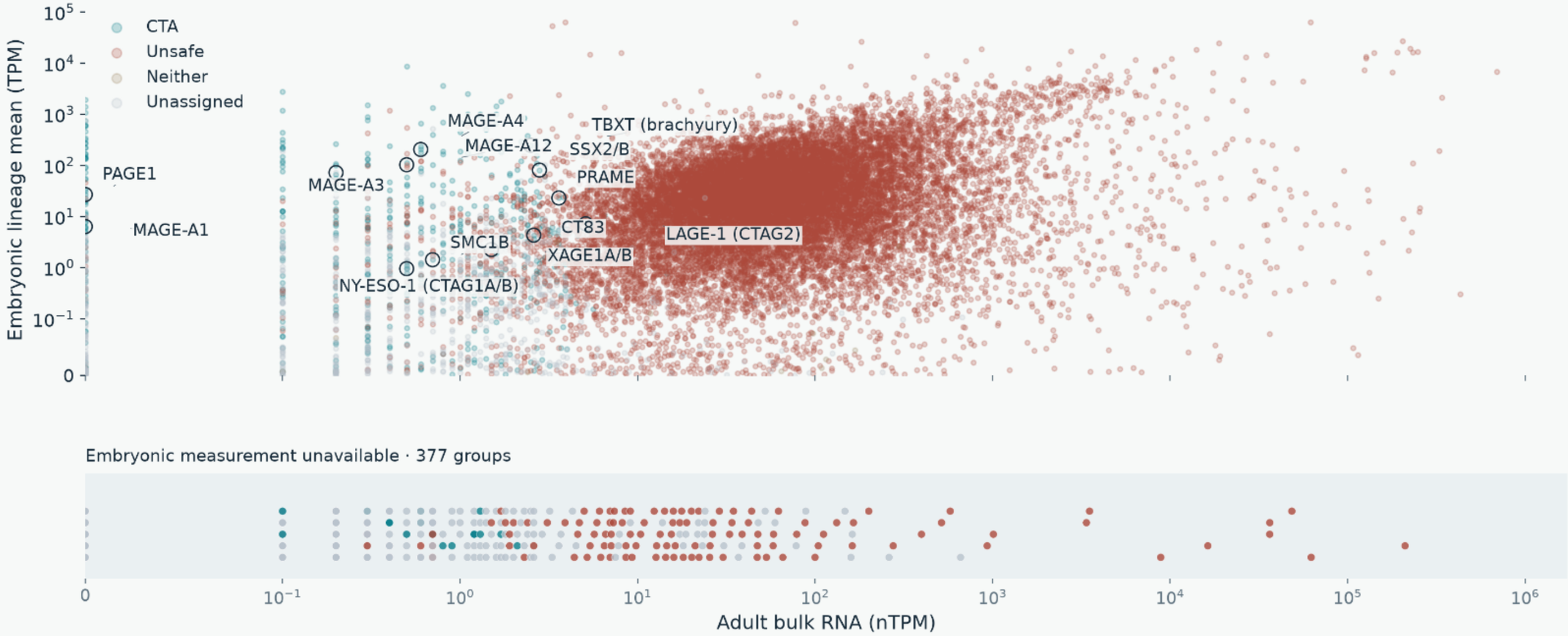
PRAME, MAGE-A4, CTAG1A/B, XAGE1A/B and CT83 now have TPM rows

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	CTA, Unsafe or Neither assigned	18,573
incomplete_evidence	Unassigned with missing coverage or unresolved evidence	694
outside_category_definitions	Tracked coverage checks pass; no definition fits	596
unassessed	No species-specific selection policy applied	0

Neither requires a measured biological profile. Unassigned does not mean Unsafe or low expression.

Which sources have incomplete evidence

Source or unresolved evidence	Proteins
HPA v23 consensus bulk	414
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	297
No tumor measurement: OncoRef + HPA	34
Measured tumor, incomplete group profile	17
HPA v23 Uncertain normal-tissue IHC	28

Overlapping gaps within 694 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 / Neither, or null when unassigned
assessment_status	Screened, incomplete evidence, outside definitions, or unassessed
gene_ids / gene_identities	All member loci, stable IDs, history and curated synonyms

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.