Tumor-Immune Intelligence (TII) Report - GBM

> **RESEARCH USE ONLY (RUO).** Educational/research analysis of public single-cell reference data. **Not for diagnostic use and not a treatment recommendation for any individual.** Archetypes and composites are research constructs positioned against a pan-cancer reference, not clinical predictions.

Dataset. GBM | tumour-type key: *glioblastoma* | 8,000 tumour-condition cells (4,441 immune = 56%, 2,680 malignant = 34%), 8,000 matched-normal cells. **Reference.** Pan-cancer solid-tumour atlas, leave-one-out (ccRCC, CRC, LUAD, Melanoma, TNBC). All z-scores are relative to that reference.

1. Archetype & composites

Archetype call: `cold-excluded`

Composite	z (vs pan-cancer)	reading
Immunotherapy-Response	-0.59	reduced effector/inflamed program
Immune-Resistance	+1.67	elevated suppressor/barrier load
Effector-suppressor balance	**-2.26**	the hot/cold index
Stromal barrier (exclusion)	+1.86	elevated

2. Immune contexture (program z-scores, hot to cold)

Programs scored in the immune compartment (barrier programs over all tumour cells), z-scored vs the leave-one-out atlas reference and bounded to +/-3 SD.

Program	z	
tam_protumor_m2	+3.00	elevated
mdsc_monocytic	+3.00	elevated
mdsc_granulocytic	+2.46	elevated
ifn_gamma_signature	+2.27	elevated
metabolic_immunosuppression	+1.97	elevated
immune_exclusion_stroma	+1.76	elevated
cdc1_recruitment	+0.81	elevated
chemokine_trafficking	+0.66	elevated
antigen_presentation_apm	+0.18	mid-range
nk_inhibitory_brake	-0.67	reduced
tcell_terminal_exhaustion	-0.99	reduced
tcell_inflamed_gep	-1.17	reduced
cytolytic_activity	-1.63	reduced
icr	-1.73	reduced
tls_signature	-1.98	reduced
tcell_stemness	-3.00	reduced

3. Exhaustion & reinvigoration potential

- **Reinvigoration potential (stemness - terminal exhaustion): -2.01** -> terminally-exhausted skew - lower reinvigoration potential.
- Terminal-exhaustion program: -0.99 (reduced); stem/progenitor (TCF7/IL7R): -3.00.

4. Antigen-presentation integrity & genomic-escape flags

- **APM integrity (z): +0.18** (mid-range). Low APM echoes HLA/B2M/JAK escape.
- **PD-L1 (CD274) RNA proxy:** low (3.8% of tumour cells positive, mean 0.03). *RNA proxy only - not a validated IHC CPS/TPS score.*
- **Tumour-specific escape candidates (vs immune internal control):** JAK2 (reduced vs immune: 13.5% malignant vs 25.3% immune), IFNGR1 (reduced vs immune: 24.4% malignant vs 63.0% immune).
- *Not assessable in this dataset (zero counts in all cells - a capture artefact, not loss): TAPBP.* Classical MHC-I (HLA-A/B/C, B2M) loss therefore cannot be evaluated from this matrix.

5. TLS, metabolic suppression & dominant suppressor

- **TLS status (z): -1.98** (reduced).
- **Metabolic suppression (z): +1.97** (elevated).
- **Dominant suppressor axis: pro-tumour TAM (M2)** (z +3.00).

6. Candidate CAR/TCR/vaccine targets (expression in malignant cells)

Antigen	class	modality	mean	%pos	vs normal	relevant
EGFR (EGFRvIII)*	surface	CAR	1.417	58.1	tumour>normal	yes
CD276 (B7-H3)*	surface	CAR/mAb	0.193	23.5	similar in normal	yes
BIRC5 (survivin)	over-expressed self	vaccine/TCR	0.192	14.1	similar in normal	
IL13RA2 (IL13RA2)*	surface	CAR	0.124	13.6	tumour>normal	yes
ERBB2 (HER2)*	surface	CAR/mAb/ADC	0.058	8.4	similar in normal	yes
CTAG1B (NY-ESO-1)	cancer-testis	TCR/vaccine	0.0	0.0	similar in normal	
MLANA (MART-1)	differentiation	TCR/vaccine	0.007	1.2	similar in normal	
PMEL (gp100)	differentiation	TCR/vaccine	0.003	0.7	similar in normal	
WT1 (WT1)	over-expressed self	TCR/vaccine	0.003	0.8	similar in normal	
PRAME (PRAME)	cancer-testis	TCR/vaccine	0.004	0.5	similar in normal	

** listed for this tumour type in the disease matrix. Expression-based discovery only; CAR/TCR development requires surface-vs-intracellular, HLA-restriction, on-target/off-tumour and clonality checks not done here.*

7. Research interpretation - rational counter-axis (educational)

Given the **cold-excluded** archetype and a dominant **pro-tumour TAM (M2)** axis, the textbook-supported, *mechanistically rational* research direction is: **macrophage repolarisation (CSF1R / CD40) + checkpoint**. This is educational mechanism-matching, not a treatment recommendation.

> Effectors present but a stromal barrier dominates - the 'excluded' archetype; priming/stroma logic applies.

8. Validated readouts requiring orthogonal data

- **TMB** (>=10 mut/Mb) and **MSI-H/dMMR** are DNA readouts - not derivable from scRNA expression. The engine would integrate them as response modifiers if WES/panel data were supplied.
- **PD-L1 IHC (CPS/TPS)** is a protein assay; only the CD274 RNA proxy is shown above.

9. Concordance / novelty flags & limitations

- **Disease-matrix expectation** for *glioblastoma*: archetype "cold/excluded", biomarker ['low TIL', 'myeloid-dominated']. **Concordance:** this dataset scored `cold-excluded` - see context note below (may reflect the specific sampled tissue).

- Single dataset, single cohort: relative positioning only; no biological replication or outcome labels.
- Cross-dataset absolute scores are offset-prone; mitigated by atlas-referenced z-scoring.
- scRNA dropout can mimic gene 'loss'; APM/escape flags are hypotheses, not calls.

Generated by tii_report.py (Phase 2). Panels: status_panels.json group J; composites + readouts: io_reference.json; reference: Phase-1 pan-cancer atlas. Textbook paraphrased (CIT), not redistributed.