Q² Solutions®

Immune Landscape Signatures for Characterization of Tumor Microenvironment and Response to Therapy

Interplay between various immune cell activities in human tumors contributes to patient responses to treatment with checkpoint inhibitors as well as overall patient outcomes. As part of a broad immuno-oncology assay portfolio, Q² Solutions Genomics offers proprietary gene expression and analysis services for the detection of **Immune Landscape Signatures** attributable to 38 key immune cell subtypes, immune functions, individually important immune-related genes and ratios (*Table 1*). RNA expression analysis can be performed on Illumina RNA sequencing, NanoString or HTG EdgeSeq gene expression platforms using RNA or total nucleic acids isolated from FFPE or fresh frozen tumor specimens. Many immune signatures are also applicable to studies using PBMC or whole blood samples. Results for the individual signatures are output as **Immune Landscape Signature Scores**, non-standardized and standardized across the project. The Immune Landscape Signature Scores can be used to determine immunogenic status of solid tumors. These signatures can also be used in a single- or multi-factor analysis of treatment response and survival, along with other clinicopathological and genomic co-factors such as tumor mutational burden.

Product highlights

- Detection of 38 Immune Landscape Signatures, characterizing key immune cell subtypes, pathways and individual genes, with potential predictive and prognostic utility across many cancer types (publication in progress).
- Gene sets comprising individual Immune Landscape Signatures have been expertly developed across thousands of RNA expression tumor samples from various cancer indications to construct co-expression clusters attributed to specific immune cell subtypes.
- All signatures are statistically associated with either event-free (progression-free or recurrence-free) survival or overall survival in multiple solid tumor cancers (publication in progress).
- We offer streamlined analysis with flexibility to include novel genes or groups of genes of interest.
- Available as an output from the following platforms:
  - Illumina RNA Access (preferred for FFPEs), Illumina TruSeq Stranded mRNA sequencing, Stranded Total Gold RNA sequencing
  - NanoString PanCancer Immune Profiling panel, NanoString PanCancer IO 360 panel
  - HTG EdgeSeq Immuno-Oncology panel, HTG EdgeSeq OBP panel

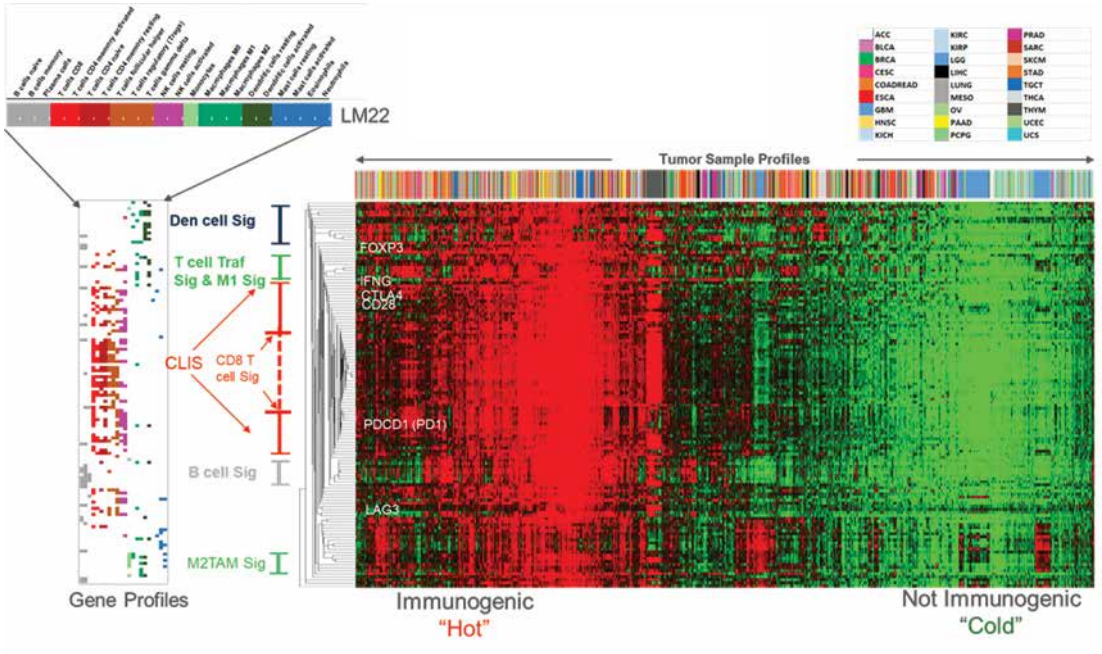
Product deliverables

- **Immune Landscape Signature Score Card**, standardized across project, per patient.
- Platform-dependent raw data output files.
- Custom statistical analysis for association with treatment response available.

Table 1: Immune Landscape Signatures

	Signature	Description
1	Cytotoxic Lymphocyte Immune Signature (CLIS)	Anti-tumor immune activity including CD8+ cytotoxic T cells, natural killer cells, and CD4+ effector T cells
2	CD8+ T cell signature	Primary adaptive immunity killer cells (cytotoxic T lymphocytes, or CTL)
3	B cell signature	Antigen presentation and antibody production and generally associated with better outcomes
4	T cell Trafficking (TCT) signature	CXCR3 Ligands, T cell recruitment
5	M2 TAM macrophage signature	Anti-inflammatory, tumor-promoting, and immune suppression activity
6	IFN-γ (IFNG)	Key marker of general immune activity (single gene)
7	TGF-β (TGFB1)	Marker of general immunosuppressive activity (single gene)
8	Wound healing signature	Promotes angiogenesis, may reflect chronic inflammation, and marker for immuno-suppressive activity, correlates with stemness
9	IFN-γ Response (IFNG response) signature	Stromal response to IFN-γ (often suppressive)
10	TGF-β Response signature	Stromal response to TGF-β (highly suppressive)
11	LAG3	Key marker of general immune activity (single gene)
12	FOXP3	Key marker of regulatory CD4+ T cells (single gene)
13	IFNG	Interferon Gamma expression (single gene)
14	TGFB1	Key marker of immune suppression (single gene)
15	VSIR	AKA VISTA, an immune checkpoint gene, inhibits T cell response (single gene)
16	Immature Dendritic Cell (iDC) signature	Marker of general dendritic cell activity (generally associated with better outcomes)
17	IL anti-inflammatory signaling	Interleukin signaling associated with anti-inflammatory processes, primarily via IL5 and IL10
18	IL pro-inflammatory signaling	Interleukin signaling associated with pro-inflammatory processes, primarily via IL6 and IL8 and frequently an indicator of worse outcomes
19	M0 macrophage signature	Biomarker of non-activated macrophage, associated with worse survival outcomes
20	M1 macrophage signature	Biomarker of polarized macrophage whose presence is generally anti-tumor
21	NK cell signature	Cytotoxic anti-tumor natural killer cell activity
22	NK CD56dim cell signature	A subtype of cytotoxic anti-tumor natural killer cells showing increased positive outcome association in certain tumor types
23	Th1 RAS GEF signature	Th1-specific aspects of the MEK/RAS pathway of extracellular signaling associated with guanine nucleotide exchange factors. High levels of this signature are overwhelming associated with worse outcomes.
24	Th2 IL signature	Indicator of interleukin Type 2 T helper cell activity.
25	Th17 signature	Subset of pro-inflammatory T helper cells that originate separately from Th1 and Th2 lineages. They are sometimes positively and sometimes negatively associated with survival, depending on the indication.
26	T cell Trafficking / M2 TAM ratio aka TCT/M2TAM	Recruitment vs. suppression of effector T cells. Useful outcome predictor in event-free and overall survival (Jones et al 2020 *Cancers*).
27	CD28/CTLA4 ratio	T cell activation (CD28) / negative regulator (CTLA4) checkpoint
28	PD1/PDL1 ratio	T cell de-activation checkpoint. Generally, high values of the PD1/PDL1 ratio imply better outcomes while low values of the ratio imply worse.
29	PD1 (PDCD1)	Important immune checkpoint gene (single gene)
30	PDL1 (CD274)	Important immune checkpoint gene (single gene)
31	CD28	Important immune checkpoint gene (single gene)
32	CTLA4	Important immune checkpoint gene (single gene)
33	NOS1	A mediator of anti-tumor activity. Its elevated presence in the TME, like TGFB1, is frequently associated with worse outcomes (single gene)
34	IRF8	A pleiotropic immune-related gene having mixed association depending on indication and outcome (single gene)
35	TOX	Supposedly a marker for T cell exhaustion but whose presence is often associated with better outcomes (single gene)
36	IL2	Cytokine important for T and B cell proliferation, and whose presence is more frequently associated with better outcomes (single gene)
37	IL6	Supports immunosuppressive MDSC and generally associated with worse outcomes (single gene)
38	IL10	A pleiotropic immune-related gene having mixed association depending on indication and outcome (single gene)

Immune Landscape Signatures – Pan Cancer Immunome Gene Set for solid tumors (RNA-Seq)



Q² Solutions: Your global laboratory partner

Q² Solutions is committed to providing customers an innovative, progressive and responsive partner with the quality focus, global experience and deep medical expertise integral to drug, medical device and diagnostic development. We work collaboratively with our customers, business partners and colleagues to lead the industry and live our customer promise of *Turning Hope* ***Into Help***™.

Our deep scientific and medical expertise, coupled with our strategic operating models, enables an impressive range of end-to-end lab solutions and one of the most robust test menus in the industry, including genomic and esoteric tests, fit-for-purpose biomarkers and companion diagnostics to support precision medicine.

Q² Solutions has a global testing footprint

Genomics	Flow cytometry / immunoassays	Anatomical pathology
• TCR Immune Sequencing • Immune Gene Signature / Epigenetic Signatures • Digital Spatial Profiling (AP-gene & protein expression) • Minimal Residual Disease (MRD) • Tumor Mutation Burden (TMB) • DNA-mismatch repair (MMR) Deficiency/ Microsatellite instability (MSI) • HLA and KIR typing • Whole Exome Sequencing • NeoAntigen discovery • Microbiome 16S rRNA	• Immuno-Phenotyping • CAR-T tracking • Receptor Occupancy (mono/bi-specific mAbs) • Tumor Infiltrating Lymphocytes (TILs) • Intracellular Cytokine Survey • Minimal Residual Disease (MRD) • Circulating Soluble Proteins • PBMC processing • ELISpot • Pembrolizumab PK and Anti-Pembrolizumab Antibody	• IHC (single & multiplex) • Tumor Infiltrating Lymphocytes (TILs) • Digital Pathology • FISH

Focus on quality

Our quality management system (QMS) follows CLSI guidelines and our laboratories are CAP accredited. Additionally, all of our CLIA validated assays are supported by bioinformatics and electronic systems that meet HIPAA, GAMP5, ICH Q9, and 21 CFR Part 11 standards.

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