Association of an Inflammatory Gene Signature With CD8 Expression by Immunohistochemistry in Multiple Tumor Types

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*At the time the studies were conducted

Background

An inflammatory signature in the tumor microenvironment (TME) has been associated with improved clinical outcomes in patients treated with immune checkpoint (IC) therapy across multiple tumor types. A limitation of CD8 T cells as a sole surrogate marker for inflammation is its inability to accurately assess the entire immune microenvironment.

Methods

1. A multiparameter tumor inflammation assay based on gene expression profiling (GEP) was developed.
2. Using a machine-learning approach, the combination of genes that gave the highest CD8 IHC was identified.
3. A 95-gene inflammation panel was used for inflammation analyses.
4. The model was considered accurate if ~95% of samples were correctly assigned to the CD8 inflammatory signature.
5. The 95% confidence interval (CI) for prediction of CD8 IHC was computed using the multiple linear regression model obtained using automated technology.

Results

1. The CD8 signature accurately predicted CD8 IHC across tumor types.
2. The modest linear correlation of CD8 IHC and CD8 signature score showed consistency across most tumor types.
3. Using this 95-gene panel assay, we have derived a 16-gene CD8 signature using GEP, which was similar for most tumor types, indicating that this gene signature may be utilized to accurately assess inflammation in the TME.

Conclusions

1. We have developed a GEP-based, investigational-use-only (IUO) assay to interrogate inflammation in the TME.
2. The CD8 signature accurately predicted CD8 IHC across tumor types, consistent across most tumor types. Using this 95-gene panel assay, we have derived a 16-gene CD8 signature using GEP, which was similar for most tumor types, indicating that this gene signature may be utilized to accurately assess inflammation in the TME.

References


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Prevalence of inflammation characterized by CD8 IHC and CD8 signature scores across tumor types

Figure 1. Correlation of CD8 IHC and CD8 signature scores across tumor types

Figure 2. Distribution of CD8 IHC and CD8 signature scores in each of the 12 tumor types

Figure 3. CD8 expression by IHC and CD8 signature scores across tumor types

Figure 4. Prevalence of inflammation characterized by CD8 IHC and CD8 signature scores across tumor types

Figure 5. Distribution of CD8 IHC and CD8 signature scores in each of the 12 tumor types

Figure 6. Prevalence of inflammation characterized by CD8 IHC and CD8 signature scores across tumor types

* The CD8 signature accurately predicted CD8 IHC across tumor types. Using this 95-gene panel assay, we have derived a 16-gene CD8 signature using GEP, which was similar for most tumor types, indicating that this gene signature may be utilized to accurately assess inflammation in the TME.