Multiplex immunohistochemistry reveals a lymphocytic immune signature associated with longer overall survival in small cell lung cancer patients

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Introduction: Small cell lung cancer (SCLC) is an aggressive neuroendocrine malignancy with limited treatment options and median survival of approximately 1 year after diagnosis, even with treatment. SCLC patients typically respond to platinum-based chemotherapies, but drug resistance and irradiation disease progression rapidly develop, driving the need for patient survival rate to 5%. The emergence of immunotherapy (IO) offers promising therapeutics for this disease. However, recently, only 5% of patients responded to first-line chemotherapy (CT) and 3% to IO. Importantly, mIHC enables cell classification via image cytometry, for identification of immune cell functional markers provide insight into immune checkpoints (PD-1, PD-L1), proliferation (Ki67), and T cell exhaustion.

Project goal: Gain a better understanding of SCC immune response through an in-depth characterization of the tumor immune microenvironment.

Figure 1: Comprehensive in-situ monitoring of the tumor microenvironment using mIHC

Abstract

Baseline demographics of SCLC patients matched for age, gender, and race

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case (n=100)</th>
<th>Control (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65 ± 15</td>
<td>60 ± 10</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>54:46</td>
<td>40:30</td>
</tr>
<tr>
<td>Race (Caucasian:Asian)</td>
<td>80:20</td>
<td>60:40</td>
</tr>
</tbody>
</table>

Conclusions:

- Increased CD8+ T cell functionality is associated with better overall survival.
- Future Directions:
  1. Confirm findings of increased T cells and dendritic cells in long-term survivors in additional cohort studies of SCLC patients.
  2. Distinguish with more power the difference between primary (lung) and metastatic sites.
  3. Identify predominating immune cell populations that correspond with clinical response to first-line therapy in stage-matched samples.

Conclusion: Patients exhibit a high variability in immune cell infiltrates, although overall total infiltrates seem to be low in comparison to control tissues. Patients with longer survival tend to be the predominant driver of immune signature.

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References:


