**Background**

- Kras mutations are the most common oncogenic mutation in non-small cell lung cancer.
- Unfortunately, targeting Kras directly has substantially failed thus far, and there are no therapies that adequately address most forms of mutant Kras.
- Immune checkpoint blockade, ICB (e.g., PD-1 blockade) has shown promise patients with non-small cell lung cancer.
- Our laboratory has previously shown that IL-6 blockade reprograms the myeloid tumor microenvironment (TME), leading to a more robust cytotoxic immune response.

Accordingly, we hypothesized that there might be an additive/synergistic effect of modulating the immunosuppressive TME and augmenting anti-tumor immunity through combined PD-1 and IL-6 blockade. We would also like to see the effectivity of anti-PD-1 treatment alone in Kras mutant lung cancer.

**Methodology**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Conditions</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (IgG)</td>
<td>200µL IP</td>
<td>Twice a week for 4 weeks</td>
</tr>
<tr>
<td>Anti-PD-1</td>
<td>Clone: 29F.1A12 (Bioxcell – BE0273-CUST)(200µg IP)</td>
<td>Three times a week for 4 weeks</td>
</tr>
<tr>
<td>Anti-IL-6</td>
<td>Clone: MP5-20F3 (Bioxcell – BE0046-CUST)(20 mg/kg IP)</td>
<td>Twice a week for 4 weeks</td>
</tr>
<tr>
<td>Anti-PD-1 + Anti-IL-6</td>
<td>Given separately</td>
<td>Two regimes combined</td>
</tr>
</tbody>
</table>

**Results**

**Figure 1.** Anti-PD-1 and anti-IL-6 treatment reduce tumor burden while their combination leads to clustered responses.

**Figure 2.** Increase in surface tumor number correlates with increased immunosuppressive hallmarks and weakened cytotoxic signature in combination treatment mice.

**Conclusions**

- Consistent with previous results, anti-IL-6 treatment results in decrease in tumor burden.
- Anti-PD-1 treatment significantly reduces tumor burden in our Kras-mutant lung cancer mouse model.
- Personalized treatment with anti-IL-6 alone might be an alternative modality for ICB in patients with Kras mutant lung cancer.
- Combination treatment results in clustered responses, with some mice responding extremely well and others receiving no benefit.
- Responders in the combination treatment group have lower expression of Treg signatures and higher CD8 T-cell cytotoxic activation, as well as lower CXCL1 and higher PD1 expression.

**Future Work**

- More repeat experiments of each group
- Dissection of why certain mice are responders or nonresponders will elucidate resistance mechanisms and help clinicians create individualized treatment strategies.

**References**


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