Development of in vivo models for evaluation of NK-TICA™, novel Bicycle®-tumor-targeted immune cell agonist® designed to engage NK cells

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INTRODUCTION

Natural Killer (NK) cells are cytotoxic cells of the innate immune system with well characterized activation and promiscuous. Their ability to directly kill malignant cells and elicit an adaptive immune response makes them a promising candidate for a precision guided immunotherapy for cancer patients.

METHODS

Summary of in vivo models assessed for NK-TICA™ preclinical studies

<table>
<thead>
<tr>
<th>Strain</th>
<th>NCG Source</th>
<th>NKp+ NCG Cells</th>
<th>NK Cells in Blood and Tumor Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>hHSC-NCG</td>
<td>human CD45+, human CD3</td>
<td>hNKp46+ (hCD45+, hCD3)</td>
<td>The tumor cell and NK cell lineages</td>
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RESULTS

Transgenic expression of hIL-15 leads to expansion of NK cells in blood

Differences in the expression of NKp46 in NK cells

- hHSC-NCG.hIL15
- hHSC-NCG IL15 HDI
- hNK-NCG.hIL15
- C57BL/6-hNKp46

CONCLUSIONS

- C57BL/6-hNKp46 mice with MC38 syngeneic tumors are immunocompetent and show the highest number of circulating and tumor-infiltrating NKp46+ NK cells across models tested. These mice, in contrast to NCG hIL15 strain, show lack of non-physiological NK cell expansion and are the donor-dependent variant. Across the models tested, hHSC-NCG.hIL15 MC38 model is the most optimal experimental tool for in vivo evaluation of NK-TICA™ providing the tumor-targeting Bicycle® cross-reacts with the mouse ortholog expressing activity as a panel of biomarkers. Mouse NK cells were defined as mCD45+, mCD3+, mCD8α−, and mNK1.2+.

REFERENCES


[Image 1]: [Tumor cell line and NK cell lineages]