Assessment of *IL-9*/*IL-9R* Expression and Therapeutic Effect of *IL-9* Blockade in a Mouse Breast Cancer Model

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Background and Hypothesis:

IL-9 is a cytokine produced by TH9, mast cells, and innate lymphoid cells. IL-9 acts on the IL-9 receptor (IL-9R) and is primarily involved in parasitic immunity and allergic inflammation. IL-9 has anti-tumor effects in solid tumors such as melanoma. IL-9 also has pro-tumor effects in various cancer types, including lung cancer. Previous studies have shown that increased serum IL-9 in breast cancer patients correlates with tumor metastasis. Therefore, we hypothesize that IL9 signaling contributes to breast tumor metastasis and blocking IL-9 may have a therapeutic benefit in reducing metastasis.

Methods:

Mice were orthotopically implanted with 4T1 breast tumor cells. Organs were harvested after 28 days. Total RNA was extracted and expression of *IL-9*/*IL-9R* and leukocyte markers were assessed. To test therapeutic effect of IL-9 blockade, tumor-bearing mice were treated with anti-IL-9 monoclonal antibody (αIL-9). Tumor sizes were monitored every 4 days. On day 28, tumor tissue was harvested and weighed. Lung was also harvested and stained with H&E for metastasis analysis.

Results:

Primary tumor growth was not altered by αIL-9. The effect of αIL-9 treatment on lung metastasis is pending pathological analysis. We further examined IL-9R to define how tumor burden alters expression of *IL-9* and *IL-9R* across tissues. Lymphoid organs, such as the thymus, spleen, and inguinal lymph node (inguinal LN), exhibit high levels of IL-9R. Additionally, the small intestine is notably enriched with IL-9R. The thymus exhibited the highest *IL-9* expression.

Conclusion and Future Directions:

Although blockade of IL-9 did not impact tumor growth in this model, this will be examined in other models to confirm the findings. Further research is needed to investigate the potential therapeutic benefits of αIL-9 with other established therapies. We observed that there is altered IL-9 and IL-9R expression in tumor bearing mice and the physiological significance of that finding remains to be determined.