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Grant title: Development of immune-based strategies to enhance theapeutic targeting of metastatic breast cancer

Lay Description of Outcomes

Metastasis is the primary cause of breast cancer-related morbidity and mortality and there is an urgent clinical need to eradicate established metastases and prevent future metastatic growth. There has been intense focus

Figure 5: Representative example of lung metastasis in the HC-11/R1 model following serial passage in vivo.

on the development and use of immunotherapy for cancer treatment. One of the prominent immune cell types within the microenvironment of metastatic lesions is the macrophage, which is normally involved in the immune response to fight infections. Macrophages are capable of communicating with other cells in the immune system, specifically those that are able to eradicate tumor cells and establish a "memory" of the tumor, leading to both eradication of the existing metastasis and inhibition of future occurrences. The studies in this proposal aimed to target the macrophages that exist within the metastatic site using pharmacological approaches and enhance their ability to induce anti-tumor immune responses. The results from these studies led to a better understanding of macrophage function within the tumor microenvironment and identified a key signaling pathway that regulates expression of key immunomodulatory factors within macrophages. Furthermore, findings from this study highlighted the complexities of macrophage function within the metastatic site and have led to further studies focused on delineating the contributions of specific macrophage subpopulations within the metastatic microenvironment (NIH/NCI R21CA235385, Wood and Schwertfeger, co-PI as well as an ACS postdoctoral fellowship). The long-term goal of these studies is to develop more effective immune-based targeting strategies that effectively enhance anti-tumor responses in metastatic sites, leading to eradication of established lesions and prevention of future recurrences.