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MAIN FIELDS OF RESEARCH; ABSTRACT

Whereas surgical resection and radio- or chemotherapy can cure primary tumors, metastatic disease is largely incurable because of its systemic nature and the resistance of disseminated tumor cells to existing therapeutic agents. This explains why >90% of mortality from cancer is attributable to metastases. Metastases represent the final step of a multistep process, which involves dissemination of cancer cells to anatomically distant organ sites and their subsequent adaptation to foreign tissue microenvironments. Each of these steps involves crosstalk between tumor cells and hematopoietic cells, including lymphocytes. Natural killer (NK) cells are immune effector cells, which act as a bridge between the innate and acquired immune system and can control tumors and virus-infected cells. We have recently found that NK cells don’t seem to control established tumors but are essential in limiting metastatic seeding to lungs and especially liver.

Most of our current knowledge of NK cells is derived from studies of mouse splenic and human peripheral blood NK cells, referred to as “conventional” NK cells. However, NK cells are also present in other tissues and organs and recent data suggest that a significant proportion of hepatic NK cells differ from peripheral NK cells in terms of surface marker expression, cytokine profiles, and cytotoxic potential. More recently, a unique NK cell subset, termed liver-resident NK cells, was characterized in both mouse and human livers. The relative abundance and unique features of hepatic NK cells suggest a distinct function of these cells. In this project we aim to examine whether and how conventional and tissue-resident NK cells in the liver are involved in controlling metastasis to the liver using preclinical models for spontaneous metastasis.

SPECIAL TECHNIQUES AND EQUIPMENT

In vivo experiments using murine model, primary cell culturing, high dimensional flow cytometry, real time quantitative PCR, fluorescence microscopy.