



The Jackson Lab: Senescence and Recurrent Cancer

Unlike liquid tumors/blood cancers, solid tumors can rarely be effectively treated without risk of recurrence using only chemotherapy. The lab of Dr. James Jackson studies why this happens in solid tumors (particularly breast cancers), with a specific focus on the role of senescent cells in cancer recurrence.

Many tumor cells will become senescent in response to chemotherapy instead of undergoing cell death. Such cells are growth-arrested, and since much of cancer chemotherapy targets highly proliferative cells, this state protects cancer cells from standard treatments. Senescent cells also secrete many cytokines and growth factors that can drive the proliferation and survival of neighboring non-senescent cancer cells. These properties of senescent cells drive recurrent disease.

The lab has identified a compound that can specifically target these senescent cells in culture, with obvious implications for the treatment of primary solid tumors to prevent recurrent disease. How senescent cells can drive recurrence following treatment can be studied in animal models by using engineered cells that can switch from green to red once they become senescent. In the simplest of terms, this means that in recurrent tumors the lineage of cells (i.e. whether they were ever senescent) can be traced by their color alone.

These cells can then be followed throughout the course of the relapsed cancer, illuminating the cellular origin of the disease. These cells are also analyzed for their cytokine and chemokine contributions to the tumor environment, potentially presenting targetable points for cancer therapy.

Cancer Biology

Breast Cancer



BRCA1 Biology: Importance in Breast & Ovarian Cancer

BRCA1 is also being studied using a unique animal model. Individuals with BCRA1-associated breast cancer are born with a defective copy of these gene in all of their tissues. However, the loss of heterozygosity of this gene and resulting tumorigenesis is only seen in breast and ovarian tissues.

Because of its essential role in DNA repair, the BRCA1 knockout is embryonic-lethal in animal models. However, this lethality is dependent on the function of p53, as double knockout animals for p53 and BRCA1 generally survive past birth. The lab has generated a unique inducible BRCA1 knockout animal to try and understand both 1) the tissue-specific role of BRCA1 deficiency in carcinogenesis and 2) the possible interplay of p53 and BRCA1 in determining this tissue-specific phenomenon.

This animal model will allow for greater understanding of the role of BRCA1 in these cancers. It also could potentially present new targetable pathway options through eventual gene expression analysis of the tissues in these mice (i.e. comparison of cancer-prone tissues and non-cancer-prone tissues after inducible deletion of BRCA1).

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