Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

Cancer cell CCR2 orchestrates escape from the adaptive immune response

By

Miriam R. Fein

CCR2 (C-C chemokine receptor type 2) is highly expressed in human breast cancer tissue by both cancer cells and host cells. CCR2 expression on host cells, especially inflammatory monocytes, promotes primary tumor growth and metastasis. To examine the relative role of CCR2 expression on host and cancer cells, I transplanted primary tumor cells derived from MMTV-PyMT;*Ccr2*$^{+/+}$ and MMTV-PyMT;*Ccr2*$^{-/-}$ mice to syngeneic *Ccr2*$^{+/+}$ and *Ccr2*$^{-/-}$ hosts. Whereas transplantation of cancer cells with wild type *Ccr2* led to rapid tumor growth, tumors from *Ccr2*$^{-/-}$ cancer cells grew very slowly. The host status of Ccr2 had no effect on tumor growth. The slow growth of tumors from *Ccr2*$^{-/-}$ cancer cells was accompanied by increased infiltration of CD8+ cytotoxic T lymphocytes (CTLs) and cross-presenting CD103+ dendritic cells (DCs). Consistently, when *Ccr2*$^{-/-}$ cancer cells were transplanted to athymic nude mice lacking an adaptive immune response, the tumors grew as fast as those derived from wild type cancer cells. Thus, tumors from *Ccr2*$^{-/-}$ cancer cells, in contrast to those from wild type cells, can be controlled by the adaptive immune system. Comparing tumors from *Ccr2*$^{-/-}$ cancer cells to those from *Ccr2*$^{+/+}$ revealed several mechanisms by which MMTV-PyMT;*Ccr2* tumors escape immune control, including cancer cell upregulation of programmed death ligand 1 (PD-L1), an inhibitory signal for T cells. Together, these results establish a novel role for CCR2- in cancer cells- in orchestrating escape from immune control in breast cancer.

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Time: 1:30 pm **Dissertation Advisor**: Dr. Mikala Egeblad
Place: Hawkins Conference Room, Wendt Building, Cold Spring Harbor Laboratory