Dynamic Control of Tumor Vessels Augments Antitumor Responses

Emmanuel M Gabriel, Assistant Professor1, Deborah Bahr2, Sanjay Bagaria2, Debrabata Muhkopadhyay2, and Keith Knutson2
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OBJECTIVES/GOALS: Our overall objective is to develop a directly observable and reproducible method of enhanced blood flow through tumor vessels (i.e. dynamic control) at the time of systemic treatment delivery. Our central hypothesis is that the dynamic control of tumor vessels will improve (1) systemic drug delivery and (2) effector cell trafficking to target tumor.

METHODS/STUDY POPULATION: B16 melanoma cells were inoculated into C57BL/6 (B6) mice (male and female) in both regional (hind leg) and systemic (flank) models. Dynamic control consisted of an IV saline bolus (500 ul) and phenylephrine (10 ug). Tumor vessel response was observed in real-time through window chambers using intravital microscopy (IVM).

CONFLICT OF INTEREST DESCRIPTION: Lonnie Shea, Myrna G Garcia1, Alvaro Padron, Yilun Deng, Harshita Gupta, Aravind Kancharla, Ryan Reyes, and Tyler Curiel
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Early life stress promotes chronicity of experimental colitis

Rachel Quinn Muir1, Barbara J. Klocke1, Kasi C. McPherson1, Jeremy B. Foote1, Jennifer S. Pollock1, and Craig L. Maynard1
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OBJECTIVES/GOALS: The overall goal of this study was to determine the effect of early life stress (ELS) on the intestinal CD4+ T cell immune compartment, at homeostasis and after induction of experimental Inflammatory Bowel Disease (IBD). METHODS/STUDY POPULATION: We used a mouse model of ELS, maternal separation with early weaning (MSEW). We used IL-10 reporter mice to enable analysis of IL-10-producing cells. Mice were examined on postnatal day 28 to determine the impact of ELS on gut regulatory T cells. Plasma levels of corticosterone (rodent stress response hormone) was determined by ELISA. Colitis was induced in MSEW and normal rear (NR) mice via intraperitoneal injection of α-IL-10R every 5 days until day 15. Mice were euthanized on days 20 and 30. Colonic tissue sections were stained for histological analysis. Remaining tissue was further processed for flow cytometric analysis of CD4+ T cells and innate lymphoid cells.

RESULTS/ANTICIPATED RESULTS: Plasma corticosterone was elevated in MSEW mice compared to their NR counterparts at 4 weeks of age. We observed that the MSEW stress protocol does not affect the baseline colonic CD4+ T cell or innate lymphoid cell populations. There was a reduction in the intestinal inflammatory/cytotoxic characteristics. These changes clearly impacted tumor cell phenotype, as cells from the scaffold increased tumor cell migration and apoptosis in vitro.

DISCUSSION/SIGNIFICANCE OF IMPACT: Early phenotypic changes at the engineered metastatic niche can identify signs of metastasis prior to colonization of tumor cells. Furthermore, dynamics of immune and stromal cells change throughout niche maturation, influencing tumor cell phenotype and may suggest targeted therapies.

CONFLICT OF INTEREST DESCRIPTION: Lonnie Shea, Jacqueline Jeruss, and Grace Bushnell are named inventors on patents or patent applications.

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