CAMB 701: The Tumor Microenvironment

Directors: Celeste Simon, PhD and Todd Ridky, MD, PhD **TA:** Ariana Majer

Tuesdays 3:30-5:30 pm BRB II/III

Syllabus Spring 2023

Class Format:

- Students present background (30-40 minutes).
- 10-minute break
- Students present key data in paper (45-50 minutes).
- Feedback from Celeste and Todd to presenters only (10 minutes).

Reminder: each week, students that are not presenting that week will submit **two questions** they would like to discuss concerning impact/novelty/implications and/or general questions about the papers to Celeste, Todd, and Ariana the day of class.

Class 1: (1/17/23). Organizational Meeting: Intro to Immunology, Tumor Microenvironment, etc. (Ariana)

Class 2: (1/24/23) Crosstalk between the Tumor and Microenvironment (Celeste) Banh et al. "**Neurons release serine to support mRNA translation in pancreatic cancer**", *Cell* (2020)

Reinfeld et al."**Cell-programmed nutrient partitioning in the tumour microenvironment**", *Nature* (2021)

Class 3: (1/31/23) Immune Surveillance (Ariana)

Li et al. **"The allergy mediator histamine confers resistance to immunotherapy in cancer patients via activation of the macrophage histamine receptor H1,"** *Cancer Cell* (2021).

Herrera et al. "Low dose radiotherapy reverses tumor immune desertification and resistance to immunotherapy," *Cancer Discovery* (2021).

Class 4: (2/7/23) Cancer Heterogeneity, Plasticity, and Tumor Evolution (Celeste) Concepcion et al. "SMARCA4 inactivation promotes lineage-specific transformation and early metastatic features in the lung", *Cancer Discovery* (2021)

Class 5: (2/14/23) Metastatic Niche (Ariana) Mukherjee et al. "Adipocyte-induced FABP4 expression in ovarian cancer cells promotes metastasis and mediates carboplatin resistance," *Cancer Research* (2020).

Class 6: (2/21/23) Tumor Angiogenesis, Lymphangiogenesis (Todd) Garcia Silva et al. "Melanoma-derived small extracellular vesicles induce lymphangiogenesis and metastasis through an NGFR-dependent mechanism" *Nature Cancer* (2021) Stella Stasso **"Lymphangiogenesis-inducing vaccines elicit potent and long-lasting T cell immunity against melanomas"** *Science Advances* (2021)

Class 7: (3/1/23) Mock Study Section (Celeste)

Spring Break: March 6-10, 2023

Class 8: (3/14/23) Systemic Factors and Tumor Progression (Celeste) Talbert et al. "**Modeling human cancer-induced cachexia**" *Cell Reports* (2021)

Queiroz et al. "Blocking ActRIIB signaling and restoring appetite reverses cachexia and improves survival in mice with lung cancer" *Nature Communications* (2022)

Class 9: (3/21/23) The Tumor Stroma, Cancer Associated Fibroblasts (Todd) Katarkar et al. "NOTCH1 gene amplification promotes expansion of Cancer Associated Fibroblast populations in human skin" *Nature Communications* (2020)

Zhang et al. "Macropinocytosis in Cancer-Associated Fibroblasts Is Dependent on CaMKK2/ARHGEF2 Signaling and Functions to Support Tumor and Stromal Cell Fitness" Cancer Discovery (2021)

Class 10: (3/28/23) Stressful Tumor Microenvironments (Hypoxia and Nutrient Scarcity) (Celeste) Lien et al. "Low glycaemic diets alter lipid metabolism to influence tumour growth" *Nature* (2021)

Ubellacker et al. **"Lymph protects metastasizing melanoma cells from ferropto**sis" *Nature* (2020)

Class 11: (4/4/23) The Influence of Microbiome on Tumor Growth (Todd) Lam et al. "Microbiota triggers STING-type I IFN-dependent monocyte reprogramming of the tumor microenvironment" *Cell* (2021)

Geller et al. "Potantial role of intratumoral bacteria in mediating tumor resistance to the chemotherapeutic drug gemcitabine" *Science* (2017)

Class 12: (4/11/23) Inflammation and Tumor Progression (Celeste) Liudahl et al. "Leukocyte Heterogeneity in Pancreatic Ductal Adenocarcinoma: Phenotypic and Spatial Features Associated with Clinical Outcome" *Cancer Discovery* (2021)

Cappellesso et al. "Targeting the bicarbonate transporter SLC4A4 overcomes immunosuppression and immunotherapy resistance in pancreatic cancer", *Nature Cancer* (2022)

Class 13: (4/18/23) Tumor-Nervous System Interactions (Ariana) Kamiya et al. "Genetic manipulation of autonomic nerve fiber innervation and activity and its effect on breast cancer progression," *Nature Neuroscience* (2019).

Pan et al. "*NF1* mutation drives neuronal activity-dependent initiation of optic glioma," *Nature* (2021)

Class 14: (4/25/23) Sex as a Biological Variable in Tumor Progression (Todd) Vellano et al. "Androgen receptor blockade promotes response to BRAF/MEK-targeted therapy," *Nature* (2022) Aguirre-Portoles et al. **"ZIP9 is a druggable determinant of Sex Diffrerences in Melanoma**" *Cancer Research* (2021)

Class 15: (5/2/23) Tumor Dormancy (Ariana) Albrengues et al. "Neutrophil extracellular traps produced during inflammation awaken dormant cancer cells in mice," *Science* (2018).

Correia et al. **"Hepatic stellate cells suppress NK cell-sustained breast cancer dormancy,"** *Nature* (2021)

Mock Study Section: each student submits a one page Specific Aims on an assigned paper from class. Each student will be assigned as the primary reviewer of someone else's aims page to present that day.

Course Grade: 40% assigned presentations, 40% overall class participation (and weekly questions), and 20% Specific Aims for Mock Study Section.