

Summer Student Research Program

Project Description

FACULTY SPONSOR'S NAME AND DEGREE: *Nicholas Bessman, PhD*

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PROJECT TITLE (200 Characters max):

Understanding biased EGFR signaling in intestinal inflammation, colitis, and colorectal cancer

HYPOTHESIS:

Our working hypothesis (informed by Bessman et al, Cell 2017) is that the seven endogenous activating EGFR ligands can induce different downstream signaling phenotypic effects in epithelial cells. We generated a new mouse model that renders EGFR incapable to distinguish between the seven activating ligands. In preliminary data, we identify that these mice are significantly protected from intestinal inflammation and colitis, but they show a strong trend toward worsened colorectal cancer and long-term survival. The goal of this project is to use mouse models and epithelial cells cultures to understand the molecular basis of these EGFR-dependent phenotypes. The long-term goal of the project is to identify improved therapeutic strategies to target EGFR in the treatment of colitis and colorectal cancer.

PROJECT DESCRIPTION (Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)

We will utilize mice bearing different genetic mutations, including in EGFR, Rag1, epiregulin, amphiregulin, and APC to dissect which molecular pathways connect biased EGFR signaling with colitis and colorectal cancer outcomes. All mouse work will be supervised by a highly trained PhD student in the lab, in collaboration with the medical student. Readouts of disease include weight loss, inflammatory gene expression, and histology, and will be analyzed in collaboration with Dr. Bessman and the senior PhD student.

Additionally, we will use intestinal epithelial cell cultures to ask how EGFR mutation and different EGFR ligand stimulations impact epithelial differentiation and function. Readouts will include microscopy and gene expression analysis, and will be analyzed in collaboration with Dr. Bessman and the senior PhD student.

SPONSOR'S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:

*Bessman NJ, Mathieu JRR, Renassia C, Zhou L, Fung TC, Fernandez KC, Austin C, Moeller JB, Zumerle S, Louis S, Vaulont S, Ajami NJ, Sokol H, Putzel GG, Arvedson T, Sockolow RE, Lakhali-Littleton S, Cloonan SM, Arora M, Peyssonnaud C, Sonnenberg GF. Dendritic cell-derived hepcidin sequesters iron from the microbiota to promote mucosal healing. *Science*. 2020 Apr 10;368(6487):186-189. PubMed Central PMCID: PMC7724573*

*Freed DM, Bessman NJ, Kiyatkin A, Salazar-Cavazos E, Byrne PO, Moore JO, Valley CC, Ferguson KM, Leahy DJ, Lidke DS, Lemmon MA. EGFR Ligands Differentially Stabilize Receptor Dimers to Specify Signaling Kinetics. *Cell*. 2017 Oct 19;171(3):683-695.e18. PubMed Central PMCID: PMC5650921*

*Choi G, Bessman NJ. Iron at the crossroads of host-microbiome interactions in health and disease. *Nat Microbiol*. 2025 Jun;10(6):1282-1293. PubMed Central PMCID: PMC12302899.*

*Goc J, Lv M, Bessman NJ, Flamar AL, Sahota S, Suzuki H, Teng F, Putzel GG, Eberl G, Withers DR, Arthur JC, Shah MA, Sonnenberg GF. Dysregulation of ILC3s unleashes progression and immunotherapy resistance in colon cancer. *Cell*. 2021 Sep*

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16;184(19):5015-5030.e16. PubMed Central PMCID: PMC8454863.

THIS PROJECT IS: Clinical Laboratory Behavioral Other

THIS PROJECT IS CANCER-RELATED

Please explain Cancer relevance

THIS PROJECT IS HEART, LUNG & BLOOD- RELATED

Please explain Heart, Lung, Blood relevance

THIS PROJECT INVOLVE RADIOISOTOPES?

THIS PROJECT INVOLVES THE USE OF ANIMALS

PENDING

APPROVED

IACUC PROTOCOL #202100008

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS?

PENDING

APPROVED

IRB PROTOCOL # M

THIS PROJECT IS SUITABLE FOR:

UNDERGRADUATE STUDENTS

ENTERING FRESHMAN

SOPHOMORES

ALL STUDENTS

THIS PROJECT IS WORK-STUDY: Yes or No

THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR

FOR INTERESTED VOLUNTEERS: Yes or No

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?

The student will learn impactful research models including genetically engineered mouse models, including models of colitis and colorectal cancer, along with emerging approaches to grow organoid cultures, which mimic the three-dimensional structure and function of intact tissues.