Student summer research opportunity

Project title: SLFN12 sensitizes Colorectal cancer to certain chemotherapy drugs

PI: Marc D. Basson, MD, PhD

Location: RGE 100

Abstract

The Basson Lab has been investigating the effects of SLFN12, an intermediate protein of the Schlafen family linked to better prognosis in aggressive and resistant cancer types, such as triple-negative breast cancer and lung adenocarcinoma. The Basson lab published an article showing that the improved prognosis observed in triple-negative breast cancer cells with high SLFN12 expression is attributed not only to the tumor's intrinsic biology when SLFN12 is expressed, but also to the sensitization of certain chemotherapy drugs. Our work on lung adenocarcinoma, which is still ongoing, confirmed this. In colon cancer, high levels of SLFN12 expression are often linked to a better prognosis, implying that elevated SLFN12 could be a positive outcome indicator, possibly because it helps suppress tumor cell growth and promotes differentiation. We look forward to testing how different chemotherapy drugs affect the cell viability of HT-29 and HCT 116, two colon adenocarcinoma cell lines, when we overexpress SLFN12, compared to the baseline SLFN12 expression in the same cell lines.

Significance

This study will provide a deeper understanding of SLFN12's role in colon adenocarcinoma, including whether its impact on prognosis is related to the tumor's intrinsic biology or its response to chemotherapy agents when SLFN12 is overexpressed. If proven to impact cells' response to chemotherapy, SLFN12 levels may one day help determine the most effective chemotherapeutic strategy for patients with colon adenocarcinoma. Additionally, targeting and activating the SLFN12 pathway might have a synergistic effect when combined with conventional cytotoxic chemotherapy in colon adenocarcinoma with low SLFN12 levels.

Research methods that will be learned by the student

- Mammalian cell culture
- Crystal violet cell viability assay
- Drug preparation
- Q-PCR
- Western blotting
- Data analysis

Proposed methods of data analysis: Standard statistical techniques, including t-tests and outlier analysis

How will the anticipated findings contribute to the success of the overall research?

Should SLFN12 levels be shown to influence cellular responses to chemotherapy, they could eventually be used to guide the selection of the most effective chemotherapy regimen for colon adenocarcinoma patients. This can be validated in mice and rats and eventually used as the basis for an IND application to the FDA for human trials.

Student fellow mentoring plan

The student will be assigned to work with a member of the Basson laboratory for daily guidance and will participate in weekly two-hour laboratory meetings that both focus on data and emphasize discussion of experimental design and data analysis. Depending on the student's level of interest, there may also be opportunities to participate in other work going on in the lab, including small animal studies, as well as clinical research projects that are ongoing in the Basson research group. It is anticipated that the student will subsequently prepare a poster or oral presentation for student research day under Dr. Basson's supervision and that the data developed will be included in a publication in which the student will be a coauthor. All research will be conducted in the Basson laboratory.