McGill Biochemistry Department | Département de biochimie

BIOC 462/491 Internship Position in Industry

Winter 2024

Restrictions

Open only to Honours Students enrolled in BIOC 462/491 during the winter 2024 semester

Company

Thryv Therapeutics Inc.
500 boulevard Cartier ouest, Suite 130A
Laval, QC, H7V 5B7
https://thryvtrx.com/

Thryv Therapeutics is a clinical-stage biotechnology company pioneering a precision medicine approach to treat genetic and drug-induced Long QT Syndromes, atrial fibrillation, and treatment-resistant cancers with potent and selective inhibitors of Serum Glucocorticoid inducible Kinase (SGK). Together we share a vision to transform the lives of people with life-threatening conditions.

Title

Characterization of novel SGK1 inhibitors for Long QT Syndrome (LQTS), Atrial Fibrillation (AF), and Treatment-Resistant Cancers

Project Description

Serum and glucocorticoid-induced kinase 1 (SGK1) is a stress-induced kinase that is involved in the mitigation of various cellular stressors, including modulation of cardiac ion channels, perturbations in metabolism, and maintenance of oncogenic signalling. SGK1 is not usually involved in normal homeostasis, which enables its inhibition to differentially target diseased tissues. Thryv has successfully developed a portfolio SGK1 inhibitors with its first one, LQT-1213, already in Phase 1b for the treatment of LQTS, and two others, THRV-1257 and THRV-1268 planned to enter the clinic in 2024 for the treatment of anaplastic thyroid cancer and atrial fibrillation respectively.

The student's project consists of carrying out experiments in the Laval laboratory using disease models to uncover novel biology of SGK1, including testing novel SGK1 inhibitors, measuring their effects on cancer cell proliferation, metabolic and immune-related readouts as well as exploring the mechanisms of SGK1 regulation at the transcription and post-translational level. The results obtained will support Thryv's clinical trials to develop biomarkers to predict patients' responses and identify additional diseases where SGK1 inhibition could benefit patients.

Contact information

Prof. Jose Teodoro, PhD
BIOC 491 Course Coordinator
jose.teodoro@mail.mcgill.ca

References:

- Giannetti et al. (2023): Gene- and variant-specific efficacy of serum/glucocorticoid-regulated kinase 1 inhibition in long QT syndrome types 1 and 2. Europace: 25(5): euad094 (link to article)
- Labit et al. (2023): The SGK1 Inhibitor THRV-1257 Induces Robust Tumor Regression and Overcomes Resistance to Standard of Care Dabrafenib Plus Trametinib in a Mouse Model of Anaplastic Thyroid Cancer (ATC) with BRAF V600E Mutation. Poster presented at the American Thyroid Association (link to poster)
- Bapat et al. (2022): Genetic inhibition of serum glucocorticoid kinase 1 prevents obesity-related atrial fibrillation. JCI Insight 7(19): e160885 (link to paper)
- Kim, Maengjo et al. (2022): SGK1 Inhibition Attenuates the Action Potential Duration in Re-Engineered Heart Cell Models of Drug-Induced QT Prolongation. Heart Rhythm 20(4): 589-595 (link to paper)
- Labit et al. (2022): Development of novel inhibitors of the serum/glucocorticoid induced kinase (SGK) family to address limitations of AKT/PI3K/mTOR inhibitors in breast cancer. Poster presented at the San Antonio Breast Cancer Symposium (link to poster)