SPECIAL DEPARTMENTAL SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

Barbara Vivash Award in Molecular Genetics

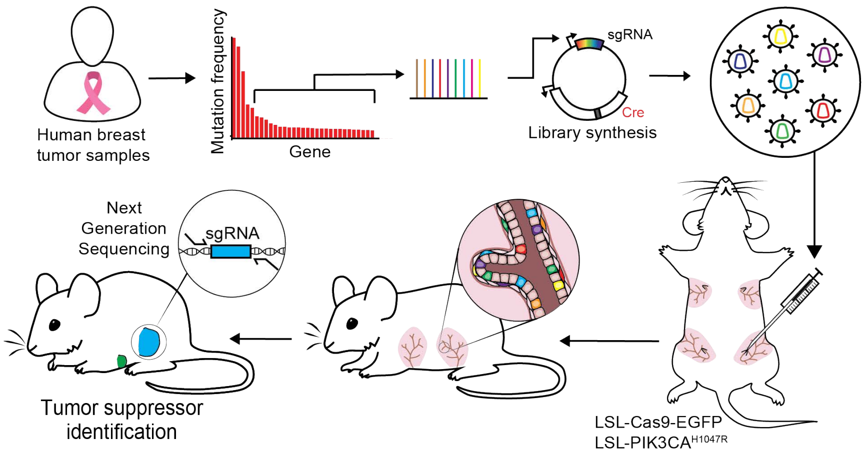
Seminar and Award Presentation

2022-2023 Recipient:

Ellen Langille, PhD

Postdoctoral Fellow
Sinai Halth | Lunenfeld-Tanenbaum Research Institute

In vivo screening for regulation of mammary tumor initiation



There are hundreds of genes mutated in breast cancer, but identification of functional driver mutations from among inconsequential bystanders remains challenging. We performed a somatic CRISPR/Cas9 mutagenesis screen to study 215 recurrent ‘long-tail’ breast cancer genes, which revealed epigenetic regulation as a major tumor suppressive mechanism. We identified that components of the BAP1 and the COMPASS-like complexes, including KDM6A, BAP1, ASXL1/2, and KMT2C/D, cooperate with PIK3CAH1047R to transform mouse and human breast epithelial cells. Mechanistically, we found that activation of PIK3CAH1047R and concomitant loss of epigenetic regulation triggered an alveolar-like lineage conversion of basal mammary epithelial cells and accelerated formation of luminal-like tumors. Mutations in epigenetic regulators are found in >39% of human breast cancers and milk protein expression can be seen in ~50% of ductal-carcinoma-in-situ, suggesting that lineage infidelity and alveolar mimicry may significantly contribute to breast cancer initiation.

Date: Monday, October 7th, 2024
Time: 3:00 PM
Place: Red Room: Donnelly Centre