**Project Outline:** Chronic myeloid leukaemia (CML) is a clonal disorder arising from the reciprocal translocation of chromosomes 9 and 22, resulting in a chimeric oncogene BCR-ABL1 that encodes a constitutively active tyrosine kinase. First-line treatment with tyrosine kinase inhibitors (TKIs), such as Imatinib, have revolutionized CML care. The unfortunate caveat is that most patients must take the inhibitors indefinitely; thus TKIs represent life-long treatment, resulting in ever-increasing costs to sustain remissions.

In our previous work, we used a comparative screen of normal vs CML stem cells and identified signalling hubs critical to *intracellular* signalling in primitive progenitor (CD34+) primary CML cells (1). Now our group would like to explore *extracellular* signalling events that happen in the tumour microenvironment that contribute to leukaemogenesis, namely extracellular vesicles(EVs), that mediate cell-to-cell communication events.

**Supervisor:** Dr. Sheela Abraham

**Project Title:** How extracellular vesicles effect stem cell function in Chronic Myeloid Leukaemia

**Keywords:** Chronic Myeloid Leukaemia, K562, extracellular vesicles, colony-forming assays

**Project Goals:** Analyze functional effects of CML EVs on normal stem cells

**Experimental Approaches:** Extracellular vesicles will be purified from K562 cell lines. Normal CD34+ cells (sourced additional from both bone marrow samples from healthy donors (Kingston General Hospital Clinical Flow Laboratory) will also be purified. The CD34+ cells will be cultured with the K562 leukaemia EVs. Extracellular vesicle-cultured cells will be functionally analyzed using specialised stem cell assays, and flow cytometry.

**References:**

