



What's raised on the island, stays on the island

Here are the ways in which your **2011 Westcoast Motorcycle Ride to Live** dollars are supporting local research:

Developing CBX7 antagonists as potential treatments for aggressive prostate cancer.

Lead Investigator: Dr. Fraser Hof

University of Victoria

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Despite advances in early detection and treatment, prostate cancer remains a leading cause of death in males in the developed world. Research focusing on what causes the invasiveness of prostate cancer has uncovered numerous proteins that are hijacked in the cancer cell. One such protein, EZH2, dramatically increases both the growth and invasiveness of prostate cancer, and its over-activity is a strong predictor of a patient's progression to the stage of hormone resistant, metastatic prostate cancer. A patient with high EZH2 levels has a much higher chance of succumbing to the disease. Our lab has discovered the first compound that blocks EZH2's product from binding to the protein (CBX7) that allows the readout of this deadly signal. Blocking CBX7's activity is a promising route to new drugs that treat cancers with this aggression-inducing signature. In order to translate this exciting result into a real advance for victims of prostate cancer, we are proposing here to conduct a large search of 55,000 drug-like chemicals in order to identify primary lead compounds that can be tested as novel treatments for advanced prostate cancer.

Small molecule inhibitors of EZH2/H3K27me3/CBX7 signaling as a targeted therapy to prevent and treat aggressive prostate cancer.

Principal Applicant: Kevin Daze

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Despite advances in early detection and treatment, prostate cancer remains a leading cause of death in males in the developed world. In addition, advanced prostate cancer diagnosed at a late stage is essentially incurable. Research focusing on what causes, or increases, the invasiveness of prostate cancer has uncovered numerous proteins that are potentially hijacked in the cancer cell. One such protein, EZH2, acts to increase both the growth and invasiveness of prostate cancer, and its over activity is an indication of poor patient outcome. Importantly, it is a driver of aggression that appears in $\geq 50\%$ of the hardest to treat, late-stage prostate cancers. Our lab has discovered a compound that blocks EZH2's mechanism of cancer promotion in a test tube. Currently there are no drug candidates available that halt the action of EZH2 — we aim to generate the first investigational drugs that shut down this promising anti-cancer target. We propose to tune our first compound to increase its potency and selectivity, with the ultimate goal of creating new prostate cancer treatments. In addition, I have developed a second approach to inhibit this same family of interactions. This is an exciting dual approach to target this pathway for treatment of prostate cancer. More synthetic chemistry work is needed to translate our initial results into real advances in the targeted treatment of prostate cancer. I am excited to be part of the **first and only** team to use chemical approaches to study and target this promising prostate cancer target.