

Depression affects 12-17% of the population, with women nearly twice as likely to be affected than men, and LGBTQ+ individuals facing a 2.5-time higher risk than heterosexual or cisgender people. Depression is a leading global cause of disability and presents a major risk factor for suicide. Anxiety and depression cost Canada nearly \$50 billion annually in healthcare, lost productivity, and reduced quality of life. Therefore, understanding how current treatments work can enhance their effectiveness, enhance their use, and inspire the development of more effective treatments. Growing evidence suggests that inhibition of hyperpolarization-activated cyclic-nucleotide gated (HCN) channels can provide an effective treatment approach. Using a combination of electrophysiology, computational docking, and molecular dynamics simulations, we aim to understand if HCN channel inhibition contributes to the mechanism of action for drugs that are currently prescribed to treat neuropsychiatric disorders (anxiety, depression, bipolar disorder, and schizophrenia). We are further attempting to identify and characterize potential binding sites for these drugs, and the chemical properties that contribute to effective protein-drug interactions.