Undergraduate research opportunities (Winter/Summer 2024) for Chemistry & Biochemistry/Biology//Physics/Chemical & Materials Engineering students

Molecular dynamics simulations to gain insights into NOTCH4 mutations in breast cancer stemness

Molecular Dynamics (MD) simulations are a potent computational tool with wide-ranging applications across various scientific fields. Their primary significance lies in their capacity to offer intricate insights into the behavior of molecules and materials at the atomic and molecular levels. MD simulations are instrumental in expanding our understanding of biology, unraveling disease mechanisms, propelling drug development, and advancing biotechnology. Moreover, it enables researchers to delve into the intricate interplay among protein structure, function, and genetic factors, ultimately fostering innovative solutions in interdisciplinary scientific pursuits.

Our drug design team focuses on the investigation of structural and transcriptional proteins from diverse pathogens and cancer types. For instance, the NOTCH homolog-4 (NOTCH4) protein coding gene is frequently mutated in several cancer types, but its role in immunotherapy is still unclear. Point mutations in the NOTCH4 gene may also play a role in tumor-suppressive or oncogenic mechanisms depending on the tissue microenvironment. However, the structural and functional effects of mutations in NOTCH4 protein mutants remain unclear. Through the application of MD simulations, we can explore various facets of NOTCH4 protein mutations, encompassing protein folding dynamics, the identification of potential drug targets, unraveling protein structure-function relationships, and elucidating mechanisms of drug resistance or breast cancer stemness.

In the proposed research project, the student will embark on a comprehensive study of the structural and functional characteristics of native and mutant NOTCH4 proteins. This work will involve the application of homology modeling, and the analysis of crucial parameters derived from MD simulations, such as root-mean square deviation (RMSD), root-mean-square fluctuation (RMSF), radius of gyration (Rg), solvent accessible surface area (SASA), and the quantification of hydrogen bonds (NH-bonds). To facilitate this investigation, the student will have access to cutting-edge computing resources within the Centre for Research in Molecular Modeling (CERMM) and the Digital Research Alliance of Canada (formerly Compute Canada). Additionally, they will benefit from the collective expertise of our scientific and technical team, participate in team meetings, and engage in scientific discussions throughout the project's duration. This collaborative and technologically advanced environment will provide an ideal platform for the student to contribute meaningfully to the field of MD simulations and their applications in human therapeutics design and development.

Keywords: cancer; homology modeling; mutation; protein-protein docking; MD simulations