UNBC UNIVERSITY OF NORTHERN BRITISH COLUMBIA

SMALL MOLECULES IN DRUG DISCOVERY AND DISEASE DIAGNOSTICS

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In this talk, I will give an overview on various scaffolds of compounds of interest in drug discovery, focusing on benzimidazoles as sirtuin inhibitors. Sirtuins are class III histone deacetylase (HDAC) enzymes that target both histone and non-histone substrates. Sirtuin 1 (SIRT1) and Sirtuin 2 (SIRT2) are the most studied among the seven sirtuins found in human (SIRT1-7). They have been implicated in various age-related diseases such as cancer, neurological disorders and cardiovascular diseases. Functionalized benzimidazoles were identified by our group as sirtuininhibitors. The benzimidazole core represents a novel scaffold for sirtuin inhibition. Hyperacetylation of p53 and α-tubulin, which are direct cellular targets of SIRT1 and SIRT2 respectively, corroborated the enzymatic results. Docking analysis indicated that the benzimidazoles were positioned in the NAD+ active site, thus supporting the notion of dislodging the co-factor as their likely inhibition mechanism. Some of the promising inhibitors displayed high autofluorescence which can be utilized to predict their localization in cells. The compounds were also found to display antiproliferative effects against a panel of cancer cell lines tested.
Other research areas of interest which will be touched upon include small molecules as ChAT modulators and hybrid molecules as antibacterial agents.

- PRESENTATION DETAILS

8 August 1:30 - 2:30	LOCATION 9-235

*This will be in-person only