Fragment-Based Ligand and Drug Discovery (FBLDD) *via* marine natural products to fight insulin resistance and inflammatory disorders associated with metabolic syndrome

This research project aims at exploiting the chemical diversity inspired by marine natural products (MNPs) for the discovery of new leads to reduce the main risk factors that promote the development of metabolic syndrome, particularly insulin resistance and obesity, and the complications, even inflammatory, of Type 2 Diabetes Mellitus (T2DM). These pathologies feature a high hospitalization and mortality rate and represent an important comorbidity factor for respiratory viral infections. MNPs may also serve as biologically validated starting points for the design of focused libraries that might provide ligands with enhanced quality and probability.[1,2] Complex MNPs are used as starting or guiding materials for generation of synthetic fragment sets of unprecedented bioactive substructures that retain only certain parts of MNP structure while modifying other portions. This project addresses the exploration of MNPs biologically relevant chemical space in an MNP-informed Fragment-Based Ligand and Drug Discovery (FBLDD) campaign[3] to enable the discovery of small molecules that bind/modulate specific targets involved in the onset of T2DM and its chronic complications. This approach exhibits several advantages over high-throughput screening campaigns, it becomes an attractive strategy in target-based drug discovery. The main goal of the research project is the development of new multitarget antidiabetic and anti-inflammatory ligands able to efficiently bind specific and selected target proteins (i.e., PTP1B, aldose reductase, human 15-lipoxygenase-1, α-glucosidase). Research activities at Department of Pharmacy will include the isolation of new molecules isolated from marine sources, their chemical manipulation, the creation of small chemical libraries for SAR studies and their chemical characterization.

References

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