Applications of computational methods in chemical biology: From designing new drugs to resurrecting the dead proteins

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Computational approaches – from bioinformatics to biomolecular modeling and simulations – have emerged as important tools in the fields of chemical biology and drug design. Recent developments in advanced computational methods coupled with sophisticated software programs and state-of-the-art supercomputing facilities have allowed them to work in tandem with experiments to understand the intricate mechanisms behind molecular recognition processes. This talk will highlight the examples where computational approaches have helped in three different applications: accelerating the initial hit-identification stage in drug discovery, developing new biocatalysts through ancestral protein resurrection, and predicting off-target-based cardiotoxic effects of drugs. The first example will present the discovery of key molecular channel properties of class I histone deacetylases (HDAC) and the design of novel HDAC inhibitors using a variety of advanced simulation methods and a hybrid virtual screening workflow. The second example will discuss the development of new computational phylogeny methods and the design of novel transaminase biocatalysts using bioinformatics-driven ancestral state reconstruction and experimental validation. Finally, an integrated computational workflow for predicting the off-target drug interactions with hERG ion channel will be presented.
Biography

Dr. Subha Kalyaanamoorthy received her Masters in Bioinformatics from Annamalai University, India in 2007. She started her research career as a junior research fellow in the AU-KBC bioinformatics center, Anna University, India. In 2009, she was awarded the post-graduate research scholarships from La Trobe University, Australia to pursue her Ph.D. under the supervision of Prof. Phoebe Chen. Her doctoral thesis titled, “Structure- and ligand-based investigation of histone deacetylases towards cancer drug discovery” focused on using computational methods to understand and develop small molecule inhibitors for targeting an epigenetic mechanism. Soon after completing her doctoral research in 2013, she received the Common wealth Scientific and Industrial Research Organization (CSIRO) OCE-post- doctoral fellowship. She worked at the Bioinformatics and phylogenomics team headed by Dr. Lars Jermiin at CSIRO. Her research focused on developing and applying computational methods for understanding and inferring the structure-function-evolution of biomolecules. Subha is currently an NSERC post-doctoral fellow at the faculty of pharmacy and pharmaceutical sciences, the University of Alberta working with Dr. Khaled Barakat. Her research at UoA is focused on modeling and simulations of cardiac ion channels and predicting the drug-induced cardio-toxic effect using computational methods. She has published peer-reviewed articles in high-impact journals, including Nature Methods, Green Chemistry and Drug Discovery Today.