Molecular Design of Therapeutics for the other “Pandemics”

Speaker: Prof. Krishna Kumar, Tufts University

Abstract: Obesity, Type 2 Diabetes (T2D) and related metabolic disorders afflict hundreds of millions worldwide. Two endogenous gut peptide hormones called ‘incretins’ have emerged as frontline treatments. These peptides, Glucagon-like Peptide 1 (GLP-1) and Glucose-dependent Insulinotropic Peptide (GIP) stimulate their cognate receptors (GLP-1R and GIPR) in different tissues with the primary function of maintaining glucose homeostasis in addition to having neuro- and cardioprotective effects. These peptides however suffer from poor metabolic stability and are rapidly degraded by the ubiquitous serine protease, dipeptidyl peptidase IV (DPP-4). We describe here the design and development of potent peptide analogues that are completely refractory to hydrolytic enzyme action while retaining full biological activity, potency, and efficacy. The platform allows for the design of hundreds of derivatives with the ability to tune the onset and duration of action, potency, efficacy, and providing a method for modulating gut and blood brain barrier (BBB) penetration. This lecture will describe the fundamental design principles, molecular pharmacology and in vivo data. Some of the compounds described here rival or better the compounds used in the clinic today and could serve as a model platform for discovery of clinically relevant molecular entities.

Biography: Krishna Kumar is Robinson Professor of Chemistry at Tufts University. His research program is at the intersection of Chemistry, Biology and Medicine. Kumar’s contributions to science have been recognized widely. He was named a DuPont Young Professor, and recognized as one of the top 35 young innovators in the world by MIT Technology Review magazine (TR35). He was awarded a Global Indus Technovator award from MIT-IBC (2006), the National Science Foundation CAREER award (2003), a Technology award from the Massachusetts Technology Transfer Center, and a BASF Distinguished lectureship in Ludwigshafen, the Indian Society of Chemistry and Biology (ISCB) award for Excellence in the Chemical Sciences (2011) and was elected fellow of the American Association for the Advancement of Science (2012) and of the Royal Society of Chemistry, UK (2018).