



SEMINAR ANNOUNCEMENT

We would like to invite you to attend this seminar hosted by Prof. Vinay Tergaonkar and Prof. Song Hai Wei:

Date: 8 May 2019, Wednesday

Time: 11:00AM – 12:00PM

Venue: Level 3, IMCB Seminar Room 3-46, Proteos, Biopolis

Speaker: Professor Liang Tong, William R. Kenan, Jr. Professor, Department Chair, Department of Biological Sciences, Columbia University, USA

Title: Structural studies on metabolic enzymes and relevance to human health

Abstract:

My laboratory has a long-standing interest in understanding the molecular mechanisms for the functions of metabolic enzymes, including their modulation by small molecules, as many of them are attractive targets for drug discovery against human diseases. The presentation will focus on our research on two of these enzymes, acetyl-CoA carboxylase (ACC) and ATP-citrate lyase (ACLY). An inhibitor against ACC is currently in phase 2 clinical trials against the liver disease NASH (non-alcoholic steatohepatitis), and an inhibitor against ACLY is in phase 3 clinical trials against hypercholesterolemia. We have determined the structure of the 500 kDa homodimer of yeast ACC by crystallography, revealing its mechanisms of catalysis, regulation by phosphorylation, and modulation by a collection of small molecules. Most recently, we have determined the structure of the 480 kDa homotetramer of human ACLY in complex with a nanomolar inhibitor by cryo electron microscopy. The inhibitor is located in an allosteric, mostly hydrophobic cavity next to the citrate binding site, and requires extensive conformational changes in the enzyme that indirectly disrupt citrate binding. This allosteric site greatly enhances the 'druggability' of ACLY and represents an attractive target for developing new ACLY inhibitors.

Biography:

Liang Tong is currently the William R. Kenan, Jr. Professor and Chair of Department of Biological Sciences, Columbia University, New York. He received his B.Sc. from Peking University, Ph.D. from University of California, Berkeley with Professor Sung-Hou Kim, and was a post-doctoral fellow with Professor Michael Rossmann at Purdue University. He was then at Boehringer Ingelheim Pharmaceuticals, Ridgefield, Connecticut, where he established the first protein crystallography/structure-based drug design laboratory in the company. He joined the faculty at Columbia in 1997, and established a vigorous research program in structural biology. He has made fundamental contributions to understanding the molecular mechanisms of many biological processes, especially metabolic enzymes and proteins involved in RNA processing. He has many papers in journals of the highest impact (Nature, Science and Cell), out of more than

280 publications (h-index 75). He was elected a fellow of the American Association for the Advancement of Science in 2009.

ALL ARE WELCOME (No registration required)

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