



Institute of
Molecular and
Cell Biology

SEMINAR ANNOUNCEMENT

We would like to invite you to attend this seminar hosted by Prof. Wanjin Hong:

Date: 11 July 2014, Friday

Time: 4:00PM – 5:00PM

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

Speaker: Prof. Ming-Wei Wang, Professor of Pharmacology, Shanghai Institute of Materia Medica, Chinese Academy of Sciences

Title: Class B GPCR drug discovery: from serendipitous findings to organized efforts

Glucagon-like peptide-1 (GLP-1)-based therapy presents a promising option for treating type 2 diabetes. However, several limitations exist relative to peptidic GLP-1 mimetics presently on the market or under development. Here, the discovery, characterization and current status of a cyclobutane derivative based non-peptidic GLP-1 receptor (GLP-1R) agonist Boc5 will be briefly reviewed. While its oral bioavailability still poses great challenges, the attainments provide significant encouragement for our ongoing search for a truly 'druggable' small molecule GLP-1R agonist.

GLP-1R belongs to class B family of G-protein coupled receptors. We have recently solved the crystal structure of human glucagon receptor (GCGR) that share 48% sequence homology with GLP-1R. Its 7-transmembrane helical domain 3-D structure, complemented by extensive mutagenesis studies and a hybrid model of glucagon bound to GCGR, gives us invaluable insights into the ligand recognition by these receptors. With the newly found knowledge and various technology platforms established, we have initiated a collaborative project to determine the structures of six GPCRs associated with metabolic disorders, including GLP-1R. Preliminary studies on 97 mutant GLP-1Rs suggest that, apart from overlapping hotspots between GLP-1R and GCGR, the differences in respective ligand interaction are significant. These efforts may lead to highly optimized drug candidates with improved efficiency.

Biography:

Following medical practices in Shanghai, Dr. Ming-Wei Wang obtained his Ph.D. from University of Cambridge in 1989. He worked for a couple of US-based biotechnology companies a year later and served as a consultant to Merck and UNDP relative to China-related projects in the mid-1990's. Thereafter, he was engaged in various entrepreneur activities. Dr. Wang was appointed to the faculty at the Shanghai Institute of Materia Medica, Chinese Academy of Sciences in 2001 and Director of the National Center for Drug Screening in 2003. In 2004, he was named by the Shanghai Pudong New District Government as a Senior Business Advisor, and in 2011, he becomes the first director of Chinese National Compound Library and one of the key project leaders of China's mega program on drug discovery and development. He presently serves as an editorial board member of *Trends in Pharmacological Sciences (TiPS)*, *Biochemical Journal* and *Acta Pharmacologica Sinica*.

ALL ARE WELCOME (No registration required)