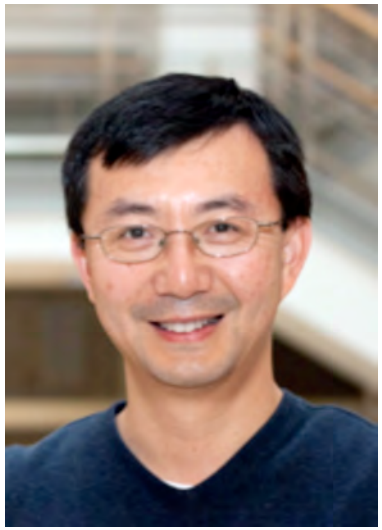

2013-2014 POCC Lecture Series

March 27, 2014, 8:00 PM

Prof. Jian Jin

University of North Carolina at Chapel Hill

A Multifaceted Strategy for Discovering Chemical Probes of Histone Methyltransferase

Carolyn Hoff Lynch Lecture Hall
Chemistry Building, University of Pennsylvania

The Philadelphia Organic Chemists' Club

POCClub.org

Dr. Jin is currently an Associate Professor in the Division of Chemical Biology and Medicinal Chemistry, Associate Director of Medicinal Chemistry in the Center for Integrative Chemical Biology & Drug Discovery, Associate Professor in the Department of Pharmacology, and Member of Lineberger Comprehensive Cancer Center at the University of North Carolina - Chapel Hill (UNC-CH). Research in his laboratory focuses on discovering chemical probes of histone methyltransferases and functionally selective ligands of G protein-coupled receptors. Prior to joining UNC-CH in 2008, Dr. Jin had > 10 years of drug discovery experience at GlaxoSmithKline, where he had most recently served as a Manager of Medicinal Chemistry from 2003 to 2008. Dr. Jin received a B.S. degree in chemistry from University of Science and Technology of China in 1991 and a Ph.D. degree in synthetic organic chemistry from the Pennsylvania State University in 1997 under the guidance of Professor Steven Weinreb. He then completed one year of postdoctoral training at Professor T.V. RajanBabu's laboratory at the Ohio State University prior to joining GSK. To date, Dr. Jin has published 77 peer-reviewed papers and delivered 46 invited talks. He is also an inventor of 9 issued U.S. patents and 37 published PCT patent applications.

Abstract: Mounting evidence suggests that post-translational modifications of histones play a critical role in diverse biological processes including chromatin compaction, gene expression, transcriptional regulation, and cell differentiation. Among the "writers", "readers", and "erasers" involved in chromatin regulation, histone methyltransferases (HMTs) have received great attention as a new class of potential therapeutic targets. Well-characterized chemical probes of HMTs will permit disease hypotheses concerning these enzymes to be tested with high confidence in cell-based and/or animal models. However, very few chemical probes of HMTs have been created despite the fact that more than 50 human HMTs have been identified and characterized. To address this issue, my laboratory has pursued a multifaceted structure-based probe discovery strategy over last 5 years. In this talk, our discoveries of substrate-competitive chemical probes of G9a and GLP, allosteric inhibitors of PRMT3, and cofactor-competitive chemical probes of EZH2 and EZH1 will be presented.