



*The Chinese University of Hong Kong
Department of Chemistry
Research Seminar Series*

Speaker: Professor Claudio J. Margulis
Department of Chemistry
The University of Iowa

Title: Using Computer Simulations to Unravel the Structure and Dynamics of Room-Temperature Ionic-Liquids

<< Abstract >>

As opposed to other more common solvents, room-temperature Ionic Liquids (ILs) are characterized by symmetries on multiple length scales defined by their amphiphilic nature as well as by networks of charge alternation. Transport in these structurally heterogeneous systems is also highly complex with local friction that is often not well described by the overall viscosity. During my talk, I plan to present a brief overview of what the current understanding is of structure and dynamics of ionic liquids and molecules dissolved in them as well as challenges that remain unaddressed.

Date: February 9, 2017 (Thursday)

Time: 2:30 p.m.

Venue: Room G35, Lady Shaw Building



ALL ARE WELCOME

Contact Person:
Prof. Steve Y.L. Tse



*The Chinese University of Hong Kong
Research Seminar Series*

Jointly Organized by
Department of Chemistry and School of Pharmacy

- Speaker:** Prof. Ram I. Mahato
Department of Pharmaceutical Sciences
University of Nebraska Medical Center, USA
- Title:** Precision Medicines of Small Noncoding RNA and Small Molecules for Treating Liver Fibrosis
- Date:** February 17, 2017 (Friday)
- Time:** 2:00 p.m.
- Venue:** L2, Science Centre

< Abstract >

Liver fibrosis is characterized by overproduction of type $\alpha 1(I)$ collagen by hepatic stellate cells (HSCs). In spite of continued research, development of therapeutic strategies to reduce and/or reverse hepatic fibrosis remains a challenge. RNA-based therapeutics is a promising approach for treating liver fibrosis. Among various RNA molecules, siRNA and miRNA have emerged as attractive target molecules and targets for amelioration of human disease. Our recent research has focused on siRNA, shRNA and miRNA-mediated gene silencing to inhibit hepatic fibrosis. We have screened various siRNA sequences targeting TGF- $\beta 1$ and chosen potent sequences for bioconjugation or conversion into shRNA. We have identified miRNAs downregulated in liver fibrosis and designed miRNA mimics to restore their expression, thereby inhibiting collagen synthesis. Furthermore, we have synthesized copolymers suitable for delivery of these RNA molecules either alone or with small molecules targeting hedgehog pathway. For their site-specific delivery, we have conjugated these RNA molecules with mannose 6 phosphate polyethylene glycol (M6P-PEG) for targeting HSCs. There was synergism in gene silencing when siRNAs targeting two different regions of TGF- $\beta 1$ mRNA were used as a pool. Bioconjugation of siRNA with M6P-PEG had beneficial effect on gene silencing even in the absence of any cationic liposomes or polymers as confirmed by transfecting M6P-PEG-siLuc to HSC-T6 cells, respectively. miR-29b1 targets several profibrotic genes, such as collagen type I & IV, c-MYC, PDGF- β and PI3K/Akt, which are upregulated in liver fibrosis. Transfection of miR-29b1 mimic in HSCs resulted in a dose-dependent decrease in collagen expression. Combination therapy was more effective in providing hepatoprotection, lowering liver injury related serum enzyme levels, reducing fibrotic protein markers compared to monotherapy. In conclusion, RNA based therapy approach holds promise to treat liver fibrosis, provided that right target, right sequence and right delivery system are chosen. I will be highlighting the importance of these three Rs and will discuss the challenges associated with their delivery.

Biography

Ram I. Mahato is a Professor and Chairman of the Department of Pharmaceutical Sciences, University of Nebraska Medical Center, Omaha, NE. He was a professor at the University of Tennessee Health Science Center, Research Assistant Professor at the University of Utah (with Sung Wan Kim), Senior Scientist at GeneMedicine, Inc., and as a postdoctoral fellow at the University of Southern California in Los Angeles (with Vincent HL Lee), Washington University in St. Louis, and Kyoto University, Japan (with Mitsuru Hashida). He received PhD in Drug Delivery from the University of Strathclyde, UK and BS from China Pharmaceutical University, Nanjing. He has published 128 papers, 17 book chapters, holds 2 US patents, and has edited/written eight books and ten journal issues (Total Google Citations= 7875 and h-Index =52). He was a Feature Editor of the Pharmaceutical Research (2006-2013) and Editorial Board Member of eight journals. He is a CRS Fellow (2011), AAPS Fellow (2010), Permanent Member of BTSS/NIH Study section (2009-2013), and ASGCT Scientific Advisor (nonviral vectors, 2006-2009). He is applying sound principles in pharmaceutical sciences in the context of the latest advances in life and material sciences to solve challenging drug delivery problems in therapeutics.

