

6th International Conference on

Structural Biology

August 22-23, 2016 New Orleans, USA



Prasanna R Kolatkar

Hamad bin Khalifa University, Qatar

Integrated methods enable re-engineering of transcription factors allowing cell fate modification

Transcription factors (TFs) are key players in early cell development which direct cells towards specific fates. The Sox family of TFs is composed of 20 members and responsible for directing a wide variety of fates. The ability of highly similar TFs to carry out such distinct outcomes had been a conundrum to date. We have studied several Sox-DNA (HMG domain) structures in my laboratory which all display essentially similar structures. The Sox binding motif is only 6-8bp long and this once again raises the question as to how specificity can be achieved. We discovered that a critical Sox17 residue involved in protein interaction with its partner Oct4 (POU domain) helps to install specificity of binding to its cognate DNA and consequently give rise to endoderm. Subsequently we were able to re-engineer Sox17 through a single residue mutant and convert it into a potent pluripotent TF by substituting Sox2 in the standard induced pluripotent stem cell cocktail composed of 4 TFs. Next we also studied the genomic profiles of native and mutant Sox TFs through a battery of ChIP-seq experiments to validate the *in-vitro* results. The integrated application of structural and genomic methods have allowed us to analyze and understand how highly similar TFs can partner each other through key interaction points which give rise to highly specific outcomes. TF function can be altered through modified TF forms as well as novel ligands which could have applications in disease and therapy.

Biography

Prasanna R Kolatkar has completed his PhD at the University of Texas at Austin in 1991 in the Department of Chemistry and Biochemistry and Post-doctoral studies in the Laboratory of Michael Rossmann at Purdue University where he has received a Jane Coffin Childs Memorial Fund Fellowship. Upon moving to Singapore in 1997, he has worked at the Bioinformatics Center and Institute of Molecular and Cell Biology in Singapore before joining the Genome Institute of Singapore in 2001. Subsequently he has joined QBRI in 2013. Recently his work has focused on re-engineering of stem cell function through directed mutagenesis of key residues involved in protein-protein interactions.

pkolatkar@qf.org.qa