TIFR Centre for Interdisciplinary Sciences
21, Brundavan Colony, Narsingi, Hyderabad 500 075

Internal Seminar

Synthesis and characterization of small molecule inhibitors for AF6 PDZ-domain

Laxman M. Alakonda

TCIS - Hyderabad

PDZ (PSD-95, Dlg, ZO-1) domains are ubiquitous interaction modules involved in many cellular signal transduction pathways and are therefore potential targets for inhibition and drug development.[1] Herein, I will be discussing the synthesis and characterization of small molecule inhibitors that are known to bind AF6 PDZ-domains. Using solution state NMR we have characterized the binding site and estimated the binding constants of small molecule inhibitor to AF6 PDZ-domains. The final aim of our project is to study changes in ps-ns dynamics of PDZ domain as a function of ligand binding affinity.

Secondly, I will discuss the synthesis and characterization of zoledronic acid (ZA),[2,3] which is a bisphosphonate drug molecule used to treat bone diseases in cancer patients. ZA exists in different pseudo polymorphs. Different solid-state forms of ZA have different impacts on its existence. Previous reports have used DSC, TG, and XRD to show that ZA exists in three different pseudo polymorphs.[4] The monohydrated and trihydrated forms have different crystal structures and show differential thermal behaviors. We are interested in studying the dynamic properties of water molecules in different pseudo polymorphs using solid-state NMR.

References:

1) Carolyn Vargas et al. ChemMedChem, 2014, 9, 1458-62; (DOI: 10.1002/cmdc.201300553)
2) Santosh K. Singh et al. Beilstein J. Org. Chem. 2008, 4, 42 ;(DOI: 10.1002/cmdc.201300553)
3) Samer S. Ratrout et al. Pharmaceutical Chem. J., 2015, 48, 12; (DOI 10.1007/s11094-015-1205-0)
4) Romina Ruscica et al. J. Pharma. Sci, 2010, 99, 12; (DOI 10.1002/jps.22223)

Wednesday, Mar 8th 2017

2:00 PM (Tea/Coffee at 1:45 PM)

Seminar Hall, TCIS