REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Structural basis for telomerase RNA recognition and RNP assembly by the holoenzyme La family protein p65

Mahavir Singh, PhD

Department of Biochemistry
University of California Los Angeles, USA

Tuesday, March 5, 2013
4:00 pm
Seminar Room

REGIONAL CENTRE FOR BIOTECHNOLOGY

Seminar series

Mahavir Singh, PhD

Abstract

Telomerase is a ribonucleoprotein (RNP) complex essential for maintenance of telomere DNA at linear chromosome ends. Low levels of telomerase activity are implicated in cellular senescence and aging, whereas high telomerase activity drives cancer cell proliferation. The catalytic core of *Tetrahymena* telomerase comprises a ternary complex of telomerase RNA (TER), telomerase reverse transcriptase (TERT), and the essential La family protein p65. p65 is a La module containing protein that has a unique C-terminal domain. The p65 C-terminal domain is essential and sufficient for the hierarchical assembly of TERT with TER. Here, I present the solution NMR and crystal structures of p65 C-terminal domain free and in complex with stem IV of TER. The structures reveal that RNA recognition is achieved by a novel combination of single- and double-stranded RNA binding, which induces a large conformational change in telomerase RNA essential for catalytic core assembly. This work provides the first structural insight into biogenesis and assembly of TER with a telomerase-specific protein. Additionally, this study defines a structurally homologous domain (xRRM) in genuine La and LARP7 proteins and suggests a general mode of RNA binding for their diverse RNA targets.