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

Seminar

Non-canonical docking mediated phosphorylation by the MAP kinase ERK2

Ranajeet Ghose

The City College of New York, NY

The mitogen activated protein (MAP) kinase ERK2 recognizes substrates containing consensus docking motifs (D-site, F-site) resulting in the phosphorylation on specific Ser/Thr-Pro sequences. The transcription factor Ets-1 possesses no canonical docking motifs, yet it is efficiently phosphorylated by ERK2 at a consensus Thr site (T38). We demonstrate that this phosphorylation is enabled by a unique bipartite mode of ERK2 engagement by Ets-1 and involves two sub-optimal non-canonical docking interactions in lieu of the usual single canonical interaction. The Ets-1 N-terminus recognizes the ERK2 D-recruitment site (DRS) through a "fuzzy" interaction, while the C-terminal pointed (PNT) domain engages in a largely rigid body interaction with a portion of the ERK2 F-recruitment site (FRS). These two spatially distinct docking interactions, while individually weak, enable the specific recognition of ERK2 by Ets-1 and the optimal localization of its dynamic phospho-acceptor at the kinase active site. This enables the phosphorylation of Ets-1 through a "proximity-mediated" mechanism that appears to be conserved between all ERK2 substrates.

Friday, June 16th 2017

4:00 PM (Tea/Coffee at 3:45 PM)

Seminar Hall, TCIS