

Seminar

NON-CANONICAL DOCKING MEDIATED PHOSPHORYLATION BY THE MAP KINASE ERK2

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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 Frecruitment 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 "proximity-mediated" of Ets-1 through а 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