

BEN TURK (OC '90)

YALE UNIVERSITY

WEDNESDAY

NOVEMBER 12, 2008

4:45 P.M.

SCIENCE CENTER A255

Protein Kinase Substrate Targeting In and Out of the Active Site

Eukaryotic organisms dedicate some 2% of their genes to encode protein kinases, underscoring the widespread importance of protein phosphorylation in the regulation of myriad cellular actions. Phosphorylation on serine, threonine and tyrosine can modulate protein function in many ways: by controlling subcellular localization, by acting as a tag for protein degradation or stabilization, by triggering the assembly of multiprotein complexes, or by allosterically regulating biochemical activity. Identifying the protein substrates for a kinase is critical to understanding its biological function. Protein kinases select their substrates through specific and complementary physical interactions. For example, sequences surrounding phosphorylation sites must have shape and charge complementarity with the kinase active site cleft. In addition, so-called docking interactions with regions outside of the active site enhance substrate affinity and specificity. Using peptide library screening, my laboratory has determined the specific sequence motifs for phosphorylation by multiple kinases that play roles in controlling cell growth, proliferation and survival. We have elucidated the fundamental mechanisms by which kinases achieve their specificity through a combination of X-ray crystallography, computational modeling, and site-directed mutagenesis. These approaches have also allowed us to identify potential protein substrates for these kinases that act as their downstream effectors in cellular signaling pathways.

THERE WILL BE A RECEPTION FOR THE SPEAKER AT 4:30 P.M.
WEDNESDAY IN LOVE LOUNGE, REFRESHMENTS WILL BE PROVIDED

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