

LECTURE #8: PHOSPHOPROTEIN PHOSPHATASES

1. General considerations
 - Phosphoprotein phosphatase super-families
 - Conserved primary structures and core catalytic domains
 - Differing modes of regulation

2. Kinetic analysis of phosphate hydrolysis
 - Substrate recognition and selectivity
 - Use of synthetic peptides
 - Use of generic protein substrates
 - Identification of authentic in vivo targets
 - Hydrolytic reaction mechanisms

3. Structural basis for substrate selectivity
 - Ser-/Thr-directed phosphoprotein phosphatases
 - Tyr-directed phosphoprotein phosphatases
 - Atypical phosphoprotein phosphatases
 - P-Ser/P-Thr-directed, e.g. Fcp1 (member of NIF-BRCT superfamily)
 - P-Tyr-directed, e.g. Eyes Absent [member of the haloacid dehalogenase (HAD)-like hydrolase superfamily]
 - Dual-specificity phosphoprotein phosphatases
 - The curious case of PTEN

4. Structural basis of regulation
 - Regulation of activity
 - PP2B (calcineurin): Ca^{2+} , calmodulin, and immunosuppression
 - PP2A: Sit4, SAPs, and TAPs, and Tor2/RAFT/mTOR
 - Regulation of localization
 - PP1 and targeting subunits
 - Receptor-associated SH2 domain-containing PTPases