Quantitative & Chemical Biology Graduate Training Program

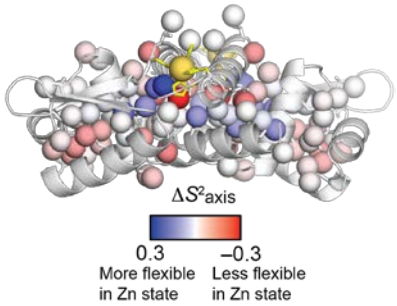
QCB Evenings

Wednesday, February 24 • 5:30pm • Chemistry C122

Entropy Redistribution Drives Allostery in a Metalloregulatory Protein

DAIANA CAPDEVILA, GIEDROC LAB

Allosteric communication between two ligand-binding sites in a protein is a central, yet poorly understood, aspect of biological regulation. Here we show that perturbations in equilibrium picosecond-nanosecond motions drive zinc (Zn)-induced allosteric inhibition of DNA binding by the Zn efflux repressor *Staphylococcus aureus* CzrA, as measured by NMR spectroscopy. DNA binding leads to an unanticipated increase in methyl side-chain flexibility and thus is stabilized by a substantial favorable entropic driving force; Zn binding specifically redistributes these motions, inhibiting formation of the DNA complex. Allosterically impaired CzrA mutants are characterized by distinct non-native fast internal dynamics "fingerprints" upon Zn binding, and DNA binding is weakly regulated. We demonstrate the predictive power of the wild-type dynamics fingerprint to identify key residues in dynamics-driven allostery. This work provides an illustration of how entropic driving forces can be harnessed by nature to evolve new allosteric ligand specificities in a compact molecular scaffold.



Proteolysis of SwrA by the LonA protease is mediated by the C-terminal region of SwrA

ANNA C. HUGHES, KEARNS LAB

Bacillus subtilis is a motile bacterium capable of swimming in liquid and swarming atop a surface. Both forms of motility are powered by the same flagellar system, however swarming motility requires approximately 2 fold more flagella than swimming motility. When inoculated on surface the transcriptional activator, SwrA, accumulates within the cell and results in an increase in flagellar gene transcription and an increase in flagellar density. Intracellular SwrA levels are low in swim cells due to proteolytic turnover by a AAA+ protease, LonA, and its putative adapter SmiA. How LonA/SmiA recognizes SwrA remains unknown. Here we show that the C-terminal region of SwrA is important for turnover by LonA. We hypothesize that the C-terminal domain of SwrA contains a specific degron sequence that is recognized by LonA/SmiA and targets SwrA for proteolysis.

All QCB Trainer Lab Personnel are invited to attend.
Food and beer will be provided.

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