

Seminar 2016



Allosteric control of protein function with disorder

We designed a regulatable multi-state protein for protein engineering. New protein, uniRapR, has a novel topology, whose conformation is regulated by the binding of a small molecule rapamycin. We validated switching ability of uniRapR in silico, in vitro, cell cultures, and in zebrafish. As a proof of concept, uniRapR is used as an artificial regulatory domain to control activity of kinases. By activating Src kinase using uniRapR in single cells and whole organism, we observe two novel phenotypes consistent with its role in metastasis. Activation of Src kinase leads to rapid induction of protrusion with polarized spreading in HeLa cells, and morphological changes with loss of cell-cell contacts in the epidermal tissue of zebrafish. The rational creation of uniRapR exemplifies the strength of computational protein design, and offers a powerful means for targeted activation of many pathways to study signaling in living organisms.

Inhibited kinase Active kinase Nikolay V. Dokholyan Michael Hooker Distinguished Professor KD Department of Biochemistry and Biophysics University of North Carolina at Chapel Hill **Genetics Medicine** KD KD Friday April 22, 2016 2:30 PM Laufer Center Lecture Hall 101 Host: Dima Kozakov **Refreshments following seminar** Stony Brook University For a disability related accommodation, please call 631-632-5400