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Simultaneous Tuning of Activation and Repression in Intrinsic Disorder-Mediated Allostery

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Intrinsically disordered proteins (IDPs) present a functional paradox because they lack stable tertiary structure, but nonetheless play a central role in signaling. Like their structured protein counterparts, IDPs can transmit the effects of binding an effector ligand at one site to another functional site, a process known as allostery. Because allostery in structured proteins has historically been interpreted in terms of propagated structural changes that are induced by effector binding, it is not clear how IDPs, lacking such well-defined structures, can allosterically affect function. Here we show mechanistically how IDPs allosterically transmit signals through a probabilistic process that originates from the simultaneous tuning of both activating and repressing ensembles of the protein, using human glucocorticoid receptor as a model. Moreover, GR modulates this signaling by producing translational isoforms with variable disordered regions. We expect this ensemble model of allostery will be important in explaining signaling in other IDPs.

Tuesday 20 October 2015 at 4.00 P.M.

COFFEE AND TEA WILL BE SERVED AT 3.45 P.M. IN FRONT OF THE SOLVAY ROOM

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