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Information transmission pathways in an allosteric protein

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Many cellular processes require allosteric proteins which contain at least two spatially separated substrate or effector binding sites with interdependent activities. Despite a large body of crystal structures there is no general knowledge about the mechanics and energetics of information transmission within such proteins. It is proposed to establish such principles from the molecular analysis of information transmission in Tet repressor (TetR), a well described tetracycline (tc) dependent regulator of transcription. TetR variants with different allostery and a peptide inducer, triggering a different structural change than tc, have already been isolated. It will be determined if there are more mechanisms of information transmission for TetR and how these depend on the chemical structure of the effector. Residues essential for transmitting information protein-internally between the binding sites will be identified by alanine scanning. The synthesis of peptidomimetics, hybrid compounds derived from the inducing peptide and tc and novel tetracycline derivates will be established and the compounds used to study their mechanism of induction. Crystal structures from all significant novel complexes will be solved to describe the propagation of information in molecular detail.

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