

s8a.m1.p51 **Reversible domain motions induced by substrate binding in ribonuclease A.** A. Zagari, R. Berisio, A. Merlino, F. Sica, L. Vitagliano, L. Mazzarella. *Centro di Studio di Biocristallografia, CNR and Dipartimento di Chimica, Università di Napoli "Federico II", Via Mezzocannone 4, 80134 Napoli, Italy.*

Keywords: X-ray structures, substrate binding, protein dynamics.

Despite the increasing number of successful determinations of complex protein structures our understanding of their dynamic properties is still rather limited. Using X-ray crystallography we demonstrate that ribonuclease A (RNase A) undergoes significant domain motions upon ligand binding. In particular, when cytidine 2'-monophosphate binds to RNase A, the structure of the enzyme becomes more compact. Interestingly, our data also show that these structural alterations are fully reversible in the crystal state. Moreover, an accurate analysis of the atomic resolution structures of RNase A [1] shows that similar effects are produced by the sulfate binding.

These findings provide structural bases for the dynamical behavior of RNase A in the binding of the substrate shown by Petsko and coworkers [2]. Finally, such domain motions may assume functional relevance for more complex systems and may play a significant role in the cooperativity of oligomeric enzymes [3].

s8a.m2.p1 **Implication of Tubby Proteins as Transcription Factors by Structure-Based Functional Analysis.** [1] T.J. Boggon, W.S. Shan, S. Santagata, S.C. Myers and L. Shapiro. *Structural Biology Program, Department of Physiology and Biophysics, Ruttenberg Cancer Center, Mount Sinai School of Medicine of New York University, New York, NY 10029, USA.*

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Tubby-like proteins (TULPs) are found in a broad range of multicellular organisms. In mammals, genetic mutation of tubby or other TULPs can result in one or more of three disease phenotypes: obesity (from which the name "tubby" is derived), retinal degeneration, and hearing loss. These disease phenotypes indicate a vital role for tubby proteins; however, no biochemical function has yet been ascribed to any member of this protein family. A structure-directed approach was employed to investigate the biological function of these proteins.

The crystal structure of the core domain from mouse tubby was determined at a resolution of 1.9 angstroms. From primarily structural clues, experiments were devised, the results of which suggest that TULPs are a unique family of bipartite transcription factors.

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