Unraveling the Structures of Antizyme and its Complexes

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Polyamine levels are regulated in multiple ways, including the role of a novel protein inactivator, antizyme (AZ), that targets ornithine decarboxylase (ODC) for degradation by the 26S proteasome. We have previously reported the X-ray structures of mouse [1] and human [2] ODCs. An extension of these studies deals with understanding the novel method of regulating ODC activity through the action of antizyme (AZ), in concert with another protein, antizyme inhibitor (AZI). Full length AZ-1 from rat has resisted crystallization, thus we have been working with several modified forms of the protein. An AZ-1 fragment encompassing amino acid residues 87-227 has been prepared in a highly soluble, stable form that is amenable to structural analysis by multi-dimensional NMR methods. This fragment retains its ODC binding activity. Many elements of the AZ secondary structure have been identified. Current efforts are focused on the determination of the tertiary structure of this AZ fragment and the characterization of its complexes with ODC and AZI using a variety of biophysical techniques. The status of these projects will be reported.

[1] Kern A.D., Oliveira M.A., Coffino P., Hackert M.L., *Structure*, 1999, **7**, 567. [2] Almrud J.J., Oliveira M.A., Kern A.D., Grishin N.V., Phillip, M.A., Hackert M.L. *J. Molec. Biol.,* 2000, **295**, 7.

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