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Human ribonuclease 6 crystal structure and conformational analysis

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Ribonucleases (RNases) are very ancient proteins present in all organisms studied so far. In addition to their conserved ribonucleolytic activities, they have been associated to a variety of biological functions such as anti-bactericidal, cytotoxic, angiogenic, immunosuppressive, anti-tumoral and/or anti-viral activities. In humans, RNase A superfamily members comprise eight rapidly evolving homologous enzymes with varying degrees of structural similarity and enzymatic activities.[1] While RNase 6 enzymatic activity against ribonucleic acid (RNA) is 40 times lower than RNase 2, a closely related homologue of RNase 6, it was found to have potent antibacterial activity against uropathogens and is expected to play other host defense roles.[1,2] RNase 6 crystal structure has been only recently elucidated in presence of sulfate anions.[3]
In this study, we present the first crystal structure of the human RNase 6 in presence of a ligand, 5'-AMP. This structure is compared to the structures of other RNase A superfamily members: RNase A and RNase 2. The position of the ligand within the catalytic site is relatively conserved (Figure 1). Nonetheless, new phosphate binding residues and ionic binding architecture within the catalytic pocket are identified in the ligand-free and ligand-bound RNase 6 structures. In addition, a new phosphate-binding site located within Loop 4 and involving His67 and its effects on ligand binding are uncovered.
Resolving the crystal structure of human RNases provides valuable insights into understanding their modes of action, which may find applications in various fields such as drug design.
Figure 1: Crystal structures of RNase A in complex with 5'-AMP (PDB ID 1Z6S, dark gray), RNase 2 in complex with adenosine-3'-5'-diphosphate (PDB ID 1HI4, red) and RNase 6 in complex with 5'-AMP (blue).
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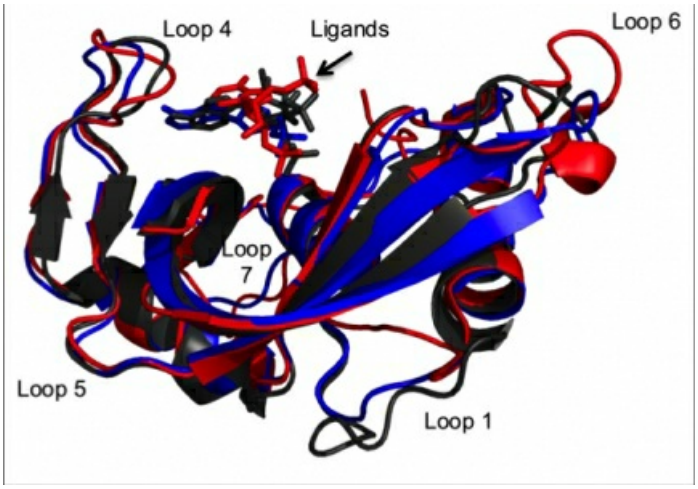

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