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Is tertiary structure really required for specific function of a protein?[1]

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A protein is folded into the unique tertiary structure spontaneously based on the information encoded in the amino acid sequence. It has been believed that the unique tertiary structure is required for the expression of its specific function. However, the discovery of intrinsically disordered proteins (IDP) raised a question whether the structure is really required to function. Some IDP's are folded by the recognition and binding of their targets called coupled folding and binding. We have created many mutants of staphylococcal nuclease (SNase) which have interesting properties. One category of mutants cannot take native structures but show enzymatic activity. Another type of mutants takes stable native structures without activity, despite that the active site residues are completely conserved. The former can be regarded as a model system of IDP. They show ligand-induced folding which is similar to the coupled folding and binding. The mechanism of induced folding has been studied intensively by stopped-flow CD. The reason why activity is lost in the latter mutants will be discussed based on the crystal structure. Consequently, I would like to discuss about the relationship among structure, function and dynamics.

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