

Deciphering the significance of protein sequence conservation with 3D structure



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Abstract

Proteins are synthesized as linear chains of amino acids. However, in this linear form, they are not functional. To become biologically active, proteins must fold into specific three-dimensional (3D) structures determined by their amino acid sequences. During the folding process, regions with adjacent amino acid residues may form local structures. In contrast, residues that are distant in the sequence can come into close proximity in 3D space to form functional sites, such as active or binding sites. Understanding the 3D structure of a protein is therefore useful for elucidating its function.

Functionally important residues tend to be evolutionarily conserved and often cluster together in the 3D structure to form a functional patch. By mapping evolutionary sequence conservation profiles onto the 3D structure, we can gain insights into the significance of these functional sites. In this talk, I will present examples that illustrate how integrating sequence conservation with structural information can help us decipher the functional importance of specific residues in proteins [1-4].

1. Ebihara A, Okamoto A, Kousumi Y, Yamamoto H, Masui R, Ueyama N, Yokoyama S, Kuramitsu S: **Structure-based functional identification of a novel heme-binding protein from *Thermus thermophilus* HB8**. *J Struct Funct Genomics* 2005, **6**:21-32.
2. Ebihara A, Yao M, Masui R, Tanaka I, Yokoyama S, Kuramitsu S: **Crystal structure of hypothetical protein TTHB192 from *Thermus thermophilus* HB8 reveals a new protein family with an RNA recognition motif-like domain**. *Protein Sci* 2006, **15**:1494-1499.
3. Ebihara A, Manzoku M, Fukui K, Shimada A, Morita R, Masui R, Kuramitsu S: **Roles of Mn-catalase and a possible heme peroxidase homologue in protection from oxidative**

- stress in *Thermus thermophilus*. *Extremophiles* 2015, **19**:775-785.
4. Ebihara A, Sugihara D, Matsuyama M, Suzuki-Nakagawa C, Nabi A, Nakagawa T, Nishiyama A, Suzuki F: **Mapping the protein binding site of the (pro)renin receptor using in silico 3D structural analysis**. *Hyperten Res* 2023, **46**:959-971.