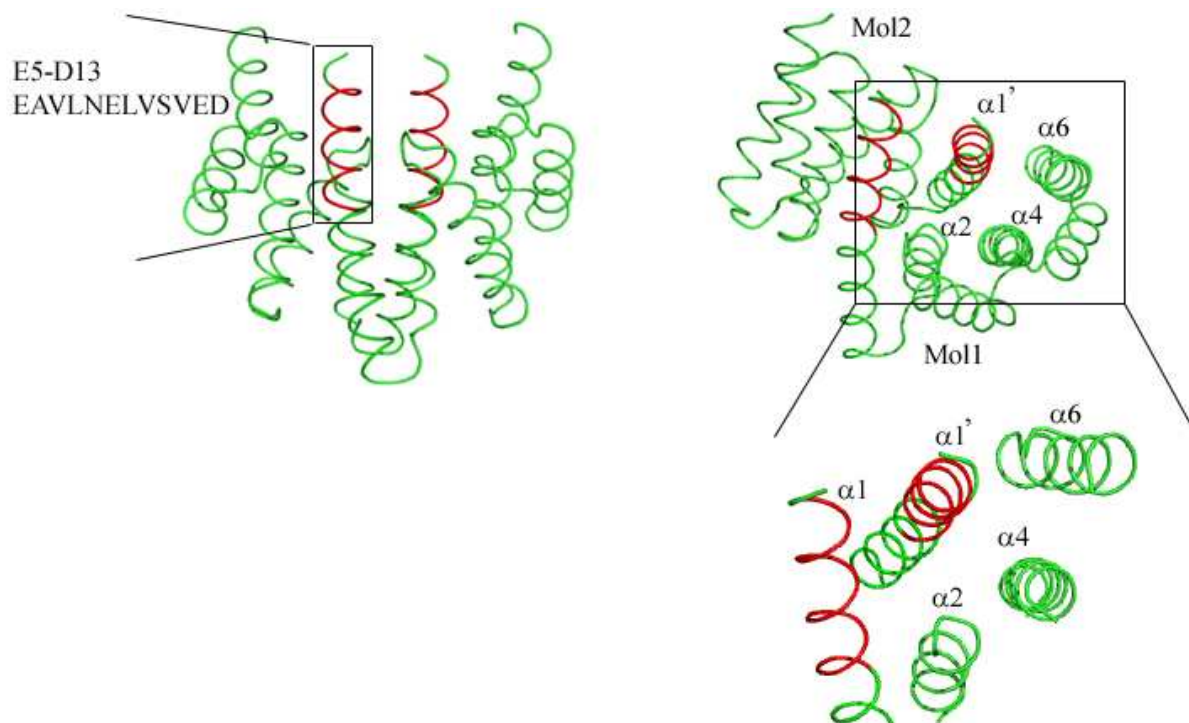


**Supplementary Figure 1. Representative examples of structural variations in protein models that can be rationalized by oligomerization or crystal packing**

**A. Human mitochondrial Fis1: 1NZN/1PC2**

Region of variation 5:13 (sequence- EAVLNELVSVED)

Human mitochondrial Fis1 (1NZN) is a dimer in the crystal structure (Dohm *et al.*, Proteins, 2004). Fis1 is composed of six helices (helices  $\alpha 2$ ,  $\alpha 4$  and  $\alpha 6$  are arranged to form an amphiphilic, concave surface). The crystal packing of Fis1 reveals one arrangement by which the concave surface mediates binding. In the crystal, a dimer of Fis1 was observed in which the concave surface of a Fis1 molecule makes contacts with helix  $\alpha 1$  of a symmetry related molecule. Fis1 is a monomer in solution- helix  $\alpha 1$  is flexible in this case (Suzuki *et al.*, J Mol Biol, 2003).



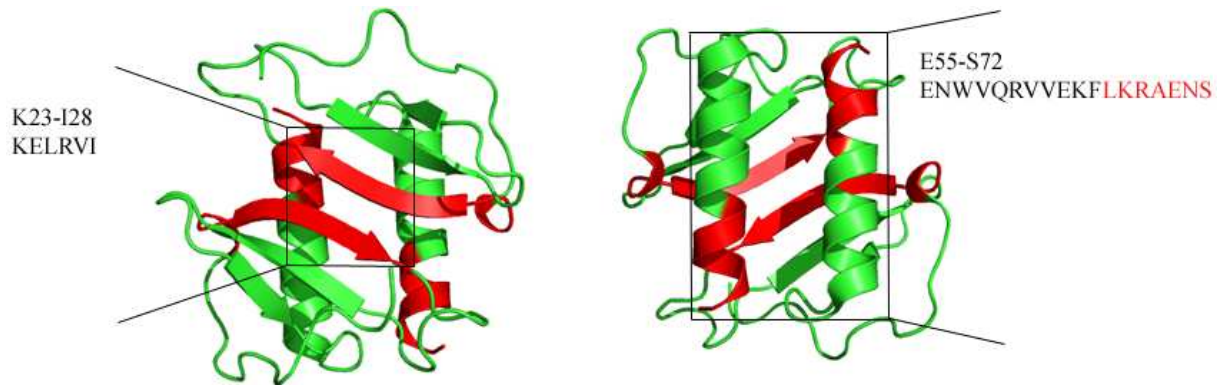
**B. Interleukin 8: 3IL8/1IKM**

region of variation 19:28 (sequence- PKFIKELRVI)

66:72 (sequence- LKRAENS)

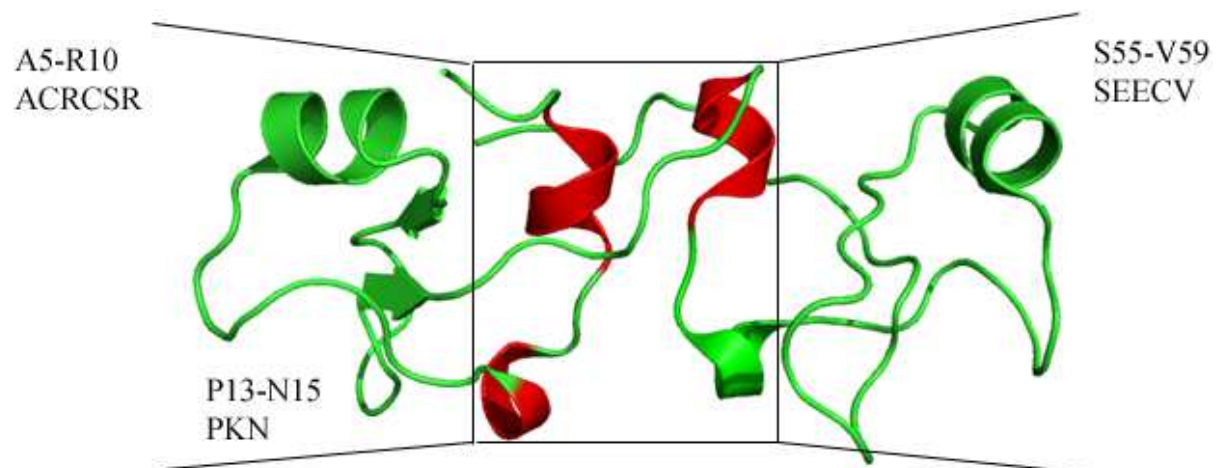
Interleukin 8 (IL-8) adopts a dimeric arrangement in the crystal, in which residues 23-29 and 55-62 play an important role in packing monomeric units. The solution structure of IL-8 is a monomer. Residues 23-28 make tight hydrogen bonding interactions to form an extended  $\beta$ -sheet comprising of six strands and two helices (residues 55-72) which are unstructured in

solution but pack at the dimer interface and are structured in the crystal (Baldwin et al, PNAS, 1991; Rajarathnam et al, Biochemistry, 1995).



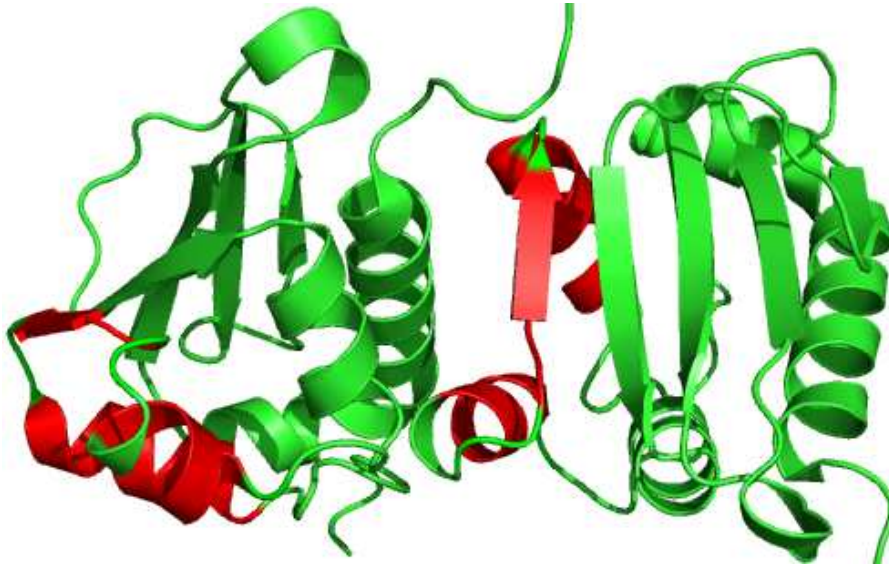
### C. Pancreatic spasmolytic peptide: 1PSP/1PCP

In the case of the pancreatic spasmolytic peptide, a member of mammalian trefoil family of peptides, conformational variations are located away from the interface.



#### D. Sterol carrier protein-2: 1C44/1QND

In the sterol carrier protein-2, the conformationally variable region (red) interacts with a symmetry related molecule.



#### E. The allergen PHL P2: 1WHO/1BMW

In the allergen PHL P2, crystal packing effects can be seen to influence conformational stability.

