Structural studies on human heat shock transcription factors (HSFs)

The heat shock response (HSR) is conserved in all organisms, which enables the cell to cope with the deleterious effects of protein-damaging stresses. Cells respond to the proteotoxic damage by elevated expression of heat shock proteins (Hsps) working as molecular chaperones. In eukaryotes, the HSR is mediated by the interplay between the heat shock element (HSE) upstream of the *hsp* genes and a group of specific activator proteins, coined heat shock factor (HSF). HSF activation is a multistep process, but most details remain veiled due to the lack of structural information. Our aim is to crystallize the full-sized or truncated human HSF1 and HSF2, and determine their 3D structures by means of X-ray crystallography. The biggest hindrance for structural study in this case lies in the difficulty in obtaining sufficient protein used in crystallization. After exhaustive optimizations, we have successfully improved the expression level of full-length HSF1 and HSF2 from 0.3 mg/L to 2.0 mg/L, and set to crystallization trails already. Recently we have made shorter constructs to express the N-terminal part only. As shown in pilot experiments, both constructs of HSF1 and HSF2 give rise to, even not 100%, soluble products.

We would like to recruit a master student to work on purification optimization of these truncated proteins and subsequent crystallization trails. Any students who are curious about structural biology and interested in working at our lab for his/her thesis project are highly welcome. He/she will learn basic skills in molecular biology and structural biology, and may have an opportunity to go to ESRF, the largest synchrotron light source in Europe, in Grenoble, France for diffraction data collection.

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