SAXS Investigations of Conformation and Stability of Eye Lens Proteins under Pressure

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We have combined small angle X-ray scattering (SAXS) and a high-pressure cell to study the effect of pressure, temperature and pH, on the conformation and the stability of γ- and α-crystallins. α-, β- and γ-crystallins are the main components of mammalian eye lenses and their structural and associative properties are responsible for lens transparency. γ are monomers (21 kDa, up to 80% sequence identity), whereas α are large hetero-oligomers of about 800kDa. The C-terminal domain of α belongs to the ubiquitous superfamily of sHSPs (small heat shock proteins): upon stress, they are able to incorporate the non-native proteins to prevent their aggregation.

High-pressure experiments performed with α-crystallins have shown a partially reversible change in size from 2 to 3kb at room temperature, and this effect was enhanced by the combination of temperature and pressure. In the case of γ-crystallins, pressure and temperature needed to be combined with pH, and the results depend upon the different γ itself. Crystallins are known to be exceptionally stable *in vivo* since they are synthesised to last for life. They therefore represent an extreme case of stability versus unfolding and these results have shown that these proteins (mainly beta strands) are also stable upon pressure.

Keywords: high-pressure SAXS, crystallins, conformation changes