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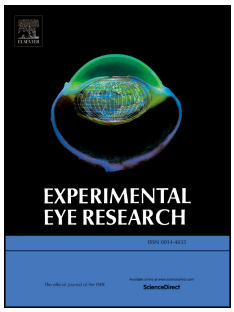

A structural and functional study of Gln147 deamidation in αA-crystallin, a major site of modification in human cataract

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A structural and functional study of Gln147 deamidation in αA-crystallin, a major site of modification in human cataract

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Abstract

Deamidation of Glu147 in human αA-crystallin is common in aged cataractous lenses (Hains and Truscott, *Invest. Ophthalmol. Vis. Sci.* 2010, 51, 3107). Accordingly, this modification may have a causative effect in cataract. αA-crystallin is a small heat-shock molecular chaperone protein that prevents aggregation of proteins and is the principal defence against crystallin protein unfolding and aggregation in the ageing lens. Deamidated Q147E αA-crystallin was structurally characterised using a variety of spectroscopic and biophysical methods, including NMR, circular dichroism and fluorescence spectroscopy and dynamic light scattering. The effect of Glu147 deamidation on αA-crystallin *in vitro* chaperone ability was determined for a variety of aggregating proteins. Compared to the wild type protein, Q147E αA-crystallin generally exhibited slightly reduced chaperone ability and a small loss of overall structure in its central α-crystallin domain while also showing significantly enhanced thermal stability and a tendency to form larger oligomers. As αA-crystallin is the major lens protein, even a small loss of function could combine with other sources of age-related damage to the crystallins to contribute to lens opacification.

Keywords

Cataract, αA-crystallin, Deamidation, Ageing, Post-Translational Modification.

Abbreviations

αAc (αA-crystallin), αBc (αB-crystallin), ADH (alcohol dehydrogenase), DTT (Dithiothreitol), HSQC (heteronuclear single quantum coherence spectroscopy), NOESY (Nuclear Overhauser