Sterol-crystallin interaction mediated by membranes

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A cataract is a common disease for the aged people and has a very high chance to lead blindness. Instead of the surgery of replacing the clouding eye lens with an artificial one, it's important to develop a non-surgical therapy. But it's difficult to be carried out due to the lack of understanding on mechanism of cataract.

In the vertebrate eye lens, alpha-crystallin(α-crystallin) is the major structural protein and consists of two subunits, αA and αB, which are used to maintain lens transparency throughout life. As a member of the small heat shock protein family (sHsp), α-crystallin exhibits chaperone-like activity to prevent misfolding as well as aggregation of key proteins in the lens associated with cataract diseases. The previous studies reported that binding capacity of α-crystallin to lens lipids increases with age [1], and high molecular complex, comprising α-crystallin and misfolding protein, showed higher association with membrane [2]. Recent evidences showed that sterols compounds can improve lens transparency [3]. Due to the strong interaction between sterols with membranes, we proposed a model based on the membrane-mediated sterol-crystallin interaction.

In this study, we used αA and αB crystallin proteins, ergosterol and membranes as a model system to study the interactions between proteins, sterol molecules, and membranes. First, the influence of membrane on chaperone-like activity of αA and αB were checked by the assays of insulin, lysozyme and alcohol dehydrogenase (ADH). Circular dichroism (CD) was used to monitor the secondary structure changes of crystallin proteins induced by binding to membranes. Lamellar X-ray diffraction (LXD) was used to probe crystallin-induced structural change of membranes. Furthermore, small-angle X-ray scattering (SAXS) was used to probe structural changes of membranes with and without ergosterol induced by protein binding. The effects of ergosterol on the interaction between crystallin proteins and membranes will be discussed.

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