Structural evolution of human αB-crystallin on UV irradiation

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Alpha-crystallin is a human lens protein which works as a chaperon to prevent from making aggregation of proteins in the lens. This protein is a water-soluble aggregate consisting of two kinds of polypeptides, αA-crystallin and αB-crystallin.

Under environmental stresses, α-crystallin makes huge aggregation and then losses its chaperone activity. Therefore, the proteins in the lens also make huge aggregation and finally the lens has become opaque, namely a serious disease, *cataract*, has developed.

The trigger of the abnormal aggregation on α-crystallin is considered to be post-translational modifications on the polypeptide such as deamidation, racemization and isomerization, truncation, phosphorylation, oxidation, an increase in intramolecular disulfide bonding and glycation. However, the abnormal aggregation process has not been clarified so far. Therefore, we have investigated the abnormal aggregation process of α-crystallin.

In order to reveal the abnormal aggregation process, we developed a UV irradiation system with which *in-situ* SANS observation can be performed. With the system, we observed the structural evolution of human recombinat αB-crystallin under UV irradiation with SANS-U spectrometer. The UV light had wavelength range with 280-360 nm (UV-B) and the SANS intensity was recorded every 30 minutes for 10 hours.

Figure 1 shows the evolution of SANS patterns of αB-crystallin under UV irradiation during 10 hours. The evolution was classified into three stages. In the first two hours (stage I), the SANS pattern was almost unchanged, where the radius of gyration was around 55 Å. Stage I could be an incubation time prior to making the abnormal aggregation. In the next six hours (stage II), the scattering intensity is going to be centering. It means that αB-crystallin is making aggregation in stage II. In the final two hours (stage III), the SANS pattern was almost unchanged again, where the radius of gyration was around 70 Å.

The investigation of the relation between the chaperone activity and the structure in each stage is now in progress.

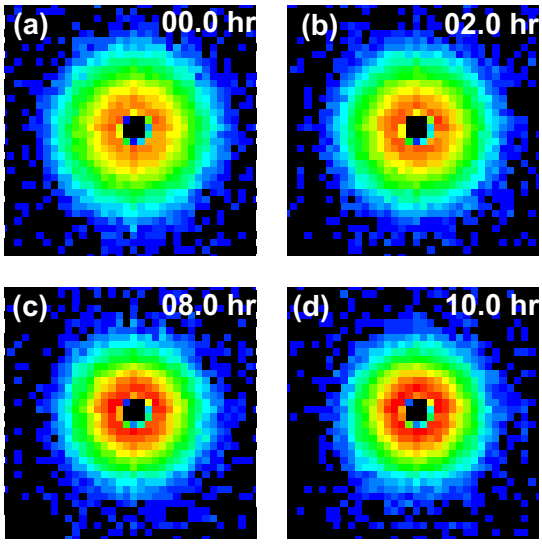

Fig. 1. Evolution of SANS patterns of αB-crystallin under UV irradiation. (a) Before UV irradiation, (b) after 2 hrs UV irradiation, (c) after 8 hrs UV irradiation and (d)after 10 hrs UV irradiation.