Pressure Effects on the Structure and Functions of Protein Disulfide Isomerase and Human Thioredoxin

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Protein disulfide isomerase (PDI) is workable as a multifunctional protein which contributes to the reduction, oxidation and isomerazation of disulfide bonds and acts as chaperones to accelerate the correct folding without aggregation *in vivo.* PDI (about 55 kDa) belongs to the thioredoxin super family and the structure is composed of 4 thioredoxin-like domains with a small domain including ER localization signal (KDEL).

In this study, we focused on the effect of pressure on the stability of PDI and human thioredoxin whose structure closely resembles the domain of PDI. The objective of this research is to clarify the relation between the structural changes and function of these proteins. The research of structural changes mainly proceeded to monitor the Trp fluorescence located in active site. It was performed not only under high pressure but also with denaturation agent or disulfide oxidant (Glutathione oxidized form). In these results, the structural change of PDI under high pressure up to 400 MPa was mainly induced by compression and its structural change returned to the native one after releasing pressure. Pressure-treated PDI also showed the similar activities to native one in both isomerase and chaperone activities. On the other hand, the structural change of thioredoxin was drastically induced by the application of high pressure up to 400 MPa which causes by the penetration of water molecules into the structural interior of thioredoxin. Thioredoxin was not completely recovered after releasing pressure in the points of both the structure and function. From these results, PDI had higher stability against pressure than thioredoxin. This thesis is summarized and discussed about the mechanism of denaturation and functions under high pressure about PDI and thioredoxin.