S56-2 Intracellular accumulation of mutant serpin and cellular response

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Serpin is a superfamily of serine protease inhibitors. Antithrombin and protein Z-dependent proteinase inhibitor in the family are important for the maintenance of normal hemostasis by means of the prevention of activated coagulation reactions. An inherited deficiency in these proteins is associated with predisposition of familial venous thromboembolic diseases. On the other hand, accumulation of mutant serpin in the cells and tissues result in various kinds of cellular disorders. For example, accumulation of mutant α_1-antitrypsin within hepatocytes and of neuroserpin within neurons to cause cirrhosis and dementia, respectively. These phenomena are recently drawing attention as folding diseases. We prepared CHO cells stable expressing novel mutant antithrombin, AT(C95R) with impaired disulfide bind formation and examined intracellular dynamics of and cellular response to AT(C95R). We found that AT(C95R) accumulated in Russell body like structures that were composed of densely arranged ER. In addition, the accumulation of AT(C95R) induced neither unfolding protein response nor ER-overload response, but decreased in cell proliferation. I will present topics of interests concerning accumulation of mutant serpins in the cells and various stress responses by their accumulation.