C-4

A proteomic approach to identify of yeast proteins that related with accumulation of misfolded protein in cell

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In growing number of diseases it has been shown that the aggregation of specific proteins has an important role in the pathogenesis of the disorder.
This has been demonstrated in structural detail with the liver cirrhosis of α_1-antitrypsin deficiency, and it is now believed that similar protein aggregation underlies many neurodegenerative disorders such as autosomal dominant Parkinson disease, prion diseases, Alzheimer disease, Huntington disease.
α_1-antitrypsin is the member of the serpin family, and functions as an inhibitor of neutrophil elastase. A numbers of well studied genetic variants of α_1-antitrypsin such as the Z (Glu342→Lys) and S_{iiyama}(Ser53→Phe), undergo polymerization which leads to retention within the hepatocyte and subsequently a decrease in the plasma concentration of active serpin. Hence α_1-antitrypsin polymerization can lead to liver disease and emphysema. Most of the newly synthesized variant α_1-antitrypsin accumulate as aggregates and are retained in the endoplasmic reticulum (ER) of the hepatocytes, which are eventually degraded.
To identify proteins that related with accumulation of misfolded protein in ER, we expressed the z and S type variant of α_1-antitrypsin in yeast, and analyzed the protein expression profile by using 2D-gel proteomic technique.
55 candidate spots were identified by peptide mass fingerprinting using MALDI-TOF MS and database search.