

REGIONAL CENTRE FOR BIOTECHNOLOGY Seminar series

A Complex Protein Network Regulates the Cytosolic Stress Response – Specific Role of Proteasome

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Swasti Raychaudhuri, PhD Abstract

Aging results from proteostasis collapse. Increased accumulation of misfolded proteins in cells leads to development of several age-related diseases including neurodegenerative diseases and cancer. In healthy cells misfolded protein load induces cytosolic stress response to counteract protein damage. However, with aging proper activation of this response is impaired. Hence it is necessary to understand the regulation of this protective pathway at cellular level. To elucidate, we have performed a genome-scale RNAi screen in HeLa cells. This study reveals an integration of multiple key pathways including chromatin remodeling, transcription, splicing, ribonucleoprotein biogenesis, membrane signaling, protein folding and post-translational modification and degradation in the activation and maintenance of cytosolic stress response. Additional quantitative proteomics experiments revealed an extensive reorganization of the nuclear proteome during and after stress. Both approaches illustrate the importance of the proteasome system in reestablishing nuclear function and in attenuating the stress response by proteasome dependent degradation of HSF1.