

Regulation of protein homeostasis in acute and chronic stress

Short summary

The balance between protein production, folding, transport, assembly and the timely degradation of proteins is defined as protein homeostasis. This process is controlled by a network of protein quality control (PQC) that includes molecular chaperone and protein degradation systems. Various situations may perturb protein homeostasis. In this thesis, we studied how acute injury and chronic diseases may lead to protein homeostasis imbalances. In particular, we tested under each of these conditions of stress, how heat shock proteins (HSPs) or other pathways in PQC may help to rebalance protein homeostasis. The experimental research in this thesis is dedicated to two entirely different challenges: 1) the poultry breeding industry in China, where animals often suffer from acute heat stress induced myocardial cell injury; 2) heritable neurodegenerative diseases in humans, in particular Huntington's disease (HD), where patients chronically express an aggregation-prone mutant protein. Our studies support the idea that acute stress and chronic stress are largely different and require different PQC networks for optimal protection. Even within one chaperone family, as was illustrated for the group of small HSPs, different members are not only differentially regulated but also protect against different forms of stress. Our data on insulin growth factor pathways further underscored how cells regulate protein homeostasis multiple ways, not only by improving chaperone capacities and degradative capacities, but even by extracellular dumping of protein damage. These multiple layers of PQC underscore the importance of maintaining protein homeostasis for cellular and organismal fitness.