

Midwest Stress Response and Molecular Chaperone Meeting
Abstract Example

Font: Times, size 12

Margins: top, bottom, left, right all 1”

Please include the following:

Title (bold)

Author names (presenting author name underlined)

Author affiliations

Abstract

All must fit on one page

Please indicate if you'd like your abstract to be considered as an oral presentation and/or a poster when you submit your abstract to Rebecca Phend at Rebecca.phend@northwestern.edu.

Unless specified, any abstracts that were not selected for oral presentations will be listed for poster presentation.

EXAMPLE:

Proteome remodeling: A missense mutation at a time

Xiaojing Sui¹, Miguel Prado², Dan Finley², Richard Morimoto¹

¹Department of Molecular Biosciences; and Rice Institute for Biomedical Research, Northwestern University, IL

²Department of Cell Biology, Harvard Medical School, Boston, MA

Protein misfolding caused by gene mutations is the basis of numerous protein conformational diseases including neurodegenerative diseases. A common feature of degenerative diseases is that patients rarely exhibit symptoms in early life, suggesting that folding mutations are buffered. Here, we propose to identify the underlying surveillance mechanisms for muscle proteome stability using an exquisitely sensitive class of metastable proteins with properties of temperature-sensitive (ts) mutations, that are functional at the permissive condition and exhibit complete loss-of-function at the restrictive condition. These ideas are based on the preliminary results using unbiased proteomics on *Caenorhabditis elegans* as the experimental model system to show that even at the permissive condition that proper folding and function of a ts missense mutation in myosin is associated with the selective increase in small heat shock proteins, but not other chaperones. This suggests an adaptive and protective mechanism to prevent proteome failure. These results lead to the hypothesis that mild folding mutations activate a protein homeostasis response that remodels the proteome to protect muscle cells against damage and failure in early adulthood. To test this, we will employ quantitative global proteomics to examine how the proteome remodels itself upon expression of different conditional metastable proteins in muscle cells, structural proteomics to monitor the conformational states of these mutant proteins and the proteome, and genetic and biochemical approaches to establish how the response protects the integrity of the muscle proteome in aging. Exploring the proteome surveillance mechanisms that detect and maintain the functional properties of a mutant protein is pivotal for understanding the earliest molecular events that prevent proteotoxicity and has broader implications on the quality control of the prevalent polymorphisms in the proteome.