

PROGRESS IN NEUROSCIENCE PINS

Seminar Series of the Brain & Mind Research Institute Weill Cornell Medical College (WCMC)



The Graduate Program in Neuroscience of WCMC and Sloan Kettering Institute

Thursday, 5/12/16, 4 PM, coffee at 3:45 PM Weill Auditorium

"The Biology of Proteostasis in Aging and Neurodegenerative Disease"

Richard I. Morimoto, Ph.D. Bill and Gayle Cook Professor of Biology Director, Rice Institute for Biomedical Research Department of Molecular Biosciences, Northwestern University

Abstract:



The health of the proteome is essential for life, and at the cellular level is orchestrated by the proteostasis network (PN) comprised of molecular chaperones, transport machineries, ubiquitin-dependent proteasomes, and autophagy pathways. Under optimal conditions, the PN balances protein flux dynamics to achieve proteome stability and functionality, and to prevent misfolding and aggregation. In *C. elegans*, the PN is regulated at the organismal level by cell non-autonomous signaling from stress sensing tissues to surrounding receiving tissues resulting in activation of components of the PN to protect against cellular damage from persistent proteotoxic stress, aging and disease. This stress protective mechanism, however, is repressed in adulthood at reproductive maturity by signals from the germline stem cells resulting in an epigenetic repression of multiple cell stress responses leading to the collapse of proteostasis. Organismal proteostasis therefore represents balance and coordination among multiple cell stress responses to ensure cellular and tissue health and longevity.

Recent relevant publications:

1. Labbadia, J. and R.I. Morimoto. Repression of the Heat Shock Response is a Programmed Event at the Onset of Reproduction. <u>Molecular Cell</u> 59: 639-650, DOI 10.1016/j. molcel.2015.06.027 PMID: 266212459 (2015).

2. Brehme, M., C. Voisine, T. Rolland, S. Wachi, J. Soper, Y. Zhu, K. Orton, A. Villella, D. Garza, M. Vidal, H. Ge, and R.I. Morimoto. A Conserved Chaperome Sub-Network Safeguards Protein Homeostasis in Aging and Neurodegenerative Disease. <u>Cell Reports</u> 9: 1135–1150, DOI: 10.1016/j, PMID: 25437566 (2014).

3. Van Oosten-Hawle, P., R. Porter, and R. I. Morimoto. Regulation of Organismal Proteostasis by Transcellular Chaperone Signaling. <u>Cell</u> 153: 1366-1378, DOI:10.1016, PMID: 23746847 (2013).



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