

CHEMISTRY Departmental Seminar

Fall 2017
CHEM 285 Schedule
Tuesdays at 4:30-5:45PM
Room Duncan Hall 250

September 5, 2017

Professor John C. Price
Brigham Young University

Investigating signal-dependent changes in ribosome activity across the proteome

Control of protein homeostasis is fundamental to the health and longevity of all organisms. Because the rate of protein synthesis by ribosomes is a central control point in this process, regulation and maintenance of ribosome function could have amplified importance in the overall regulatory circuit. Indeed, ribosomal defects are commonly associated with loss of protein homeostasis, aging and disease, whereas improved protein homeostasis, implying optimal ribosomal function, is associated with disease resistance and increased lifespan. To maintain a high quality ribosome population within the cell, dysfunctional ribosomes are targeted for autophagic degradation. It is not known if complete degradation is the only mechanism for eukaryotic ribosome maintenance or if they might also be repaired by replacement of defective components.

We used RNAseq, stable-isotope feeding and protein mass-spectrometry to measure the *in vivo* activity for >1000 substrates and structural dynamics of assembled ribosomes in mouse liver. In general, peripheral r-proteins and those with more direct roles in peptide-bond formation are replaced multiple times during the lifespan of the assembled structure, presumably by exchange with a free cytoplasmic pool, whereas the majority of r-proteins are stably incorporated for the lifetime of the ribosome. Dietary signals impact the general ribosome activity, rates of new ribosome assembly, and component r-protein exchange. The results indicate that gene specific changes in ribosome activity are accompanied by variations in *in vivo* maintenance mechanisms. Also, the signal-specific modulation of ribosomal repair and degradation could provide a mechanistic link in the frequently observed associations between diminished rates of protein synthesis, increased autophagy, and greater longevity.