Seminar

Dr. Gustavo Silva

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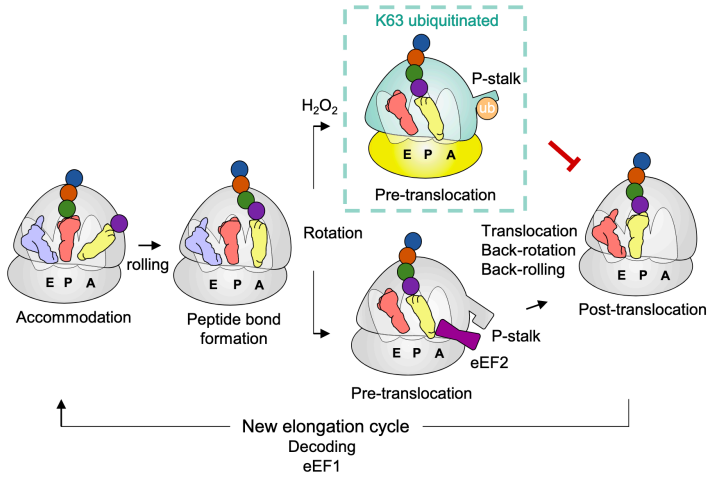
"K63 ubiquitin and translation control during oxidative stress"



Rapid reprogramming of gene expression is essential for cellular survival during exposure to harmful environments. Although transcriptional regulation has been largely studied during stress, a variety of regulatory mechanisms exist to regulate protein synthesis at the translation level. In response to oxidative stress, protein synthesis is globally inhibited while translation regulation allows synthesis of stress-response proteins. However, the mechanisms by which eukaryotic cells regulate translation in a fast and refined manner under stress still remains elusive. My group has shown that an unconventional ubiquitin chain (K63-linked) accumulates during oxidative stress due to the redox regulation of a trio of ubiquitin enzymes (Rad6, Bre1, and Ubp2). Using a novel proteomics method for linkage-specific ubiquitination, we identified several ribosomal sites of K63 ubiquitination, particularly at the decoding center and at the 40S-60S interface. To understand the impact of this modification on ribosome structure and function, we resolved the 3D structure of K63 ubiquitinated ribosomes using cryo-EM. Our analysis revealed that K63 ubiquitin regulates elongating ribosomes by inducing flexibility of the P-stalk, a 60S ribosome structure involved in the translocation stage of translation. Our results highlight a new pathway named Redox control of Translation by Ubiquitin (RTU), in which K63 ubiquitin serves as a master regulator of translation, supporting translation reprogramming and cellular resistance to stress.

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12:00 PM **tiny.ucsf.edu/SilvaSeminar**

Hosted by Stephen Floor