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Ribosomes are giant molecular machines that produce all proteins necessary for life. In eukaryotic cells, their assembly is a highly elaborate and carefully coordinated process. The Klinge lab's research is aimed at understanding the molecular mechanisms that govern early stages of eukaryotic ribosome assembly.

Ribosomes are responsible for decoding the information contained in messenger RNA to synthesize proteins used in all domains of life. In eukaryotes, approximately 200 factors must work in a precise and coordinated manner to build ribosomes from proteins and segments of RNA, and most are essential. These factors are involved in all stages of ribosome assembly, from transcription of ribosomal RNA in the nucleolus to export into the cytoplasm, where the final stages of maturation and quality control occur. As ribosome assembly progresses, more and more of this machinery is released from intermediate complexes until the ribosomal subunits complete maturation.

The structure of this molecular machinery and the mechanisms by which it functions remain poorly understood. The Klinge lab's major focus is to elucidate them in the context of intermediate complexes formed during the early stages of ribosome assembly, using the model system Saccharomyces cerevisiae. The group combines yeast genetics with novel biochemical tools, x-ray crystallography, and cryo-electron microscopy.

Klinge's lab has studied the temporal order by which 70 factors associate with nascent pre-ribosomal RNA to form the small subunit processome, a giant pre-ribosomal particle. By studying ribosome assembly as a function of transcription, his lab has assigned proteins to particular stages of early ribosome assembly. In parallel, the researchers have used biochemical and structural biology methods to elucidate the functions of multi-protein complexes within the small subunit processome. More recently, they used cryo-electron microscopy to obtain the first three dimensional views of nucleolar precursors of both the small and large ribosomal subunit. These structures, elucidated in conjunction with complementary chemical biology, genetic, and biochemical approaches, have provided the first molecular snapshots of eukaryotic ribosome assembly at near-atomic resolution.

The lab ultimately aims to define the entire sequence of events that drive the formation of the eukaryotic ribosome at an atomic level.

EDUCATION

B.A. in biochemistry, 2005
Ph.D. in biochemistry, 2009
University of Cambridge

POSTDOC

Swiss Federal Institute of Technology in Zurich, 2009–2013

POSITIONS

Assistant Professor, 2013–2019
Associate Professor, 2019–2024
Professor, 2024–
The Rockefeller University

AWARDS

Human Frontier Science Program Career Development Award, 2014

Alfred P. Sloan Research Fellowship, 2014

Irma T. Hirschl/Monique Weill-Caulier Trust Research Award, 2014

Rita Allen Foundation Scholar, 2014

NIH Director's New Innovator Award, 2016

SELECTED PUBLICATIONS

Sanghai, Z. et al. Modular assembly of the nucleolar pre-60S ribosomal subunit. *Nature* 556, 126–129 (2018).

Barandun, J. et al. The complete structure of the small-subunit processome. *Nat. Struct. Mol. Biol.* 11, 944–953 (2017).

Chaker-Margot, M. et al. Architecture of the yeast small subunit processome. *Science* 355, eaal1880 (2017).

Chaker-Margot, M. et al. Stage-specific assembly events of the 6-MDa small-subunit processome initiate eukaryotic ribosome biogenesis. *Nat. Struct. Mol. Biol.* 22, 920–923. (2015).

Klinge, S. et al. Crystal structure of the eukaryotic 60S ribosomal subunit in complex with initiation factor 6. *Science* 334, 941–948 (2011).