

## SMS Fall 2022 Seminar Series

Friday Oct 21 | 2:30pm | Biodesign Auditorium

### Imaging Biological Systems at the Single-Molecule Scale

Single-molecule fluorescence imaging has renewed interest in the transient interactions and conformations of biological systems that underpin function and regulation. The protein synthesis mechanism, a process defined by rapid transactions and directional movements, is an exemplar in this regard where transient interactions define the genetic code and directional movements along the messenger RNA template. In this context, published and anecdotal observations over the past several decades have led our team to ask whether the translation mechanism may be influenced by endogenously encoded sequence variations that potentially exist within the ribosomal RNA component of the assembled ribosome. Our findings reveal that the functioning ribosome pool in most species is intrinsically heterogeneous at the level of its ribosomal RNA composition. They also show that the relative expression levels of variant ribosomal RNA alleles within the assembled ribosome can vary with physiological context and that specific variant alleles in the model *E. coli* organism have the capacity to modulate transcriptional control of gene expression and phenotype. These findings lead us to speculate that natural sequence variations within the hundreds of ribosomal DNA alleles present in the mammalian genome have the capacity – at least in principle – to provide a mechanism for templating and regulating heterogeneity into the expressed ribosome pool.

### Scott C. Blanchard, PhD

*Endowed Chair, St. Jude Children's Research Hospital*

Dr. Scott C. Blanchard received his PhD in Biophysics from Stanford University, and is currently a member of St. Jude Faculty and Endowed Chair in Molecular Imaging. Current research in the Blanchard laboratory focuses on examining structure-function relationships in macromolecular assemblies using genetic, biochemical, and spectroscopic techniques. Our mission is to develop novel approaches, including single-molecule fluorescence imaging methods, to elucidate the conformational and compositional processes critical to the functions of biological systems. The regulation of protein synthesis and ribosome biogenesis in development and disease, mechanisms of integral membrane protein signaling, and small-molecule interventions in infectious disease, are key focus areas.

A principal goal of investigating this diversity of biology systems is to reveal regulatory paradigms that explain how cellular factors and small-molecules modify the function of essential molecular machines. We seek to leverage the information obtained from our discovery research initiatives to improve the efficacy of clinical interventions for the betterment of the human condition.

