













SEMINAR SERIES 2023 14 NOVEMBER

Dr. Susan Buchanan

Deputy Scientific Director, Lab Chief & Senior Investigator NIDDK, National Institutes of Health Bethesda, Maryland USA

Susan obtained a M.A in biophysical chemistry from Princeton and PhD in biochemistry from Johann-Wolfgang-Goethe Universität, Frankfurt, Germany. In 2018, she was elected a Fellow of the American Academy of Microbiology and has recently been recognized with numerous NIH Director's awards for equity, diversity and inclusion; mentorship; and the promotion of women in leadership.



During her PhD and Postdocs, Susan trained with three Nobel

Laureates in crystallography, learning the determination of membrane protein structure at the very foundation of the field. Her early research resolved the second membrane protein structure, worldwide; resulted in the biochemical characterization of mitochondrial respiratory enzymes; and led to the first structural determination of the bacterial TonB-dependent transporter.

Today, her lab combines structural (X-ray crystallography, cryo-electron microscopy), biophysical and biochemical (small angle X-ray scattering, electron spin resonance, thermal denaturation, targeted crosslinking, analytical ultracentrifugation) techniques to understand the essential processes of membrane protein folding and integration, transport of vital nutrients into bacteria and mitochondria, and transport of protein toxins across the outer membrane.

Structural Insight into Outer Membrane Protein Folding in Bacteria & Mitochondria

Gram-negative bacteria, mitochondria, and chloroplasts contain an inner and outer membrane. The outer membrane contains a host of beta-barrel proteins commonly called outer membrane proteins (OMPs), which serve essential functions in cargo transport and signaling and are also vital for membrane biogenesis. In Gram-negative bacteria, OMPs are synthesized in the cytoplasm and then transported across the inner membrane into the periplasm via the Sec translocon. Once in the periplasm, chaperones guide the nascent OMPs across the periplasm and peptidoglycan to the inner surface of the outer membrane. Here, the nascent OMPs are recognized by a complex known as the beta-barrel assembly machinery (BAM) complex which folds and inserts the new OMPs into the outer membrane. Similar mechanisms for OMP biogenesis exist for mitochondria (SAM), where interaction of the bacterial or mitochondrial signal sequence located in the final transmembrane beta strand associates with the first beta strand of BamA/Sam50, followed by strand integration into the BAM/SAM complex. We solved structures of BamA (2013), the BAM complex (2016), and the SAM complex (2021). However, even with these structures being known, the mechanism for how the BAM or SAM complex recognizes, folds, and inserts nascent OMPs into the outer membrane remains to be determined. Current experiments on the SAM complex probe the binding of mitochondrial beta signals to Sam50, as well as studying binding of a novel antibiotic that has been shown to bind to BamA and inhibit strand integration.