Youxing Jiang

Structural Insights into the Assembly, Gating, and Selectivity of Mitochondrial Calcium Uniporter

Mitochondria can take up large amounts of Ca^{2+} from their environment, a process that can modulate ATP production, alter cytoplasmic Ca^{2+} dynamics, and trigger cell death. Ca^{2+} enters the mitochondrial matrix through the mitochondrial calcium uniporter, a highly selective Ca^{2+} channel that is localized to the inner mitochondrial membrane. In humans, the uniporter is a protein complex or uniplex consisting of at least four components: the ion conducting pore MCU, the essential membrane spanning subunit EMRE, and the Ca^{2+}-sensing gate-keeping proteins MICU1 and MICU2. While MCU is found in all major eukaryotic taxa, EMRE is metazoan-specific and is required for the conductivity of MCU in these organisms. On the contrary, the pore-forming MCU is the only component of the uniporter in most fungi based on genome sequence analysis and likely represents the minimal channel component of the uniporter for Ca^{2+} uptake. My lab aims to address the fundamental questions about the uniporter's assembly, gating, and ion permeation properties by determining the structure of the uniporter, focusing first on the MCU component and then, ultimately, the uniplex.