“The cytoplasmic domain of the rhomboid intramembrane serine protease: What the crystal structures don’t tell you”

Rhomboid proteins comprise the largest class of intramembrane protease known, being conserved from bacteria to humans. A wealth of x-ray crystallographic data on the bacterial rhomboid has revealed an aqueous-exposed active site formed by its six transmembrane segments. However, domains of the rhomboid that exist outside this catalytic core have not yet been resolved, nor has a functional role for these regions been elucidated. In this presentation I will describe our progress in identifying the functional contributions that these regions make to rhomboid protease activity. This has led to the identification of new functionally critical sequences, and an unanticipated domain-swapping interaction that is facilitated by interactions with membrane-mimetic micelles.