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Signaling from inside the membrane: mechanism of rhomboid proteases

Rhomboid proteases are integral membrane proteins endowed with the extraordinary ability to hydrolyze protein segments within the membrane. This ancient family of membrane-immersed enzymes plays key roles in cell signaling events during bacterial growth, animal development, and mitochondrial quality control. Although high-resolution rhomboid structures have been achieved, translating these static images into a sophisticated understanding of rhomboid's functional properties remains incomplete. We have been integrating spectroscopic, structural, and enzymatic methods to rhomboid proteases and their substrates reconstituted into defined proteoliposomes. These approaches indicate that rhomboid proteases have evolved unexpected properties precisely by virtue of being immersed inside the membrane. A new model for rhomboid intramembrane proteolysis will be discussed.

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