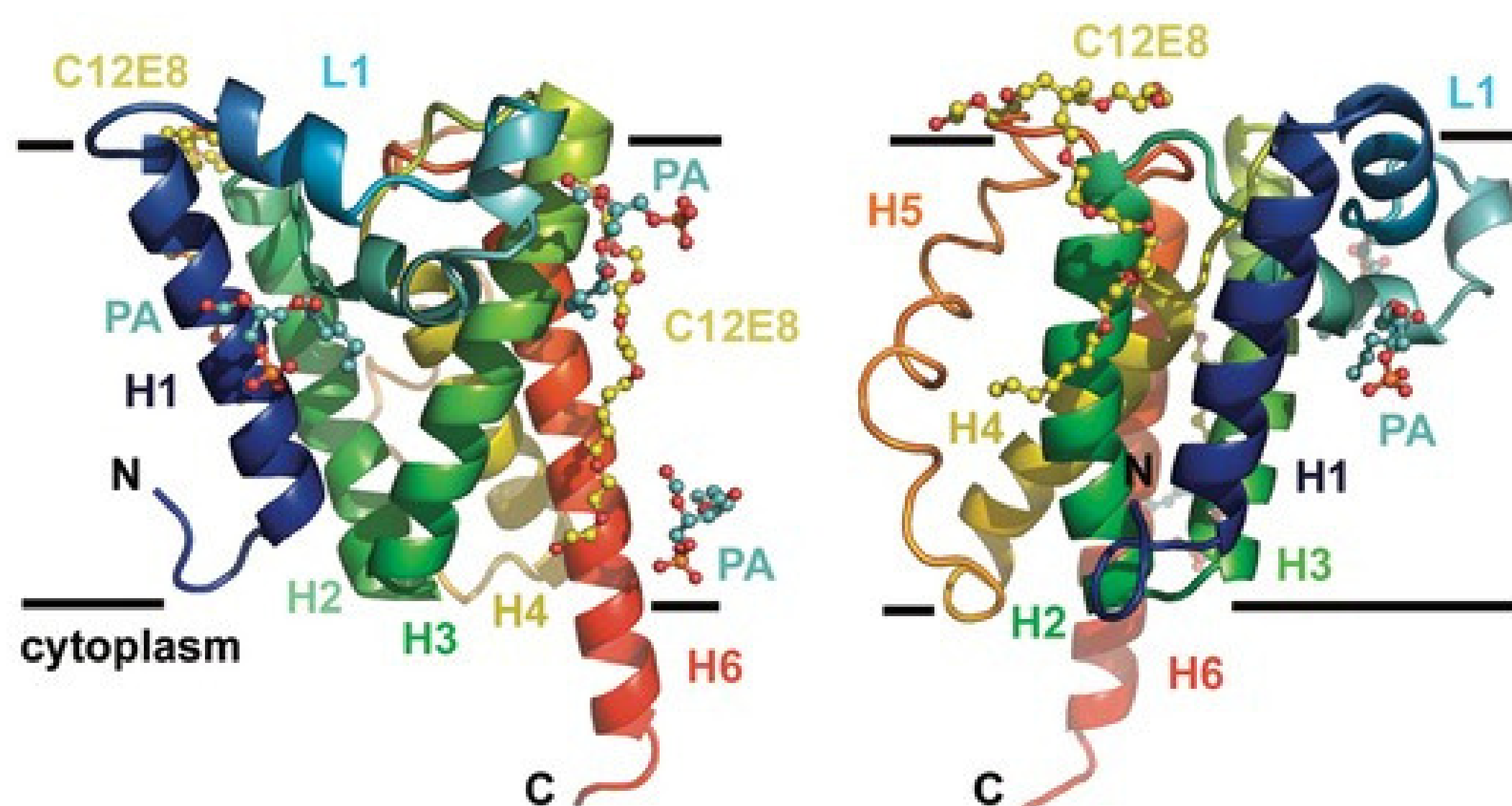




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## The rhomboid protease family – How does peptide bond hydrolysis occur within the lipid bilayer?



Rhomboid proteases are serine proteases that are located in cellular membranes. Discovered in *Drosophila* they were shown to cleave transmembrane proteins and release signalling molecules. Initially there was doubt that these were indeed proteases since water is required for peptide bond hydrolysis. Proof that these were proteases came from both biochemistry and crystallographic studies, that revealed a catalytic site buried in an alpha-helical bundle. This activity site is located within an aqueous cavity on the helical bundle separating it from the hydrophobic lipid bilayer. Members of the rhomboid intramembrane protease family are found in all kingdoms from bacteria to humans. In eukaryotic cells, they are found in the plasma membrane, ER and Golgi membranes with various functions from the unfolded protein response to protein trafficking. Also, a rhomboid protease family member is found in the mitochondrial membrane. This protease plays a role in mitochondrial homeostasis and is important in neurological function. In this talk I will discuss crystallography studies on the rhomboid protease family and biochemical kinetic analysis of substrate cleavage. I will cover its roles in various cell types and end with the unexplored role of this protease family in bacteria.