

# Phylogeny unites apicomplexan and fungal transmembrane proteins in an ancient eukaryotic superfamily

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Eukaryotic pathogens are more closely related to their vertebrate hosts than bacterial pathogens, making drug discovery more challenging. The ideal drug target is essential in the pathogen and lacks homologs in the host, therefore accurately detecting homology is important for drug target identification.

We identified a new family of transmembrane proteins that are found in diverse eukaryotic clades but not in vertebrates. Members of this family include Cysteine Repeat Modular proteins (CRMPs) which are required for host cell invasion in the apicomplexan parasite *Toxoplasma gondii*, and fungal FLC proteins which are required for virulence in diverse fungal pathogens. Our phylogenetic analysis suggests this protein family could be targeted to treat a range of eukaryotic pathogens, however, we have almost no understanding of how these proteins function at the molecular level.

We show that structural predictions of CRMPs and FLCs share a unique arrangement of nine transmembrane helices, and we identify conserved motifs shared by members of this family. Topology predictions show that these proteins have an extracellular N-terminus that is highly variable in domain composition and length, and an unstructured cytosolic C-terminus. Overall, the conserved transmembrane domain coupled to variable extracellular domains is characteristic of transmembrane sensory signalling proteins. Future work will determine if and how these proteins sense and transduce environmental signals.