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S E M I N A I R E

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" Dissecting protein-membrane interfaces and usage on viral proteins".

Peripheral membrane proteins (PMPs) include a wide variety of proteins that have in common to bind transiently to the chemically complex interfacial region of membranes through their interfacial binding site (IBS). In contrast to protein-protein or protein-DNA/RNA interfaces, peripheral protein-membrane interfaces are poorly characterized.
I collected a dataset of PMP domains representative of the variety of PMP functions: membrane-targeting domains (Annexin, C1, C2, discoidin C2, PH, PX), enzymes (PLA, PLC/D) and lipid-transfer proteins (START). The dataset contains 1328 experimental structures and 1194 AphaFold models. I mapped the amino acid composition and structural patterns of the IBS of each protein in this dataset, and evaluated which were more likely to be found at the IBS compared to the rest of the domains' accessible surface.
I find that about two thirds of the PMPs in the dataset have protruding hydrophobes (Leu, Ile, Phe, Tyr, Trp and Met) at their IBS. The three aromatic amino acids Trp, Tyr and Phe are a hallmark of PMPs IBS regardless of whether they protrude on loops or not. This is also the case for lysines but not arginines suggesting that, unlike for Arg-rich membrane-active peptides, the less membrane-disruptive lysine is preferred in PMPs. Another striking observation was the over-representation of glycines at the IBS of PMPs compared to the rest of their surface, possibly procuring IBS loops a much-needed flexibility to insert in-between membrane lipids. The analysis of the 9 superfamilies revealed amino acid distribution patterns in agreement with their known functions and membrane-binding mechanisms. Besides revealing novel amino acids patterns at protein-membrane interfaces, our work contributes a new PMP dataset and an analysis pipeline that can be further built upon for future studies of PMPs properties.
Finally, I'll discuss how these discoveries can advance our understanding of the HEV viral protein pORF1 by modeling and predictions of membrane interactions.

Jeudi 15 décembre 2022

14h00

Salle des conférences