

## MS34-P08 | UNDERSTANDING OF CHOLESTEROL TRANSPORT IN NPC FAMILY PROTEIN: A COMPUTATIONAL STUDY

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Even though there has been significant progress of understanding the dietary cholesterol exchange in cellular environment, many of the details still remains unclear. The transmembrane protein NPC1 inside lysosome plays one of the major roles in cholesterol transport mediated by NPC2. Meanwhile, NPC1L1 (Niemann-Pick type C1 like 1), which is related to the dietary cholesterol absorption process in small intestine, shares sequence homology with NPC1. However, unlike NPC1, NPC2 is not involved in cholesterol internalization with NPC1L1. The structure of N-terminal domain (NTD) of NPC1 in complex with cholesterol (PDB id: 3GKH and 3GKI) was known while only cholesterol free NTD (PDB id: 3QNT) is known for NPC1L1. It is noted that the whole cryo-EM structure of NPC1 is determined (PDB id: 3JD8).

We compared the NPC1L1 and NPC1 in complex with cholesterol with molecular docking followed by molecular dynamics study for better understanding of these underlying behavior. The NTD molecular dynamics simulation shows different structural and dynamical features. The difference in cholesterol internalization mechanism between NPC1 and NPC1L1 might be closely related to these structural and dynamical characteristics. We believe the current study can provide better understanding of cholesterol absorption/re-absorption process via NPC1 and NPC1L1 and their difference with atomic detail.