第140回 病態生化学セミナー
新興感染症ワクチン・治療用抗体研究開発センター共催

日時：令和 5 年 2 月 24 日（金曜日） 17 時00分～

場所：医学部第二研究棟 1階 セミナー室

演題：Structural insights into the hepatitis B virus receptor and bile acid transporter NTCP（日本語での講演となります）

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Roughly 250 million people are infected with hepatitis B virus (HBV) worldwide, and perhaps 15 million also carry the satellite virus HDV, which confers even greater risk of severe liver disease. Almost ten years ago the HBV receptor was identified as NTCP (sodium taurocholate co-transporting polypeptide), which interacts directly with the first 48 amino acid residues of the N-myristoylated N-terminal preS1 domain of the viral large (L) protein. Despite the pressing need for therapeutic agents to counter HBV, the structure of NTCP remains unsolved. This 349-residue protein is closely related to human apical sodium-dependent bile acid transporter (ASBT), another member of the solute carrier family SLC10. Crystal structures have been reported of similar bile acid transporters from bacteria, and these models with ten transmembrane helices are believed to resemble strongly both NTCP and ASBT. Using cryo-electron microscopy we have solved the structure of NTCP bound to an antibody, clearly showing the transporter has no equivalent to the first transmembrane helix of other SLC10 models, leaving the N-terminus exposed on the extracellular face[(1)]. Comparison of the different structures indicates a common mechanism of bile acid transport, but the NTCP structure also displays a pocket formed by residues known to interact with preS1, presenting new and enticing opportunities for structure-based drug design.

(1) Nature. 2022 Jun;606(7916):1027-1031. doi: 10.1038/s41586-022-04857-0.

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