Unraveling the Mechanisms of Site Selectivity in Fucosylation by Fucosyltransferases

Abstract

Fucosylation plays a pivotal role in a range of biological processes, including cell recognition, adhesion, and immune responses. The site-selectivity of fucosylation is essential for the precise incorporation of fucose into glycans, which underpins their diverse biological functions. In this talk, I will present our latest work on the investigation of the mechanisms underlying site-selective fucosylation of lacto-N-tetraose (LNT) and lacto-N-neotetraose (LNnT) catalyzed by FucTa from *Helicobacter pylori* and Bf13FT from *Bacteroides fragilis*, utilizing a combination of molecular dynamics simulations and experiments. The influence of glycosidic linkages and aglycones on the site-selectivity of fucosylation is examined. Upon the change in the glycosidic linkage from LNT to LNnT, the narrow binding pocket of Bf13FT restricts glycan accommodation, forcing it into the adjacent cleft. In contrast, FucTa exhibits a larger binding site, accommodating glycan conformation change upon the change in the glycosidic linkage. On the other hand, aglycone modifications induce conformational changes in glycans, resulting in an increase in site-selectivity. These insights advance our understanding of the enzymatic mechanisms of these fucosyltransferases and provide the mechanistic foundation for the rational design of fucosyltransferases tailored for the precise synthesis of different glycans.