Human milk oligosaccharides (HMO) are a family of structurally related glycans that are highly abundant in breast milk. Oligosaccharide fraction is the third largest solid component in human milk after lactose and lipids. There is an accumulating evidence that HMO can provide significant benefits to the breast-fed infants. However, understanding of the exact HMO functions is still incomplete due to the lack of individual compounds in sufficient quantities. Therefore, development of expeditious strategies for the synthesis of HMO has been increasingly important.

Among all the methods available for oligosaccharide synthesis, armed-disarmed strategy introduced by Fraser-Reid is based on chemoselective activation of different building blocks. Later, the scope of this armed disarmed strategy was broadened by the introduction of other reactivity levels that included superarmed glycosyl donors. One of those was invented by Bols and co-workers wherein the superarming property was achieved by the conformational change to the glycosyl donor. The other type of glycosyl donors was introduced by our lab wherein the superarming was achieved using conventions of the O2/O5 cooperative effect (electronic effect).

Presented herein is the expansion of our work on the investigation of hybrid glycosyl donors that combine aforementioned conformational and electronic effects. The major emphasis of this study was to compare the reactivity of differently protected glycosyl donors by competition studies. The applicability of the developed glycosyl donors in one-pot oligosaccharide synthesis has been demonstrated. This ultimately led us to the development of general chemical strategies for the synthesis of HMO. To demonstrate the versatility of this approach, we synthesized four common core HMO: lacto-N-tetraose, lacto-N-neotetraose, lacto-N-hexaose, and lacto-N-neohexaose.