PROGRESS REPORT for Mizutani Foundation Research Grant

Reference Number: 200080
Principal Investigator: Hongzhi Cao
Organization: National Glycoengineering Center, Shandong University
Period: April 1, 2020 – March 31, 2021
Grant Title: Chemoenzymatic synthesis and functional study of 0-series gangliosides
Progress Report:

(a) Abstract:

The lack of structurally well-defined oligosaccharides and glycoconjugates is a major obstacle in glycobiology and glycomedicine. Due to the structural complexity and diversity of oligosaccharides and glycoconjugates, their synthesis is challenging. Therefore, there is an urgent need to develop a general strategy for the diversity-oriented synthesis of glycans and their conjugates. Chemical synthesis of glycans and is a time-consuming process and requires well-trained personnel. In contrast, chemoenzymatic methods, combining the advantages of both chemical and enzymatic synthesis, are more efficient, convenient and environmentally friendly. **The objectives of this project** are to develop convenient and efficient chemoenzymatic synthetic strategies for the rapid and diversity-oriented assembly of complex oligosaccharides of biological importance. **The methods used in this project** included 1) enzymatic modular assembly (EMA), in which bacterial glycosyltransferases were used in combination with sugar nucleotide donor generation enzymes for the *in situ* sugar nucleotide donors production and glycosidic linkage construction occur in one-pot; 2) substrate engineering strategy, which was based on the insight of the promiscuity and substrate adaptability of enzymes and careful tuning of the substrate structures to realize the precise control of enzymatic reactions; 3) high throughput glycan array technology for the functional studies of the obtained glycans. We have obtained the following **research results and progress**: 1) the diversity-oriented synthesis of 0-series gangliosides; 2) the diversity-oriented synthesis of poly-N-acetyllactosamine derivatives; 3) the diversity-oriented synthesis of complex blood group Sd^a antigens and hybrid Lewis antigens; 4) the development of a general methodology for the site-specific enzymatic fucosylation; 5) the development of a rapid enzymatic assembly strategy of oligosaccharides.