

The Fifth Green and Sustainable Chemistry Award
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Automated Glycoconjugate Synthesis by Artificial Golgi Apparatus

The fact that automated synthesizers of nucleotides (DNA/RNA) and peptides (proteins) are already commercially available, establishes them as indispensable devices for the investigation of functional roles of genomes and proteins as well as the development of a variety of therapeutic reagents. Advent of practical method for the synthesis of glycoconjugates has been strongly required in order to reveal essential functions of carbohydrates in biological events. Although recent progress has been made in the liquid-phase and solid-phase chemical syntheses allowed for making a variety of oligosaccharides and glycopeptides, the general approaches based on organic chemistry are still limited regarding the target structures and were found technically troublesome by general biochemists or medical scientists. Enzymatic synthesis is a potential alternative for the chemical syntheses of complicated oligosaccharides, because they have the advantage of stereo- and regio-selectivities in the glycosylations without tedious procedures for protection/deprotection and toxic reagents/solvents.

We have developed an automated carbohydrate-synthesizer (glycoconjugates-synthesizer) “GolgiTM” by mimicking biosynthetic system of the Golgi apparatus in cells. The significant fact that biosynthesis of glycoproteins in cells needs both random coil polypeptides displaying multiple sugar-acceptors and a series of membrane-immobilized glycosyltransferases have greatly motivated us to design versatile strategy for the polymer-supported enzymatic syntheses of various glycoconjugates such as oligosaccharides, sugar derivatives, and sphingoglycolipids. The present GolgiTM system was improved by using tailored-magnetic beads for immobilizing glycosyltransferases and fine-filter membrane system to achieve fully automated synthesis in 36 or 96-well reaction vessel. The computer system was also well designed to be user friendly machine for broad area of researchers. In combination with convenient molecular shuttle with hetero-bi-functional linker, it was demonstrated that combined use of GolgiTM with conventional peptide synthesizer allows for high throughput parallel/combinatorial synthesis of biologically important glycopeptides related to tumor antigenic structures.

It is our belief that this concept and an innovative technology will become part of the entrenched repertoire for the practical and green chemical synthesis of glycoconjugates and carbohydrate-containing materials as bio-industrially attractive target molecules.