The Logic of Automated Glycan Assembly

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Carbohydrates are the dominant biopolymer on earth and play important roles ranging from structure (cellulose as building material for plants and chitin for animals) to function in many biological systems. While the other two major classes of repeating biopolymers, oligonucleotides (DNA and RNA) and proteins, are now well understood, glycans remain poorly studied since access to pure samples from natural sources is exceptionally difficult. Automated solid phase synthesis of oligopeptides and oligonucleotides has fundamentally impacted biology and medical research. Similarly, the glycosciences would benefit from synthetic tools.

The synthesis of glycans was for many decades a highly specialized, technically demanding and time-consuming undertaking. To spend several years for the synthesis of a trisaccharide was not uncommon until just a few years ago. The goal of my laboratory since its start in 1998 was to develop a general method for the automated assembly of glycans that could be used by anybody. After the initial proof of principle,[1] we spent many years[2] to address all aspects of glycan synthesis including the development of solid support and linkers, the design and synthesis of building blocks, the creation of an automated synthesizer. [3] In the context of the synthesis of ever more complex oligo- and polysaccharides,[4-6] we developed automated synthesis protocols, post-synthesis manipulations and purification methods to access complex glycans quickly and reliably. Finally, oligosaccharides as long as 50-mers are now accessible within days.

The general protocols we developed resulted in the commercialization of the Glyconeer 2.1™ synthesizer as well as the building blocks and all reagents.[7] Several laboratories around the world are now using the automated glycan assembly platform to meet the demand of biologists for defined carbohydrates. Rapid access to defined oligosaccharides has been the foundation to many applications including synthetic tools such as glycan microarrays, glycan nanoparticles and anti-glycan antibodies. The platform technology is helping to address real-life problems by the creation of new vaccines and diagnostics. After addressing mainly mammalian glycobiology, material science and plant biology are benefitting increasingly from synthetic glycans.

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