

SYNTHESIS AND STRUCTURAL ANALYSIS OF ANTIPARALLEL GLYCAN HAIRPINS

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Natural biopolymers have inspired the development of synthetic analogues – i.e. foldamers – capable of adopting defined conformations and forming programmable three-dimensional architectures. These compounds are mainly based on peptides and nucleic acids, that are well understood at the molecular level. Following these examples, we recently designed a glycan adopting a stable secondary structure, challenging the common belief that glycans are not capable of folding due to their flexibility [1].

Herein, we present new design principles to access a linear glycan capable of spontaneously folding into an antiparallel arrangement, establishing a new class of synthetic oligosaccharide foldamers. We have rationally designed a rigid turn unit sustained by a non-conventional hydrogen bond. This turn unit allowed for the construction of a glycan antiparallel hairpin, stable secondary structures not identified in nature. Automated glycan assembly facilitated rapid access to synthetic analogues of different lengths. Nuclear magnetic resonance (NMR) and SAXS conformational analysis provided definitive evidence of the folded conformation of the synthetic glycan hairpin. These results offer a basis for designing new glycan architectures, with potential applications in glycobiology and material sciences.

References:

1. Fittolani, G., Tyrikos-Ergas, T., Poveda, A., Yu, Y., Yadav, N., Seeberger, P. H., Jimenez-Barbero, J., Delbianco, M., *Nature Chemistry*, **2023**, 15(10), 1461-1469.