Carbohydrate foldamers and assemblies

Martina DELBIANCO [1]

[1] Max Planck Institute of Colloids and Interfaces, Potsdam-Golm Science Park, Am Mühlenberg 1 OT Golm, 14476 Potsdam, Germany

martina.delbianco@mpikg.mpg.de

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. In contrast, the complexity of carbohydrate synthesis and structural analysis have prevented access to synthetic carbohydrates capable of adopting defined geometries. In the Delbianco group, we prepare well-defined carbohydrates to understand how the primary sequence affects the carbohydrate conformation.1 With multiple analytical techniques, we study the conformation of single carbohydrate chains2 and explore how several carbohydrate molecules aggregate to form a material3.

Building on this fundamental knowledge, we present the rational design and synthesis of a glycan adopting a stable secondary structure, challenging the common belief that glycans are not capable of folding due to their flexibility. By combining natural glycan motifs, stabilized by a non-conventional hydrogen bond and hydrophobic interactions, we have designed a glycan hairpin, a secondary structure not present in nature. Automated glycan assembly enabled rapid access to synthetic analogs, including site-specific 13C-labelled ones, for NMR conformational analysis. Long-range inter-residue nuclear Overhauser effects (NOEs) unequivocally confirmed the folded conformation of the synthetic glycan hairpin. The ability to control the conformation of glycans could lead to the generation of 3-D architectures, with applications in catalysis and nanotechnology.

Bibliographic references:

[1] Y. Yu, T. Tyrikos-Ergas, Y. Zhu, G. Fittolani, V. Bordoni, A. Singhal, R. J. Fair, A. Grafmüller, P. H. Seeberger, M. Delbianco, Angew. Chem., Int. Ed. 2019, 58, 1433-7851

[2] X. Wu, M. Delbianco, K. Anggara, T. Michnowicz, A. Pardo-Vargas, P. Bharate, S. Sen, M. Pristl, S. Rauschenbach, U. Schlickum, S. Abb, P. H. Seeberger, K. Kern, Nature 2020, 582, 375-378.

[3] G. Fittolani, D. Vargová, P. H. Seeberger, Y. Ogawa, M. Delbianco, J. Am. Chem. Soc. 2022, 144, 12469-12475.