ISBN:
978-1-917892-15-5

Darón I. Freedberg OVRR, CBER, FDA

Silver Spring, Maryland, USA

Unveiling solution glycan conformations

Abstract:

Despite the vast diversity of glycans, we face common, and often interconnected, challenges in their solution NMR structural studies:
1) discrimination of distinct conformations amongst a conformation-rich landscape,
2) limited structural data and
3) spectral overlap, especially observed for homopolymers.

We've addressed these issues by improving spectral analysis, sensitivity and resolution, though not simultaneously. To address the first challenge, we've developed new methods to determine solution conformations and extract thermodynamic and kinetic data for these conformational equilibria in glycans in the fast exchange limit. We will show how using labile ^{1}H signals help alleviate two of these challenges and thus increase the repertoire of structural data. To address the second and third challenge, we've added OH detection as a way to increase spectral dispersion. Once detected, we can also detect hydrogen bonds through heteronuclear J-coupling. Ultimately, these help to discriminate unique, potentially biologically active conformations and refine structural models and improve vaccines and therapeutics. Finally I will present our latest results in structure determination demonstrating the combined power of the methods we developed and our latest results that use the above methods in our efforts to enable and enhance the structural studies of larger homo- and hetero-oligosaccharides.

Keywords: glycan conformation, hydrogen-bonding, hidden conformation, NMR

Biography: My group has been working to characterize the three-dimensional structure and dynamics of polysaccharides in solution. Our prime tool is NMR spectroscopy because it allows us to obtain structural details at atomic resolution. We have characterized larger and larger oligosaccharides by developing new methodologies that overcome technical limitations. These will help us enhance our understanding of polysaccharide structure-function relationships