



QSB SEMINAR SERIES 291

NMR of Glycans ON and OFF cells

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ABSTRACT

Carbohydrates are ubiquitous in nature and participate in a wide variety of cellular processes. They make up bacterial capsules, play roles in cell-cell interactions such as immune responses, fertilization, inflammation, and cell growth, influence protein folding and stability, and may be involved in signal transduction. Given the variety of monosaccharides, linkage types, and functional group modifications, oligosaccharides alone have potential structural complexity unmatched by any other biomolecule.

Despite their importance, carbohydrate structure-function relationships, or “glycan code”, are poorly understood. Our group is delineating carbohydrate three-dimensional solution structure to gain insight into how carbohydrates function, which should facilitate development of vaccines, drug delivery systems, and antibiotics of the future. Our goal is to unveil carbohydrate structure-function relationships using heteronuclear multidimensional NMR to delineate conformation and dynamics of ^{15}N , ^{13}C enriched oligo- and polysaccharides.

In recent research, we sought to understand why a, 2->8 polysialic acid induces almost no immune response in humans, while other polysaccharides induce a stronger immune response. We hypothesized that a three-dimensional structural difference between polysaccharides on and off cells may be the source of this difference. To test this hypothesis, we deciphered the structure of ^{15}N , and ^{13}C polysialic acid on bacteria and found that the structure is quite similar to purified polysialic acid. In a continuing effort to address this question, we are studying a, 2->8 tetrasialic acid in solution. Our recent studies of the labeled tetramer show evidence for a helix with two residues per turn. Finally, we recently developed methods to observe hydrogen bonding involving hydroxyl groups in carbohydrates. We are able to directly detect hydrogen bonds and assign directionality. We also recently developed methods to measure hydroxyl group H/D exchange rates in glycans, to infer hydrogen bonds in systems in which we cannot directly detect them. Direct detection of hydrogen bonds is a powerful structural descriptor since only certain conformations can explain their presence. Therefore, hydrogen bonds, in opposition to other NMR observables, provide evidence of unique three-dimensional structures even when coexisting with other conformations in solution. Together, these experiments are helping to expand the repertoire of methods available to determine carbohydrate three-dimensional solution structures.