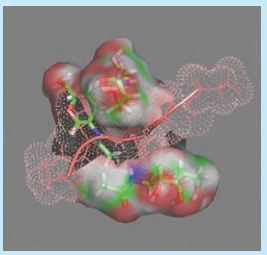
Sensing Sugar's Shape

Changes in the type and distribution of carbohydrate groups adorning a protein can have serious biological implications. For example, the appearance of otherwise-rare serine- or threonine-linked α-*O*-*N*-acetylgalactosamine (GalNAc) glycan modifications, known as Tn antigens, is associated with a poor cancer prognosis.

Existing analytical methods generally lack the sensitivity to closely characterize the structural effects of changes in glycan modification patterns or how those changes alter interactions between a protein and its partners. Borgert *et al.* have tackled this challenge in a new study that pairs nuclear magnetic resonance and glycopeptide microarray binding studies to analyze Tn antigen-containing peptides and other representatives of the larger mucin glycoprotein family.

To begin, they obtained structures for seven differentially glycosylated variants of a mucin-derived peptide sequence containing multiple sequential threonines. Their data showed that as glycosylation density increased, the glycan molecules exhibited higher levels of organization, with twists in the peptide backbone allowing individual GalNAc residues to maintain the same overall orientation in either the presence or absence of adjacent glycans. These new structures have been deposited in the PDB, which previously contained coordinates for only two mucin motifs.

The researchers subsequently examined the relative specificity of Tn antigen-targeting antibodies with an array containing dozens of different α-*O*-GalNAc-containing peptides. Unlike lectins, which bind promiscuously to α-GalNAcs, the seven different monoclonals could be grouped into three classes, recognizing different subsets of glycopeptides. Likewise, polyclonals elicited against three different mucin glycopeptides exhibited clear differences in their specificity profiles. Given the broad structural similarity shown for individual GalNAc residues, this indicates that preferential antibody recognition for individual Tn antigens is mediated by interaction with elements formed through interplay of glycan and peptide structure. – *Michael Eisenstein*



Borgert, A. *et al. ACS Chem. Biol.*, Published online 23 Mar 2012, doi: 10.1021/cb300076s

Damage Control

'Smart' hydrogels differ from their less enlightened counterparts in their capacity to react quickly to changes in the environment or to return automatically to a particular shape after undergoing deformation. However, although scientists have developed other classes of synthetic materials with the capacity for self-repair of damage, this remains a test that even smart hydrogels have failed.

A polymer developed by Phadke *et al.* now appears to make the grade. Their team identified acryloyl-6-aminocaproic acid (A6ACA), which forms hydrogel structures with dangling hydrocarbon chains that can potentially crosslink under appropriate environmental conditions. Seconds of exposure to acidic pH caused A6ACA hydrogel chunks to fuse tightly together, and longer-term exposure (up to 24h) further toughened both the bond and the individual hydrogel segments. The researchers determined that this effect is mediated by extensive hydrogen bonding between protonated carbonyl groups within the side chains with other carbonyl and amide groups. At alkali pH, these carbonyl groups are deprotonated and the interaction between hydrogel segments is promptly disrupted. This fusion between hydrogels is exquisitely dependent on chain length; short chains fail to form the interactions required for tight bonding,

while long chains create steric interference and are prone to unproductive self-interaction.

A6ACA strikes a perfect balance, and performed well in a number of tests. For example, mechanical damage to polymer layers was healed nearly instantly by exposure to low-pH buffer, and A6ACA proved equally effective at patching damage to gastric tissue isolated from rabbits. The researchers were also able to assemble complex structures by fusing together individual hydrogel segments, suggesting that this polymer or its derivatives could offer a versatile tool for diverse applications. – *Michael Eisenstein*

Phadke, A. *et al. Proc. Natl. Acad. Sci. USA*, 109(12), 4383–4388 (2012).