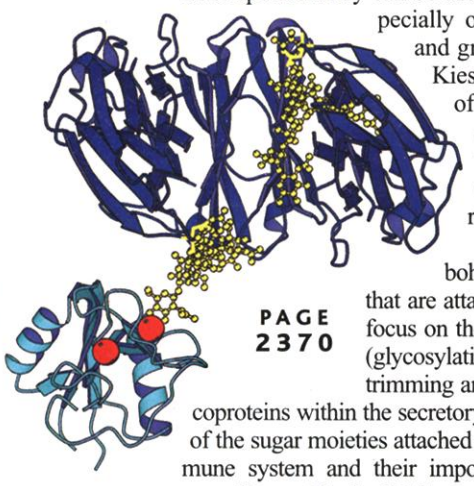
# Cinderella's Coach Is Ready

The chemistry and biology of carbohydrates has been a Cinderella field: an area that involves much work but, alas, does not get to show off at the ball with her cousins, the genomes and proteins. What has rescued this Cinderella from the shadows is no fairy godmother but a plethora of new synthetic and analytic methods that a previous generation of researchers would have found nearly magical nonetheless. Carbohydrate modifications of proteins and lipids are key factors in modulating their structure and function within cells. In the extracellular milieu, they exert effects on cellular recognition in infection, cancer, and immune response, but details of the specific mechanisms have often been sketchy. This special issue looks at advances in chemistry and biology aimed at understanding and controlling the outcomes of carbohydrate recognition.*

Pharmaceutical companies and biotech firms have long been interested in carbohydrate drugs, but successes have been few and far between. Prospects may be improving, however. In News stories, Alper (p. 2338) charts the recent ups and downs of the field and explores carbohydrate compounds that are currently in clinical trials aimed at fighting everything from inflammation and tissue rejection to hepatitis and cancer. Service (p. 2340) looks at the recent fortunes of companies trying to bring carbohydrate drugs to market and at a variety of strategies they are pursuing. Finally, four short profiles (pp. 2339, 2340, 2342, and 2343) offer a broader look at research taking place in labs investigating the role of carbohydrates in areas ranging from prion diseases to human evolution.

For chemists, studying carbohydrates has been labor-intensive compared to nucleic acids and proteins because of their branching and stereochemistry. Sears and Wong (p. 2344) overview emerging synthetic methods, including enzymatic routes, for synthesizing oligosaccharides and attaching them to peptides and proteins, which should allow these steps to become more automated. Dell and Morris (p. 2351) outline how ultrahigh-sensitivity mass spectrometry can be used to determine oligosaccharide structure, especially of glycoproteins, despite the small amounts and great complexity of the samples. Bertozzi and Kiessling (p. 2357) show how chemical inhibition of glycosynthetic pathways can be used to elucidate function in cells and how these pathways could be hijacked to control oligosaccharide structure at cell membranes to alter recognition or target drugs.



PAGE 2370

Our overview of the biological aspects of carbohydrates has mainly focused on carbohydrates that are attached to proteins. Helenius and Aebi (p. 2364) focus on the role of cotranslational carbohydrate addition (glycosylation) and subsequent modification by sugar trimming and addition in the folding and transport of glycoproteins within the secretory system. Rudd *et al.* (p. 2370) look at the role of the sugar moieties attached to many proteins and to some lipids of the immune system and their importance in immune recognition and immune surveillance. Finally, Wells *et al.* (p. 2376) focus on the modification of cytosolic proteins by the addition of O-linked *N*-acetylglucosamine and its potential role in intracellular signal transduction mechanisms.

The additional complexity and variety generated within the proteome by carbohydrates will provide further challenges beyond the one-to-one correlation of genetic sequence and protein sequence. We have already heard the word "glycomics" being whispered by guests at the ball.

–STELLA HURTLEY, ROBERT SERVICE, PHIL SZUROMI

* Online, we have included a number of links to Web sites that may prove helpful to readers; see www.sciencemag.org/feature/data/carbohydrates.shl

CONTENTS



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