

This Week's Citation Classic

Spiro R G. Glycoproteins. *Adv. Prot. Chem.* 27:349-467, 1973.

[Depts. Biological Chem. and Med., Harvard Med. Sch.; and Elliott P. Joslin Res. Lab., Boston, MA]

By 1973 it had been recognized that the attachment of sugar residues represents one of the major posttranslational modifications which a protein may undergo. This article reviews the information available on glycoproteins at that time in regard to their distribution, biological properties, composition, structural features, and metabolism. [The SC® indicates that this paper has been cited over 185 times since 1973.]

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"It was as a medical student that I first became interested in glycoproteins after being introduced to the pathological manifestations of diabetic microvascular disease. The nodular lesions in the kidney glomerulus particularly fascinated me as they were known to react intensely with the periodic acid-Schiff stain and were presumed to consist of glycoprotein material.

"When I started my postdoctoral biochemical training under A. Baird Hastings at the Harvard Medical School in 1956, I became aware that very little was known about glycoproteins at that time and indeed I remember that all the pertinent reprints could comfortably fit into one file folder. It therefore became evident to me that, as so often happens in science, I would have to take a long detour in order to understand the diabetic glomerular deposits. I soon developed a keen interest and commitment to the study of the biochemistry and biology of glycoproteins which has stayed with me to the present day.

"The 1960s proved to be an exciting period in which work from a small number of laboratories defined the structural features of carbohydrate-containing

proteins and characterized some of the enzymes involved in their assembly. My laboratory concentrated at that time on fetuin, α_2 -macroglobulin, thyroglobulin, collagens and basement membranes and eventually showed that the diabetic glomerular lesions were made up of basement membrane material. Moreover, during this period sophisticated analytical and structural techniques were developed which permitted the study of glycoproteins at high levels of sensitivity and which revealed that they are widely distributed in nature as biologically important molecules, including enzymes, hormones, immunoglobulins, lectins, transport and clotting proteins, lubricants, and membrane components.

"When I reviewed this rapidly expanding field for the *New England Journal of Medicine* and the *Annual Review of Biochemistry*, I discovered that investigators in quite diverse fields had developed a desire to know more about these molecules. The decision to write an article for *Advances in Protein Chemistry* was based on a perception that this interest in glycoproteins would further escalate and that a comprehensive review would serve a useful function. Indeed in recent years there has been a veritable explosion of activity in the area of glycoproteins.

"I believe that my review in *Advances in Protein Chemistry* may be cited by investigators who are attempting to correlate structure with function after becoming aware of the biological role of glycoproteins, particularly at the cell surface, where the sugar components appear to be specific determinants involved in recognition phenomena. Another group of researchers who may refer to this review are cell biologists interested in the assembly of membrane and secretory proteins, since carbohydrate attachment can occur at an early stage through the mediation of lipid-saccharide donors, followed by processing reactions to yield the mature carbohydrate units."