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Obituary:
An appreciation of Gilbert G. Ashwell — A pioneer of Glycobiology

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Gilbert G. Ashwell July 16, 1916 - June 27, 2014.
This picture was taken 1976 at his office in NIH.

It is with great sadness that we learned the passing away of George Gilbert Ashwell at the age of 97. Gil Ashwell was a pioneer in the field of glycobiology and is best known as a discoverer of the asialoglycoprotein receptor in the liver. Recently, Ashwell proposed this receptor be named Ashwell-Morell receptor, taking his friend and collaborator's name, Anatol G. Morell, who was at the Albert Einstein College of Medicine [1]. With this as momentum, a host of carbohydrate recognizing receptors have been identified such as selectin, siglec, macrophage lectins and dendritic cell lectins on various cell surfaces, mannan (or mannose)-binding protein (or lectin) and galectin in serum and the matrix, respectively and calnexin, calreticulin among others in organelles. These carbohydrate recognizing receptors may be collectively defined under the concept of "endogenous lectin". Endogenous lectins are known to play pivotal roles in various biological pathways in immunology, cell differentiation, tumors and many other diseases.

Ashwell was born in Jersey City, New Jersey in 1916. After high school, he attended University of Illinois, where he earned his B.A. in 1938 and M.S. in 1941. He then joined Columbia University and received his M.D. in 1948. After graduating, he remained at Columbia University as a research fellow for 2 years. In 1950, Ashwell joined the NIH National Institute of Arthritis, Metabolism, and Digestive Diseases. He became chief of NIAMD's Laboratory of Biochemistry and Metabolism in 1967 and held that position through most of his NIH career. Afterwords, this institute has split into the National Institute of Arthritis and Musculoskeletal and Skin Diseases and the National Institute of Diabetes and Digestive and Kidney Diseases.

The initial collaboration with Morell was undertaken with the aim of developing a radioactive preparation of ceruloplasmin specifically labeled at the carbohydrate residue. The development of this new technology included removal of sialic acid with neuraminidase, enzymatic oxidation of the exposed galactose residues and reduction of the resultant aldehyde derivative with tritiated borohydrate. When the highly radioactive human asialoceruloplasmin was injected into a rabbit, essentially all of the labeling disappeared from the animal's circulation in a matter of minutes. This disappearance was found to be accompanied by an equally rapid accumulation in the liver. Further investigation demonstrated that majority of normally circulating serum glycoproteins behaved in a manner similar to ceruloplasmin and that plasma membranes

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of the liver were the primary binding sites for circulating asialoglycoproteins [2]. Subsequently, they isolated and chemically characterized the receptor involved as the first mammalian lectin [3, 4]. This was perhaps the first receptor ever to be described. As for the physiological function of the Ashwell-Morell receptor, Dr. Marth's group showed recently that it mitigates the lethal coagulopathy of sepsis [5]. In addition, Ashwell-Morell receptor has had an impact on the manipulation of drugs and biologics for their specific delivery to the liver thus increasing biological efficacy in the body.

In recognition of his contribution to science, Ashwell was elected as a member of the National Academy of Sciences in 1979, received the prestigious Gairdner Foundation Prize in 1982; the ASBC-Merck Prize in 1984; an honorary doctoral degree from the University of Paris in 1988; the Alexander von Humboldt Foundation Senior Scientist Award in 1989; and the Society for Glycobiology's Karl Meyer Award (with Dr. Saul Roseman) in 1993. Ashwell was named NIH Institute Scholar in 1984. This was a special title created to recognize his distinguished scientific achievements and he was the only recipient of such rank.

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