Furthermore, at present it remains unclear whether blocking the Ashwell receptor—for instance, with synthetic high-affinity ligands—may diminish thrombocytopenia once full-blown DIC has developed and whether this could have a beneficial effect in severe sepsis.

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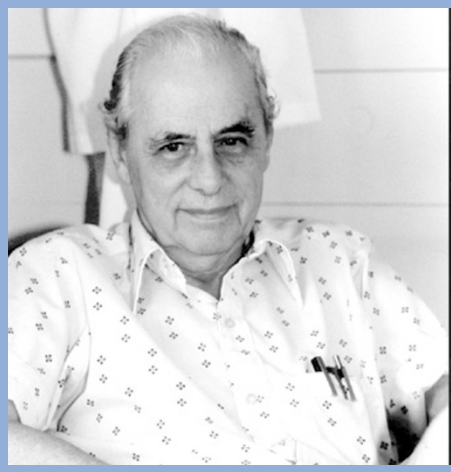
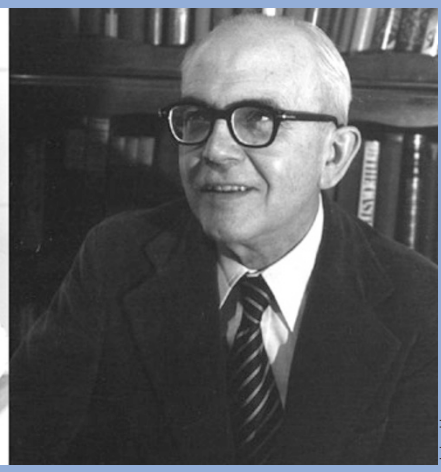
Gilbert Ashwell: sweet on science

In 1974, Gilbert Ashwell and Anatol Morell discovered a receptor in the liver that recognizes particular glycoproteins, dubbed asialoglycoproteins. We asked Ashwell about his discoveries and what he thinks of the study by Grewal *et al.*[1] in this issue, which suggests that the receptor is involved in regulating sepsis.



Gilbert Ashwell



Anatol Morell

John Hanover

How did you discover the receptor?

It came by accident, as many things do in science. I was on sabbatical at Columbia University in 1965–1966, and my dear friend Anatol G. Morell and his wife, Halina, frequently invited me to dinner, as I was alone in New York—my family was in Washington. During one of those times, Anatol, who was at the Albert Einstein College of Medicine, brought up that he had a problem determining the half-life of the glycoprotein he was working on, ceruloplasmin, a copper-carrying protein. Since my background was more in carbohydrates, I suggested that we label a terminal galactose with a long-lasting tritium isotope to determine the serum half-life.

This material, when injected into a rabbit, rapidly disappeared from the serum within five to ten minutes and was recovered essentially complete in the liver. The critical problem then was the demonstration that galactose was the unique sugar required for hepatic recognition by the then–unknown carbohydrate-binding protein.

From there we went on to isolate and chemically characterize the appropriate receptor as the first mammalian lectin. We both feel that if this receptor is to be identified, other than as an asialoglycoprotein receptor, a more appropriate name would be the Ashwell-Morell receptor.

What were some of the early implications of the finding?

For years it had been known that hormones were inactive if they had been desialyated in preparation; with this finding it became immediately clear what happened: the hormones never got to their target organ—they were disposed of in the liver. Since then, people have used the receptor in experiments to deliver drugs specifically to the liver. I worked for years and years to finally convince people that the carbohydrates were more important than just glucose.

What do think of the study of Marth and his colleagues in this issue?

I was dumbfounded. I was so completely taken aback, because I had been working on this for over 30 years, trying find out the real biological function of this protein. I, and others, had worked with the knockout mice and found that they had perfectly normal lives, as far as we could tell. We had figured originally that we had discovered the normal mechanism for the turnover of serum glycoproteins, and when I found out that wasn't right, I was very despondent. Hence my delight in learning of Dr. Marth's success; this was the first real evidence of physiological function.

You still go into the lab every day. What are you working on now?

I still work, as a guest worker, in the lab of John Hanover at the National Institutes of Health. I have been involved in studying changes in carbohydrate metabolism in various mutant forms of *C. elegans*. With the exception of the last few weeks, when I've been combating a neck problem, I get to the lab at seven and work until noon. I will be 92 in July, so I feel I have a right to take only part of the day. I can't stay away.

1. Grewal *et al. Nat. Med.* **14**, 648-655 (2008).