between monomers and dimers of GAL1 as a general phenomenon regulating its activity has to be questioned. As no data shows a monomerization of human GAL1, one must be careful before concluding that results on monomer–dimer equilibrium obtained on a rodent model have relevance to human GAL1. Furthermore, several lines of evidence strongly support the concept of a dimeric stable structure of human GAL1. On reducing SDS–PAGE, a faint band is often observed representing dimers of the protein that are not fully dissociated even after heating in SDS and β-mercaptoethanol. And in tissue and cell extracts there is some evidences that GAL1 is not free but associated with its biological partners to form high mass complexes. In light of the fact that multivalent interactions require at least a bivalent lectin, it is likely that human GAL1 occurs in the cytosol as a dimer. The same is expected to be true for externalized galectin interacting with glycosylated cell surface receptors. Dimeric GAL1 should be necessary to induce biological effects for which clustering of receptors is required (Sharon, 1994).

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Albert Neuberger (1908–96): founder of modern glycoprotein research

Albert Neuberger, who passed away in London on August 14, 1996, was an outstanding scientist of enormous intellectual stature, a distinguished biochemist, and an inspiring teacher. He also rendered many services to the scientific community and to society in his country, in Israel and elsewhere.

Sixty years ago Neuberger proved for the first time the existence of glycoproteins, by demonstrating that carbohydrate is an integral part of a protein. Some 25 years later he identified, together with his coworkers, the first carbohydrate-peptide linking group. He thus laid the foundation for modern glycoprotein research. Neuberger also made seminal contributions to other areas of biochemistry, primarily porphyrins and lectins.

Ovalbumin—the first identified glycoprotein

Most proteins are now known to be glycosylated, and the detection, purification, and characterization of glycoproteins pose hardly any problems, even when available only in microgram

quantities. To appreciate Neuberger's pioneering achievement, it should be recalled that in 1936, when he first became interested in these substances, it was generally believed that, apart from mucins, ordinary proteins consisted only of amino acid residues, and that the presence of sugars in protein hydrolyzates was due to impurities. Moreover, the techniques for investigation of proteins and carbohydrates were primitive and required gram quantities of material. Methods such as electrophoresis, gel filtration, and chromatography of various types did not exist and the homogeneity of a protein preparation could not be easily assessed, except by crystallization. Neuberger chose to work on hen egg albumin, or ovalbumin, because it was the only protein available in quantity that could be crystallized and that was shown by colorimetric methods to contain carbohydrate. He could not separate the carbohydrate from ovalbumin by repeated crystallization, prolonged dialysis, ultrafiltration, heat denaturation, or mild acid treatment. For these experiments, *20 g* of the protein was needed. Another *120 g* of ovalbumin was then incubated for a period of 4–6 weeks with a mixture of pancreatic proteases and peptidases, sold under the name trypsin (luckily, no exo- or endoglycosidases, nor *N*-glycanases were present). Digestion appeared to have produced a material consisting almost entirely of free amino acids and unhydrolyzed carbohydrate. Removal of the amino acids was achieved mainly by their conversion to *N*-acetyl derivatives, which were extracted by chloroform. The remaining material was fully acetylated and purified by chloroform extraction, and the *O*-acetyl groups were removed by alkaline hydrolysis. Finally, 4.1 g of glycopeptide (originally referred to as "polysaccharide") was obtained. It contained only two monosaccharides, isolated after acid hydrolysis as crystalline derivatives, mannose as its *p*-bromophenylhydrazone and glucosamine as a Schiff base formed by condensation with 2,4-dihydroxybenzaldehyde. The molecular weight of the glycopeptide was estimated as 1200. It contained three acetyl groups; two were thought to belong to *N*-acetylglucosamine residues and the third to an amino acid to which the carbohydrate was linked. Four nitrogen atoms were present per molecule, two of which were accounted for by the glucosamine, and one represented the ammonia released upon hydrolysis, and which was assumed to be derived from an amide linkage. The fourth nitrogen was believed to come from the amino acid to which the carbohydrate was linked, and which could not be identified at the time (somewhat later, Neuberger thought it could be aspartic or glutamic acid). In the landmark article describing this work (Neuberger, 1938), Neuberger concluded that it "places beyond all doubt the question of the occurrence of carbohydrate in crystalline egg albumin and this glycoprotein contains a single carbohydrate prosthetic group that consists of four molecules of mannose and two of *N*-acetylglucosamine, with one point of attachment to the protein."

Because the clouds of war had gathered over Europe, Neuberger was unable to continue the work on glycoproteins. He returned to these substances again only in 1956. Together with Robin Marshall and other colleagues he identified in 1961 the carbohydrate-peptide linking group in ovalbumin as β-*N*-acetylglucosaminyl-asparagine (GlcNAc-Asn; Johansen *et al.*, 1961; Marks *et al.*, 1963; Marshall and Neuberger, 1964), both by degradation and by chemical synthesis. This linking group, the first of its kind, was identified almost simultaneously in three other laboratories, of Leon Cunningham in Nashville, TN; Ikuo Yamashina in Kobe, Japan; and V. P. Bogdanov in Moscow, and was synthesized by Roger Jeanloz in Boston. It was subsequently shown to be widespread in nature. A few years later, Neuberger and Marshall proposed that carbohydrate-linked asparagine is part of the sequon Asn-X-Ser/Thr (Neuberger and Marshall, 1968), a rule subsequently found to apply generally.

Studies on porphyrins and lectins

Research done by Neuberger from the late 1940s to the middle 1950s, and in parallel by David Shemin at Columbia University, New York, demonstrated that all four nitrogen atoms of the tetrapyrrole ring of the porphyrins are derived from glycine, and that δ-aminolevulinic acid is a key intermediate in the synthesis of these vital constituents of hemoglobin and of chlorophyll (Neuberger, 1960). This work helped explain the biochemical defect in acute porphyria, a disease believed to be the cause of insanity of King George III of England.

In 1971 I spent six months in Neuberger's laboratory at St. Mary's Hospital, and, as a result, he became interested in lectins. Together with A. K. (Tony) Allen, we purified wheat germ agglutinin by conventional techniques, found that it was composed of three isolectins, and that, contrary to earlier suggestions, it was not a glycoprotein (Allen *et al.*, 1973). We also proposed that the combining site of the lectin consists of three or four subsites with differing specificities, and occupies a cleft in the molecule resembling that of hen egg white lysozyme. The paper became a Citation Classic.

Over the next decade and a half, the lectin field was explored by Neuberger mainly with Allen, David Ashford, and Neila Desai. Among the several other plant lectins purified and characterized were those of the thorn apple (*Datura stramonium*) and potato (*Solanum tuberosum*). The latter lectin has a combining site similar to that of wheat germ agglutinin. Structurally, it is a most unusual glycoprotein, containing a large amount of hydroxyproline to which oligomers of the furanose form of L-arabinose are attached, in addition to galactose in α-linkage to serine (Ashford *et al.*, 1982).

Childhood and youth in Germany

Neuberger was born on April 15, 1908, in Hassfurt, a small town in northern Bavaria, to middle-class parents who were religious Jews (Neuberger, 1990). He received his early education first at home, mainly by private teachers or clergymen, with much emphasis on classics, including Latin and Greek, then at high school in Würzburg where besides classics, he also studied mathematics and physics, but not biology or chemistry. In addition, he received a remarkably good Jewish education, which had a permanent impact on his life. During his medical studies at the University of Würzburg, Neuberger took courses in chemistry, and his interest in the subject continued throughout his career. He also spent some time in a research laboratory in Berlin where he established a long lasting friendship with Ernst Chain, one of the many future Nobelists with whom he became closely associated (in 1945, Chain shared the Nobel Prize with Alexander Fleming and Howard Florey for their work on penicillin). After receiving a summa cum laude medical degree from the University of Würzburg, Neuberger worked for a short time as a clinician. However, with the situation in Germany becoming more uncertain, he decided to explore the possibility of transferring his activities elsewhere. A brief visit to England in 1932 convinced him that he would be quite happy living there. As soon as Hitler came to power in January 1933, he left Germany and came to London.

A fast rising career in England

Neuberger adapted rapidly to the British way of life, and achieved a remarkable mastery of the English language. In 1936 he obtained a Ph.D. degree from the University of London on the electrochemistry of amino acids and proteins, and remained to continue his postdoctoral research there. Just before the outbreak of World War II, he moved to the Department of Biochemistry at Cambridge University, which was at the time one of the world centers of biochemical research. It was headed by Frederick Gowland Hopkins, the father of British biochemistry and a Nobel Prize winner in 1929 with Christian Eijkman for their discoveries of the growth-promoting activities of vitamins. Unlike many refugees from Nazi Germany, he had a comfortable life at Cambridge, since he was awarded the prestigious Beit Memorial Fellowship. For some time during the war Neuberger served as consultant in nutrition to the Medical Directorate, General Headquarters, India Command, which gave him the opportunity to travel all over India, and to become familiar with a variety of medical problems of that country.

From 1950 to 1955 he was Head of the Department of Biochemistry at the National Institute for Medical Research that listed on its staff the Nobel laureates A. J. P. Martin (corecipient with R.L.M. Synge of the prize in 1952 for the invention of paper chromatography) and J. W. Cornforth (who was awarded the prize in 1975 for stereochemical investigations of enzyme-catalyzed reactions). He then moved to St. Mary's Hospital Medical School, where he was appointed Professor of Chemical Pathology. During 1958–1962 he also served as Principal of the Wright-Fleming Institute of the hospital, a position held earlier by Sir Alexander Fleming, the discoverer of lysozyme and penicillin. Neuberger was instrumental in bringing Rodney Porter to this Institute from Oxford (Porter shared in 1972 the Nobel Prize with Gerald Edelman for the discovery of the chemical structure of antibodies). Neuberger remained at St. Mary's until he reached the retirement age of 65. This did not mean, however, an end to active research, because he received an appointment at Charing Cross Hospital Medical School where he continued his studies and to publish scientific articles until his 80s.

Honors and awards

Neuberger was elected to the Royal Society in 1951, and derived enormous pride from the election to the Society in 1993 of his youngest son Michael, a noted biochemist at the MRC Molecular Biology Laboratory, Cambridge. It was one of the rare cases of father and son both being FRS. Among the other honors bestowed on him are the awards of CBE in 1964, then the Heberden Medal of the Royal Society of Medicine, and the Frederick Gowland Hopkins Medal of the Biochemical Society. In 1973, he was elected as Honorary Member of that Society. In the previous year he became Foreign Honorary member of the American Academy of Arts and Sciences. He was awarded the honorary degrees of Doctor of Laws from the University of Aberdeen in 1967, Doctor of Philosophy from the Hebrew University of Jerusalem in 1968, and Doctor of Science from the University of Hull in 1981.

A deep sense of duty

Neuberger believed that since "an academic scientist is in a privileged position in that he is being paid for doing exactly what he wants to do . . . this imposes a duty and a responsibility to give some of his time to work (not directly concerned with his own research) which might be beneficial to society as a whole, or to other scientists and academic colleagues." Thus, in England he was member of the Medical Research Council, the Agricultural Research Council, the Council of Scientific Policy, and of many other high-level committees. He also served as chief editor of several leading scientific journals, among them The Biochemical Journal (1947–55), published by the British Biochemical Society of which he was chairman (1967–69), and as associate managing editor of Biochimica and Biophysica Acta (1968–81). He was Chairman of the Governing body of the Lister Institute of Preventive Medicine from 1970; when the building housing the research laboratories was closed, he established, from the proceeds of the sale, the Lister Fellowships in medical research that have had an enormous impact on young scientists in Britain.

Since the 1960s, Albert Neuberger and his wife Lilian had developed a keen interest in, and became closely attached to Israel. They visited the country several times a year, making their home in the apartment they purchased in the heart of Jerusalem, where they made many friends. He even went back to his Hebrew, which he studied in childhood. During this period, Neuberger devoted much time and energy to the Hebrew University, Jerusalem, serving for almost two decades as Chairman of the Academic Committee of the Board of Governors of the University. The Committee had a great influence on the organization of the curricula and research in life sciences, including agriculture. These activities for the Hebrew University were part of the debt he felt he had to the people of Israel.

A penetrating mind with wide interests

Neuberger was a warm and kind person, a family man, modest and unassuming, with a clear penetrating mind and balanced views, who was liked and admired by many and whose advice was very often sought. He was widely read, not only in scientific subjects but also in literature, history, and Judaism and was keenly interested in many aspects of human life.

He had an interesting and varied life and was blessed with an exceptionally happy marriage to Lilian (née Dreyfus), whom he married in 1943. She provided him with great but unobtrusive support. Their four sons made each a successful career in a different field—law, economics, medicine, and science. The Neubergers were avid travelers, visiting countries near and far until not long ago. Lilian recorded these travels both in writing and in drawings, at which she is a master.

An inspiring teacher

Neuberger had numerous students and coworkers, many of whom made illustrious careers for themselves. Most prominent of them is undoubtedly Fred Sanger from the MRC Laboratory of Molecular Biology at Cambridge, twice Nobel laureate, in 1958 for elucidating the amino acid sequence of insulin, and then in 1980, together with Walter Gilbert, for a method for DNA sequencing. Sanger obtained his Ph.D. under Neuberger's guidance in 1943 for work concerned with protein metabolism and also did with him some studies of the nutritive value of potatoes, within the framework of the war effort. He regards Neuberger as his main teacher, "both by instruction and by example." In the obituary for Neuberger, (*Independent*, Aug. 19, 1996) Sanger wrote:

Not only did he teach me biochemistry, but he taught me how to do research, particularly how not to be afraid to venture into untrodden ground, and how not to worry too much when experiments did not work, but to get on and try something else . . . . I was always impressed by his wide knowledge of different aspects of biochemistry and his ability to work on them and produce fruitful results . . . . I was his only research student at the time, so we worked together at the same bench and I was able to benefit from his experience, ability and great kindness. I feel eternally grateful for what he did for me.

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Announcement

ISOBM International Workshop for Monoclonal Antibodies Against Sialyl Le^a and Related Antigens

The International Society for Oncodevelopmental Biology and Medicine (ISOBM) has initiated the Tissue Differentiation (TD) Workshops as a follow-up to the successful Workshop on Monoclonal Antibodies against CEA. The primary goal and purpose of these workshops is to characterize the wide array of monoclonal antibodies raised against molecules that have shown potential as tumor markers.

The sialyl Le^a antigen is the subject of the sixth workshop in the series (TD-6), and this work will be presented at the ISOBM meeting in Lausanne, Switzerland, in September 1997. The aim of this workshop is to fully characterize a broad panel of anti-sialyl Le^a and related antibodies, in order to determine their relative value in assay systems for monitoring patient disease in pancreatic, hepatobiliary and gastrointestinal cancer.

Members of the TD-6 Workshop committee are:
Phil D. Rye, Oslo, Norway (Chairman)
Nicolai V. Bovin, Moscow, Russia (Co-chairman)
Ben Appelmelk, Amsterdam, The Netherlands
Franz-Georg Hanisch, Koln, Germany
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Meeting Announcements

Boston Glycobiology Discussion Group

This group consists of glycoscientists in the Boston area who hold regular meetings that begin with a social hour including dinner and proceed to a presentation on a variety of topics in the glycosciences. Scheduled meeting dates, speakers, and topics include:
—May 15, Peter Lansbury, Molecular Mechanism of Amyloid Formation in Alzheimer's Disease
—June 25, Paul Goetinck, C-Terminal G-3 Domain of Aggregan: Its Influence on Glycosaminoglycan Addition
Meetings take place at the Massachusetts Institute of Technology Faculty Club in Cambridge.

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Eurocarb 9
9th European Carbohydrate Symposium

The Jaarbeurs Congress Center
Utrecht, Netherlands
July 6–11, 1997

The scientific program has been designed to cover all aspects of chemistry, biochemistry, (molecular) biology, and (bio)technology of carbohydrates. It will include plenary lectures, in-