CC/NUMBER 44
OCTOBER 30, 1989

This Week's Citation Classic®

Bennett G, Leblond C P & Haddad A. Migration of glycoprotein from the Golgi apparatus to the surface of various cell types as shown by radioautography after labeled fucose injection into rats. *J. Cell Biol.* 60:258-84, 1974.
[Dept. Anatomy, McGill Univ., Montreal, Quebec, Canada and Dept. Morfologia, Fac. Medicina São Paulo, Brazil]

This study used light and electron microscope radioautography to document the addition of fucose residues to glycoproteins in the Golgi apparatus in virtually all cell types. These molecules were seen to migrate to lysosomes, secretory products, and especially to the cell surface where they contributed to the "cell coat" of the plasma membrane. [The *SCI*® indicates that this paper has been cited in over 310 publications.]

Golgi Apparatus Production of Cell Surface Glycoproteins

Gary Bennett
Department of Anatomy
McGill University
Montreal, Quebec H3A 2B2
Canada

July 28, 1989

For my part the present work represented the culmination of several years of graduate studies during which I was privileged to work under the supervision of Dr. Charles Philippe Leblond at McGill University. I had joined Leblond's laboratory in 1965, just in time to receive some supervision from Marian Neutra and to witness the publication of Neutra and Leblond's landmark paper on the uptake of ^{3}H-glucose label in the Golgi apparatus of intestinal goblet cells—the first dynamic evidence for Golgi involvement in glycosylation.[1]

Neutra and Leblond had also provided light microscope (LM) radioautographic evidence for the migration of glycoproteins from the Golgi complex to the plasma membrane of intestinal columnar cells. Plasma membranes had been studied biochemically in only a few cell types at this time, but evidence for the presence of carbohydrate at the surface of all cells had been provided by Leblond's laboratory in the form of histochemical studies using the periodic acid Schiff or colloidal iron techniques.

During the 1960s many common sugars became commercially available in tritiated form, and each was used for radioautographic investigation by me and others in Leblond's laboratory. The introduction of ^{3}H-fucose was a great advance, since this highly specific label was incorporated exclusively into fucose residues of glycoconjugate side chains.

The *in vivo* radioautographic experiments carried out during this period required large amounts of costly isotope. Thus our studies were team efforts, and tissues from any one experimental animal were parceled out to a number of different investigators, e.g., Antonio Haddad examined thyroid tissue, Melvin and Alfred Weinstock studied odontoblasts, and I concentrated on intestinal tissues and liver.

In some secretory cells, no obvious labeling of the plasma membrane was detected, but in intestinal columnar cells and hepatocytes, Leblond and I showed passage of ^{3}H-fucose-labeled glycoproteins from the Golgi apparatus to the whole cell surface.[2] An important question was to determine whether this latter phenomenon occurred to some extent in all cell types. In the above experiments, it was my task to take samples of every organ and tissue in the body for LM radioautography. Since all of these could be embedded in one large paraffin block, sections of the latter provided an immediate survey of reactions in virtually every cell type, and these were used to produce most of the illustrations in the 1974 paper. The paper also contained preliminary electron microscope (EM) data obtained by Haddad and me in kidney tubule cells. These data were published in more detail in a later publication.[3] (Dr. Haddad is currently at the Departamento de Morfologia, Faculdade de Medicina de Ribeirão Preto, Universidad de São Paulo, Brazil.)

The reasons as to why this paper has been highly cited may be various. The work came from Leblond's laboratory and gave some of the first evidence for what is now known as a fundamental principle of cell biology, i.e., that plasma membrane glycoconjugate molecules are continuously synthesized in the rough endoplasmic reticulum and Golgi apparatus in all cells and continuously migrate to the plasma membrane where they undergo turnover.

The final chapter in our radioautographic study of glycoprotein synthesis came with the use of ^{3}H-N-acetylmannosamine as a specific precursor of sialic acid residues. It was shown that this residue was also added to glycoproteins in the Golgi apparatus (often at the trans face). Our findings with this and other sugars formed the subject of keynote addresses given in 1976 to the International Congress of Cell Biology in Boston[4] and to the Royal Microscopical Society in London. The sialic acid findings were published in more detail in 1981,[5] and large review articles on the role of the Golgi apparatus in glycoconjugate synthesis were published in 1984 and 1988.[6]

1. **Neutra M & Leblond C P.** Synthesis of the carbohydrate of mucus in the Golgi complex as shown by electron microscope radioautography of goblet cells of rats injected with glucose-H^3. *J. Cell Biol.* 30:119-36, 1966. (Cited 465 times.)
2. **Bennett G & Leblond C P.** Formation of cell coat material for the whole surface of columnar cells in the rat small intestine, as visualized by radioautography with L-fucose-^{3}H. *J. Cell Biol.* 46:409-16, 1970. (Cited 210 times.)
3. **Haddad A, Bennett G & Leblond C P.** Formation and turnover of plasma membrane glycoproteins in kidney tubules of young rats and adult mice, as shown by radioautography after an injection of ^{3}H-fucose. *Amer. J. Anat.* 148:241-74, 1977. (Cited 45 times.)
4. **Leblond C P & Bennett G.** Role of the Golgi apparatus in terminal glycosylation. (Brinkley B R & Porter K R, eds.) *International cell biology, 1966-1967.* New York: Rockefeller University Press, 1977. p. 326-36. (Cited 105 times.)
5. **Bennett G & O'Shaughnessy D.** The site of incorporation of sialic acid residues into glycoproteins and the subsequent fates of these molecules in various rat and mouse cell types as shown by radioautography after injection of [^{3}H]N-acetylmannosamine. I. Observations in hepatocytes. *J. Cell Biol.* 88:1-15, 1981. (Cited 65 times.)
6. **Bennett G.** Radioautographic and cytochemical studies on the synthesis and intracellular transport of glycoproteins. *Acta Histochem.* (Supp. 36):9-49, 1988.