

HARRY SCHACHTER

Annette Antoinette Herscovics
1938-2008



Annette (Antoinette) Herscovics, one of the true pioneers of glycobiology research, passed away in Montreal, Canada, on September 6, 2008, after a long battle with cancer. She made seminal contributions to the field for more than 40 years and was still very active shortly before her death, having published two important papers in 2007 and two in 2008.

Annette, the daughter of Polish Jews, was born in Paris, France, in 1938, and was a hidden child survivor of the Holocaust during her years in Nazi-occupied France. In 1963, she obtained a PhD in Biochemistry under the direction of Rose M. Johnstone at McGill University in Montreal. Her first academic appointment was in the Department of Anatomy at McGill University (1967–1971). This Department was headed by the brilliant cell biologist C.P. Leblond, an expert in autoradiography.

Annette made important discoveries on the glycosylation of thyroglobulin using autoradiography and other techniques to monitor the incorporation of radioactive sugar precursors *in vivo* and *in vitro*. These studies first demonstrated the progressive addition of core mannose to a glycoprotein in the rough endoplasmic reticulum followed by the addition of more terminal galactose and fucose in the Golgi apparatus, proving that the Golgi was not the only site of protein glycosylation. These prophetic findings laid the foundation for our current understanding of protein *N*-glycan processing.

In 1971, Annette moved to Harvard Medical School in Boston as an Associate in Biological Chemistry in the laboratory of Roger W. Jeanloz. She remained at Harvard until 1981 and published more than 20 original papers with Jeanloz and other collaborators on the synthesis and structure of polyisoprenyl β -D-mannopyranosyl phosphates and other activated sugar donors. She was among the first to demonstrate the existence of the dolichol pathway in *N*-glycan synthesis. She showed that calf pancreas microsomes synthesize dolichol phosphate mannose and dolichol phosphate glucose and that these dolichol derivatives act as mannose and glucose donors in the formation of dolichol-linked oligosaccharide containing GlcNAc, Man, and Glc, the precursor of all *N*-glycans.

Annette returned to McGill University in 1981 as an Associate Professor in the McGill Cancer Centre and remained at McGill until her death. In 1987, she was appointed as a Professor in the Departments of Medicine and Biochemistry at McGill and in 1992 as a Professor in the Department of Oncology.

On returning to McGill, Annette made what are probably her greatest contributions, *i.e.*, her discovery of the important roles played by glycosidases in glycoprotein processing. In both collaborative and independent work, Annette Herscovics and Kelley Moremen did most of the seminal work on this topic.

Annette purified and cloned yeast and mammalian glucosidases and mannosidases that are essential components of *N*-glycan processing. She cloned the yeast ER α 1,2-mannosidase and

eventually, in collaboration with Lynne Howell at the Hospital for Sick Children in Toronto, determined its structure by X-ray crystallography. The structure of the yeast ER α 1, 2-mannosidase served as a model to determine the structure of several other family members. She showed that there are three distinct mammalian Golgi α 1,2-mannosidases, IA, IB, IC, derived from different genes, with similar specificities, but distinct patterns of tissue-specific expression in the adult and during mouse embryonic development. She also discovered that a family of compounds, derivatives of deoxynojirimycin, is potent inhibitors of processing glycosidases, thus interfering with the maturation of *N*-glycans to complex structures. These compounds have subsequently been used extensively as tools to study the calnexin cycle and also as antiviral agents.

Annette later went on to make important contributions to the glycosyltransferase field. She purified and determined the specificity of several yeast mannosyltransferases, not found in mammalian cells, that add α 1,2- and α 1,6-linked mannose to *O* and *N*-glycans, respectively. In a collaborative study, she determined the structure of one of these enzymes by crystallography. This was the first yeast glycosyltransferase structure to be determined. Annette also created the first Golgi α 1,2-mannosidase knock-out mouse and demonstrated that the absence of this enzyme produces a unique “respiratory distress” phenotype. She showed that a few membrane glycoproteins in a subset of bronchiolar lung epithelial cells disappear in the knock-out lungs. Annette Herscovics was a major figure in the field of glycobiology. Although she has always had a relatively small research group, she produced work of very high quality and importance. She received many awards and honors over the years and was appointed as a Fellow of the Royal Society of Canada in 1998. Annette has published 110 peer-reviewed papers since 1964 and has been a pioneer in several important fields in glycobiology.

She was an excellent violinist and had many interests outside of her science. She leaves behind her son Philippe Herscovics, daughter-in-law Jackie Mercer, and grandchildren Max, Alex, and Zara. Annette Herscovics will be greatly missed by her many friends and colleagues.

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(Author's title given as of the time of writing)