



Continuing down memory lane (Preface for glycoconjugates and drug research—Part 2)

The second part of the 6th ICSM Proceedings issue is dedicated to the memory of late Professor Lars Svennerholm. Professor Svennerholm was a renowned neurochemist, who also devoted his life to the research of Glycoconjugates and Drug Research. Like late Professor Bachhawat, who organized the first four ICSM symposiums, Professor Svennerholm worked to find the cause and cure of many inborn diseases.

My first memories of Professor Svennerholm are from 1966, when I met him for the first time in the elevator of Mergenthaler Hall at the Johns Hopkins University Homewood campus. At that time, he had come all the way from Sweden to visit the laboratory of my mentor, Professor Saul Roseman, to see how a carbohydrate laboratory all of a sudden published its first paper on the *in vitro* biosynthesis of GM1 ganglioside from GM2 (or Tay Sachs disease) ganglioside in the October 1965 issue of *Journal of Biological Chemistry*. He gave both of those nomenclatures before 1965, after their isolation in the purest forms. Of course, Professor E. Klenk first isolated the GM2 ganglioside in 1938 in Germany. However, the world came to know the easy isolation procedures, tentative structures, simple nomenclature, and many physiological roles of those gangliosides from the papers published by the laboratory of Professor Svennerholm. Before he passed away, the number of papers rose to 300.

As a result of his visit to Johns Hopkins University, both Manju and I ended up touching his benches in the summer (May and June) of 1968. I remember when we arrived at his laboratory, they were almost ready to lock-up for the summer; that was the Swedish tradition for summer. Due to our urgent Romanian-mission he was kind enough to keep the laboratory doors open for the next two months. Not only were we given an open lab, but also provided with a very helpful graduate medical student, Rolf Ohmen, MD to aid us. Rolf educated us in the human fetal brain physiology and also worked hard with us on the project “Characterization of Ganglioside-synthesizing Glycosyltransferases in the Human Fetal Brains.” Previously we established the *in vitro* biosynthetic pathway of GD1a ganglioside from GM3 in embryonic chicken brains. However, during our informal lunch-time discussions we learned how serendipitously he first isolated GD1a ganglioside (NeuAc α 2-3Gal β 1-3GalNAc β 1-4-

Gal β 1-4Glc-Ceramide) and then, later on, all other short chain gangliosides, GM1 (Gal β 1-3GalNAc (NeuAc α 2-3) β 1-4Gal β 1-4Glc-Ceramide), GM2(GalNAc(NeuAc α 2-3) β 1-4Gal β 1-4Glc-Ceramide), and GM3 (NeuAc α 2-3Gal- β 1-4Glc-Ceramide), one by one. Technicians wanted some short name to identify fractions as and when they were discovered; GD1a was isolated first, because it is the major ganglioside of normal human brains. The GM3 was isolated at the end as we know now, being the precursor of the bigger gangliosides, it exists in lower quantities in the normal brains. Later on Lars (that’s the way he insisted we call him) realized that the nomenclature went backwards, 3- should have been for the bigger oligosaccharide chain and 1- should have been for the shortest oligosaccharide chain. However, by that time a world full of neurochemists loved his short nomenclature and had already published hundreds of papers using that nomenclature.

Starting from the isolation of gangliosides to their functional roles, all were areas of research quite dear to Professor Svennerholm. However, his high regard always existed for the enzymologists in the ganglioside field. Before this series of ICSM meetings we used to have meetings on “Gangliosides” in France (Organized by late Professor Paul Mandel in 1973, 1979, and 1985; in Italy (organized by late Professor Paoletti and Professor Guido Tettamanti in 1975), in Venezuela (organized by Professor Robert Ledeen in 1987) and in Japan (organized by Professor Yamakawa in 1981 and in 1989). Those were the platforms where we met many times and discussed the biological roles of the macromolecules. Professor Svennerholm’s dream was to use GM1 ganglioside for the cure of Alzheimer patients; as a medical person he had the privilege to start those experiments and in this country it is still in the trial stage. In recent years a number of papers have been published on the role of gangliosides in biological functions (including in this series) on the roles of disialosyl-gangliosides (GD3 and GD1b) in the apoptosis of human carcinoma cells.

Besides his 300 papers Professor Svennerholm published a few books on “Biological Function of Gangliosides”. However, he was always proud of his first “Cook Book” which he claimed was translated into at least seven different languages at that time. If ganglioside has become a household word in the world of Neurochemistry, then it is due to a lifetime love

and dedication for the subject by Professor Svennerholm. Out of his hundreds of talks at different conferences around the world, his most significant talk at the Nobel Symposium in 1992 on "Biological Function of Ganglioside" is worth mentioning. For many years he was an active member of the Nobel Committee. Of course the name Lars Svennerholm will remain in the literature forever, but the person Lars Svennerholm will be

remembered in the hearts of friends whom he met in his fruitful lifetime.

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