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PREFACE

Preface to the Special Issue Honoring Bob Ledeen

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Bob Ledeen

It is a special privilege that we have compiled a Special Issue of *Neurochemical Research* to honor Dr. Robert W. Ledeen, Professor of Neurology and Neurosciences, University of Medicine and Dentistry of New Jersey, Newark, New Jersey, USA. A total of 23 articles from contributors from all over the world are included in this issue, and they cover a wide range of topics, including neurochemistry, neurobiology, glycobiology, signal transduction, and developmental neurobiology. Dr. Ledeen is no doubt one of the most prominent scientists in neurochemistry and glycobiology and his seminal work has greatly influenced these fields for many years.

Dr. Ledeen received a BS degree in chemistry at the very early age of 20 from the University of California, Berkeley and subsequently obtained his PhD degree in organic chemistry in 1953 from the University of Oregon, Corvallis. Postdoctoral training at the University of Chicago was interrupted by military service and then resumed at Mt. Sinai and Albert Einstein College of Medicine in

Special Issue: In Honor of Bob Leeden.

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New York. He was appointed by Dr. Saul Korey as an instructor in 1961, in the Einstein Department of Neurology, eventually becoming a tenured professor. He credits Saul Korey as the one who introduced him to gangliosides, of interest at that time in relation to Tay-Sachs and other lipid storage diseases. At Einstein, he and Drs. William T. Norton and Kunihiko Suzuki among others, rapidly established a prominent research and educational program in neurochemistry. In 1991, he was recruited to the University of Medicine and Dentistry of New Jersey as Professor and Director of Neurochemistry in the Department of Neurosciences, and there has continued his enduring efforts in neurochemical research.

Dr. Ledeen has been involved in glycolipid research for half a century ("believe it or not", he says.). His work has continued to influence the direction of the field till today. He was the first to establish the correct structure of Tay-Sachs ganglioside (GM2) in 1965. He subsequently elucidated the ketosidic configuration of sialic acid in sialoglycoconjugates in 1969. These early contributions were followed by a series of careful studies on the cellular and subcellular distribution of gangliosides in the nervous system, including the demonstration of gangliosides in neuronal and glial membranes, myelin, synaptic vesicles, and growth cones. He further demonstrated fast axonal transport as the distribution mechanism of gangliosides and other lipids to axonal and nerve ending membranes. These studies led to work on the neuritogenic effects of gangliosides in the nervous system, adding to the pioneering work of Dr. Dominick Purpura and others. He further made the fundamental discovery that GM1 ganglioside in the plasma membrane modulates the calcium concentration in neuronal cells, which accounts in part for its biological effects in promoting neuritogenesis. More recently he made another surprising discovery that GM1 ganglioside is also present in the nuclear membrane where it occurs in close association with the sodium-calcium exchanger protein that regulates intracellular calcium homeostasis. Those and other findings are contributing to the growing recognition of the importance of intracellular gangliosides in regulating a number of neuronal functions, leading to his current exciting work on the beneficial role of GM1 in relation to Parkinson's disease.

In addition to the above, Dr. Ledeen has also carried out numerous fundamental studies on the chemistry and metabolism of myelin metabolizing enzymes. His discovery of myelin-associated G proteins linked to cholinergic receptors is particularly noteworthy as it demonstrated for the first time the existence of signaling pathways in myelin. Subsequent work revealed the presence of aspartoacylase in myelin and its role in providing acetyl groups for lipid biosynthesis within that membrane. These studies contributed substantially to an altered view of metabolic activity within myelin, which had for many years been considered as an inert membrane.

After decades-long devotion to the study of ganglioside function in the nervous system, Dr. Ledeen's recent interests have turned to the immune system where his group has sought to elucidate the mechanism of immune suppression and the reasons for its failure in autoimmune disorders. This work revealed the role of GM1 in effector T cells which, when cross-linked by galectin-1 from regulatory T cells, opens TRPC5 calcium channels thereby inactivating and eliminating autoreactive effector T cells. His group is actively probing the potency of GM1-galectin-1 interaction in T cells of autoimmune patients, with an eye toward potential new therapies.

Neurochemical Research conferred an unusual honor on Bob a while back in publishing a poem he wrote on the occasion of his colleague Bill Norton's retirement, in which he imagined Bill reminiscing on the relative ease of grant funding early in his career compared to the current situation:

> Sweet milk did flow from the NIH cow,
> Playing the grant game was the cat's meow;
> But the times they have changed, my colleagues are blue,
> What once gave us milk now gives us 'mooo'.

Bob confides to his friends that he is more excited than ever about research and the progress so many are making in the glycosphingolipid field. It is remarkable that he has maintained such a consistent level of scientific excellence for so many years, and continues as vigorously as ever. It should be noted that his research has been supported by numerous funding agencies for many years including virtually continuous NIH funding from the beginning of his ganglioside studies. An acute understanding of the problem, a mastery of technology and experimental design, and a high level of intelligence and insight mark his science. He has indeed set an example for many of us in the field to follow.

Representative publications of Dr. Ledeen (from a total of 175 full papers)

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