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GUEST EDITORIAL

Special Issue in Honor of Baruch Kanner

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It is with great pleasure that I have this opportunity to write the preface for this special issue of *Neurochemical Research*, in honor of Professor Baruch Kanner. Baruch has made very important contributions to the field of neurotransmitter research, through decades of a highly-productive career, in particular with respect to the cloning and molecular identification of secondary-active transporters for two key neurotransmitters, glutamate and γ-aminobutyric acid (GABA). In the following paragraphs, some of the highlights of his outstanding career are summarized.

Initially a citizen of the Netherlands, Baruch went to college at Delft Technological University, where he graduated with a B.Sc. degree in chemical engineering in 1968. As common at the time in Europe, Baruch stayed in Delft for a Master's degree, but switching fields to Biochemistry, a discipline that became interesting to him for the rest of his career. After immigrating to Israel in 1970, he started working on his doctoral degree in microbiology under the guidance of David Gutnick at Tel Aviv University. He graduated with a Ph.D. degree in 1974, after several years of highly productive research, with seven published papers. In the Gutnick laboratory, Baruch worked on bioenergetics projects, including purification and functional characterization of a Ca^{2+}-dependent F1-ATPase from *E. coli*, as published in *PNAS* (1974).

With his growing expertise in protein purification in the bioenergetics field, it was no surprise that Baruch stayed in academia, after getting the opportunity of a postdoctoral position in Ef Racker's laboratory at Cornell University in Ithaca, NY, a very prominent lab in the bioenergetics field. Ithaca, with its long and cold winters, quite a change from the Israel climate, provided a challenge for the Kanner family, by balancing the requirements of long work hours, as

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common for postdocs at Ivy League schools, with the needs of a growing family with his wife Nechama. Nevertheless, Baruch managed these challenges very well, working on several projects, ranging from light-driven proton transport to F1 ATPase, with several publications as the result.

When he concluded with his postdoctoral work in 1976, he decided to move back to Israel, where he was offered a lecturer position at Hebrew University in the Faculty of Medicine. Baruch stayed at Hebrew University until today, as Emeritus Professor, after rising through the ranks to become Professor in 1990. As a new faculty member at Hebrew University, Baruch needed to find a new research direction, and he quickly started focusing on neurochemistry, becoming interested in the secondary-active transporters for the neurotransmitters glutamate and GABA. While also publishing work on monoamine transporters, Baruch's breakthrough contributions were the functional characterization, solubilization and reconstitution of glutamate and GABA transporters, for example published in Kanner, BI, *Biochemistry* (1978) and Kanner, BI and Sharon, I, *Biochemistry* (1978). These early developments in the Kanner laboratory led to a long series of important functional studies on these transporters. Just to highlight two very important examples: (1) The discovery of K^+ counter-transport and its binding order mechanism in glutamate transporters (Kanner, BI and Bendahan, A, *Biochemistry*, 1982). (2) The identification of chloride coupling of substrate flux in the GABA transporter with a stoichiometry of 1:1 (Keynan, S and Kanner, BI, *Biochemistry*, 1988).

Baruch's work on GABA and glutamate transporters culminated in the cloning and expression of a GABA transporter (GAT1), published in 1990 in *Science*, and the cloning and functional characterization of the glutamate transporter subtype Glt-1, published in *Nature*, 1992. The importance of these seminal contributions cannot be overstated, because the availability of the protein sequence, and the ability to express these transporters in systems such as mammalian cells and *Xenopus* oocytes resulted in an explosion of research in the neurotransmitter transporter field, eventually leading to determination of the structures of the glutamate transporter homologue GltPh and the GABA transporter homologue LeuT, the development of pharmacological tools to study these transporters, and the identification of, as Baruch always says "the molecular mechanism" of how these transporters operate.

Of course, Baruch's research did not stop with the cloning of the transporters, the cloning just gave him the tools to continue with his passion, i.e. to figure out how these transporters work. In consequence, a large number of papers were published with diligent structure function analysis of GABA and glutamate transporter. His publications are too numerous to discuss, with a total number of 139 papers, showcasing a very prolific career. However, two additional major contributions should be highlighted: (1) The identification of the chloride binding site of the GABA transporter, published in *Nature* in 2007. This breakthrough was possible because of Baruch's keen eye in identifying minor differences in sequences of GAT1 (SLC6) family members, which, in combination with careful site-directed mutagenesis approaches allowed the prediction of this important binding site. (2) The discovery of the inverted repeat structural fold of glutamate transporters, in collaboration with Lucy Forrest, which led to the prediction of an inward facing structure of the transporter. This structure was soon after confirmed by x-ray crystallography with GltPh.

This special issue of *Neurochemical Research*, which I had the honor of guest editing, celebrates the totality of Baruch's work, which he contributed in a long and outstanding career. The issue contains original research articles, as well as reviews, ranging from topics as diverse as transporter regulation, animal models and behavior, to computational aspects of transporter modeling. The wide range of contributions highlights the impact that Baruch's work had not only on our understanding of transporter "molecular mechanism", but also on how transporters are trafficked and how they contribute to specific disease states. While all of the articles in this special issue are important and would deserve commentary, I would nevertheless highlight one particular article with the title "*Forty Four Years with Baruch Kanner and the Chloride Ion*" by Gary Rudnick. This article summarizes the history of Baruch's research in a very personal manner and gives insight into the circumstances that led to some of the key early discoveries, eventually leading to the molecular identification of GABA and glutamate transporters.

In summary, Baruch has to be congratulated on an outstanding career that is not only notable for the scientific contributions, but also for the many young scientists Baruch has trained throughout the years, who could not have received any better training to become successful in science and research. Baruch has moved to Tel Aviv, to be able to spend more time with children and grand children. While this meant that the laboratory at Hebrew University in Jerusalem had to be closed, it is hoped that Baruch will continue to present at scientific conferences, so that the next generation of transporter scientists can benefit from his immense knowledge.