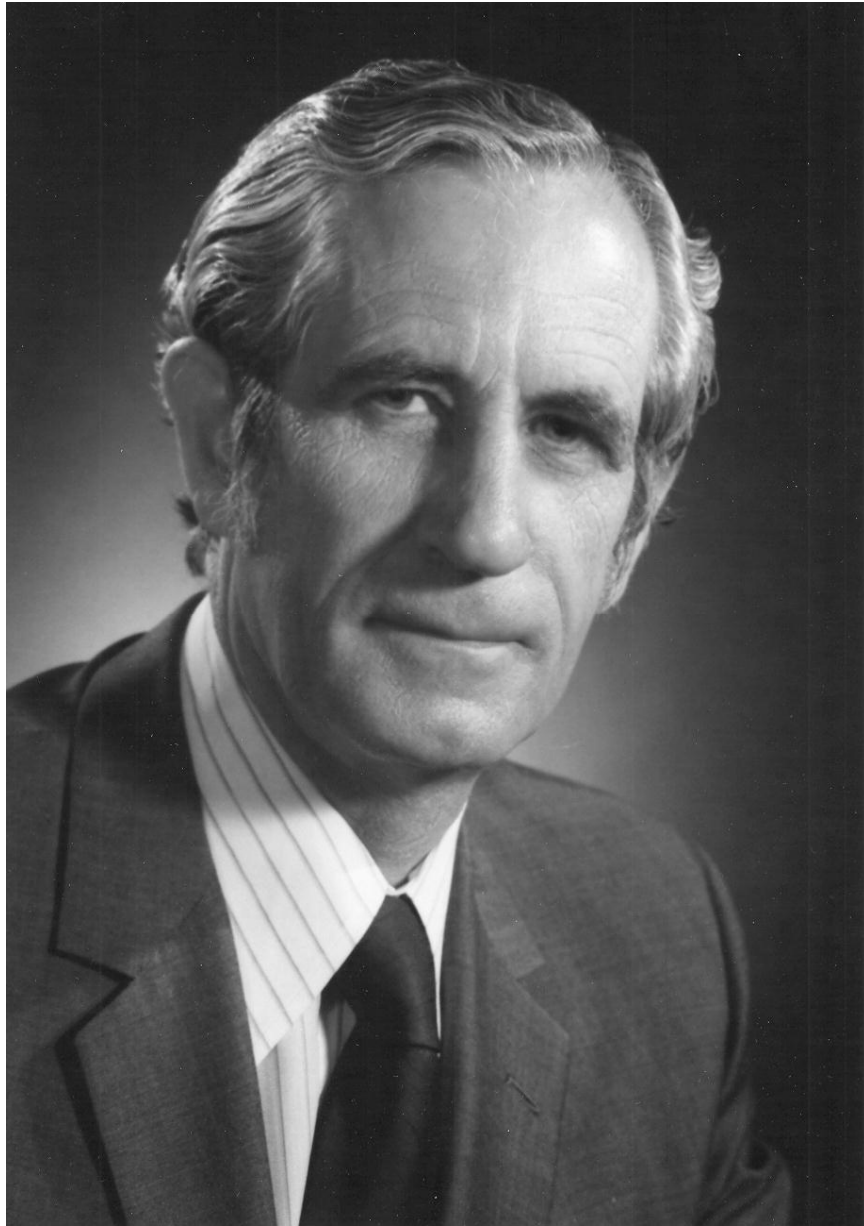


UNIVERSITY OF TORONTO

Werner Kalow
1917-2008



The pharmacogenetics community lost one of its founding fathers earlier this year with the passing of the Emeritus Chairman of the Editorial Board of this journal, Professor Werner Kalow of the University of Toronto, in February, 2008, at the age of 91 years. The internationally recognized pharmacologist, educator, mentor, trusted colleague, and valued friend played a seminal role in the establishment and evolution of the now-burgeoning fields of pharmacogenetics and pharmacogenomics, and he remained active and engaged in his scientific passion until his death.

Werner Kalow was born to a German missionary family and raised in the town of Cottbus in what was later to become East Germany. Following medical studies in Greifswald and Koenigsberg, he was drafted into the German Navy and became a ship's surgeon on a merchant vessel that was captured during the Second World War. During a period of internment as a prisoner of war in Arizona, he became the camp's physician, and he began his familiarization with North American culture that would later lead to his return. After the war, Dr Kalow returned to Germany and in 1947, he took up a position in the Department of Pharmacology at Humboldt University in Berlin, and later at the Free University of Berlin upon its formation in the American-occupied sector of the city. It was at this time that the unexpected death of a patient, after injection with the local anesthetic, procaine, led to studies with Hans Herken that would later evolve into Dr Kalow's seminal work on the pharmacogenetics of the serum esterases. In 1949, Dr. Kalow received an invitation to become a visiting scientist at the University of Pennsylvania from Carl Schmidt, Chairman of its Department of Pharmacology, where he produced his first observations on the metabolism of procaine and benzoylcholine by the same serum esterase. Subsequent discussions with Ken Ferguson, Chairman of the Department of Pharmacology at the University of Toronto, led to the acceptance of an offer to take a permanent faculty position in Canada. Dr. Kalow joined the University of Toronto in 1951, where he remained active until the end of his life.

Werner Kalow is known for his many key contributions to the field of pharmacogenetics. He was one of the first to demonstrate the existence of inherited variants of plasma cholinesterase, and to devise a sensitive method, using dibucaine inhibition, to distinguish variant forms of the enzyme. On the basis of the interest kindled in him by these observations and by other examples emerging in the literature, Dr. Kalow then undertook to publish in 1962 the seminal monograph in the emerging discipline of pharmacogenetics entitled *Pharmacogenetics. Heredity and the Response to Drugs*. With Beverley Britt, he then went on to investigate the pharmacogenetics of malignant hyperthermia, a disorder caused by exposure to general anesthetics, which is now known to be caused by variants of the ryanodine receptor. With his longtime colleagues, Drs Ted Inaba and Bing Tang, Dr. Kalow perfected the concept and use of 'probe drugs' as innocuous predictors of variable drug-metabolizing enzyme capacity, and used these methods to uncover numerous instances of significant interethnic differences in drug-metabolizing enzyme function. His laboratory was one of the first to establish that the defective oxidations of debrisoquine and sparteine are caused by a defect in the same cytochrome P450 enzyme, now known as CYP2D6. Dr Kalow also conceptualized and led the development of caffeine as a noninvasive probe for CYP1A2 and NAT2 functions. Since that time, his interests in pharmacogenetics have been far ranging, including studies of CYP2C19, UGT2B15, and CYP3A4. Finally, the contributions of his laboratory and his collaborations in the area of molecular pharmacogenetics are also impressive, including important studies of the biochemistry and molecular genetics of the

CYP2D6 genetic polymorphism. He was also an avid advocate of the field of pharmacogenetics in general, and had recently written a number of insightful reviews on multiple aspects of pharmacogenetics, in addition to editing two versions of a book on pharmacogenomics.

Dr Kalow was recognized for his accomplishments with numerous honors and awards, including Fellowship of the Royal Society of Canada (1977), the Upjohn Award from the Pharmacological Society of Canada (1981), the Bernard B. Brodie Lectureship (1990), the Oscar B. Hunter Award from ASCPT (1993), the Killam Prize (2001), and nomination for the Nobel Prize (1990).

Dr Kalow's infectious enthusiasm for science and its role in society, his inquisitive nature, his wealth of innovative ideas, and his constructively critical rigor will always be remembered. Beyond this, Werner Kalow was a true gentleman, a gracious colleague, and a wonderfully kind and supportive friend – facts that will be his even more enduring legacy. He will be deeply missed.

University of Toronto
With excerpts from Pharmacogenetics and Genomics