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In Memoriam
Fridolin Sulser

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Dr Fridolin Sulser, a pioneer in psychopharmacology research, died on 3 January 2016 at the age of 89, surrounded by his loving family. A renaissance-style man, he was a brilliant scientist with an intense interest in philosophy, literature, music, and nature. He will be remembered for his enthusiasm and innovative thinking, which inspired and challenged those around him.

Born in Grabs, Switzerland, Fridolin grew up in the town of Maienfeld, nestled in the Swiss Alps. He left his beloved home to attend medical school at University of Zurich with an interest in psychiatry. He earned the MD degree in 1955 and served a mandatory 2-year term as medical officer in the Swiss army. As a medical student, Fridolin was influenced profoundly by the MD and existentialist philosopher, Karl Jaspers. This influence contributed to Fridolin's recognition that he was drawn to experimental biology and culminated in a decision to move from psychoanalysis to pharmacology. After a brief stint in industry, he began an academic career as Assistant Professor in Pharmacology at University of Bern, where his research focused on cardiac function. Two years later, he embarked on a quest to pursue his long-standing interest in brain research and obtained funding from the Swiss Academy for postdoctoral training in the laboratory of Bernard Brodie at the NIH. He joined the Brodie laboratory in 1958 and began working on the mechanism of action of the antidepressant drug imipramine. Using the reserpine model of depression, he showed that norepinephrine is required for imipramine reversal of reserpine. Collaboration with Jim Dingell (in James Gillete's laboratory at NIH) led to the discovery of desmethylimipramine (DMI), which accumulated in brain after chronic imipramine administration. DMI, not imipramine, was a potent norepinephrine uptake inhibitor, supporting Brodie's theory of a prodrug, which is activated by *in vivo* metabolism.

When his student exchange visa expired in 1962, Fridolin was forced to leave the NIH, moving to Burroughs-Welcome as Director of Pharmacology. In 1965, he was recruited to Vanderbilt University to head up a new psychopharmacology research unit and to Tennessee Neuropsychiatric Institute (TNI). TNI was housed off-campus at a local mental health hospital; Fridolin envisioned that proximity to patients would foster an emphasis on clinically relevant research. TNI prospered and Vanderbilt gained a national reputation for excellence in psychopharmacology research. This recognition, in turn, set the stage for the university, as a whole, to take advantage of the explosion of interest and funding in neuroscience. In addition to his dynamic leadership, Fridolin was an incredibly supportive mentor and friend. Looking back, I marvel at the environment that he created at TNI, an environment that promoted cutting edge science and was equally nurturing and supportive of individuals. I was fortunate to be in his laboratory—I felt it then and know it now. At a time when females were uncommon in lab settings and often overlooked, I was given exceptional opportunities to develop independence and gain recognition.

Fridolin championed the theory that acute effects of tricylic antidepressant drugs were not directly responsible for their therapeutic action. His research on the mechanism for the delayed effect of antidepressants was influenced by his friend and Nobel Prize winner, Earl Sutherland, who suggested that he should look beyond the synapse at the norepinephrine/adenylate cyclase signal transduction cascade. This strategy led to the discovery that antidepressant treatments (tricyclics, MAO inhibitors, and ECT), given on a clinically relevant time basis, reduced the responsiveness of the β-adrenoceptor-coupled adenylate cyclase system to norepinephrine in limbic and cortical structures of the rat brain. Further work found that chronic, but not acute, treatment with noradrenergic antidepressants, downregulated the biologically active form of the transcription factor, CREB-P, in the frontal cortex, indicating a net deamplification of the β-adrenoceptor—cyclic AMP cascade. This research switched the emphasis on the mode of action of antidepressants from acute presynaptic to delayed postsynaptic second messenger-mediated cascades and opened up the gateway for subsequent studies of events beyond the receptors including changes in gene expression. Fridolin was eager to move his own research from the membrane to the nucleus, an interest fueled by a 1-year sabbatical at the Roche Institute of Molecular Biology. Back at Vanderbilt, he collaborated with Richard Shelton (in Psychiatry), using fibroblasts from patients with major depression to model signal transduction in affective disorders. These early studies were productive but, as is still the case today, identifying alterations in gene expression that may be crucial to the pathophysiology of major affective disorders remains an elusive goal.

Fridolin was active in the ACNP for more than 40 years, serving in many roles, including President in 1979. He was a loyal attendee through the years, contributing to lively discussions and challenging the *status quo*. Other honorific recognitions include the prestigious Anna-Monika Prize. He is survived by his wife, Johanna, two daughters, Anna and Bettina, and two sons, Adrian and Daniel. They, as well as his trainees and scientific colleagues, will cherish the memories of this remarkable man.

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