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# Obituary

## Henry Ichiro Yamamura (1940–2008)

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On 4 September 2008 Henry (Hank) Yamamura died peacefully at his home in Tucson, Arizona after a battle of almost 2 years with lung cancer. Hank handled his final illness with the same grace and good humor that characterized his entire life. Throughout his bouts with chemotherapy he remained active professionally, conversing regularly with friends all over the country—more interested in their lives than in bemoaning his own fate. He is survived by his wife Susan and his son Mark, a surgeon who lives in Hawaii.

Hank was a pioneer and one of the country's leaders in molecular studies of neurotransmitter receptors. His doctoral research with Akira Horita at the University of Washington dealt with classical receptor pharmacology but with a spin. He demonstrated an unsuspected link between $\beta$- and $\alpha$-adrenergic receptors in experiments elucidating influences of propranolol upon $\alpha$-adrenergic pharmacology. Hank and Susan moved to the east coast to do his military service at the Army's chemical warfare research center at Edgewood, Maryland. It was during his years at Edgewood that I first came in contact with Hank. The Army labs were large and well equipped with abundant technical assistance but with very little meaningful science. Hank asked whether I might serve as an informal mentor and suggest projects on which he could work during his abundant free hours. Knowing of the Army's interest in anticholinergics for chemical warfare, and because our lab was, at the time, characterizing neurotransmitter transporters, I suggested that Hank seek a transporter for choline. In short order Hank identified and characterized the choline transporter, the chief regulatory mechanism for acetylcholine synthesis, with his paper published in *Science* impacting the field in a major way.

Following his army service Hank joined me as a postdoctoral fellow. Shortly before he arrived, I was visiting George Aghajanian at Yale to talk about our recent work identifying opiate receptors. George, who had done his military service at Edgewood, commented that a major Edgewood effort was administering an extraordinarily potent and long acting muscarinic antagonist to soldier 'volunteers.' If we could get hold of this agent, quinuclidinyl benzilate (QNB) and radiolabel it, we might be able to find muscarinic receptors. George's only concern was that QNB might be classified 'top secret.' When I returned to Baltimore, I asked Hank about QNB whereupon he gasped, 'How did you know?' He said nothing further, but a month later when he arrived in the lab, he brought with him a vial with the magic drug. We sent it to New England Nuclear for tritiation. Utilizing radiolabeled QNB Hank identified and elegantly characterized muscarinic cholinergic receptors. [$^3$H]QNB binding soon became an indispensable tool to characterize anticholinergic actions of drugs and for over 30 years remained the most widely employed receptor radioligand. Because of the very high affinity of QNB for receptors, Hank was able to label them in intact rodents and, with Michael Kuhar, he localized receptors by autoradiography. With this simple, sensitive, and specific ligand-binding approach, Hank elucidated muscarinic interactions of many classes of drugs, clarifying important clinical phenomena. For instance, he showed that extrapyramidal adverse effects of neuroleptics could be explained by their relative anticholinergic effects. He characterized the muscarinic receptor activity of numerous antidepressants, discovering a relationship to therapeutic efficacy.

After 3 extraordinarily productive years, Hank set up his own laboratory in the pharmacology department at the University of Arizona in Tucson and rose rapidly through the ranks, ultimately to a Regents Professorship. Hank continued his interest in muscarinic receptors, establishing himself as the country's authority in this area. As heterogeneity of muscarinic receptors became evident with therapeutic implications for drugs acting at individual subtypes, Hank emerged as a national leader. He also studied a variety of other neurotransmitter receptors with a particular focus on their heterogeneity.

For many years a major portion of Hank's effort involved elucidating opiate receptor subtypes and how their differential linkage to G proteins impacts their analgesic interactions. He collaborated with Victor Hruby, utilizing novel peptides to move receptor research to a biophysical level and dissecting how receptor recognition leads to second messenger influences and differentiation of agonists and antagonists. With novel spectroscopic techniques he showed how $\delta$-opiate receptors desensitize and resensitize and worked out similar mechanisms for cannabinoid receptors. He made related contributions to studies of GABA and central as well as peripheral benzodiazepine receptors.

Besides his important research activities, Hank was a beloved teacher and mentor. His many graduate students and postdoctoral fellows over the years uniformly attest to his good-natured and patient demeanor. Hank was never too busy to help young faculty colleagues plan their research, apply for grants, and set up their teaching programs. Hank was a giant as a scientist, as a teacher, as a citizen, and as a friend. He will be sorely missed.

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