

A Tribute to Robert Jacobs (1933-2015)

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Robert Jacobs in his later years enjoying the outdoors.

Although Dr. Robert Jacobs passed away in 2015, he is still greatly missed. On the second anniversary of his passing, his friends and colleagues have taken the opportunity to reminisce and prepare this tribute.

Robert Jacobs passed away on August 26, 2015. Bob, as his students would call him, was born April 2, 1933

in Chicago, IL to Robert S. and Betty Ester Jacobs. Bob initiated his pharmacology career by joining G.D. Searle, LLC in 1957 and circa 1960 became head of the Pharmacology Screening Lab there. While at G.D. Searle, he earned his undergraduate degree at Northwestern University in 1964 and PhD in pharmacology at Chicago's Loyola University, Stritch School of Medicine in 1971 (dissertation available at [Loyola University of Chicago eCommons](#)). Alexander Karczmar, a true centenarian in life and likely in the pharmacology literature, served as chair of the Department and chair of the Jacobs Thesis Committee. See the companion obituary on page 264.

Bob moved to Santa Barbara in 1974, was hired as an assistant professor to initiate an undergraduate degree program in pharmacology at the University of California, Santa Barbara (UCSB), which became "the first campus in the nation to offer a full undergraduate pharmacological sciences curriculum." In contrast to professional programs in medicine, nursing, and pharmacy, which emphasize the therapeutic principles and applications of pharmacology, Bob developed

an undergraduate pharmacology program that emphasized pharmacology as a basic science focusing on drug discovery and mechanism of action. An aspect that set this program apart encompassed extensive laboratory preparations demonstrating pharmacological principles using primary tissues and in vivo models. Today, the major includes courses that represent "state of the art" pharmacology for students with research interests in all of health sciences (<https://undergrad.biology.ucsb.edu/majors/pharmacology>). The program continues as a vigorous undergraduate major, where many of its graduates continue for advanced degrees and hold leadership positions in industry and academia. Other UC campuses and universities, such as UC, San Diego; UC, Davis; SUNY, Stony Brook and Duke, followed Bob's lead in the undergraduate arena. He was ably assisted by the late Jean Devlin in instruction, organizing the major, and mentoring students at UC, Santa Barbara. The major, its courses, and the preparation of students for graduate study or professional school in medicine, pharmacy, and dentistry continue today at UC, Santa Barbara with Drs. Carol Vandenberg and Leslie Wilson providing the continuity and oversight of the major.

Bob's internationally recognized research centered on the pharmacology and toxicology of marine natural products (MNPs) that blossomed after joining UC, Santa Barbara. He built an internationally recognized center of marine pharmacology by developing extensive collaborations with marine natural product chemistry laboratories and pharmaceutical companies around the globe. Bob uniquely integrated his passion for MNPs with teaching pharmacology by developing in vitro and in vivo assays that were taught in the hands-on undergraduate pharmacology laboratory and then used by student volunteers in the lab to screen

MNPs. Initially the lab focused on discovering compounds that modulated neuronal transmission at the neuromuscular junction in skeletal muscle, which resulted in the discovery of lophotoxin, isolated from *Lophogorgia sp.*, as an irreversible antagonist of the nicotinic acetylcholine receptor. Broadening the focus of the lab and screening efforts to identify potential anti-cancer, anti-inflammatory, and anti-pyretic compounds led to the discovery of novel pharmacology of MNPs. Using the sea urchin embryo assay as a model to identify potential inhibitors of cell division led to the discovery of stypoldione, a novel inhibitor of microtubule assembly.

While investigating potential inhibitors of beta bungarotoxin neurotoxicity, a novel anti-inflammatory MNP, manoalide, was identified through in vivo evaluation in the PMA-induced ear edema assay. Mechanism of action studies identified irreversible inhibition of phospholipase A2 lipase, a key enzyme in arachidonic acid release, resulting in anti-inflammatory effects similar to non-steroidal anti-inflammatory agents. Manoalide was eventually evaluated by several pharmaceutical companies for anti-rheumatic and dermatological applications. MNPs became a rich source of anti-inflammatory compounds identified in the lab, e.g., sclaradiol, fuscoidin, and the pseudopterosins. The pseudopterosins isolated from the sea whip *Pseudogorgia elizabethae* were found to affect many aspects of inflammatory signaling cascade. These activities were ultimately harnessed as an ingredient in a cosmetic to prevent wrinkles and were found to possess notable wound healing properties. Development of the pseudopterosins for their unique wound healing properties through Phase 2 clinical trials was managed by the biotech company Terosin, co-founded by Bob. Bob used



his passion for pharmacology and MNPs to train his students by guiding them through the discovery of novel mechanisms of action of these MNPs.

Bob retired from UCSB in 2010 at the age of 77. Alejandro Mayer (postdoc 1985-1988), Keith Glaser (graduate student 1985-1987), and Peer Jacobson (graduate student 1987-1990) carried Bob's enthusiasm and legacy in the pharmacology of marine natural products forward by curating a dedicated website (<http://marinepharmacology.midwestern.edu/>), contributing reviews on marine pharmacology (<http://marinepharmacology.midwestern.edu/preclinicalPipeline.htm>) and providing rigorous editorial assistance to the only journal dedicated to the preclinical and clinical pharmacology of marine natural products (<http://www.mdpi.com/journal/marinedrugs>).