

A Tribute to Gavril W. Pasternak

Submitted by Kelly Standifer, Dennis Paul, Ying-Xian, Grace Rossi, and Steven Childers

It is with great sadness and loss that we report the passing of the distinguished scientist and long-time ASPET member, Professor Gavril W. Pasternak, MD, PhD on February 22, 2019, at the age of 71 after a brief battle with pancreatic cancer. In recognition of the impact of his scientific career, "Gav" was honored with the 2012 ASPET Julius Axelrod Award in Pharmacology.

Dr. Pasternak was a graduate of Johns Hopkins University (BS chemistry, MD, and PhD). During his undergraduate years at Hopkins, Gav's primary interest was playing lacrosse, but his lifelong passion with opioids began when he joined the laboratory of Dr. Solomon Snyder for his PhD work. Those were exciting days with Sol's group, which was one of the labs who first identified opioid receptors by radioligand binding. Gav joined Candace Pert as the first students to work on opioids in Sol's lab, and he began with isolating brain extracts to identify potential endogenous opioids, called morphine-like factors in those days. Of course, Hans Kosterlitz, John Hughes, and their colleagues at the University of Aberdeen were the first to purify enkephalins, so Gav switched his focus to characterizing pharmacological and biochemical properties of opioid receptors. He was the first to show that sodium distinguished agonist and antagonist binding to opioid receptors by selectively decreasing affinities for agonists, a finding that would provide one of the foundations for exploring opioid receptor crystal structure decades later. But his lifelong interest in mu receptor subtypes began with a serendipitous finding. In characterizing the actions of novel irreversible alkylating ligands, which he hoped could be used as long-acting agonists and antagonists at opioid receptors, he found that the alkylating antagonist naloxonazine only reacted with a subset of mu receptors. From that finding, he deduced that mu receptors must exist as multiple discernible subtypes. This was more than simply an academic interest for Gav. From his clinical work, he knew the enormous variation in the response of patients to analgesic drugs, and he theorized that multiple mu receptor subtypes not only provided the opportunity to design novel analgesics



with fewer side effects, but could also individualize pain therapy with different patients. From these early beginnings ultimately came his pioneering work on alternative RNA splice variants of mu receptors.

Following completion of his neurology residency at Johns Hopkins in 1979, Gavril joined the Neurology Department of Memorial Sloan-Kettering Cancer Center, where he was the model of the classic clinician/scientist until his passing. From the development of receptor binding assays to the recognition of splice variants of mu opioid receptors that may explain individual differences in response to opioid drugs, Dr. Pasternak devoted his career to contributing to our understanding of how opioids produce analgesia and their undesired effects. In recent years he was awarded several patents for the development of novel opioid analgesics that do not produce many of the adverse effects of morphine. Among the many NIH grants that funded these endeavors, Dr. Pasternak was especially

proud of the Research Scientist Development, MERIT, Senior Scientist awards and most recently, a UG3 grant from NIDA to develop ‘...a new class of potent, safer analgesics’ that target one type of mu receptor splice variants identified in his lab.

In addition to his Julius Axelrod Award, he has been recognized with many other scientific awards for his work in the fields of pain including the John J. Bonica (International Association for the Study of Pain), Raymond W. Houde (Eastern Pain Association), Frederick W. L. Kerr Basic Science Research Awards (American Pain Society), the Founders Award (International Narcotics Research Conference), 2018 Award in Excellence in Pharmacology/Toxicology awards (PhRMA Foundation), and the Harrington Scholar-Innovator Award for being a physician-scientist innovator.

Gavril believed that mentoring was an important aspect of research and teaching, and his lab always included a cadre of summer students (high school and college), graduate and medical students, postdoctoral fellows, residents, and visiting professors from all over the world. Gav’s irreplaceable enthusiasm for science was contagious. Most of his mentees produced at least one paper and presented their work with Gav at a national or international meeting; all of them received thoughtful guidance and attention geared toward helping them identify and achieve their career goals.

What many did not know about Gav was that he was a two-time U.S. Lacrosse Man of the Year awardee (NY Metro Division), and he continued to play in lacrosse tournaments through age 70. Gav’s passion for lacrosse and mentoring young talent were combined when he co-founded the Doc’s NYC Lacrosse program in 1996 so that children in NYC had a place to play lacrosse in their home town. Because few NYC public schools offered lacrosse as a team sport in high school, Gav suggested that a public-private partnership might help fund lacrosse teams in inner city public schools. In 2006, the non-profit organization CityLax partnered with the NYC Board of Education to make that happen. This enabled a diverse group of kids from all over NYC to play from elementary age through high school and to become eligible for college scholarships.

Gavril was predeceased by his beloved wife Sandra and daughter Katie Pasternak. The condolences of the ASPET community are with his daughter Anna Pasternak and son David Avram Pasternak. He is also survived by his academic family of undergraduate and graduate students, post-doctoral fellows, visiting scientists, collaborators, colleagues, and friends.

You can add a note of remembrance at: <https://www.legacy.com/obituaries/berkshire/obituary.aspx?n=gavril-william-pasternak&pid=191661024&fhid=2086>

IN SYMPATHY

ASPET notes with sympathy the passing of the following members.

Paul Greengard
Gavril W. Pasternak
Jeremy G. Richman

Raymond W. Ruddon
Paul Talalay
William Schumacher