Twenty-second lecture in the series

James P. Holland Memorial Lecture

Monday, October 11, 2021, at 4:00pm
On Zoom
(Learn more/register: https://go.iu.edu/holland-lecture)

Vitamin K_2 synthetic enzyme UBIAD1 moonlights as a key regulator of cholesterol synthesis

Russell DeBose-Boyd, Ph.D.

(https://profiles.utsouthwestern.edu/profile/34046/russell-debose-boyd.html)

Beatrice and Miguel Elias Distinguished Chair in Biomedical Science
Professor of Molecular Genetics
University of Texas Southwestern Medical Center

UbiA prenyltransferase domain-containing protein-1 (UBIAD1) utilizes geranylgeranyl pyrophosphate (GGpp) to synthesize the vitamin K2 subtype menaquinone-4 (MK-4). Mutations in UBIAD1 cause Schnyder corneal dystrophy (SCD), which is characterized by corneal opacification owing to over-accumulation of cholesterol. Our studies disclosed a key role for UBIAD1 in regulating endoplasmic reticulum (ER)-localized HMG CoA reductase, the rate-limiting enzyme in synthesis of cholesterol and nonsterol isoprenoids including GGpp. Feedback control of reductase involves sterol-induced ubiquitination, an obligatory reaction for its ER-associated degradation (ERAD) that is augmented by GGpp. Sterols also cause UBIAD1 to bind reductase, which inhibits ERAD and allows continued synthesis of nonsterol isoprenoids in sterol-replete cells. GGpp triggers release of reductase from UBIAD1, enhancing ERAD and stimulating translocation of UBIAD1 to Golgi. SCD-associated UBIAD1 resists GGpp-induced release from reductase and becomes sequestered in ER to inhibit ERAD.

Gene knockout studies in mice were attempted to explore the in vivo function of UBIAD1; however, homozygous germ-line deletion of Ubiad1 caused embryonic lethality. We generated homozygous deletion of Ubiad1 in knock-in mice expressing ubiquitination-resistant HMGCR, implying embryonic lethality results from enhanced ERAD of HMGCR. The study of Ubiad1-deficient mice offers the opportunity to determine the physiological significance of UBIAD1-mediated synthesis of MK-4.

Thanks to our generous Indiana University Holland lecture sponsors:

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Office of the Vice Provost for Faculty and Academic Affairs
Office of the Vice Provost for Research
College of Arts and Sciences
Department of Biology
Medical Sciences Department

About Russell DeBose-Boyd

Russell DeBose-Boyd is a dynamic speaker and has provided a lecture for iBiology. His research focuses on how cholesterol synthesis is regulated through endoplasmic reticulum-associated degradation.

Professional Experience

Department of Molecular Genetics, University of Texas Southwestern Medical Center; Dallas, TX
- Beatrice and Miguel Elias Distinguished Scholar in Biomedical Science, 2016-
- Professor, 2013-
- Associate Professor, 2007-2013
- Assistant Professor, 2003-2007
- Instructor, 2001-2003

Education

University of Texas Southwestern Medical Center, Postdoctoral Fellow, 2001
University of Oklahoma Health Sciences Center, PhD, 1998
Southeastern Oklahoma State University, BS, 1993

Honors

Edwin Bierman Award, American Diabetes Association, 2021
John J. Abel Award in Pharmacology, American Society for Pharmacology and Experimental Therapeutics, 2010
Early Career Scientist, Howard Hughes Medical Institute, 2009-2015
Distinguished Young Scholar in Medical Research, W.M. Keck Foundation, 2006-2011
Established Investigator, American Heart Assoc., 2005-2009
David L. Williams Memorial Lectureship Award, 2005
Scholar, National Center on Minority Health and Health Disparities Health Disparities, 2002-2008
Mentored Minority Faculty Development Award, NIH/NHLBI, 2002-2007
Fellow, Jane Coffin Childs Memorial Fund for Medical Research, 1998-2001

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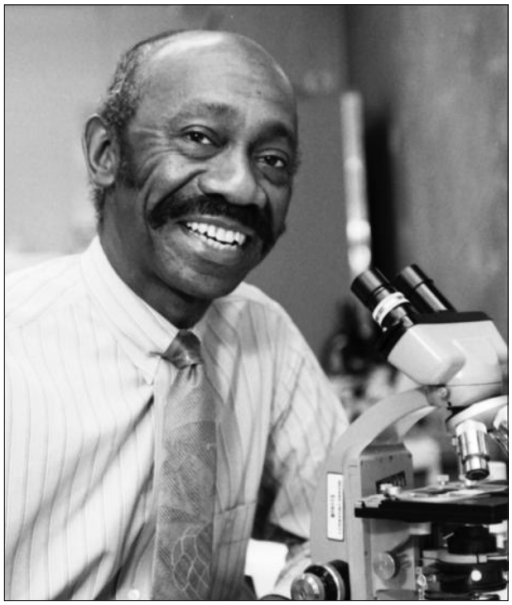
About James Holland and the Lecture Series



Professor James P. Holland, 1934–1998

The James P. Holland Memorial Lecture Series was initiated in the fall of 2000, and is now organized by the Herman C. Hudson and the James P. Holland Scholars Program and the Department of Biology. The lectures honor the memory of one of the most beloved faculty members on the Bloomington campus. Professor Holland had a passion for teaching that earned him virtually every teaching award offered on campus, including the President's Award for Distinguished Teaching. This lecture series honors his legacy and is designed to bring awareness of and support to diversity in the life sciences.

Professor Holland worked tirelessly to address the needs of minority students. He created Biology's summer enrichment program, which brings Indiana minority high school students to campus to attend science lectures and participate in hands-on laboratories. The program is designed to spark their interest in science and provide a taste of college life. Holland and the late Herman C. Hudson joined forces to found IU's Minority Achievers Program (MAP) and the Mathematics and Science Scholarship Program (MASS). In 2003 the programs were named after Hudson and Holland to honor the efforts of these two men.

James Holland came to Indiana University to study zoology, earning a master's degree in 1958 and a doctorate three years later. Holland was on the Howard University faculty until 1967, when he returned to IU as an associate professor in the Department of Biology, advancing to full professor in 1974. His research involved reproductive endocrinology, and he examined the mechanism by which thyroid hormones influence female reproductive physiology.

From recruiting and mentoring students to serving as associate dean and interim dean of the graduate school, Professor Holland's commitment to the university was exceptional. He was a recipient of IU's Distinguished Service Award, the Herman B Wells Lifetime Achievement Award, and the Distinguished Alumni Service Award. Jim Holland taught over 11,000 undergraduates during his IU career, and his talent for teaching earned him a FACET award, given to exceptional teachers who inspire both students and colleagues. He was the first to receive the Chancellor's Medallion for his "transcendent efforts on behalf of the university."

About the Holland Teaching Award

It was Holland's wife, Constance, who created the **James Philip Holland Teaching Award for Exemplary Teaching and Service to Students**. Mrs. Holland—a highly respected, award-winning secondary school teacher—established the award to recognize others who shared the Hollands' passion for teaching. **Linda Charnes, Professor of English, is this year's recipient.**

About the Holland Fellowship

Biology established the James P. Holland Graduate Fellowship in Biology to honor Professor Holland, a member of our faculty for 31 years. He was a truly dedicated teacher and mentor who loved science.

The Holland Fellowship supports the training of a first-year Ph.D. graduate student from groups underrepresented in the life sciences. It provides stipend, tuition, and health insurance during the first year of graduate training for the Ph.D. degree.

Allan Gramillo

Allan Gramillo, **the 2021–22 Holland Fellow**, is pursuing a Ph.D. in microbiology through the Department of Biology. His research interests include biofilm formation and antibiotic resistance. Gramillo is from Los Angeles, California, and is a first-generation student. He received his undergraduate degree in microbiology from California State University, Los Angeles, and completed his master's in microbiology in the lab of Dr. Peter Bergholz at North Dakota State University in Fargo.

Visit https://go.iu.edu/252c for more information about the Holland Graduate Fellowship.