

Demetrios Vavvas, MD, PhD, is the Monte J Wallace Ophthalmology Chair in Retina, the J.W. Miller Scholar in Retina Research, Associate Professor of Ophthalmology at Harvard Medical School, co-director of the Ocular Regenerative Medical Institute and Co-Director of the Angiogenesis Laboratory.

Dr. Vavvas has received his B.Sc. (first Class Honors) in Neurosciences from McGill University. Subsequently he studied regulation of muscle metabolism and proto-oncogene regulation during his combined MD/PhD training at Boston University. He completed his ophthalmology residency training at Harvard/MEEI and was selected to be the chief resident. After residency he served as the Director of the Eye Trauma Service and Associate Chief of Residency affairs. Subsequently he completed his fellowship in studies and surgeries of diseases of the Vitreous and retina at Mass. Eye and Ear/Harvard Medical School. He was selected to serve as the chief fellow and he received the fellow of the year teaching award.

As a clinician scientist, Dr. Vavvas is a full-time member of the Mass. Eye and Ear Retina Service and has a highly productive translational research laboratory. His clinical interests focus on diabetic retinopathy, ocular tumors, and the "dry" form of age-related macular degeneration (AMD), for which effective therapies are currently lacking. Based on his involvement with several clinical studies, Dr. Vavvas has completed a physician-sponsored Investigational New Drug (IND) approved phase I-II study for dry AMD using high dose Atorvastatin showing reversal high risk features without progression to atrophy or neovascular AMD. A larger phase III is being planned based on these results.

Dr Vavvas' lab identified receptor interacting protein kinases (RIPK) mediated programmed necrosis as significant mode of photoreceptor cell loss and showed that simultaneous inhibition of both RIP kinase and caspase pathways is necessary for effective neuroprotection. In addition we showed that RIPK mediated necrosis and not apoptosis is the mechanism of the non autonomous cone cell death in diseases where rods but not cones harbor the deleterious gene mutations. We have also shown for the first time a novel non-necrotic function for RIPK1 on regulating angiogenesis through modulation of infiltrating macrophages, suggesting that inhibition of RIPK1 may aid in pathologic angiogenesis that is seen in several degenerative eye conditions. This work has implications in novel therapeutic strategies for neurodegenerative disorders and several patents have been issued in this work. A startup company has been formed.

Another interest has been the role of inflammatory cells and microglia in the pathophysiology of retinal diseases after various noxious stimuli. We have uncovered the intricate relationship of inflammation and retinal degenerations and in collaboration with Eleftherios Paschalis we have shown that there is a permanent neuroglia remodeling in the retina after infiltration of CSFR1 inhibition resistant peripheral monocytes. This supports that changes in the epigenetics of infiltrating immune cells are needed in order to promote tissue neuroprotection and recovery.

Other areas of contribution in the lab include the first description of Verteporfin as a YAP inhibitor in Ocular oncology and second in all of Oncology. Furthermore, we showed methodological issues in working with Verteporfin as a non light activated modulator of YAP, that can affect the interpretation of many published results. We have also debunked the hypothesis of NLRP3 inflammasome in the RPE as a cause of AMD and we led an international effort publishing in *Nature* about deficiencies and questionable data in the purported lens regeneration in infants.

Dr. Vavvas has published more than 190 peer reviewed manuscripts and several book chapters. His research is well funded, with support from Research to Prevent Blindness, Alcon Research Institute, an R01 and R21 from the National Eye Institute, and funding from several foundations. His work has resulted in 11 patent filings with 6 issued and 5 pending.

Dr. Vavvas' outstanding contributions to research have been aptly recognized. In 2010, the Harvard Medical School Department of Ophthalmology selected Dr. Vavvas as the Joan W. Miller Scholar in Retinal Research. Subsequently, in 2012, he received a Club Jules Gonin Retina Research Foundation Travel Grant to present his work on photoreceptor death in inherited rod retinal degenerations in Reykjavik, Iceland. He has received the 2013 Physician Scientist Award from RPBI, the 2014 Macula Society Research Grant, the 2015 Alcon Research Institute Young Investigator Award, the 2016 ARVO Foundation/Pfizer Ophthalmics Carl Camras Translational Research Award and the 2016 New England Hellenic Medical and Dental Society HYGEIA Award. He was selected in the Ophthalmologist 2019 Power list (Top 50/ Top 10 Mentors Worldwide) He was nominated for the prestigious 2019 Barbara J. McNeil Faculty Award for Exceptional Institutional Service to Harvard Medical School.

Committed to training the future leaders of ophthalmology, Dr. Vavvas has served as a primary mentor to over 35+ research trainees and 35+ clinical trainees in ophthalmology and vision research. Many of them are now Assistant or Associate Professors at institutions in the USA and abroad. Has won awards for his teaching along the years and for the last 10 years co-organizes the annual Mass. Eye and Ear Vitrectomy Course, for first year vitreoretinal fellows from over 20 different programs in the nation. This is an intensive course that consists of lectures, wet labs, and "dry labs" using virtual reality simulators. The course is designed to give beginning fellows a brief but comprehensive introduction to techniques in vitreoretinal surgery, to better prepare them for the fellowship OR experience. He also has served as the co-Director of the Medical Retinal Fellowship at Mass. Eye and Ear and along with Dr Michael Young organizes the Biennial Ocular Regeneration Symposium which is supported by the NIH R13 program and helps many trainees and young investigators to learn from outstanding faculty and start collaborations with experts in the field.