BIOGRAPHICAL SKETCH

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NAME: Puro, Donald G.

POSITION TITLE: Professor of Ophthalmology & Visual Sciences and Molecular & Integrative Physiology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Pennsylvania, Philadelphia, PA	B.A.	05/1969	Biochemistry
University of Rochester, Rochester, NY	M.D.	05/1974	Medicine
University of Rochester, Rochester, NY	Ph.D.	05/1975	Physiology
Strong Memorial Hospital, U of R, Rochester, NY	Internship	06/1975	Pathology
National Institutes of Health, National Institute of General Medical Sciences, Bethesda, MD	Postdoc	06/1977	Pharmacology
University of Miami, Bascom Palmer Eye Institute, Miami, FL	Residency	06/1980	Ophthalmology

A. Personal Statement

I am an ophthalmologist/scientist. As the Principal Investigator on NIH/NEI-supported research projects for ~35 years, I have carried out a series of R01-funded projects chiefly focusing on the role of ion channels in retinal neurons, Müller cells and microvessels. Recently, my research focus changed from the retina to the front of the eye. With receipt of an RPB Stein Innovation Award in 2016, I was able to initiate a quest to elucidate how ion channels impact the response of conjunctival goblet cells to the electrolyte imbalance (hyperosmolarity) that is the universal hallmark of dry eye. My hope is that elucidation of previously unsuspected pathophysiological mechanisms will reveal new targets for novel pharmacological treatments of this common, uncomfortable, sight-impairing disorder.

Throughout my career, I have sought to mentor research-oriented medical students, ophthalmologists, physicians and PhDs. More than 30 postdoctoral fellows have trained in my laboratory. Two UM medical students received Rearch to Prevent Blindness fellowships to take a year out to perform research in my lab; both are now members of academic ophthalmology departments. Of my postdocs, 25 currently hold academic positions; another is a Division Director in the Food and Drug Administration. Four have become department chairs.

B. Positions and Honors

Positions and Employment

1980-1985 Medical Officer, United States Public Health Service; Principal Investigator, National Eye Institute, NIH, Bethesda, MD
1985-1990 Associate Professor, Department of Ophthalmology (Bascom Palmer Eye Institute) and Department of Physiology & Biophysics, University of Miami, Miami, FL
1990-1995 Professor, Department of Ophthalmology and Associate Professor, Department of Physiology, University of Michigan School of Medicine, Ann Arbor MI
1995- Professor, Departments of Ophthalmology & Visual Sciences and Molecular & Integrative Physiology, University of Michigan, Ann Arbor, MI

Honors

1973 Alpha Omega Alpha Honor Medical Society
1974 Robert Kates Award for excellence in clinical medicine and research, University of Rochester
1974 National Foundation Award for Research in developmental biology

1986 Research to Prevent Blindness-William and Mary Greve Research Scholar Award
1992 Research to Prevent Blindness-Senior Scientific Investigator Award
2002- American Ophthalmological Society membership
2002 Harrington RPB Senior Scientific Investigator
2007- Listed as one of the 'Best Doctors in America'
2009 Inaugural class of Fellows in the Association for Research in Vision and Ophthalmology (ARVO)
2012- Selected as a Castle Connolly 'Top Doctor'
2016 Research to Prevent Blindness Stein Innovation Award
2018 Elected a Fellow in the American Association for the Advancement of Science (AAAS)

C. Contributions to Science

1. During my first years as a Principal Investigator (PI), I focused on the functional development of retinal neurons. One of the most important findings was the discovery of a functional role for insulin and its receptors, whose existence in the retina and elsewhere in the CNS had only recently been reported. Our early projects contributed to a better understanding of the role of extracellular molecules in regulating the functional development of the retina. (Selected publications are listed below.)

   Puro DG, Battelle B-A and Hansmann KE. Development of cholinergic retinal neurons of the rat retina. *Developmental Biology* 91:138-148, 1982.

   Puro DG and Agardh E. Insulin-mediated regulation of neuronal maturation. *Science* 225:1170-1172, 1984.

2. Subsequently, I shifted my research focus to retinal Müller cells. My aim was to use the patch-clamp technique to better understand Müller cell physiology and pathobiology by analyzing the function and regulation of ion channels expressed by these glia. In the course of electrophysiological studies of human and primate Müller cells, I (along with others) found that glial physiology is dynamic, rather than static as previously thought. Our studies also contributed to a better understanding how a breakdown of the blood-retinal barrier breakdown can disrupt neuronal function.

   Puro DG and Mano T. Modulation of calcium channels in human retinal glial cells by basic fibroblast growth factor: a possible role in retinal pathobiology. *Journal of Neuroscience* 11:1873-1880, 1991.

   Puro DG and Stuenkel EL. Thrombin-induced inhibition of potassium currents in human retinal glial (Müller) cells. *Journal of Physiology* 485:337-348, 1995.

   Puro DG. Growth factors and Müller cells. *Progress in Retinal and Eye Research* 15:89-101, 1995.

3. To maintain a fresh perspective, my strategy has been to change projects every ~10 years. The next focus of my research was the retinal microvasculature. Utilizing a novel method for isolating vast complexes of retinal microvessels, we used techniques such as patch-clamping, fluorescence imaging and time-lapse photography to test mechanistic hypotheses concerning retinal vascular physiology and pathobiology. Contributions made during a series of NEI R01 grants included the first characterization of the electrotonic architecture of the retinal microvasculature and the first assessment of the roles of $P2X_7$ receptor/channels in retinal pathophysiology.

   Ishizaki E, Fukumoto M and Puro DG: Functional K_{ATP} channels in the rat retinal microvasculature: topographical distribution, redox regulation, spermine modulation and diabetic alteration. *Journal of Physiology*, 587:2233-2253, 2009. PMCID: PMC2697296.

   Zhang T, Wu DM, Xu G-z and Puro DG: The electronic architecture of the retinal microvasculature: modulation by angiotensin II. *Journal of Physiology*, 589:2383-2399, 2011. PMCID: PMC3098709.

   Fukumoto M, Nakaizumi A, Zhang T, Lentz SI and Puro DG: Vulnerability of the retinal microvasculature to oxidative stress: ion-channel-dependent mechanisms. *American Journal of Physiology*, 302: C1413-C1420, 2012. PMCID: PMC3361947.

   Puro, DG: Retinovascular physiology and pathophysiology: New experimental approach/new insights. *Progress in Retinal and Eye Research*,31:258-270, 2012. NIHMSID #355389.

4. Building upon a decade of experience studying blood vessels within the retina, I then shifted my focus to the study of pathological pre-retinal neovascularization. With support of a new NEI R01 grant, my laboratory performed the first bioelectric analysis of pathological angiogenesis in any tissue. In studies of

animal models and human specimens of retinal neovascularization, we discovered that pathological neovessels generate an extremely high voltage, whose transmission into the retinovascular network exerts a function-altering impact that likely boosts the pathobiological process of hypoxia-driven angiogenesis.

Puro DG, Kohmoto R, Fujita Y, Gardner TW and Padovani-Claudio DA. Bioelectric impact of pathological angiogenesis on vascular function. *Proceedings of the National Academy Sciences USA*. 113:9934-9939 (2016). PMCID: PMC5024585.
This paper was featured in an accompanying Commentary in *PNAS* 113:10458-10460 (2016).

5. After studying the retina for many years, I shifted my attention to the front of the eye and began an RPB-supported project focusing on dry eye. By applying the patch-clamp technique, as well as other experimental methods, I am exploring how ion channels play a role in the response of the tear-stabilizing goblet cells to hyperosmotic stress, which is the hallmark of dry eye.

In 2018, my first dry eye paper was published in the *American Journal of Physiology* and was highlighted by the American Physiological Society as one of "best of the best" in their APS*select* program; a press release was also issued: http://www.the-aps.org/mm/hp/Audiences/Public-Press/2018/30.html

Puro, DG. Role of ion channels in the functional response of conjunctival goblet cells to dry eye. *American Journal of Physiology*. 315: C236-246, 2018. PMCID: PMC6139504.

D. Research Support

A Novel Experimental Approach to Dry Eye: Role of Ion Channels in the Physiology and Pathobiology of Conjunctival Goblet Cells. Funded by the Research to Prevent Blindness (Stein Innovation Award). This new avenue of research is based on the premise that new knowledge of how ion channels play a role in the function of conjunctival goblet cells will provide new targets for pharmacological therapy of dry eye.
Role: Principal Investigator

Michigan Vision Clinician/Scientist Development Program (K12 EY022299; PIs: Drs. Gardner and Lee)
Role: Mentor and former executive committee member