

The Distinguished Lecture Series Presents:



**“Uncovering rules of
photoreceptors long life”**

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Thursday, April 1st, 2021: 4:00PM – 5:00PM
Zoom Meeting

<https://harvard.zoom.us/j/97426411271?pwd=NGp2bndzSzJQVlB1V1NhWEJsK1I2UT09>

Meeting ID: 97426411271

Password: 747000

About Dr. Bazan's research:

My research is focused on understanding cellular and molecular mechanisms that preserve photoreceptors and retinal pigment epithelial (RPE) cell functional integrity for decades in healthy eyes despite their hostile environment (light exposure, high oxygen consumption, highly reactive retinoids; peroxidation-susceptible polyunsaturated fatty acids; and other adversities). Similar mechanisms likely operate to sustain successful brain aging. My laboratory has begun to uncover molecular principles involved in the retention/conservation and function of docosahexaenoic acid (DHA) and other molecules in RPE cells and photoreceptors. We participated in the discovery of Neuroprotectin D1 (NPD1) and coined its name. Under conditions of uncompensated oxidative stress, NPD1 is made on demand from DHA when homeostasis is disrupted, and the response needs to be modulated to protect cell integrity. We found that neurotrophins (mainly PEDF) are agonists for the synthesis of this mediator in RPE cells, that 15-lipoxygenase-1 (15-LOX-1) is the enzyme that catalyzes its synthesis, that it targets protein phosphatase 2A to regulate anti-/pro-apoptotic proteins during uncompensated oxidative stress, and that it regulates proteostasis as well. We identified transcription of pro-inflammatory genes as a target of NPD1 and demonstrated that the CA1 hippocampus from early-stage Alzheimer's patients displays a 25-fold loss of NPD1 as well as of the enzyme for its synthesis.

Most known lipid mediators are derived from 18-22C fatty acids. However, we recently discovered a new family of mediators, which we named the elovanoids (ELVs), made from 32C or 34C fatty acids. The ELV precursors are made by photoreceptor-specific elongase ELOVL4 (ELongation of Very Long chain fatty acids-4). We reported the detailed structure and stereochemistry of ELVs and demonstrated that they are low-abundance, highly potent pro-homeostatic mediators that also arrest senescence gene programming and the senescence-activated secretory phenotype in RPE cells upon homeostasis disruptions.

Our common thread of concepts includes homeostatic regulation, metabolomics, and genetic and epigenetic events. A central theme is to understand early responses to uncompensated oxidative stress, immune-inflammatory responses, and mutations that lead to retinal degenerations. Our aim is to contribute to prevent, ameliorate, and cure age-related macular degeneration, inherited retinal degenerations, and other neurodegenerative diseases.

About Dr. Bazan:

He is the founding Director of the Neuroscience Center of Excellence at the School of Medicine, Louisiana State University Health New Orleans. He is also the inaugural founder of The Ernest C. and Yvette C. Villere Chair for Research in Retinal Degeneration (1984-present) and has been appointed to the highest academic rank in the LSU System, a Boyd Professor (1994-present). He is also a Foreign Adjunct Professor of Neuroscience, Karolinska Institutet, Stockholm, Sweden. He devoted his life to studying fundamental cellular and molecular lipid signaling taking place in the early stages of neurodegeneration and other brain and retinal dysfunctions. He has discovered cellular and molecular principles that reveal novel pro-homeostatic mediators as well as their relevance in early stages of Alzheimer's disease, in experimental stroke, experimental epilepsy, Parkinson's disease, traumatic brain injury, and age-related macular degeneration. Currently, he is beginning to apply his discoveries (patents exclusively licensed from the University in three startup companies that he co-founded). They are NeuResto Therapeutics, LLC (novel discoveries for Alzheimer's, Parkinson's, retinal degenerations, stroke, traumatic brain injury, and other brain and retina diseases; <http://www.neuresto.com/>), South Rampart Pharma, LLC (novel non-addictive, non-toxic painkiller; <https://www.southrampartpharma.com/>) and CurVirBiotech (innovative therapeutic approaches to block/attenuate SARS-CoV-2, and other viruses, into the eye, brain and other organs; <https://www.curvirbiotech.com/>)

Lab Website: https://www.medschool.lsuhsu.edu/neuroscience/bazan_lab.aspx