Team discovers retina protein that may help conquer blindness

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Human eye. Image: Wikipedia.

Research led by Nicolas Bazan, MD, PhD, Boyd Professor and Director of the LSU Health New Orleans Neuroscience Center of Excellence, discovered a protein in the retina that is crucial for vision. The paper reports, for the first time, the key molecular mechanisms leading to visual degeneration and blindness. The research reveals events that may be harnessed for prevention, as well as to slow down progression of retinal degenerative diseases. The paper is published in the March 4, 2015, issue of *Nature Communications*.

There is growing evidence of the significance of the essential omega-3 fatty acid family member, docosahexaenoic acid (DHA), for photoreceptor function and in retinal degenerative diseases, but not much understanding about what governs it. The research team found that

the protein receptor for adiponectin, a hormone that promotes insulin sensitivity and is involved in the metabolic syndrome, has a heretofore unrecognized function. The receptor also regulates DHA retention and conservation in cells in the eye and is necessary for photoreceptor cell function.

"This is the first time that such an integral membrane protein has been localized in the photoreceptor cells and shown to have the capacity to support sight," notes Dr. Bazan, the paper's corresponding author.

Working with a novel genetic mouse model they developed with the adiponectin receptor gene deleted, the researchers found that total and free retinal DHA were diminished in the gene-deficient mice. When they incubated normal retinas with labeled DHA, they measured abundant levels of it, demonstrating that a functional AdipoR1 gene must be present for DHA uptake and retention. Additionally, when cultured human Retinal Pigment Epithelial (RPE) cells were incubated with labeled DHA, DHA within the medium decreased with time while increasing within the cells. Also, when the AdipoR1 gene activity was ramped up in these cultured RPE cells, much more labeled DHA was taken up and incorporated. But when silenced, labeled DHA was diminished, indicating that human RPE cells can also take up DHA and that the AdipoR1 gene plays a significant role in this activity, too.

DHA in brain and retinal cells also builds reservoirs for molecules called into action when normal functions are disrupted, resulting in such conditions as retinal degeneration, Parkinson's or Alzheimer's disease. Dr. Bazan and his colleagues previously discovered neuroprotectin D1 (NPD1), one such molecule made from DHA when cell survival is compromised. Loss of, or diminished, retinal DHA leads to visual impairment and may play an important role in the development of blindness from retinitis pigmentosa and other retinal degenerative diseases, as well as age-related macular degeneration (AMD), the

foremost cause of blindness in people older than 50 years.

"Our model and newly discovered molecular mechanism allow therapies to be testedmore rapidly," notes Dr. Bazan. "We feel an urgency to address blindness and cognitionimpairments of dementias because of their heavy burden on patients, families, care givers andthe health care system."

DHA, found in fish oil, is an essential omega-3 fatty acid and is vital for proper brain function. It is also necessary for the development of the nervous system, including vision. Dr. Bazan has been a pioneer in the understanding of the biology and impact of DHA in medicine.

More information: *Nature Communications*, www.nature.com/ncomms/2015/150 … full/ncomms7228.html

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