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# What Do Lipids from Beeswax and Fish Oils Have to Do with Dry Skin, Macular Degeneration, Seizures, and Male Infertility?

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A common link between beeswax and fish oil lipids is that each contains very long chain fatty acids (VLC-FA) greater than 26 carbons in length. Those in beeswax are saturated (VLC-SFA), while those in fish oils are polyunsaturated (VLC-PUFA). Each has vastly different melting points (64 °C vs. 10-15 °C, resp.) that give them distinctly different biophysical properties when incorporated into biological membranes. VLC-SFA and VLC-PUFA are synthesized by the same enzyme, ELOngation of Very Long Chain Fatty Acids-4 (ELOVL4), which is found in only a few tissues, such as skin, retina, brain, and testes. VLC-SFA are the main products in skin and brain, while VLC-PUFA are most abundant in retina and sperm. Dominantly expressed mutations in ELOVL4 lead to several different neurological and somatic diseases, depending on the type of mutation. A 5bp deletion in exon 6 of ELOVL4 causes Stargardt-like macular dystrophy (STGD3), a juvenile form of macular degeneration, without any skin or CNS involvement. However, a point mutation in ELOVL4 causes spinocerebellar ataxia-34 (SCA34), a late adult onset disease that causes cerebellar atrophy and subsequent gait and balance problems, but without any retinal involvement. SCA34 patients may also develop a skin rash (erythrokeratoderma, EKA), that usually occurs before any signs of ataxia.

Recessive inheritance of the STGD3 mutation in humans has catastrophic consequences, including intractable seizures, severe mental retardation, somatic developmental abnormalities, and skin lesions. Death usually occurs within the first decade of life. Mice with recessive inheritance of the STGD3 mutation die at birth from dehydration, due to the

absence of a VLC-SFA-containing lipid that makes up the permeability barrier. We prevented this by expressing ELOVL4 in their skin under the control of the keratin-14 promoter. They survived, but to our surprise, at age P19 developed seizures and died by P21. Our electrophysiology studies on hippocampal slices of these mice found significant differences in electrical responses in mutant and WT neurons. This behavior was observed in hippocampal neuronal cultures as differences in the kinetics of synaptic vesicle fusion and neurotransmitter release, which we could correct by adding VLC-SFA.

Sperm and retina appear to be the only tissues in the body that have VLC-PUFA. Reduction in VLC-PUFA in the human retina occurs in STGD3 as well as in age-related macular degeneration (AMD). Deletion of the gene (Elov12) that makes the precursors of VLC-PUFA leads to male infertility in rodents. Our recent analysis of sperm from 70 healthy males found a positive correlation between the levels of VLC-PUFA and sperm count/motility ( $P < 0.0001$ ).

We hypothesize that the biophysical properties of VLC-SFA provide stability to synaptic vesicle membranes and reduce spontaneous fusion that could cause seizures. They accomplish this because their great length allows them to span the entire lipid bilayer and increase Van Der Waals interactions and thereby reduce spontaneous fusion events. On the other hand, the VLC-PUFA with their great length and 5-6 methylene-interrupted cis double bonds increase the fluidity of the lipid bilayer, facilitating events that require this type of environment. Interestingly, photoreceptors and sperm have prominent cilia that are essential for their function.

**6:00 pm Reception**

**6:30-7:30 pm Dinner**

**7:30-8:30 pm Presentation**

**Buffet Menu by Bad Brad's**

Brisket, pulled pork

potato salad, cowboy beans

bread, relish tray

bar-b-q sauce, cherry cobbler, tea.

*RSVP is NOT required to attend the presentation.*

**Speaker Bio Sketch on next page.**

**Oklahoma State University**

Edmond Low Library, Oklahoma State University

Peggy Helmerich Browsing Room, 2nd Floor, East Side

map: <https://parking.okstate.edu/parking-map>

**Cost**

\$16 members

\$5 students

**RSVP Deadline**

Tuesday, Nov 27<sup>th</sup>, 5 pm

Contact: Allen Apblett

[allen.apblett@okstate.edu](mailto:allen.apblett@okstate.edu)

**Park in lot 31**



OSU campus map  
QR code



OSU parking map  
QR code

## Robert Eugene Anderson Biographical Sketch

Dr. Anderson's entire research career has been devoted to studies on the chemistry of lipids and their role in cell structure and function. The highlights presented below are divided into three time periods: his education/training (1963-68), his first faculty appointment at Baylor College of Medicine in Houston, TX (1969- 4), and his second faculty appointment at the University of Oklahoma Health Sciences Center and the Dean McGee Eye Institute (1995-present). More details are given for the studies carried out in Oklahoma. Dr. Anderson has mentored 15 graduate students, 29 postdoctoral fellows, and a large number of college and high school students.

Dr. Anderson completed graduate work at Texas A&M, did a post doctorate at Oak Ridge Association Universities, and then accepted an Assistant Professorship at Baylor College of Medicine. He rose through the ranks to become a full Professor and remained at Baylor for twelve years before matriculating to the OUHSC in 1995 where he is currently a Professor and also has an appointment in the Dean McGee Eye Institute.

Dr. Anderson's research focuses on the metabolic pathways that (1) provide molecules essential for the normal function of the retina and (2) protect against stress-induced retinal

degenerations. Disruptions in the former, which occurs in dominantly inherited Stargardt Macular Dystrophy (STGD3), leads to macular degeneration in children. We recently discovered that a unique group of fatty acids found primarily in photoreceptor membranes is greatly reduced in retinas of an animal model of STGD3. Current studies are focused on finding ways to deliver these essential fatty acids to the retina with the goal of preventing the retinas from degenerating. Environmental and hereditary stresses can lead to retinal degeneration. We discovered that the insulin receptor can be activated by light and initiate a series of "downstream" reactions that can protect the retina from light stress-induced degeneration. Current studies are focused on finding ways to fortify these pathways so that the retinas of persons susceptible to retinal diseases become more resistant to stress-induced degeneration. Finally, we have identified a number of synthetic and naturally occurring compounds that can protect the retina from oxidant stress-induced degeneration. Current research focuses on identifying the specific metabolic pathways these compounds affect and to test their efficacy in animal models of human age-related macular degeneration.

## DRIVING DIRECTIONS TO THE EDMON LOW LIBRARY

### Directions from Tulsa via Cimarron Turnpike

- Take Hwy 64 to the Cimarron Turnpike - toll gate (manned - \$0.75)
- Take the OSU "Y" turnoff (approximately 20 miles) - toll gate (unmanned - \$0.50)
- Continue on the turnpike. It will curve left into Stillwater and become Washington Street.
- Drive thru four traffic lights (Richmond Rd, The Links Apartments, & Airport and Lakeview Rds)
- Just before the next traffic light, go right at the "Y" (do not go through the light). This will keep you on Washington.
- Pass through two more traffic lights (Will Rogers Elementary School and McElroy Street).
- At the next traffic light, take right to Hall of Fame going west.
- Turn left (south) into Monroe Street at the first traffic light on Hall of Fame.
- When you reach the intersection of Monroe Street and Farm Road, take left to the parking lot #31 and park somewhere. This is a large lot and no parking hang tag is necessary after 5 PM.
- From the parking lot, you will walk south east in between two buildings towards the tower which is the Edmon Low Library.

### Directions from Tulsa via State Highway 51

- Travel through Stillwater to Duck Street.
- Turn right (north) onto Duck Street
- From Duck street, take left (west) onto the Hall of Fame
- Turn left (south) into Monroe Street from Hall of Fame.
- When you reach the intersection of Monroe Street and Farm Road, take left to the parking lot #31 and park somewhere. This is a large lot and no parking hang tag is necessary after 5 PM.
- From the parking lot, you will walk south east in between two buildings towards the tower which is the Edmon Low Library.

### Directions from Oklahoma City via I-35 North

- Take the Stillwater Exit and turn right on State Highway 51 (you are approximately 17 miles west of Stillwater).
- As you enter the edge of Stillwater, turn left (north) at 4th traffic light, which is Western.
- As you round the curve, it becomes Hall of Fame.
- When you reach the intersection of Monroe Street and Farm Road, take left to the parking lot #31 and park somewhere. This is a large lot and no parking hang tag is necessary after 5 PM.
- From the parking lot, you will walk south east in between two buildings towards the tower which is the Edmon Low Library

