

Investigating the role of AdipoR1 in pro-homeostatic fatty acid metabolism pathways

Eric Prestenburg, Alise Aucoin, Marie-Audrey Kautzmann-Guerin, PhD, Bokkyoo Jun, PhD, William Gordon, PhD, and Nicolas Bazan, MD, PhD



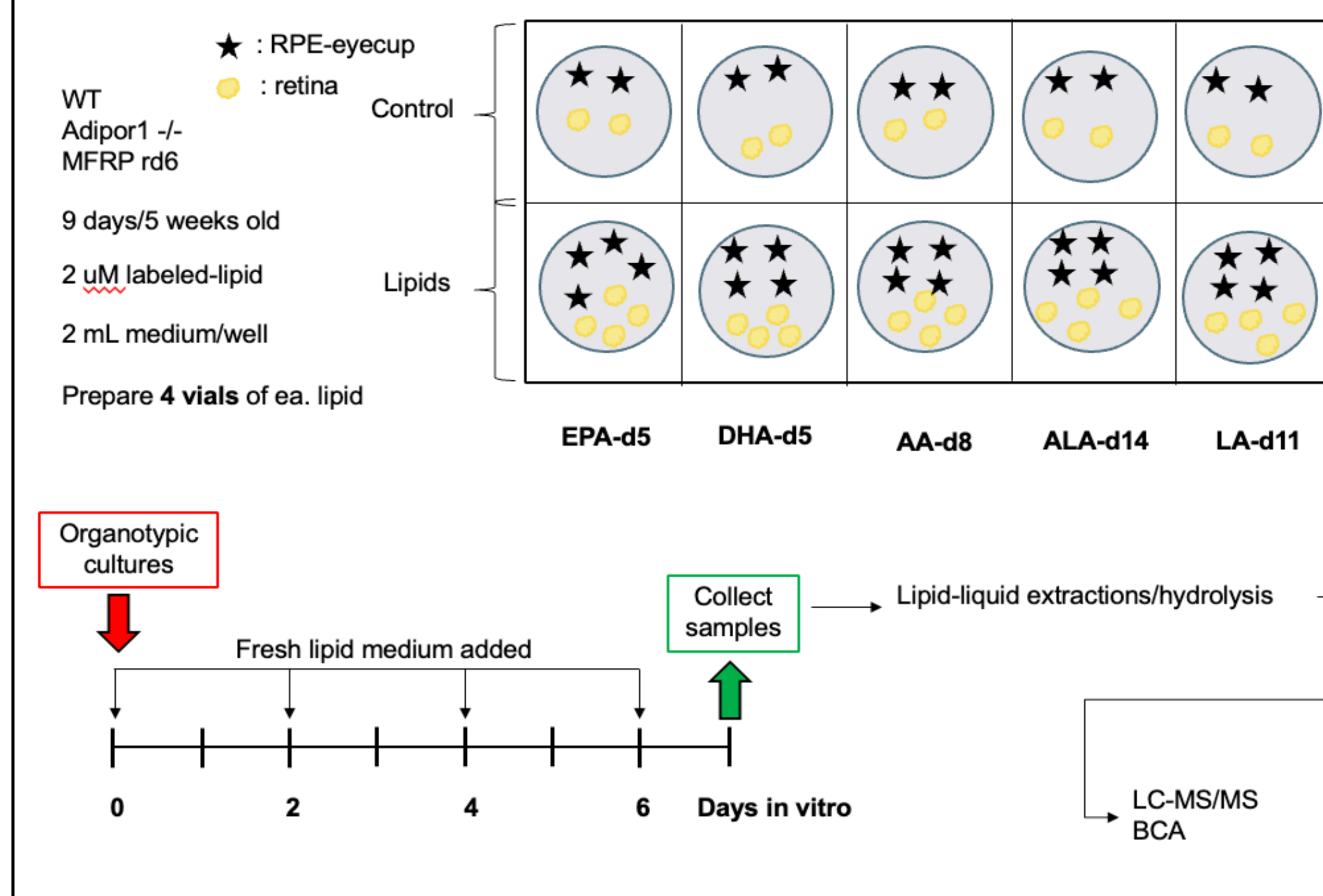
Neuroscience Center of Excellence, School of Medicine, LSU Health Sciences Center

Introduction

- Docosahexaenoic acid (DHA, 22:6) has widely been accepted as a fatty acid that has a critical role in maintaining homeostasis in the retina as a substrate necessary for the synthesis of very-long-chain polyunsaturated fatty acids (VLC-PUFAs).
- This class of fatty acids are precursors for elovanoids (ELVs), which have been indicated to respond to inflammation and oxidative stress encountered by the retina. Elovans are synthesized in the retinal pigmented epithelial (RPE) cells and induce expression of anti-apoptotic and pro-survival proteins.
- AdipoR1 double-knockout mice have been demonstrated to have lower concentrations of DHA and VLC-PUFAs in ocular tissue. This genetic anomaly is medically significant, as clinical studies have correlated mutations of the Adipor1 gene with patients suffering from retinitis pigmentosa and age-related macular degeneration.

Goals and Methods

- We intend to elucidate the significance of AdipoR1 with the concentrations of DHA, VLC-PUFAs, and ELVs in retina and RPE.
- We also intend to determine tissue specificity of fatty acids and enzymes involved in the generation of VLC-PUFAs.



VLC-PUFA Synthesis Pathway

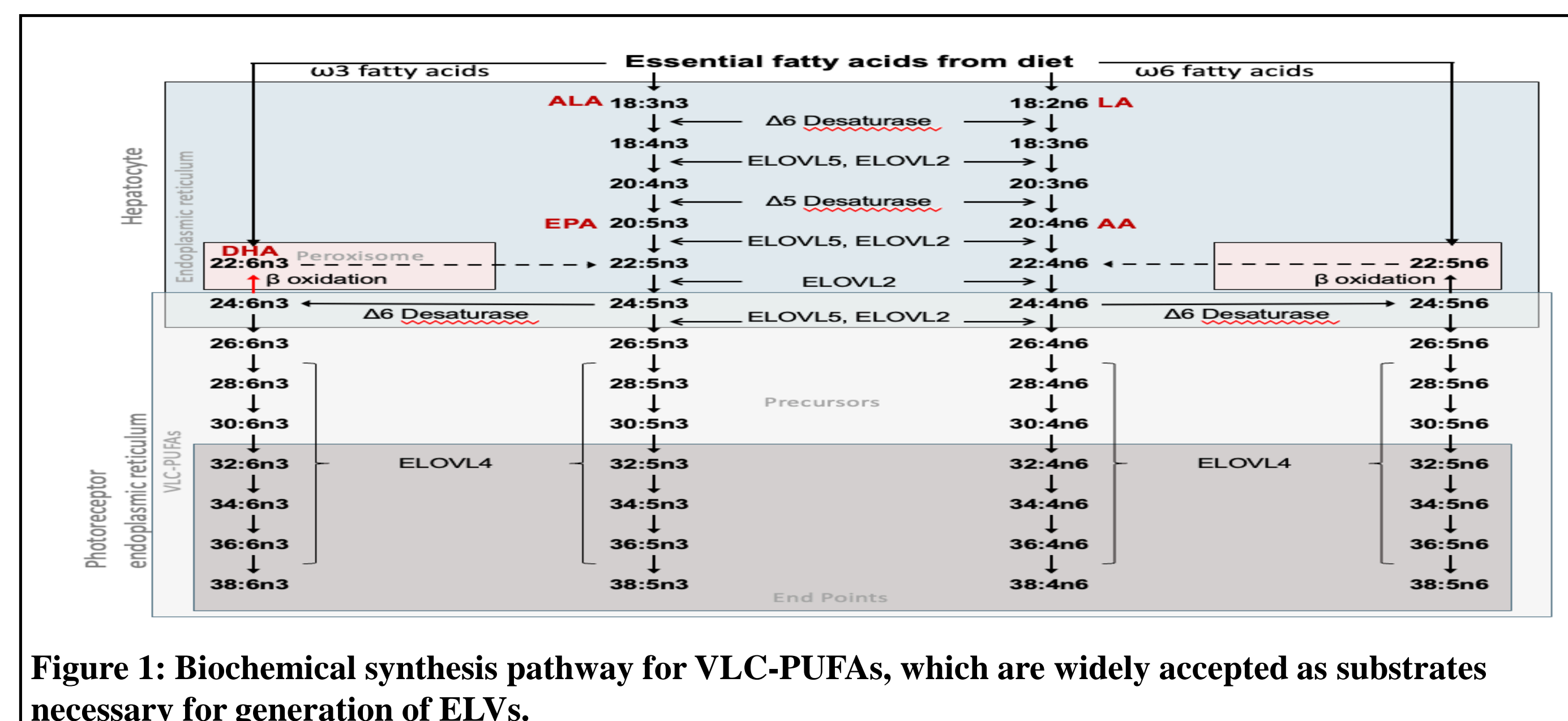


Figure 1: Biochemical synthesis pathway for VLC-PUFAs, which are widely accepted as substrates necessary for generation of ELVs.

Total FA Concentrations in Retina

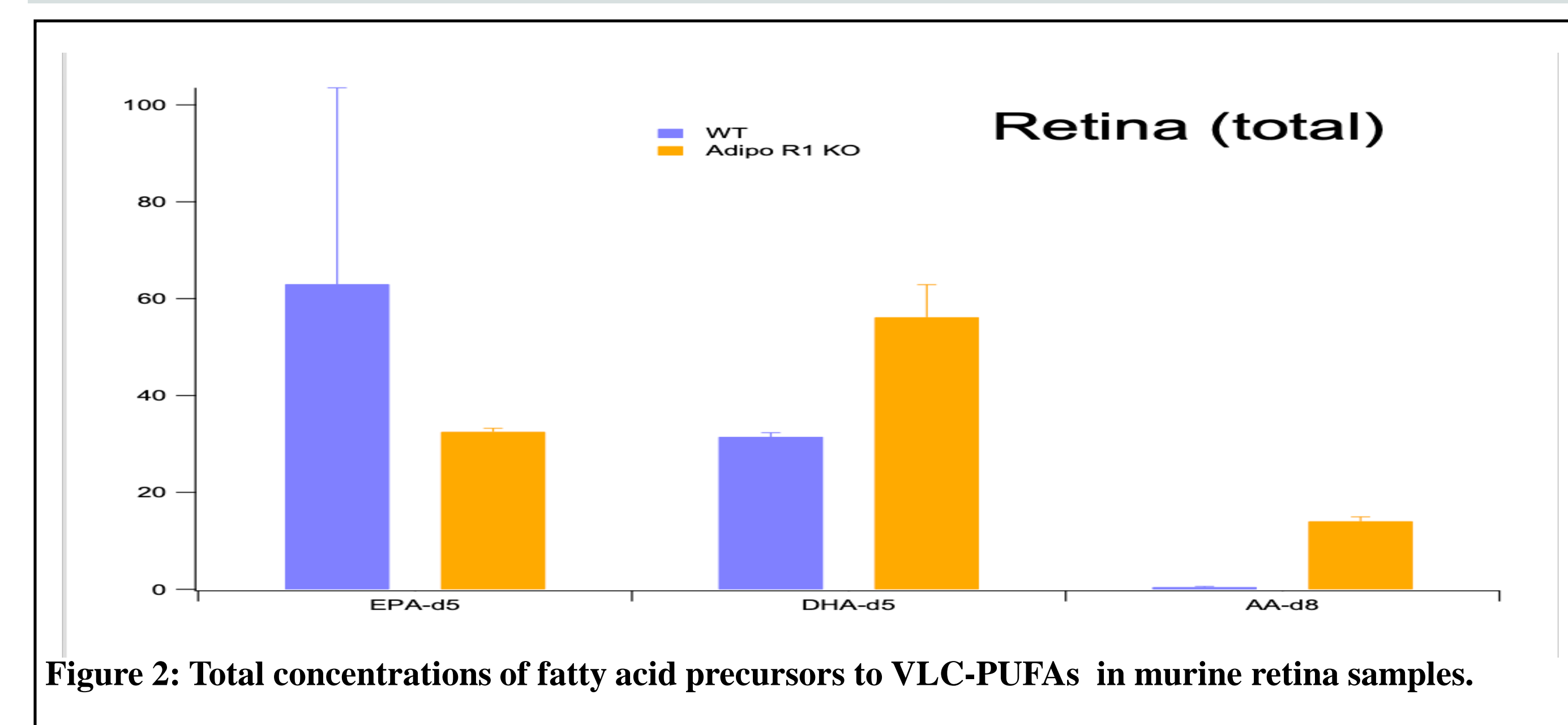


Figure 2: Total concentrations of fatty acid precursors to VLC-PUFAs in murine retina samples.

Total FA Concentrations in RPE

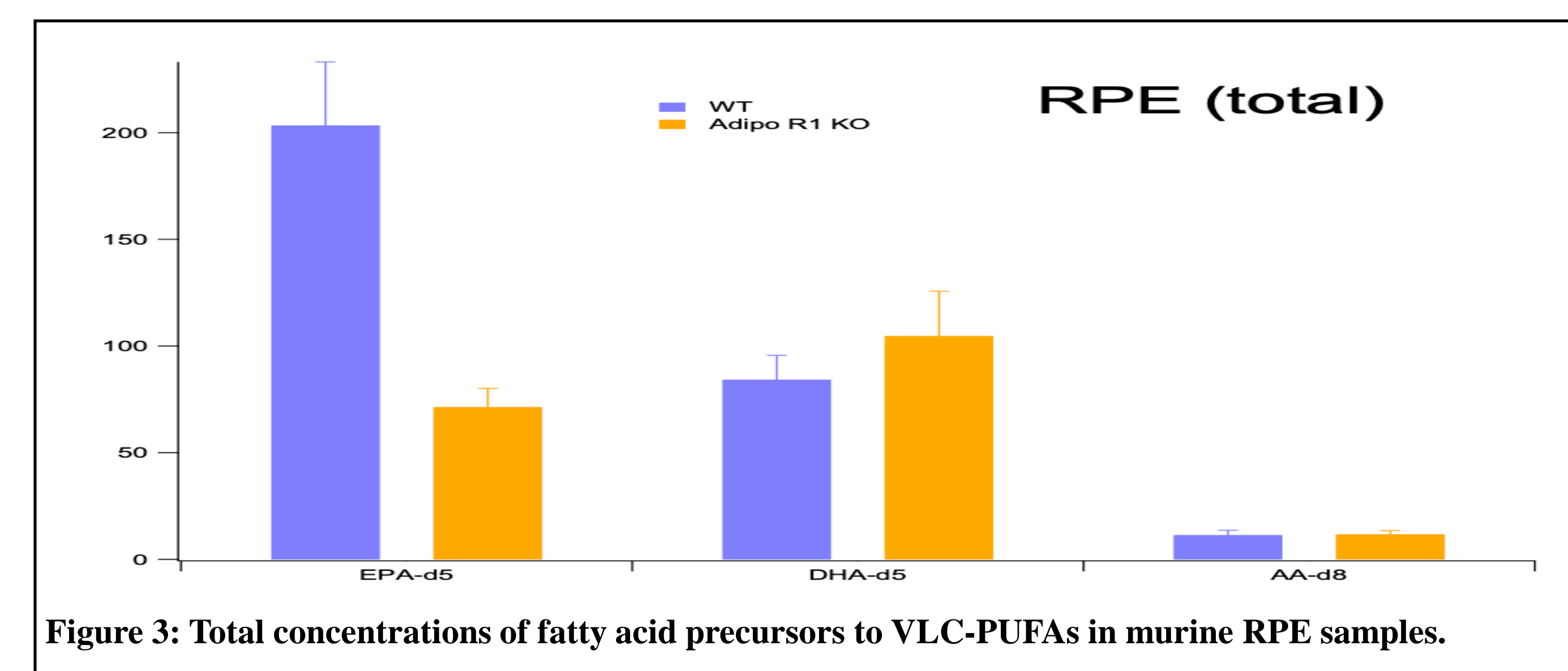


Figure 3: Total concentrations of fatty acid precursors to VLC-PUFAs in murine RPE samples.

Ret. FA Concentrations – DHA-d5

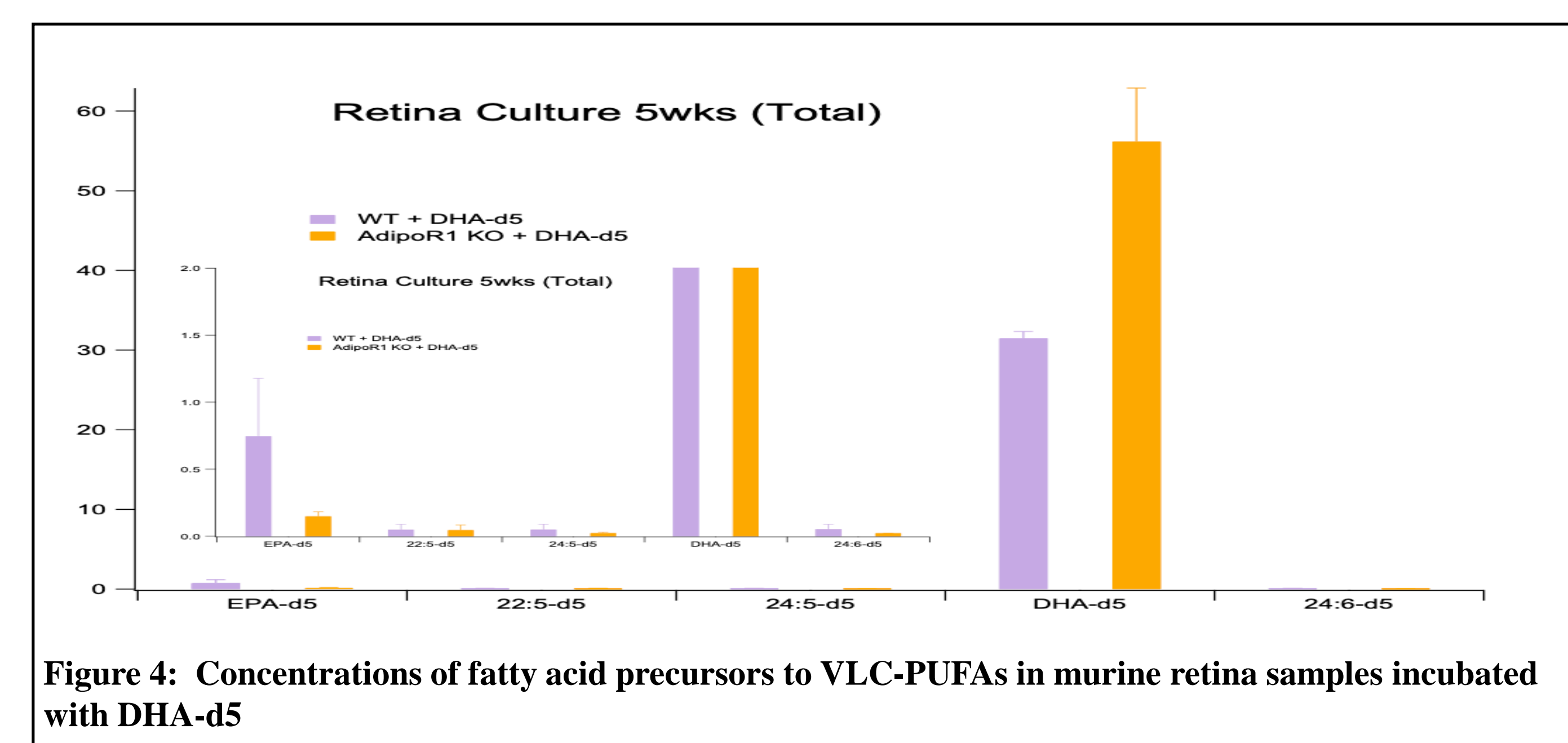


Figure 4: Concentrations of fatty acid precursors to VLC-PUFAs in murine retina samples incubated with DHA-d5

Ret. FA Concentrations – EPA-d5

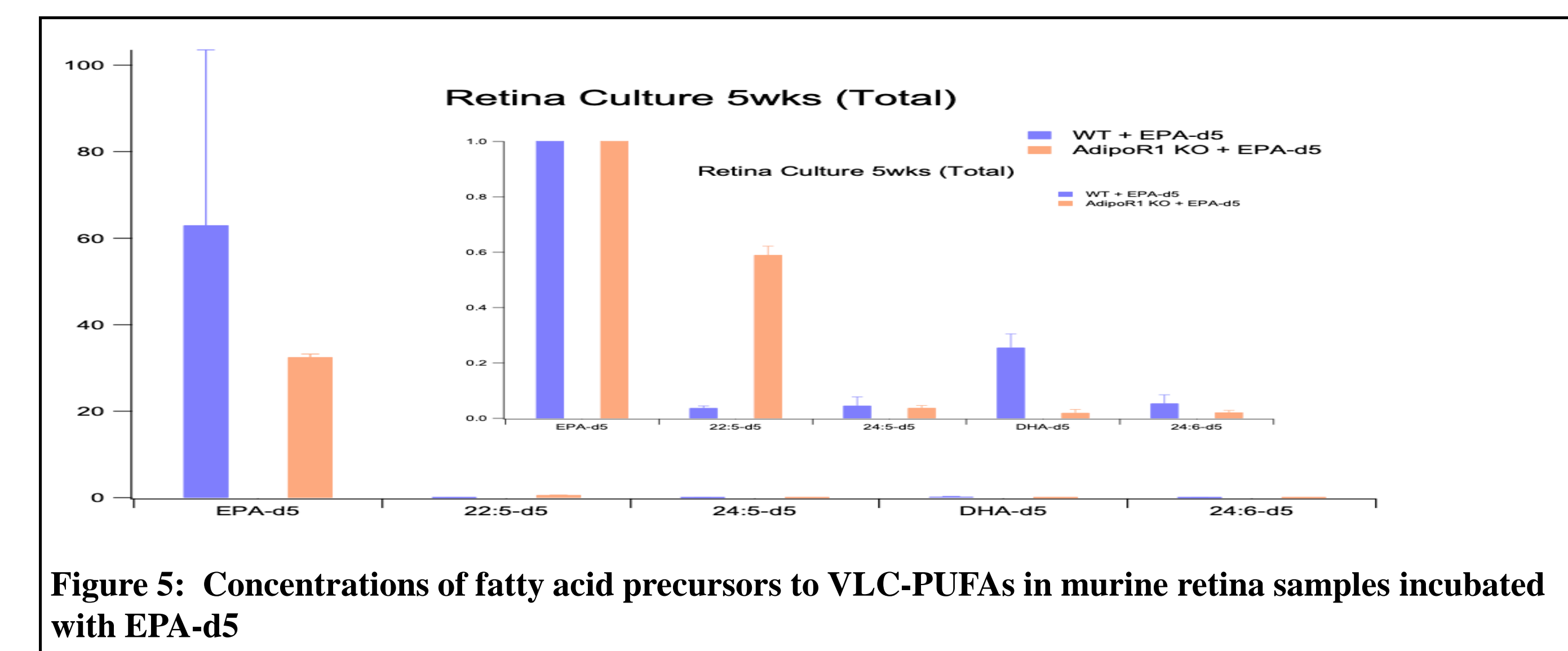


Figure 5: Concentrations of fatty acid precursors to VLC-PUFAs in murine retina samples incubated with EPA-d5

Discussion and Future Endeavors

- Unfortunately, our generated data is unreliable based on unexpected results from our internal standards. This may be due to problems with our lipid extraction protocol or errors in benchtop preparation of retina and RPE tissues. A root cause analysis will be conducted to identify the problems and properly correct them.
- Once more reliable mass spectrometry results are generated, we plan to supplement those finding with MALDI imaging for retina sections of *wild-type* and *AdipoR1* *-/-* mice.
- Western blotting of retina and RPE samples for enzymes participating in the elongation pathways will also be used to determine tissue specificity of these proteins.