# ApoB is the oldest human Apolipoprotein and its fly homolog ApoLpp transits the adult blood brain barrier then accumulates near Myoglianin expressing glia

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The Apolipoprotein (Apo) family is not a traditional protein family where all members share sequence similarity inherited from a common ancestor. Instead, Apo family membership is determined the ability to bind lipids. ApoB is unique member of the family. ApoB has two isoforms ApoB100 and ApoB48 that are known to physicians as components of "bad cholesterol". Recent associations of ApoB with cognitive impairment and Alzheimer's are considered byproducts of cerebrovascular atherosclerosis. On the other hand, a Drosophila Apo family member called ApoLpp also has two isoforms (ApoLppI and ApolppII) with ApoLppII crossing the blood brain barrier in second instar larvae to deliver lipids. Our hypothesis is that ApoLpp's role in the brain is also a role for ApoB, providing a distinct explanation for ApoB association with dementia. First, we demonstrated via interspecific trees of Apo family members that human ApoB is conserved in flies as ApoLpp and in nematodes as Vitellogenin-6. Next, we bridged the life-stage gap between ApoB studies of adult cognitive impairment and ApoLpp studies of larval lipid delivery by analyzing ApoLpp in adult brains. We employed new GFP tagged proteins created in my lab. Imaging data showed that both isoforms of ApoLpp cross the blood brain barrier in adults then coalesce into distinct patterns in the cortex and the medulla. The patterns suggest ApoLpp's lipid delivery role persists in adult brains, perhaps serving glia that express Myoglianin. We are examining this possibility now. Two reports in zebrafish indicate that ApoB is present in their larval and juvenile brains, providing our hypothesis with a foothold in vertebrates. Confirmation of ApoB presence in the brain of adult fish and a role there delivering lipids would validate our hypothesis that ApoB has a role in dementia independent of the circulatory system. This in turn would suggest new mechanisms of human adult brain homeostasis.