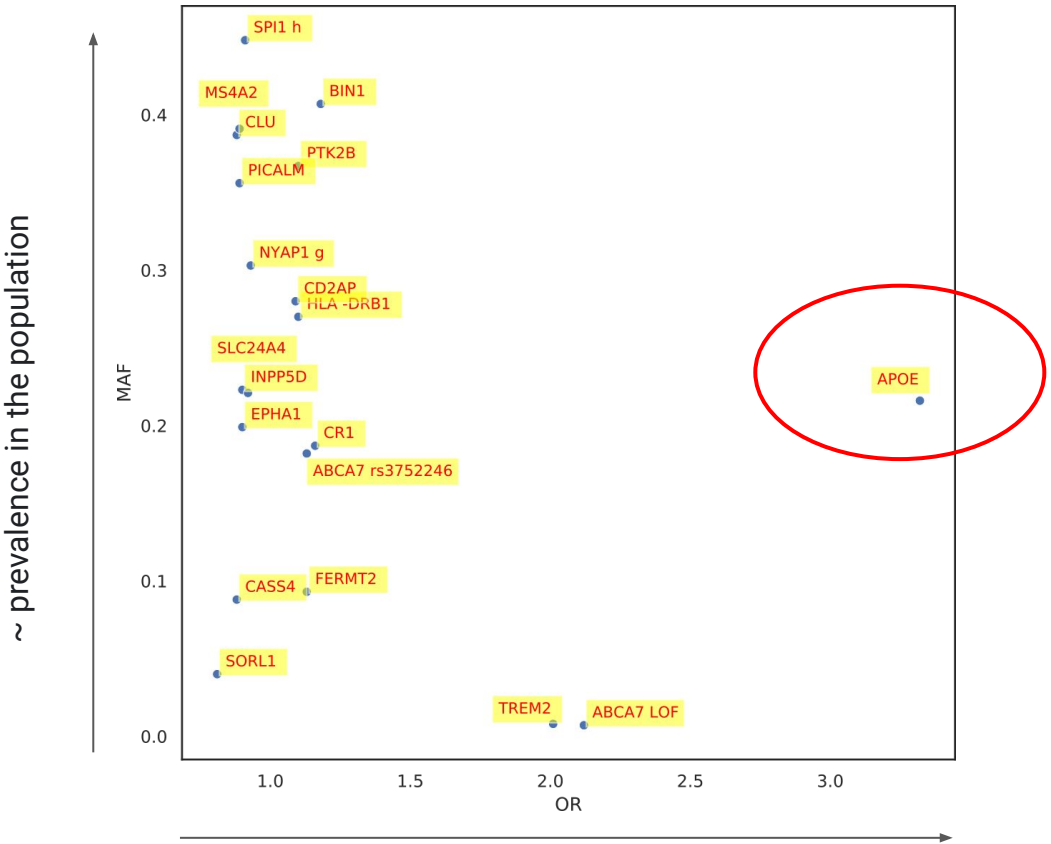
How does APOE4 impair cellular function in the brain?

Joel Blanchard, Leyla Akay, Jose Davila, Djuna von Maydell

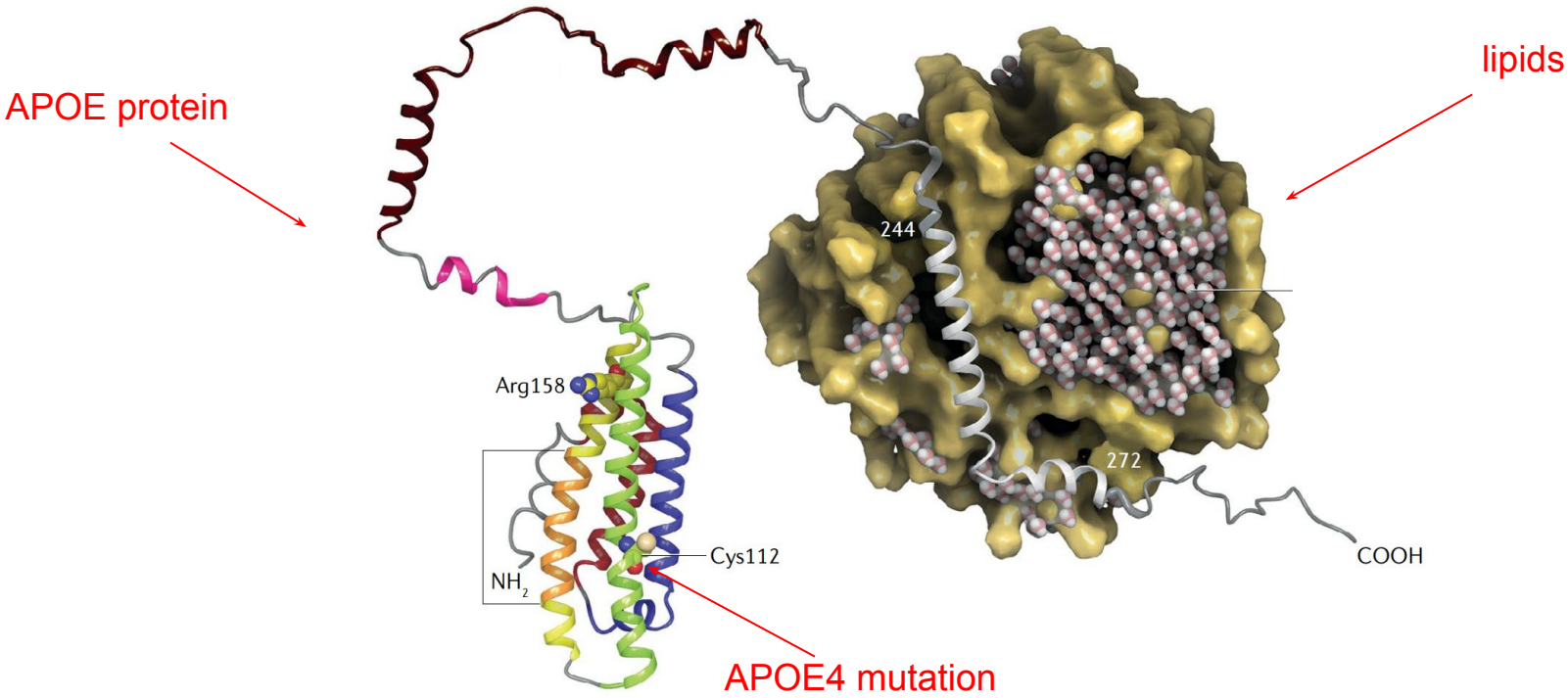
Tsai & Kellis labs

APOE4 is the strongest genetic risk factor for Alzheimer's disease



Adapted from
Kunkle *et al*, 2019, Nature Genetics
Steinberg *et al*, 2015, Nature Genetics

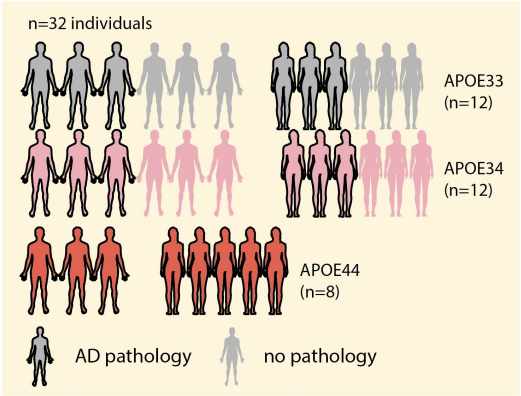
The APOE4 mutation impairs lipid transport by the APOE protein

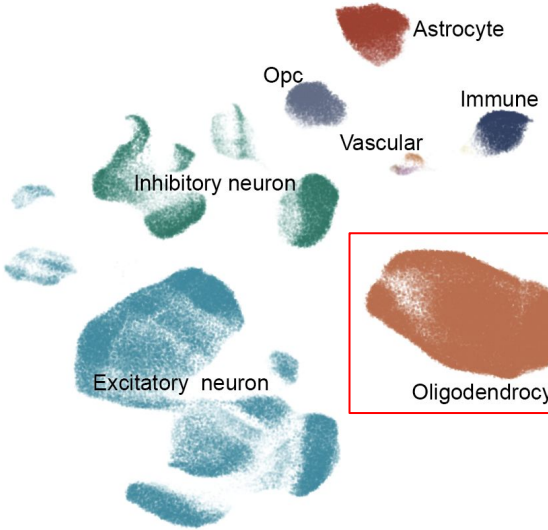


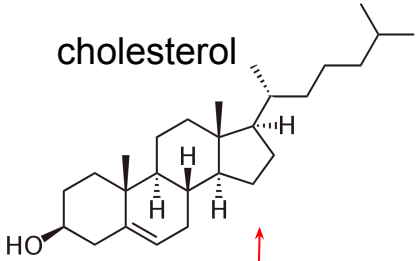
Adapted from Yamazaki *et al*, 2019, Nature Rev Neurology

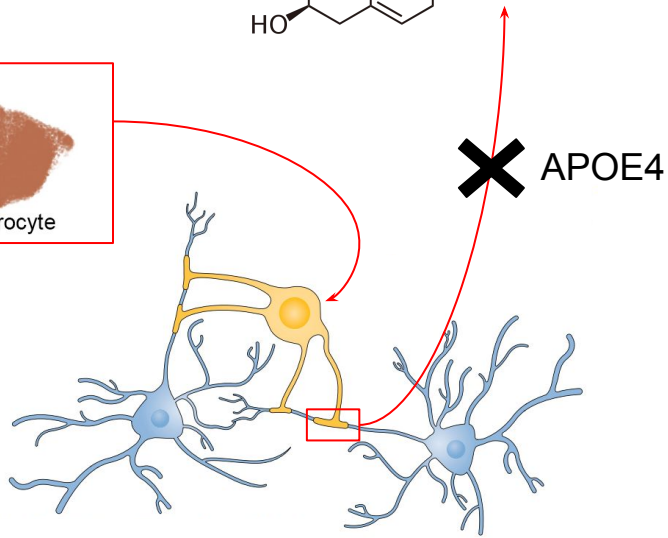
What are the cell-type-specific effects of APOE4 in the human brain?

ROSMAP cohort



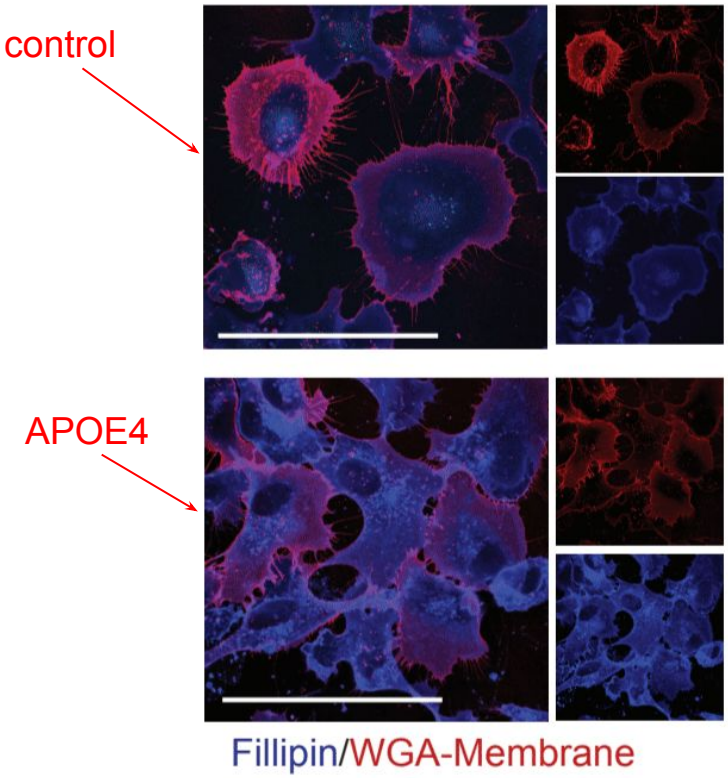


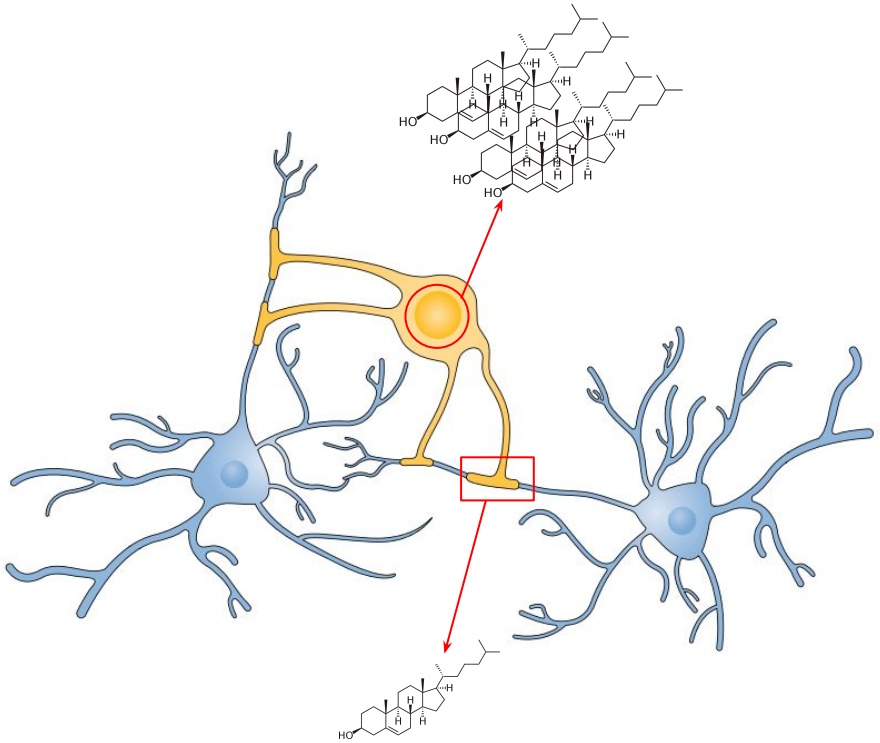




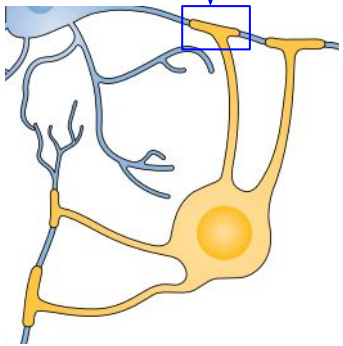
Oligodendrocyte cartoon: Ridler, Nature Rev Neurology, 2019

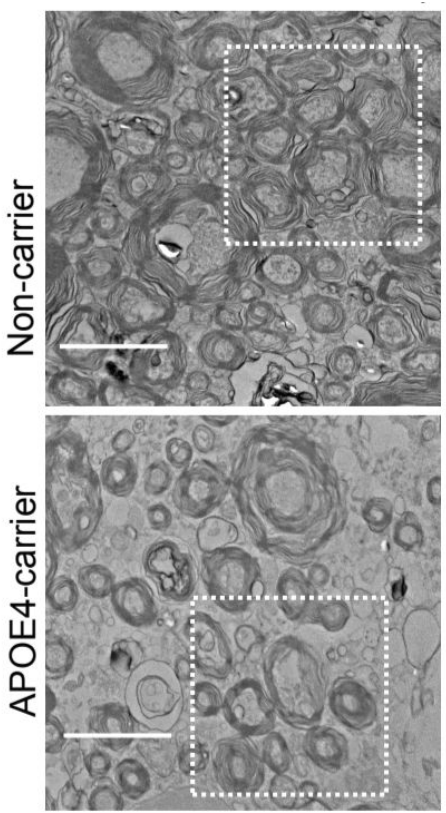
APOE4 impairs cholesterol transport to the cellular membrane

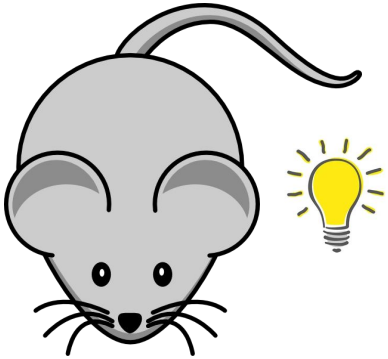




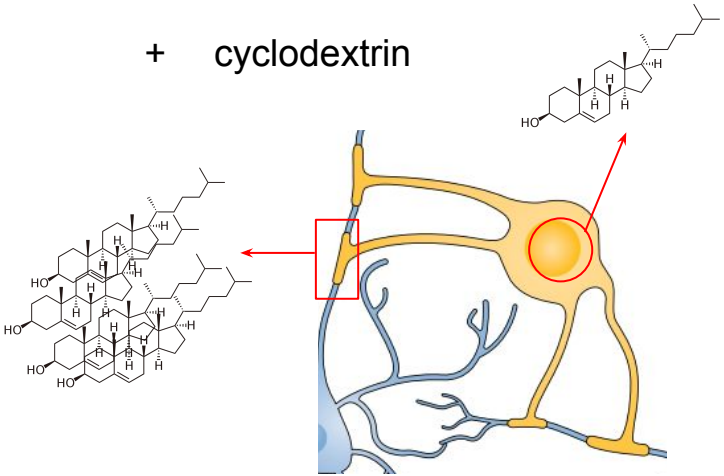
Enhanced cholesterol transport improves myelination and cognition in APOE4 mice







+ cyclodextrin



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