KU ALZHEIMER'S DISEASE CENTER
The University of Kansas Medical Center

APP Metabolism and Mitochondria

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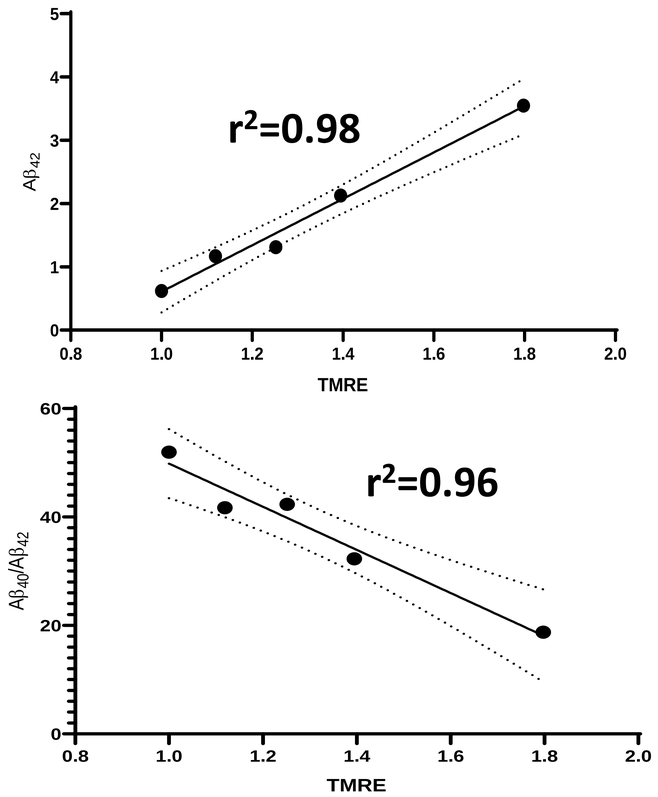
A relationship between mitochondrial function and amyloid beta (Aβ) is well established. The exact mechanism of this relationship and its effects on amyloid precursor protein (APP) processing homeostasis and secretase enzyme function is not understood. Our goal is to elucidate the relationship between bioenergetics, mitochondrial function, and the molecular machinery of APP processing.

Mitochondrial membrane potential is an important factor for secretase activity and APP localization. Mitochondrial membrane potential likely influences pH balance (in a compartmentalized manner) and could alter autophagy, endosome function, lipid raft formation, and alter APP processing homeostasis. Further studies will focus on the affects of mitochondrial membrane potential on APP processing and secretase function in induced pluripotent stem cell derived neurons.

Data Highlights



Lab Directions:

Mitochondrial membrane potential influences Aβ production.

There is a clear relationship between APP localization to mitochondria, mitophagy, and APP metabolism.

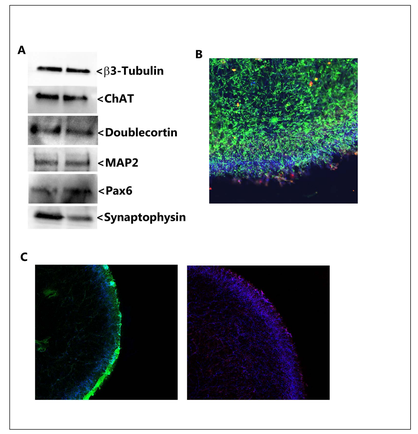
How do AD genetic risk factors interact with brain aging?

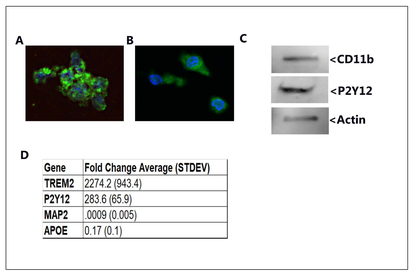
VIEW NOW

New Model Systems

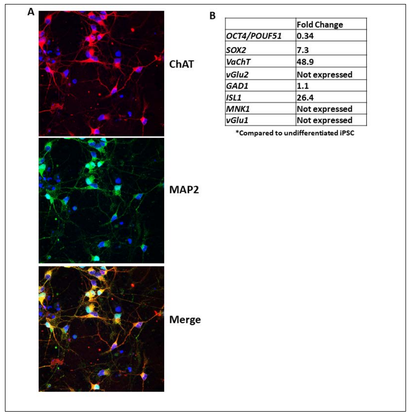
We are developing cerebral organoid models, microglial, and neuronal differentiations of induced pluripotent stem cells from the KU ADC cohort autopsy program. The goal is to use these models to understand the intersection between AD genetic risk factors and aging.

Data Highlights





Gene	Fold Change Average (STDEV)
TREM2	2274.2 (943.4)
P2Y12	283.6 (65.9)
MAP2	.0009 (0.005)
APOE	0.17 (0.1)



	Fold Change
OCT4/POUF51	0.34
SOX2	7.3
VaChT	48.9
vGlu2	Not expressed
GAD1	1.1
ISL1	26.4
MNK1	Not expressed
vGlu1	Not expressed

*Compared to undifferentiated iPSC

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