The Role of iPSC Research at the Shiley Marcos ADRC

Lawrence Goldstein, PhD
ALZHEIMER’S DISEASE (AD)

- **AD IS COMMON, PROGRESSIVE, AND INCURABLE**
  - ONLY A FEW TREATMENTS KNOWN-HAVE MINIMAL EFFECT
- **SYNAPSE LOSS**
- **EVENTUAL MASSIVE NEURONAL DEATH**

**PLAQUES**

**TANGLES**

**THE AMYLOID CASCADE HYPOTHESIS**

FROM [WWW.MEDLIB.MED.UTAH.EDU/WEBPATH/WEBPATH.HTML](http://www.medlib.med.utah.edu/webpath/webpath.html)

FROM [www.northwestern.edu/nuin/faculty/Binder_L/](http://www.northwestern.edu/nuin/faculty/Binder_L/)
AD PHENOTYPES IN FAD AND SAD HIPSC DERIVED NEURONS

**THE AMYLOID CASCADE HYPOTHESIS**

**PLAQUES**

**TANGLES**

ISRAEL ET AL., NATURE 2012

- $A\beta$ PEPTIDE?
- GSK3 KINASE?
- PHOSPHO-TAU?

![Graphs showing secretion of $A\beta_{1-40}$, active GSK3$\beta$, and pTau/Tau ratios for NDC, SAD, and FAD conditions.](image-url)
WHAT IS UPSTREAM OF P-TAU?

VAN DER KANT AND LANGNESS
CELL STEM CELL 2019
ARE ALL PATIENT LINES AFFECTED?
Does p-tau depend on Abeta?

VAN DER KANT
AND
LANGNESS
CELL STEM CELL
2019
WHAT ARE LIKELY MECHANISTIC CONCLUSIONS?
APPROVED DRUGS THAT ALTER CHOLESTERYL-ESTER SUPPRESS NFT PHENOTYPE
THANK YOU!!

CHOLESTEROL AND P-TAU
CHERYL HERRERA
DAN WILLIAMS
STEVE WAGNER
ANNE BANG
VANESSA LANGNESS
RIK VAN DER KANT

HUMAN MODELS OF AD
MASON ISRAEL-UCSD
SHAUNA YUAN-UCSD
GRACE WOODRUFF-UCSD
SOL REYNA-UCSD
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