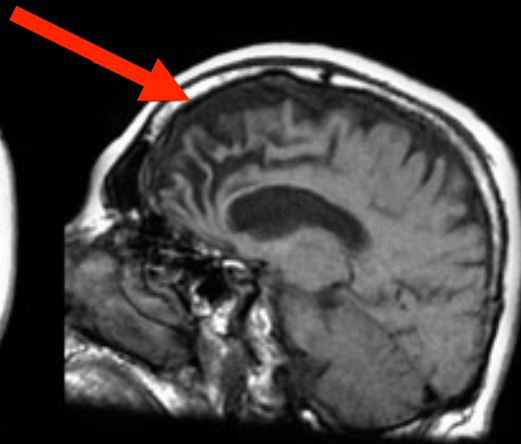


Normal



Frontotemporal dementia

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Tau gene and Frontotemporal Dementia (FTD)

Kassandra Ford

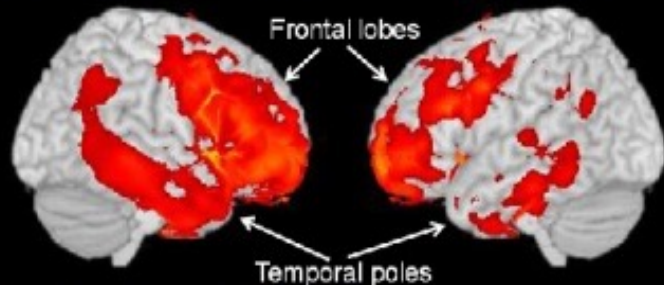
What is FT Dementia?

Early onset

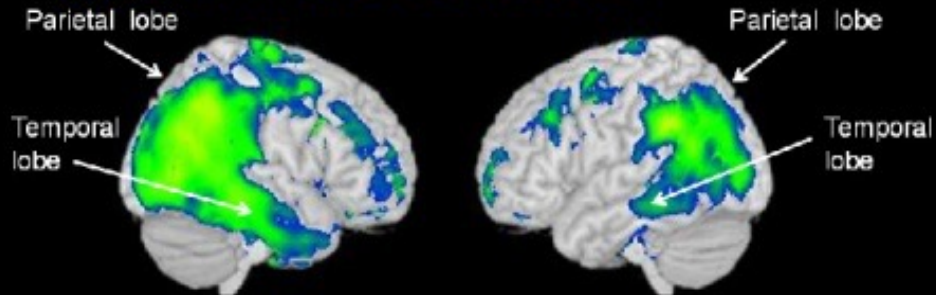
Two types

Poor prognosis

Frontotemporal Dementia



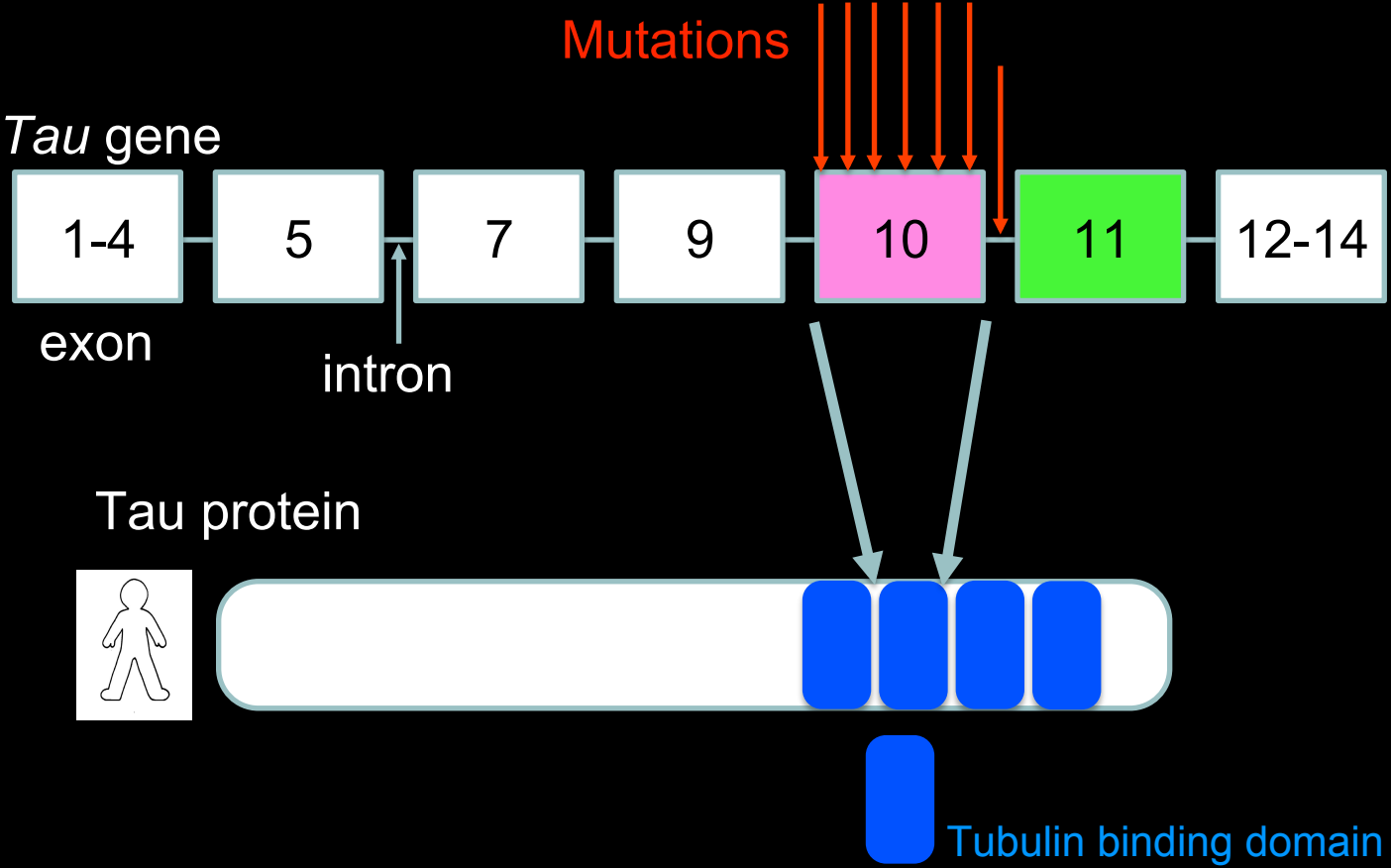
Alzheimer's Disease



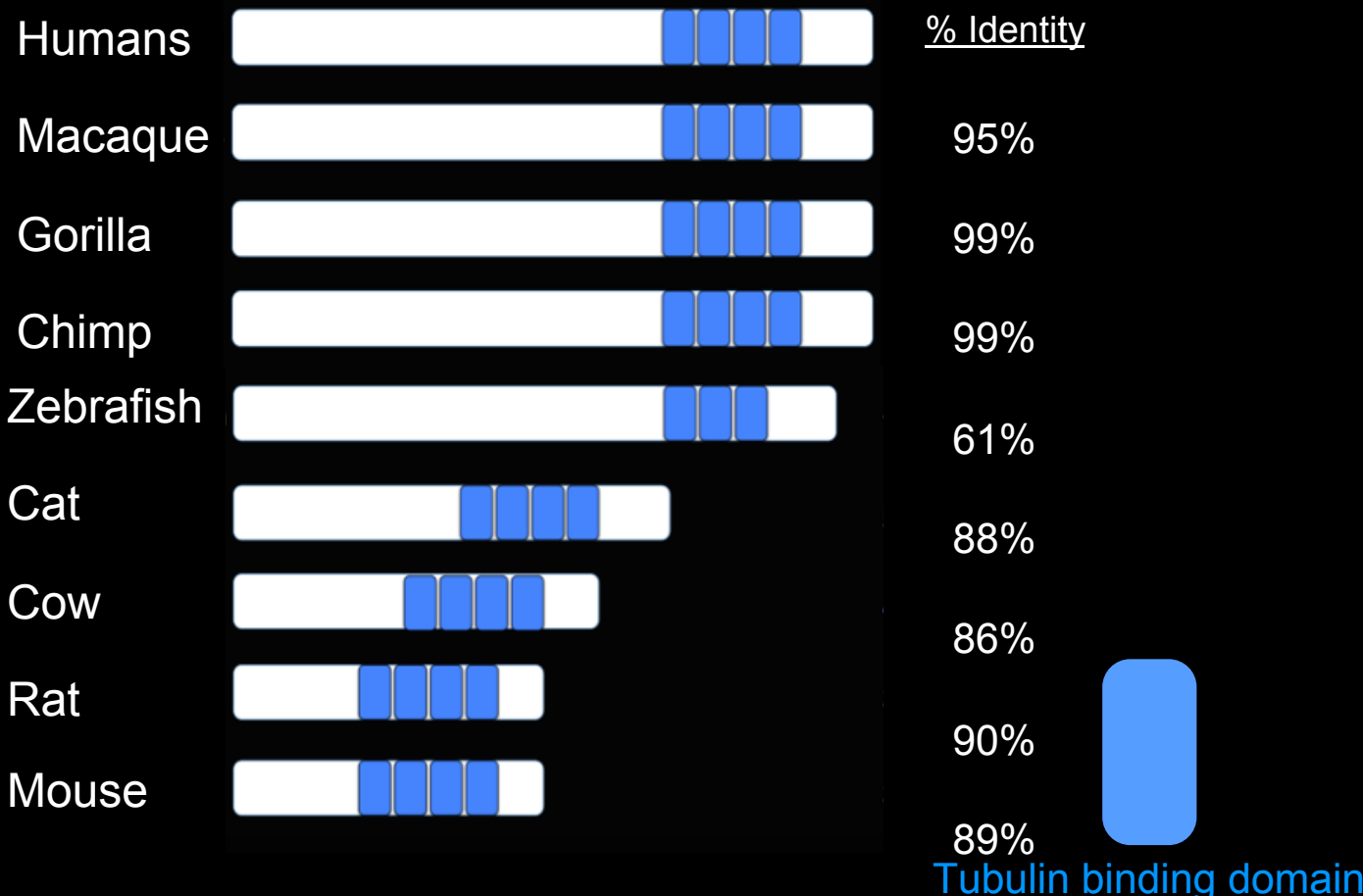
FT Dementia phenotype

<https://youtu.be/RcWPCgm22Nk>

Tau is associated with FT Dementia



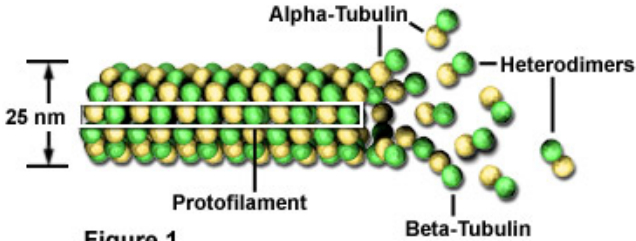
How conserved is the Tau protein?



Cellular Components

Microtubule formation

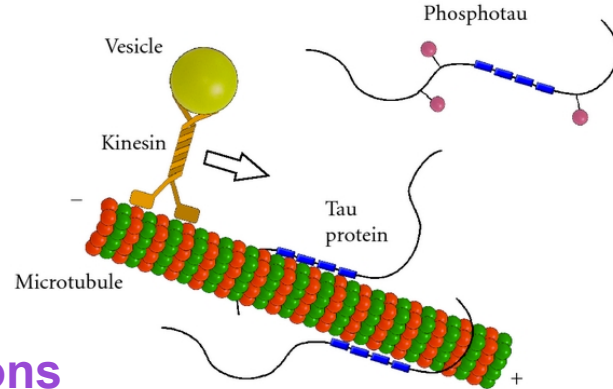
Microtubule Helical Structure



Biological processes

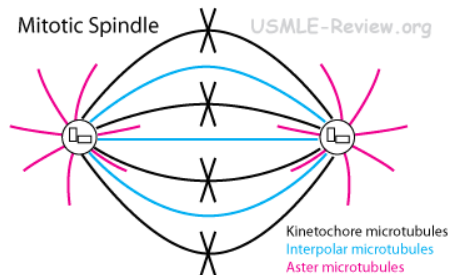
Microtubule Polymerization

Microtubule-based Movement

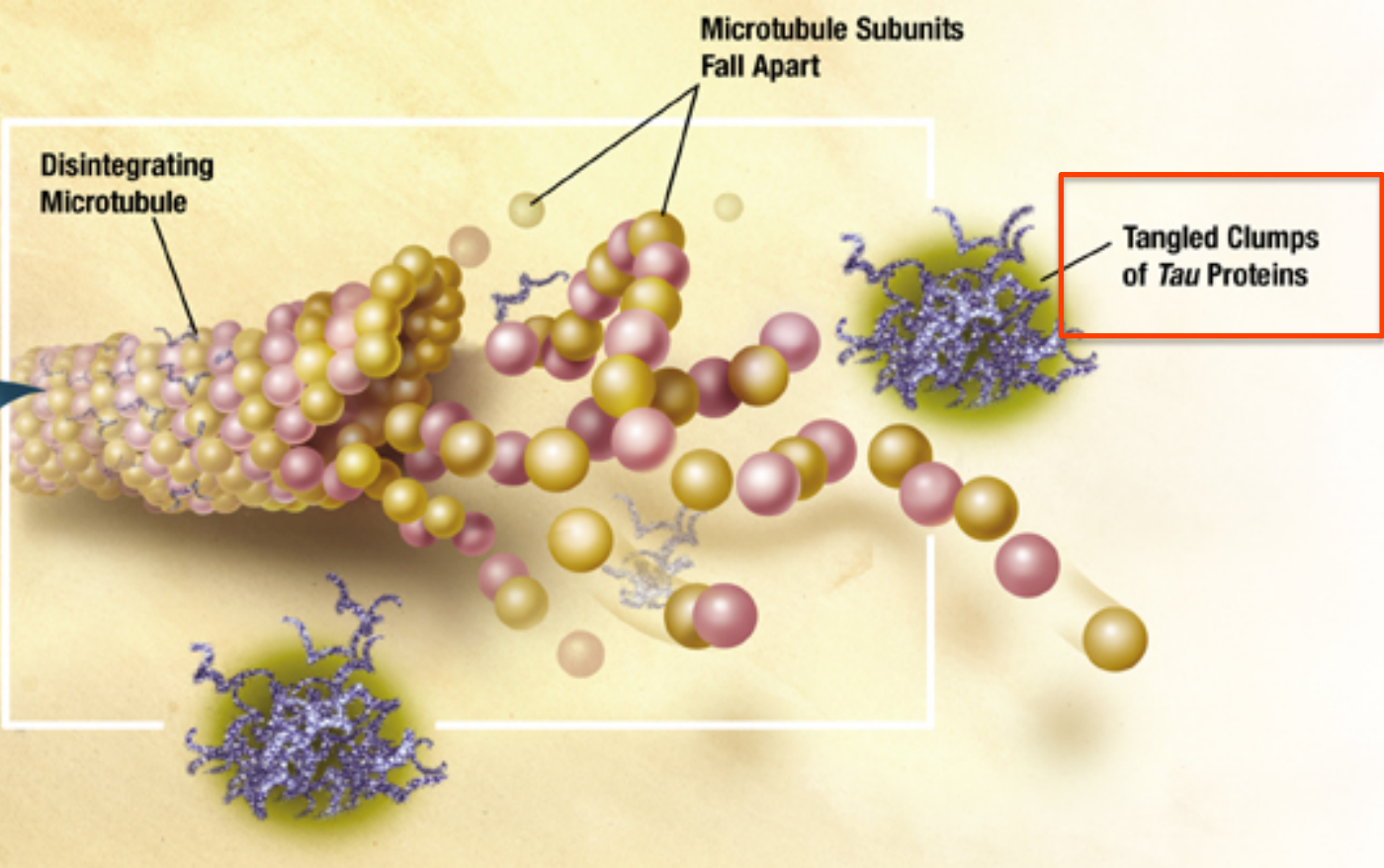


Molecular functions

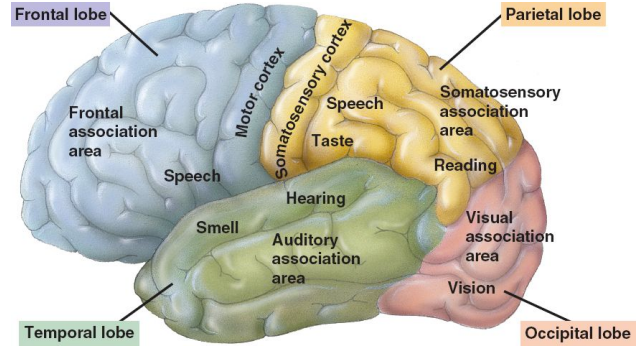
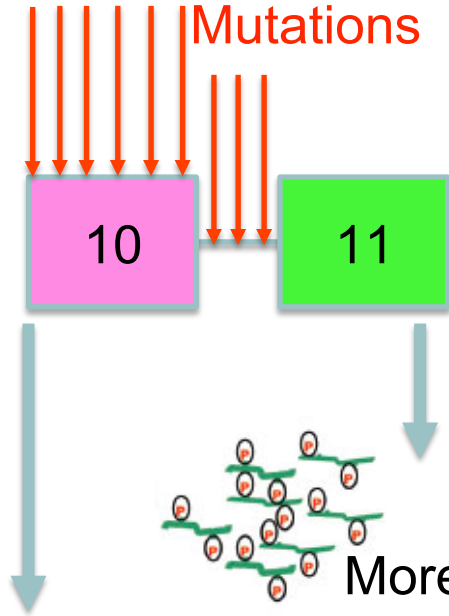
Microtubule binding



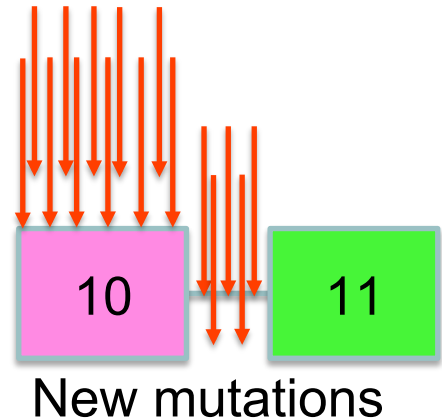
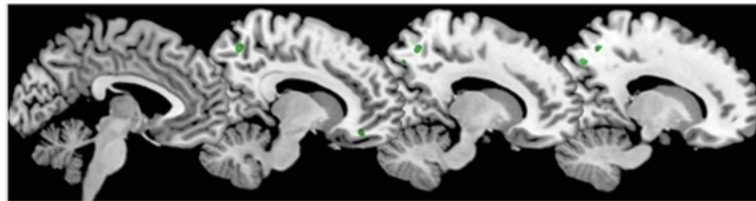
What happens in FT Dementia?



Phenotypic changes in the FT Dementia brain



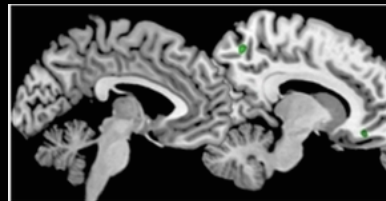
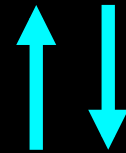
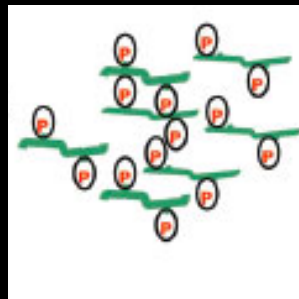
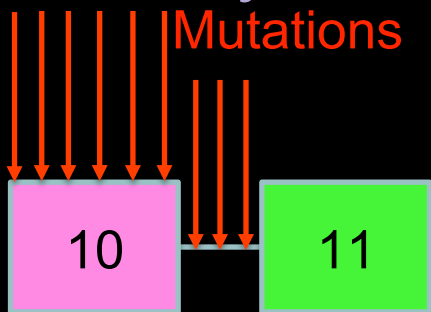
Brain areas affected



Connect exon/intron 10 mutations to phenotypic changes

Primary:

Mutations



Long term:

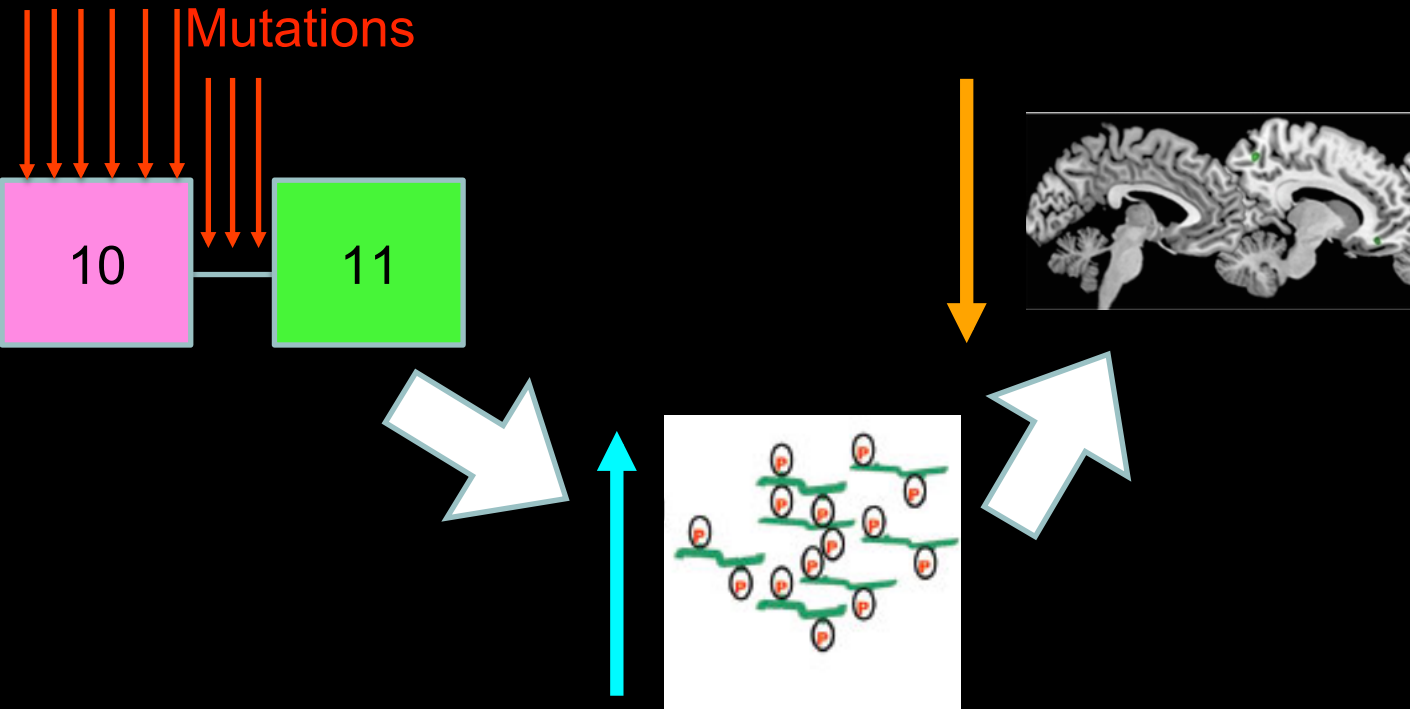
Differences from Alzheimer's

Treatment

Cure!

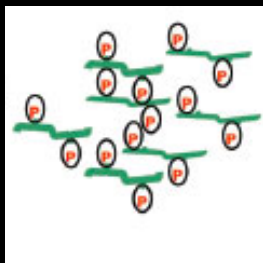
Hypothesis:

Tau mutations in exon 10 and intron 10 lead to increased Tau protein and decreased GM density

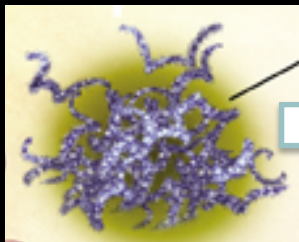


Rationale:

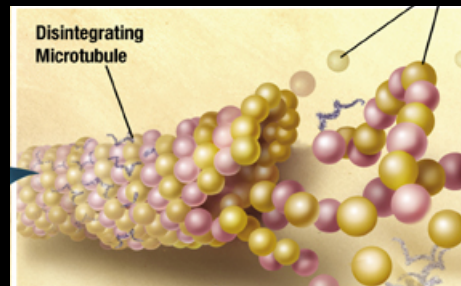
Increase
Tau protein



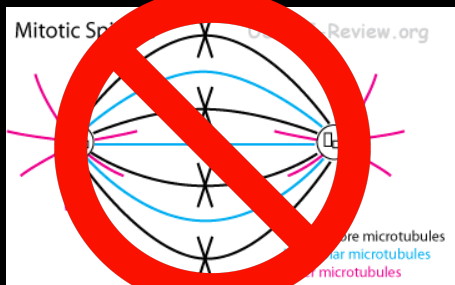
Tau protein
aggregates



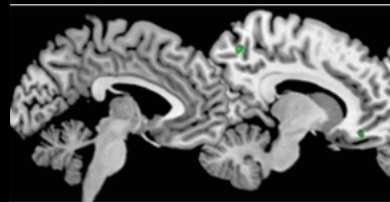
Microtubule
destabilization



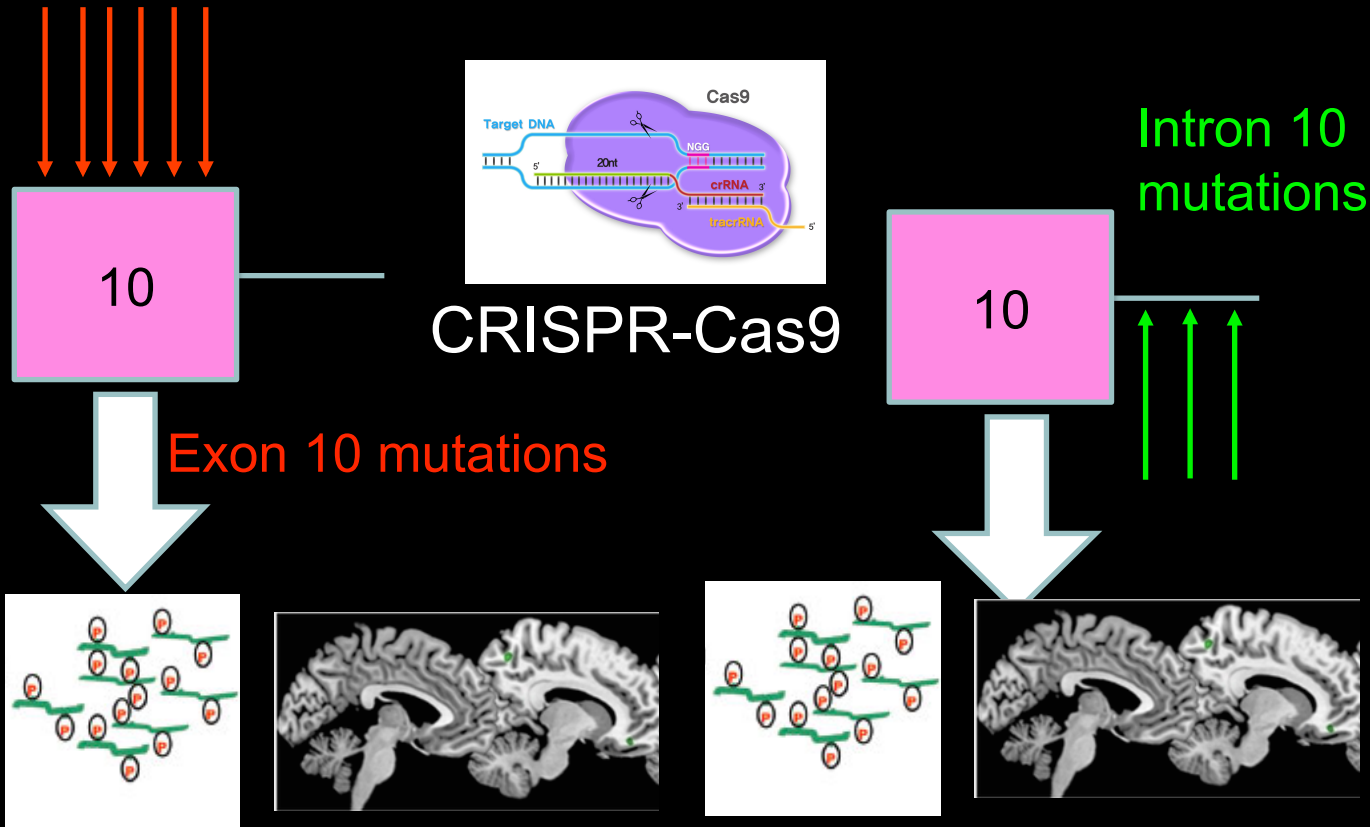
Decreased cell
differentiation



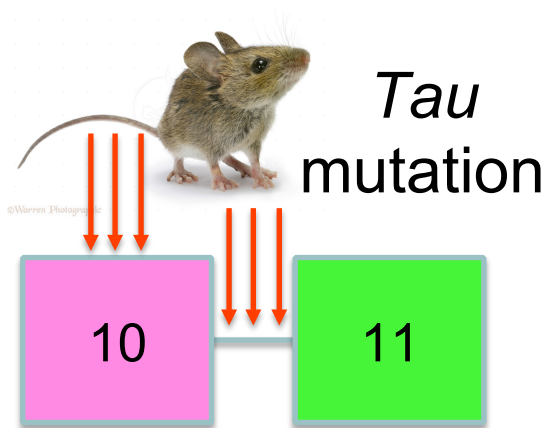
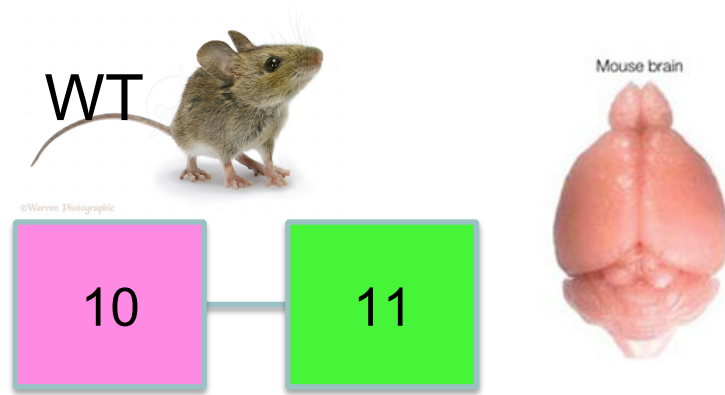
Cell death and
brain deterioration



Aim 1: Determine Tau protein expression and GM density with the exon/intron 10 mutations

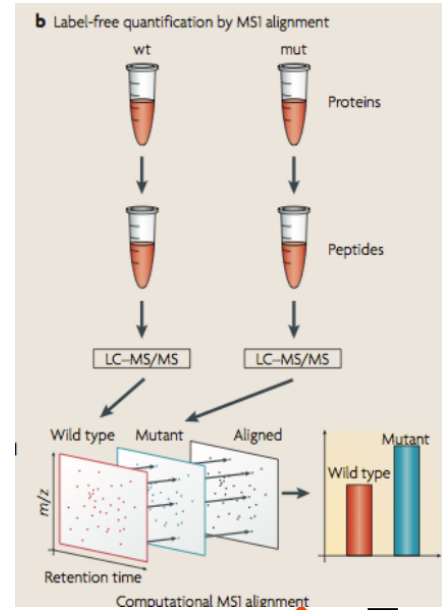


Aim 1: Determine Tau protein expression and GM density with the exon/intron 10 mutations



Tau mutations

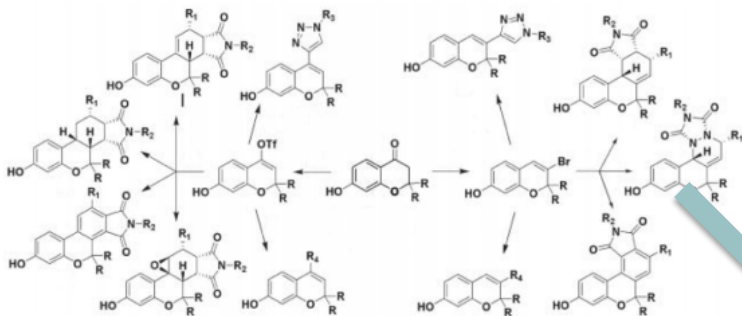
WT



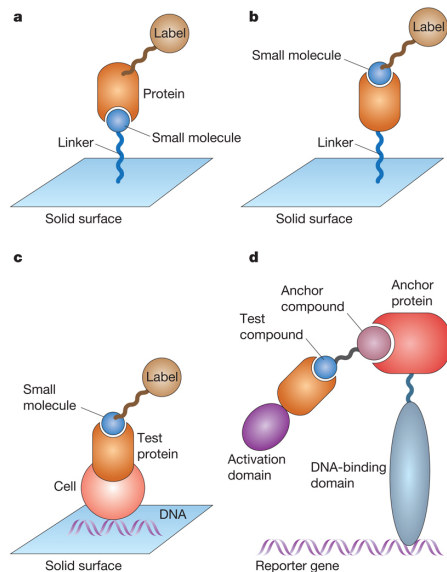
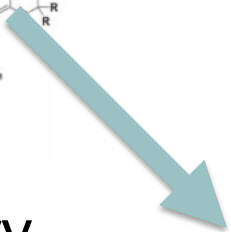
↓ Tau protein

↑ Tau protein

Aim 2: Determine chemical genetic compounds that will alter Tau protein levels

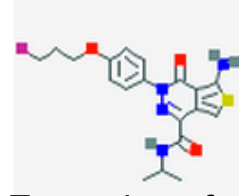
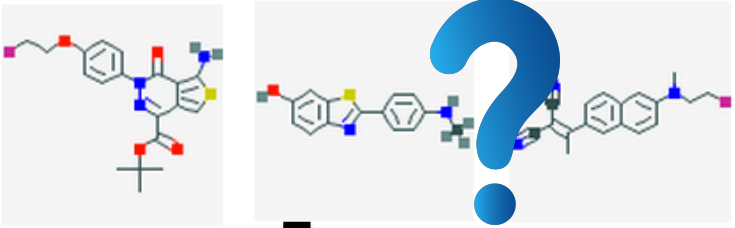


Diversity-oriented library

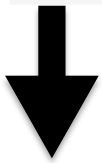


Protein binding assay

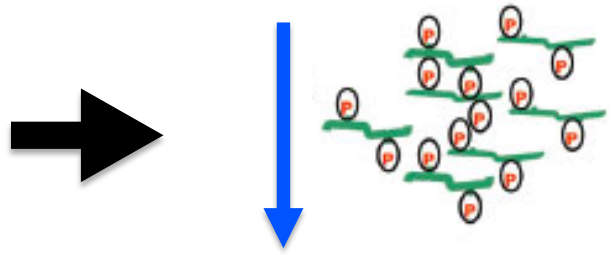
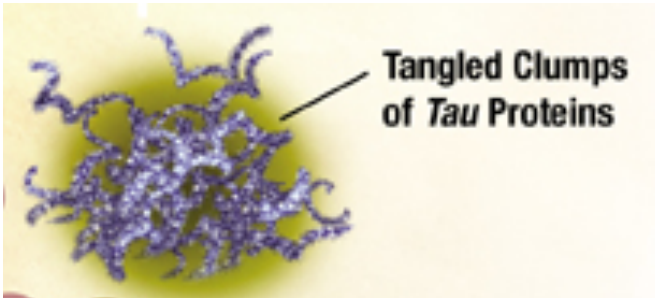
Aim 2: Determine chemical compounds that will decrease Tau protein levels



Examples of chemicals associated with Alzheimer's



Target Tau protein tangles

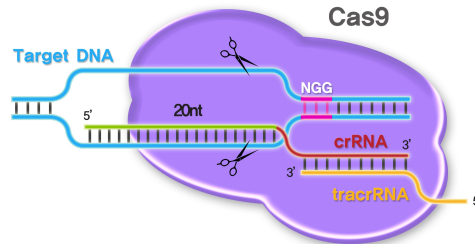


Decrease Tau protein

Aim 3: Evaluate changes in learning based on induced mutation in *Tau*

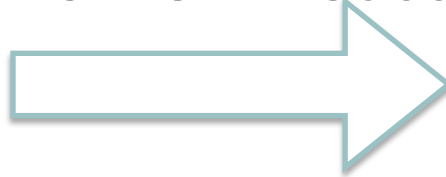


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CRISPR-Cas9



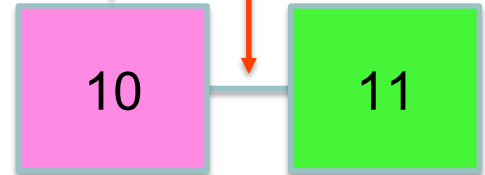
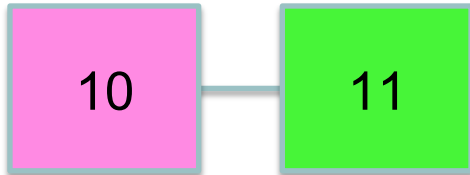
Mutations

10

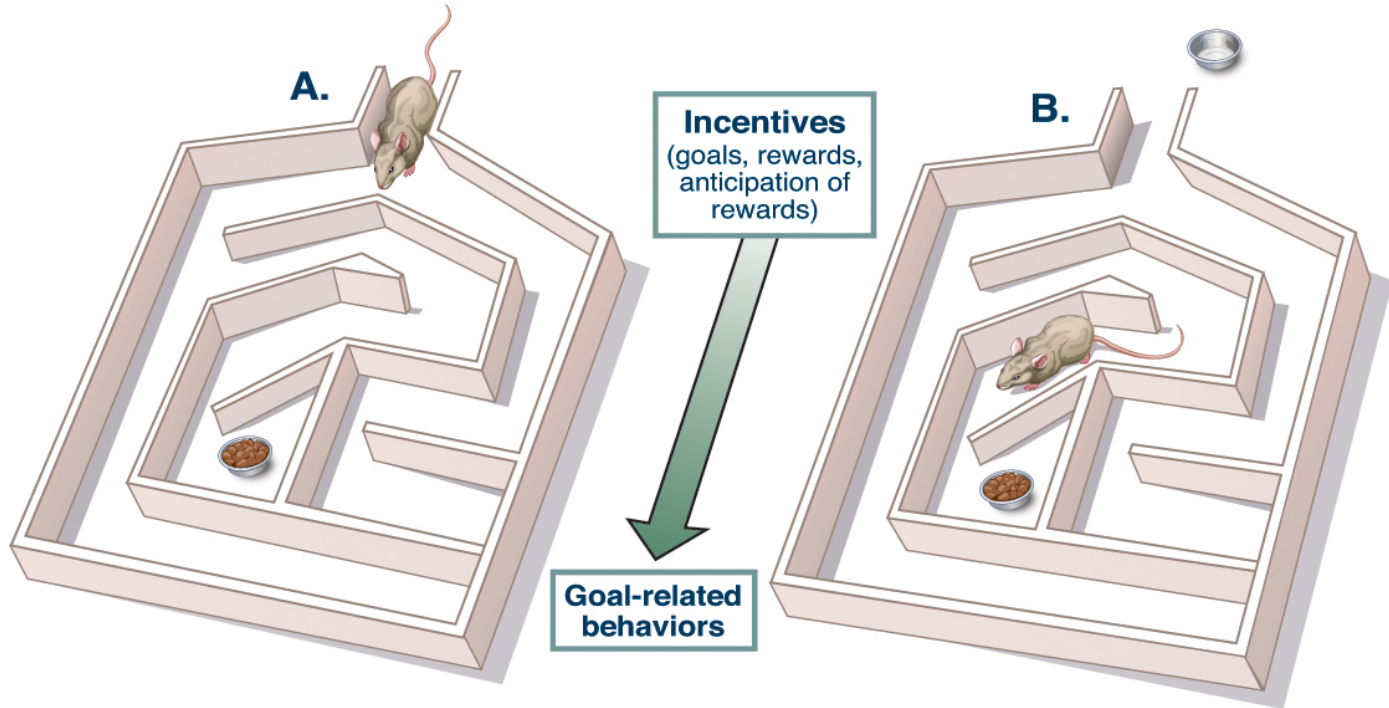
11

10

11

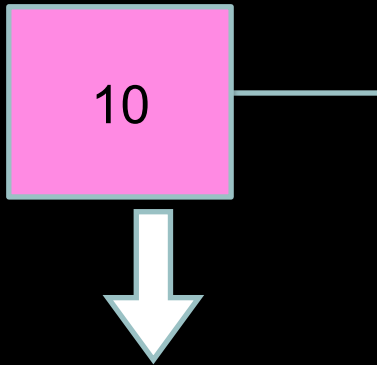


Aim 3: Evaluate learning with the Hebb-Williams maze

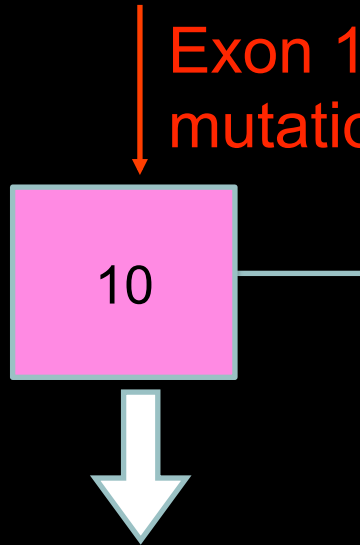


Aim 3: Prediction of changes in learning based on induced mutation in *Tau*

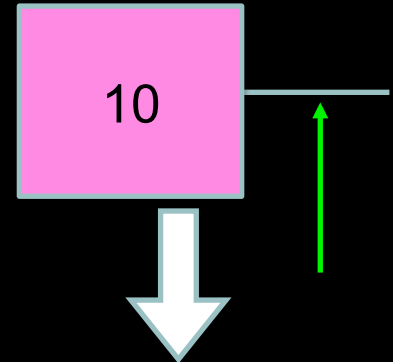
WT



Exon 10
mutation



Intron 10
mutation

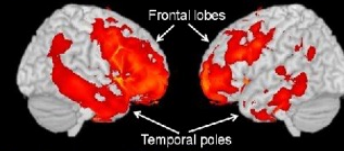


Future research

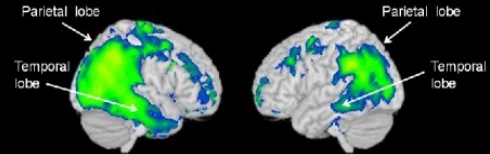


New neuro-imaging techniques

Frontotemporal Dementia



Alzheimer's Disease



FTD vs. Alzheimer's



New pharmaceuticals

Questions?

References

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