

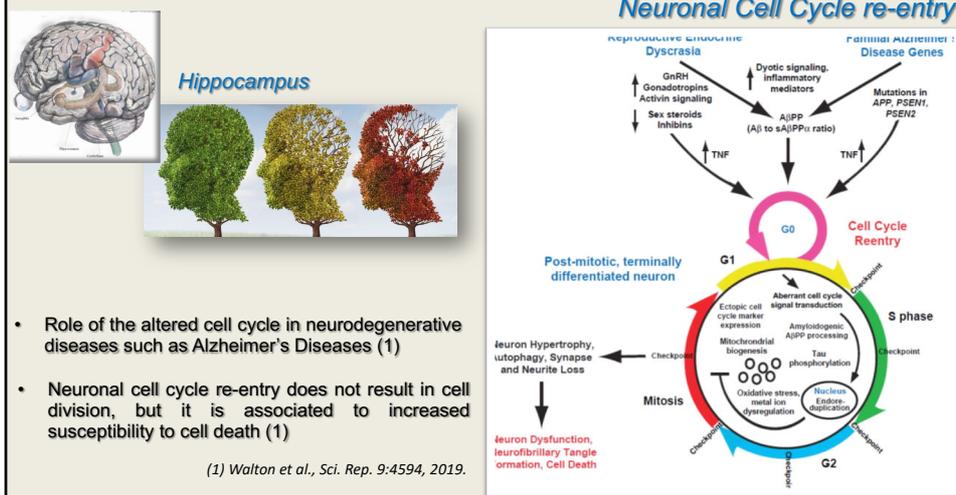
## The nuclear tau as an early molecular marker of Alzheimer's disease

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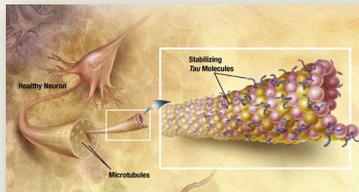
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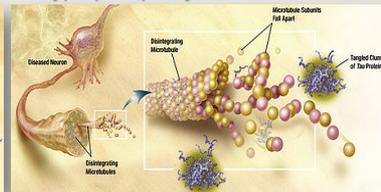


## The nuclear tau as an early molecular marker of Alzheimer's disease

Normal tau

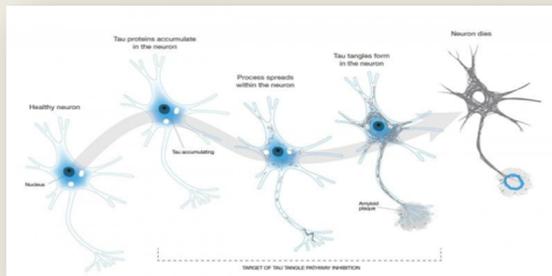


Hyperphosphorylated tau

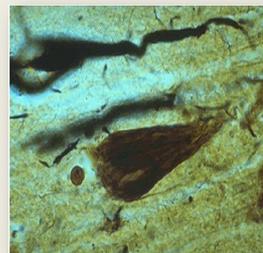


Destabilization of microtubules

Neuronal death



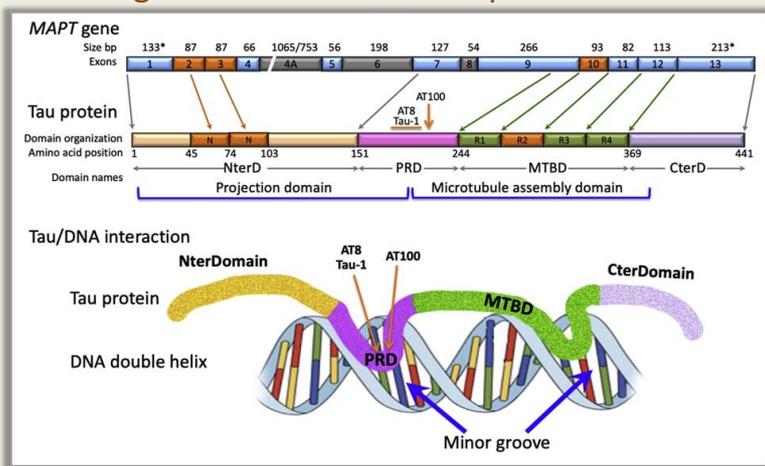
TAU aggregation



Neurofibrillary Tangles (NFT)

## The nuclear tau as an early molecular marker of Alzheimer's disease

### MAPT gene structure and tau protein domains

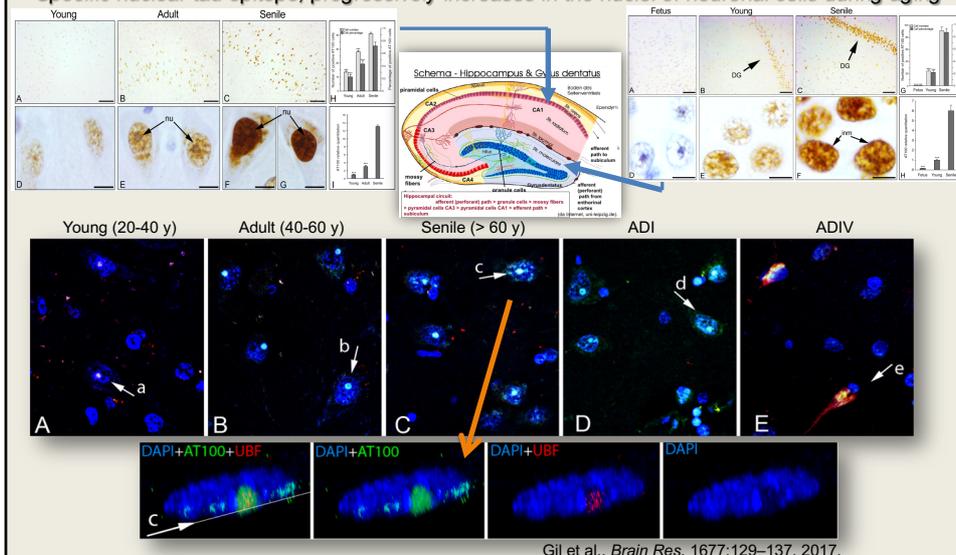


Federico et al., In: Factors affecting neurological aging: Genetics, neurology, behavior, and diet. Elsevier Inc., 2019.

## The nuclear tau as an early molecular marker of Alzheimer's disease

### AT100 epitope

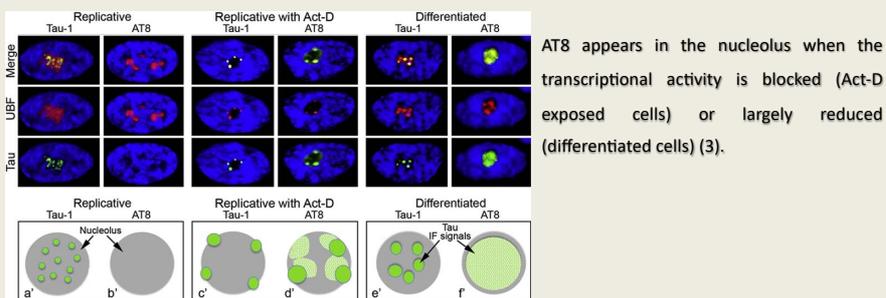
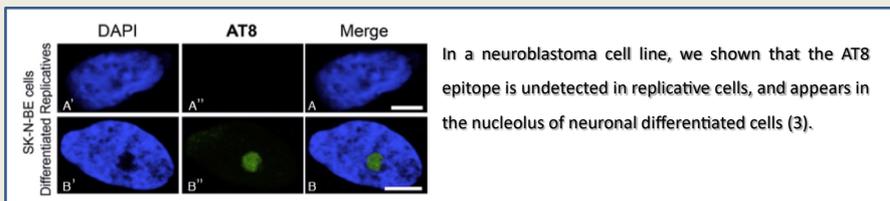
Specific nuclear tau epitope, progressively increases in the nuclei of neuronal cells during aging



## The nuclear tau as an early molecular marker of Alzheimer's disease

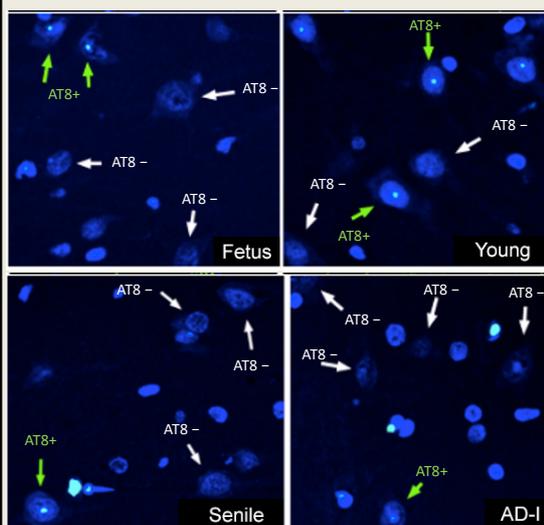
### AT8 epitope

Specific nuclear phosphorylated tau epitope, that appears to be related with neuronal differentiation



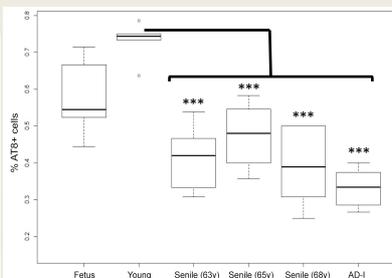
## The nuclear tau as an early molecular marker of Alzheimer's disease

### Phosphorylated AT8 epitope in the human neurons from the CA1 region



The percentage of neurons with nucleolar AT8:

- increases from foetal to young brain
- decreases from young to senile brain
- is low at the start of AD (AD-I)



### *The nuclear tau as an early molecular marker of Alzheimer's disease*

- The results showed that the AT8 epitope disappears in senile neurons respect to cells from younger subjects, indicating a possible role of AT8 in the ectopic activation of the cell cycle in differentiated cells.
- These data improve the knowledge on the role of nuclear tau in the neuronal differentiation and cell degeneration in AD, involving the presence/absence of AT8 in the nucleolus of neurons related to a re-entering in the cell cycle.
- The molecular mechanisms related to the start of AD are not yet clear, so their understanding is very relevant if we consider the social impact of this disease in the human populations.