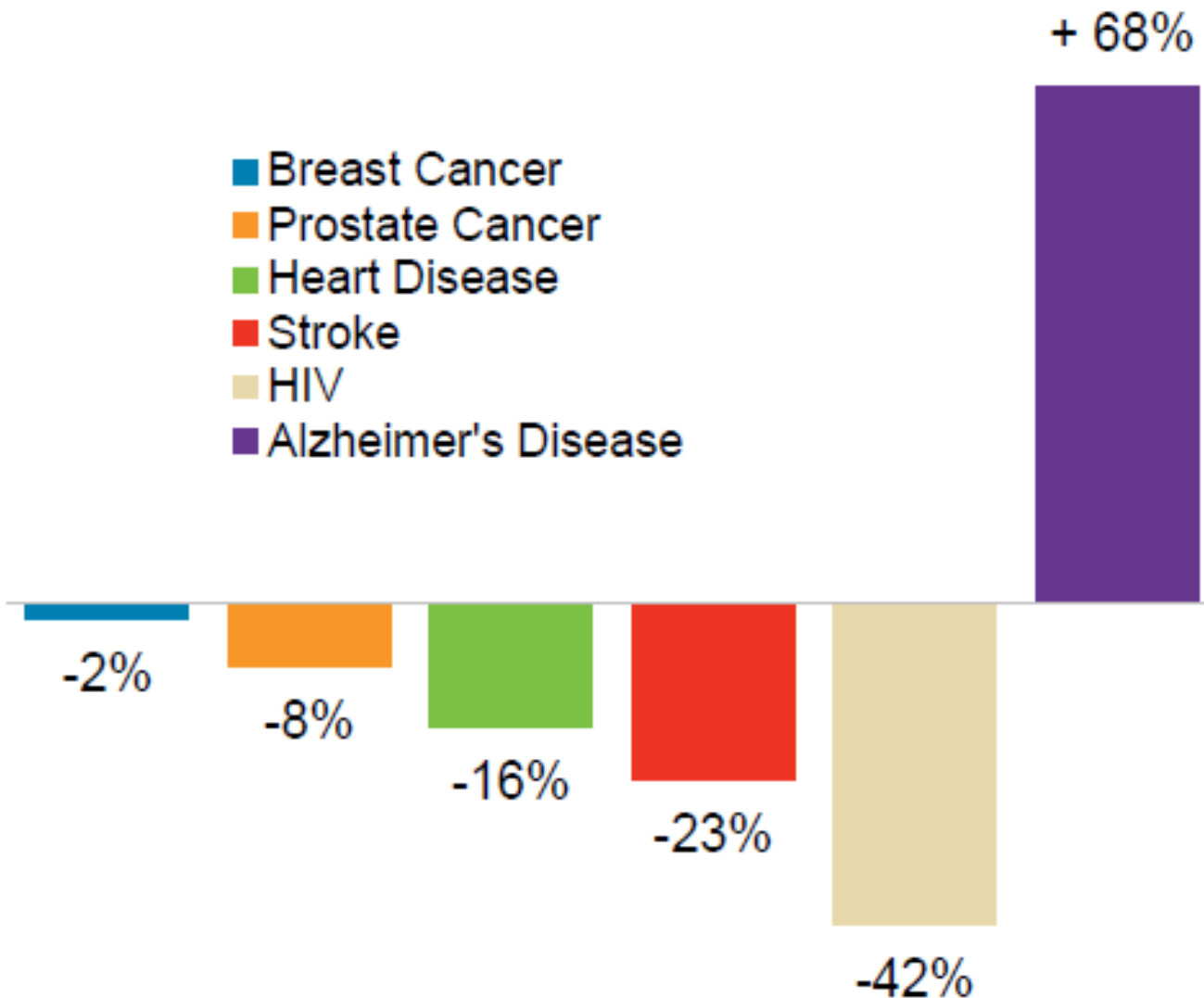




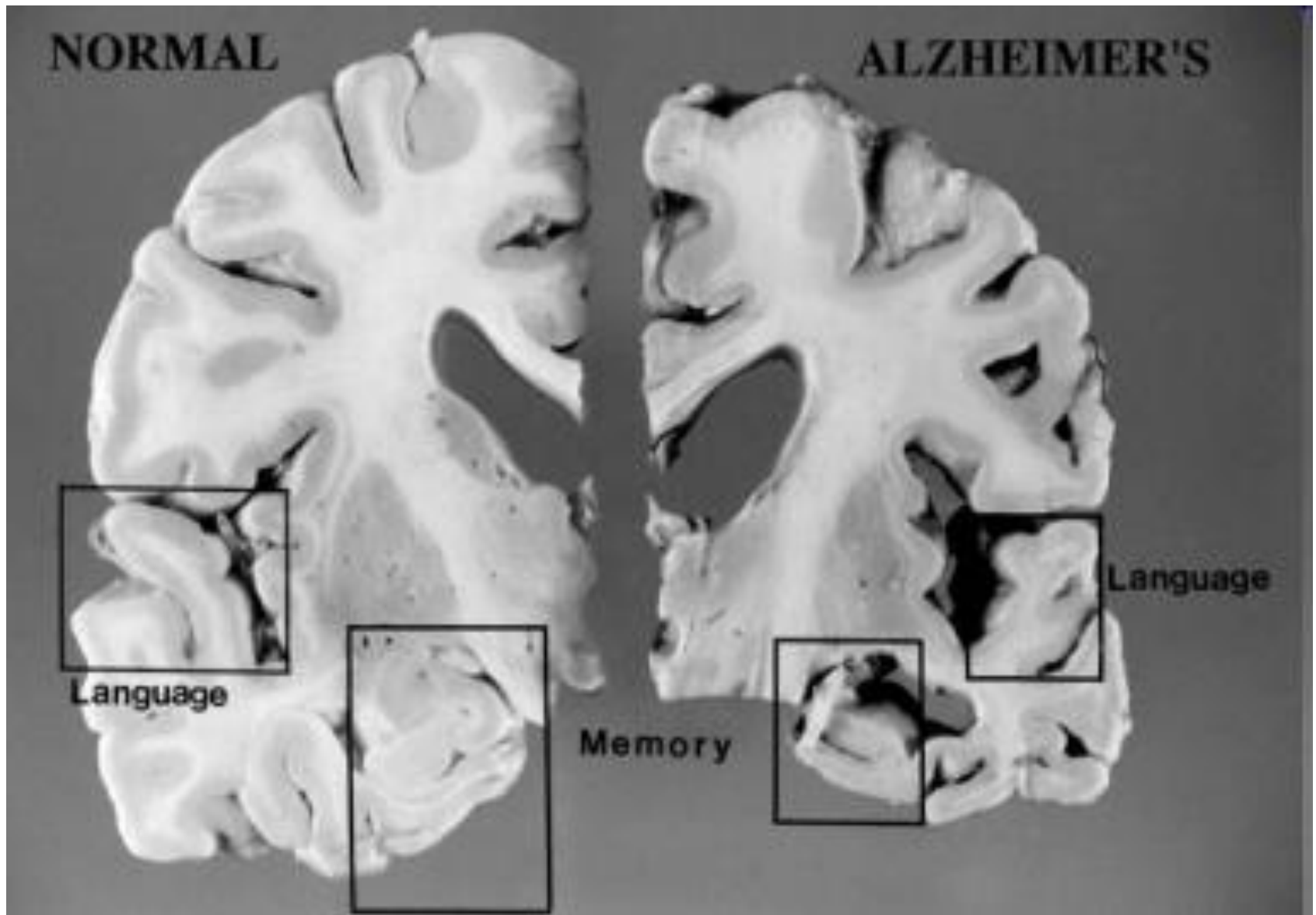
# Alzheimer's Disease

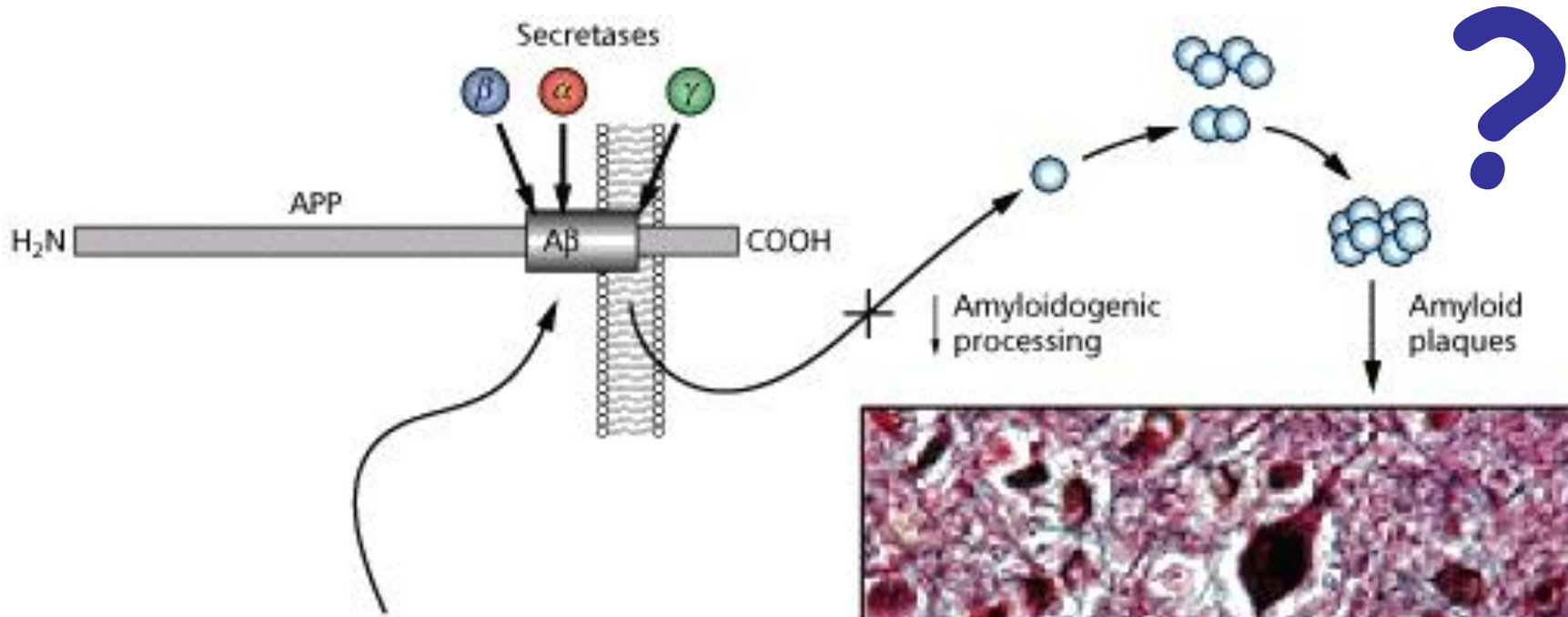
- 1 in 9 people in the US aged 65 and older
- 1 in 3 people aged 85 and older
- 2/3 are women
- Annual cost of more than 200 billion dollars
  - By 2050 estimated to cost 1.2 trillion dollars annual
- Currently the 6<sup>th</sup> leading cause of death in the US.
- Familial (genetic) Alzheimer's disease (FAD) only accounts for ~15% of cases. The remaining are sporadic.
  - APP and PSEN1/2 primary mutations for early onset AD (EAOD)
  - APOe4 high risk for sporadic AD (>20x increase risk) (LOAD)
- Amyloid peptide thought to be the primary causative species
  - Many types of amyloid peptide
  - Many downstream effects such as Tau phosphorylation

## Change in Number of Deaths Between 2000 and 2010

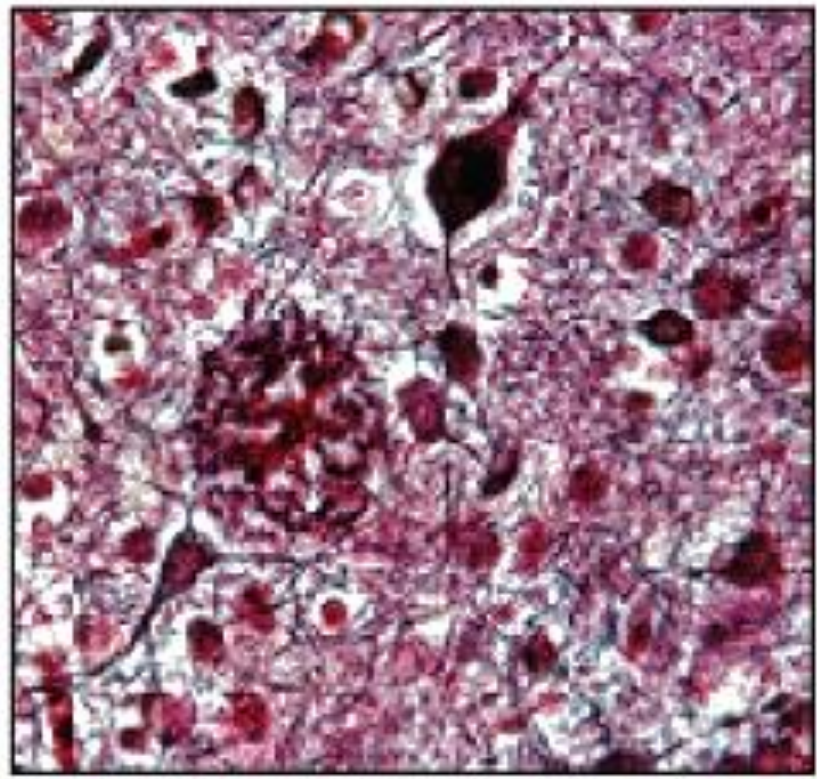


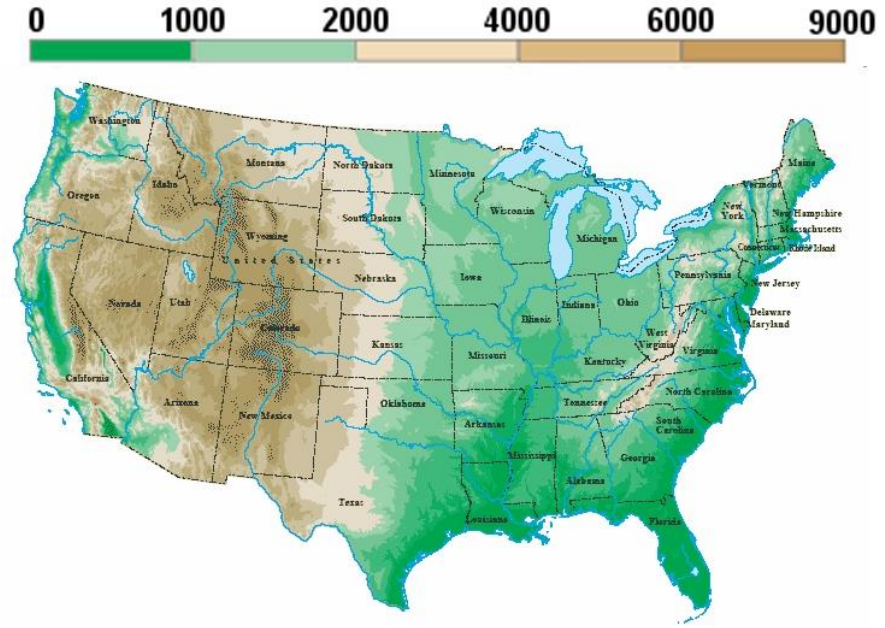
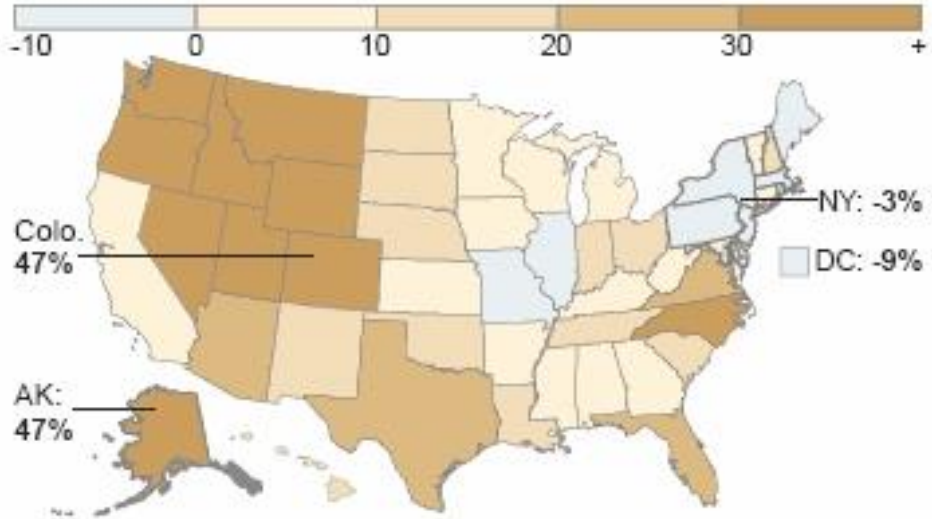
# Disease





- APP enhanced processing
- PSEN1/2 enhanced processing
- APOE cholesterol?!
- Hypoxia ROS
- TAUphos

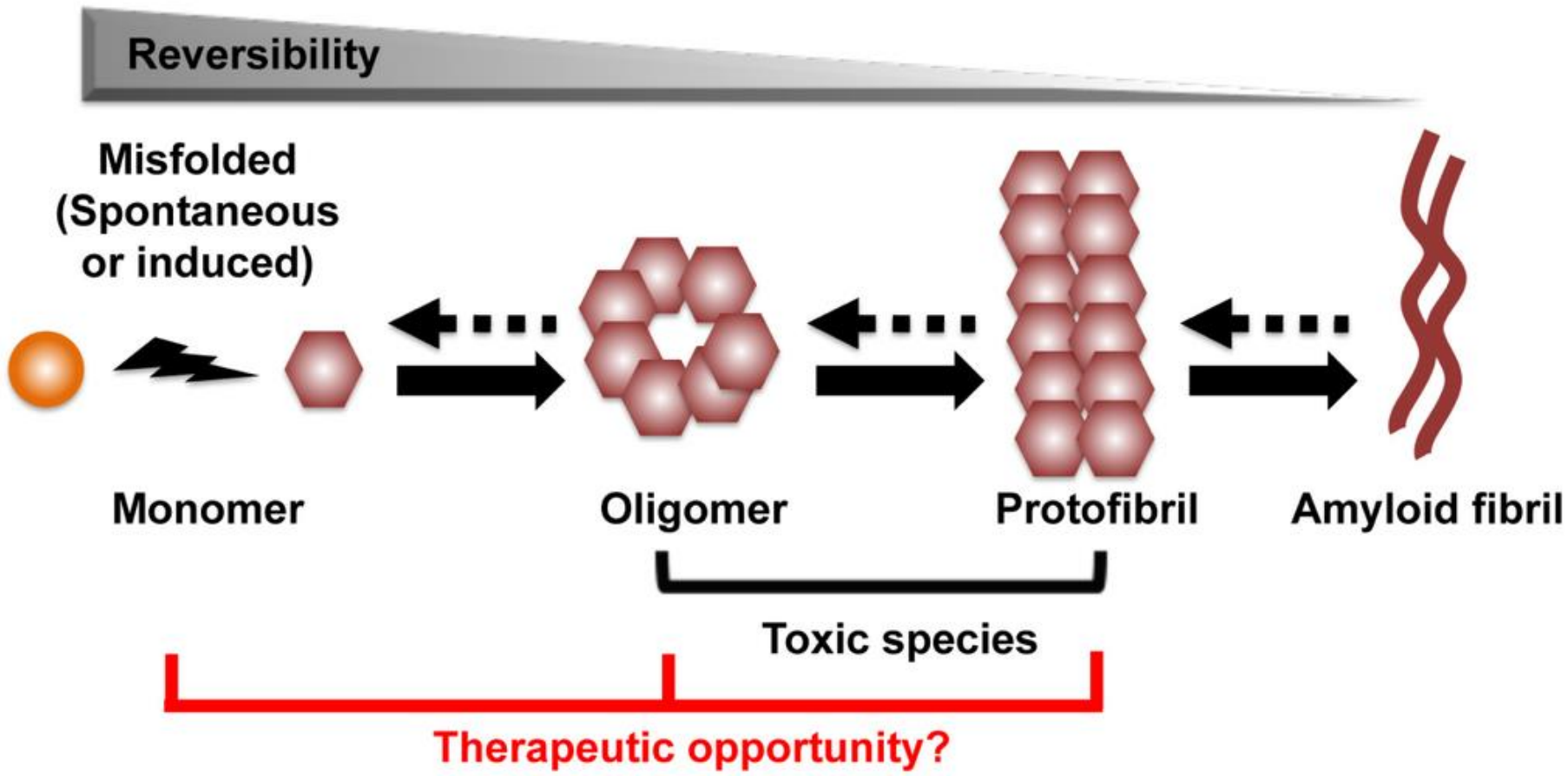




Percent increase in Alzheimer's 2000-2010 (65+) and U.S. topographic map with values in feet above sea level (USGS).

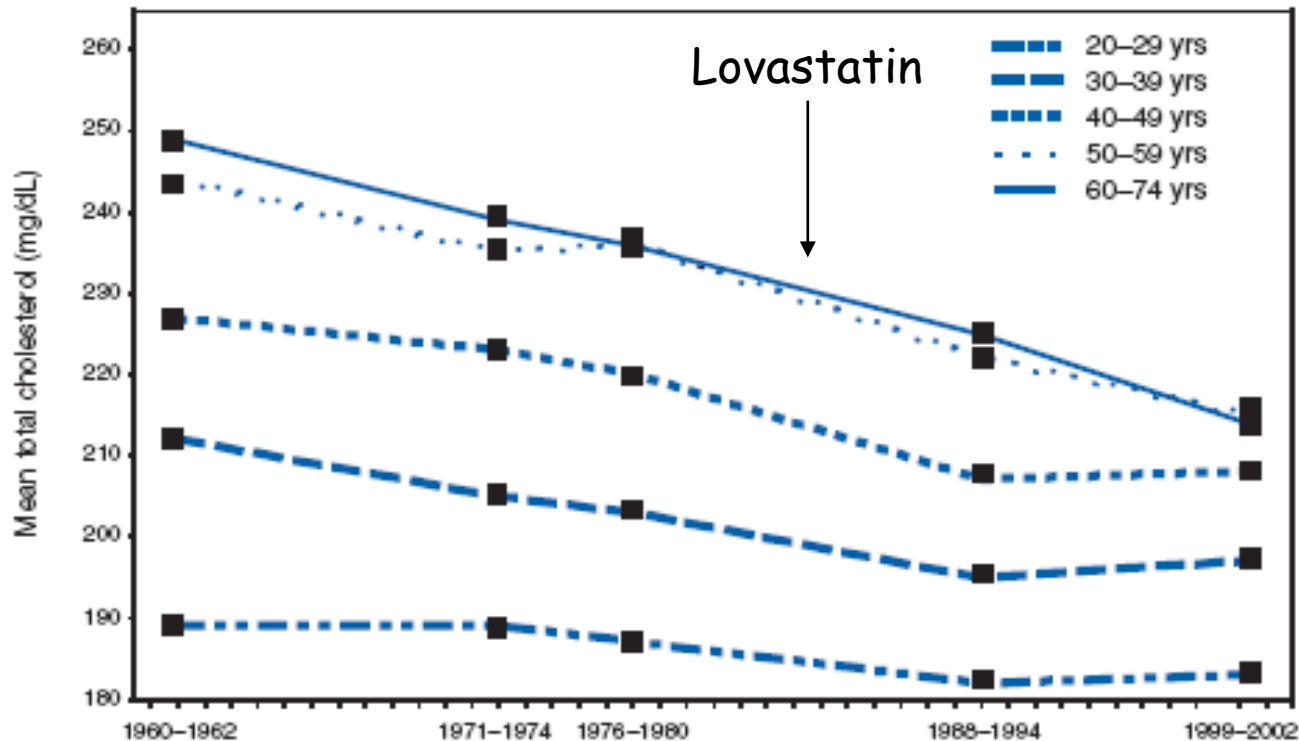
At mile high there is 17% less available oxygen than at sea level

Hebert, L. E., P. A. Scherr, et al. (2004). "State-specific projections through 2025 of Alzheimer disease prevalence." Neurology 62(9): 1645.

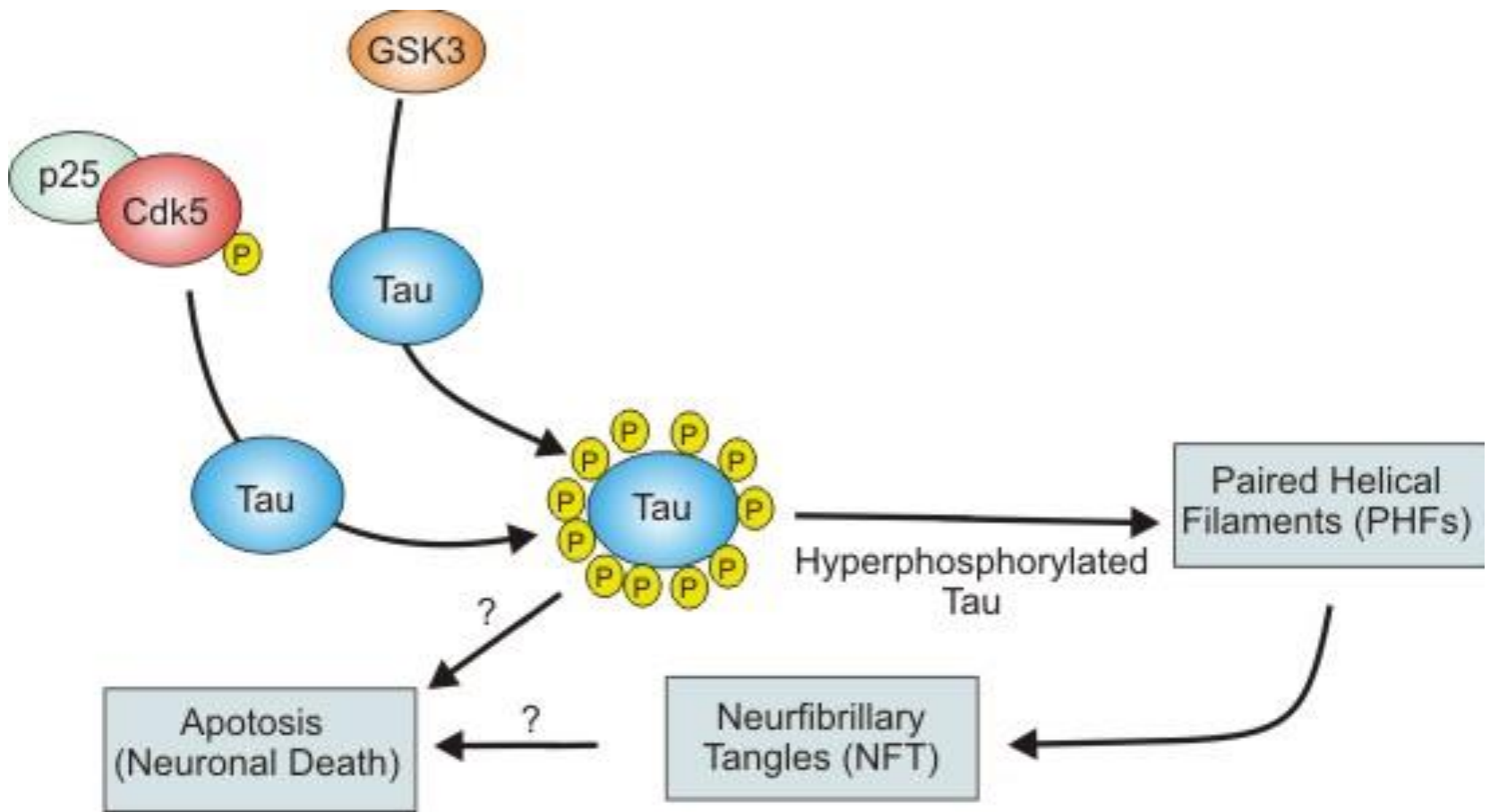


Team Workshop 1: Find and write down the sequence of amyloid beta 1-42 ( $A\beta_{42}$ ) and amyloid beta 1-40 ( $A\beta_{40}$ ). Now use PASTA to predict the aggregation free energy of both peptides. Where in the sequence would you target a drug to inhibit aggregation?

## Trends in Mean Total Cholesterol Among Adults Aged 20–74 Years, by Age Group — United States, 1960–1962 to 1999–2002\*



Team Workshop 2: The use of statins has been accredited for the overall decrease in blood cholesterol and decreased cardiovascular diseases. Use the Cochrane library to determine if there is evidence linking statins to AD

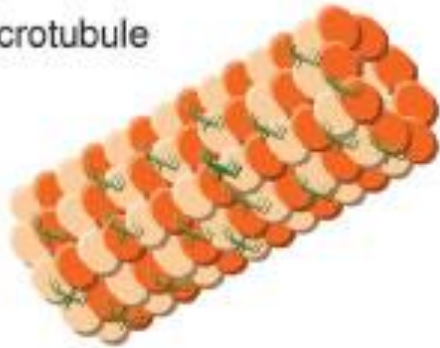


Team Workshop 3: Use STRING to discover Tau interacting proteins that may play a role in Apoptosis of neurons and propose a mechanism for how Tau hyperphosphorylation triggers apoptosis.

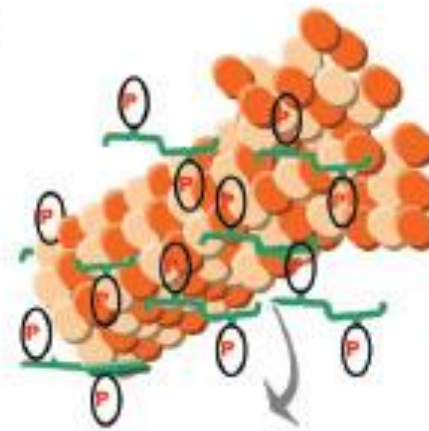




Microtubule



Destabilized Microtubules



Phosphorylated TAU Protein



Paired Helical Filaments



Team Workshop 4: Determine the mechanism of nocodazole and compare this to hyperphosphorylation of Tau. Design an experiment to distinguish microtubule disassembly toxicity from Tau-NFT toxicity?



# Remember

- Before 12 PM of the next class day:
  - go to [b.socrative.com/student/login](https://b.socrative.com/student/login) and complete the quiz