

Scan Me!



Alzheimer's Disease: Current Treatments and New Studies

An Honors Capstone Enhancement

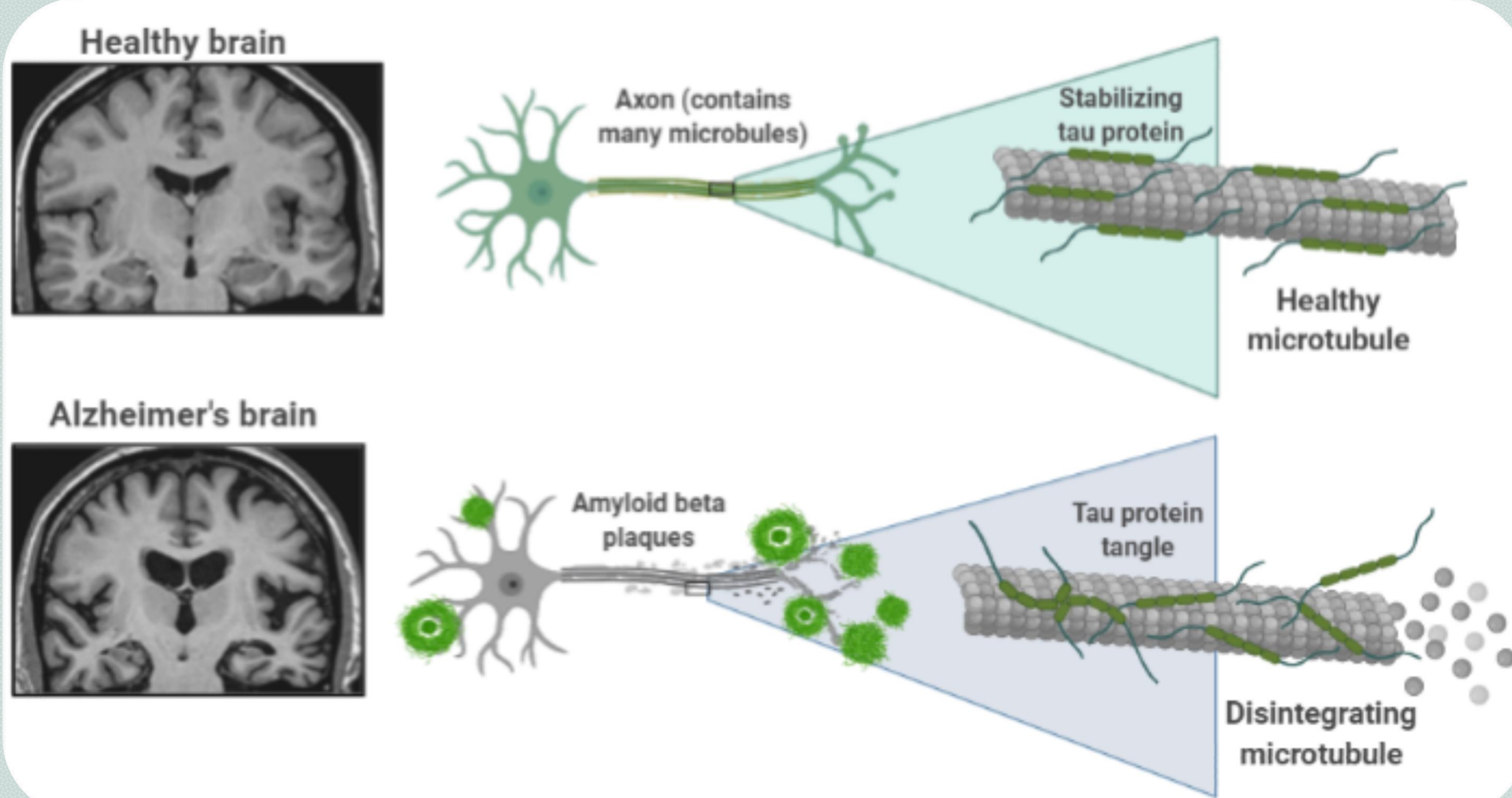
Melissa Gouge



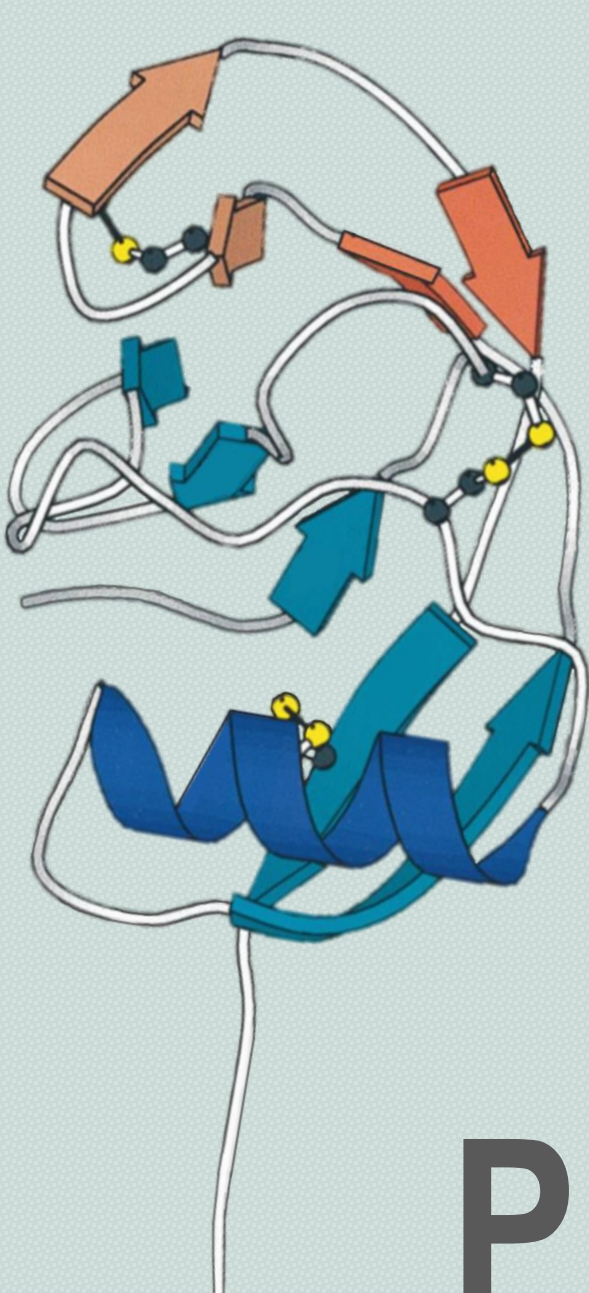
What is Alzheimer's Disease?

Definition: progressive loss of cognition and other important mental functions

Impact: ~5.8 million Americans, doubling every 20 years until 2050



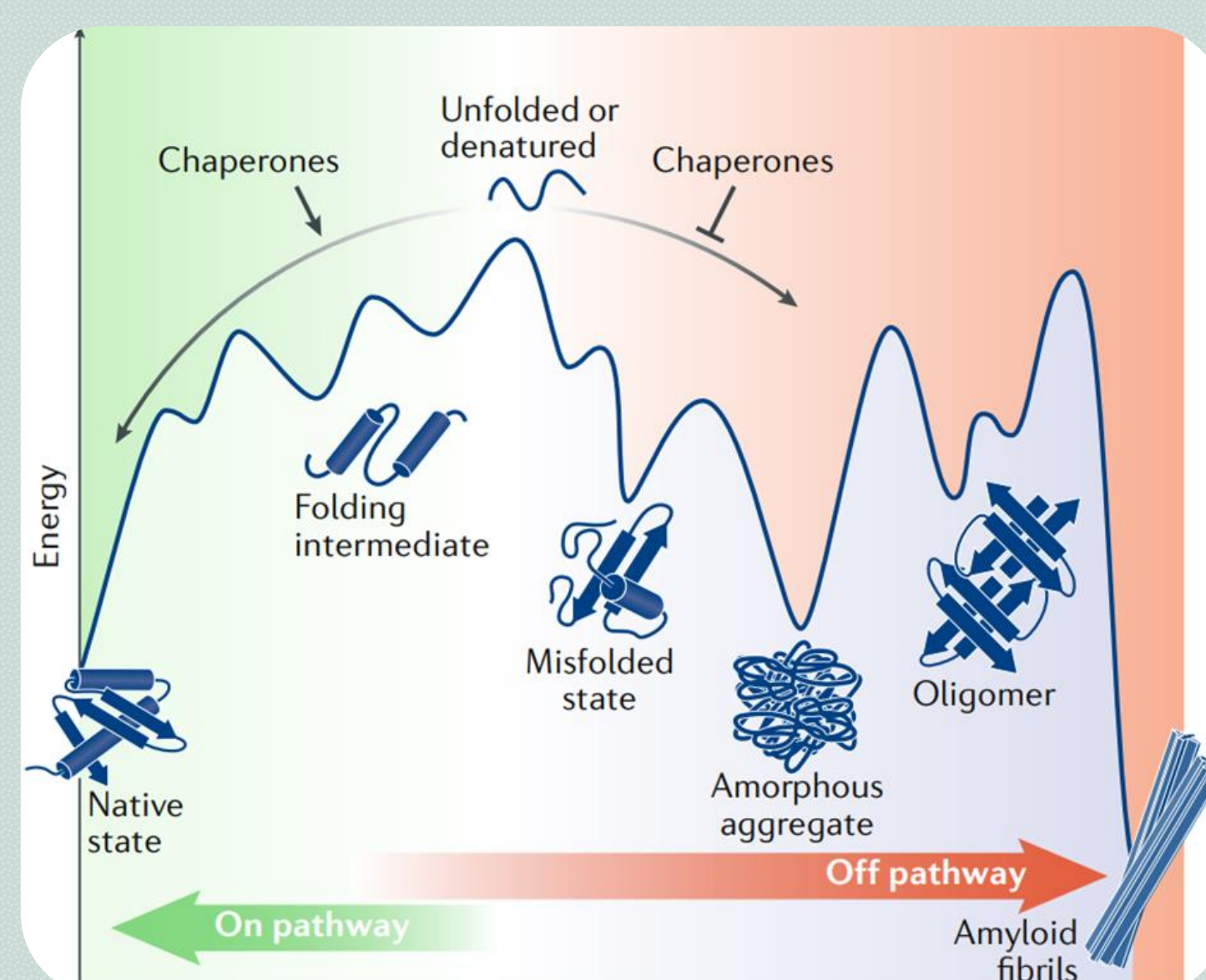
Amyloid-β Peptides



- **Senile Plaques:** misfolded Amyloid-β peptides
- 40-42 residues long
- Function unknown
- Deposit of plaques in an ongoing process

Proteostasis Network

- Recognizes misfolding proteins and returns them to their native state
- Fails in AD patients



Three Stages of Disease

Preclinical

- Brain changes including buildup of amyloid peptides and study of CSF fluid shows increase in tau and phosphorylated tau levels
- No significant clinical symptoms apparent

Mild Cognitive Impairment (MCI)

- Memory and cognition impairment at a higher level than typical aging
- No interference with independence of individual

Alzheimer's Dementia

- Memory loss, word-finding difficulties, visual/spatial problems
- Significant impairment to independence of individual

Current AD Diagnostic Tools

Imaging Tools: MRI, PET Scan

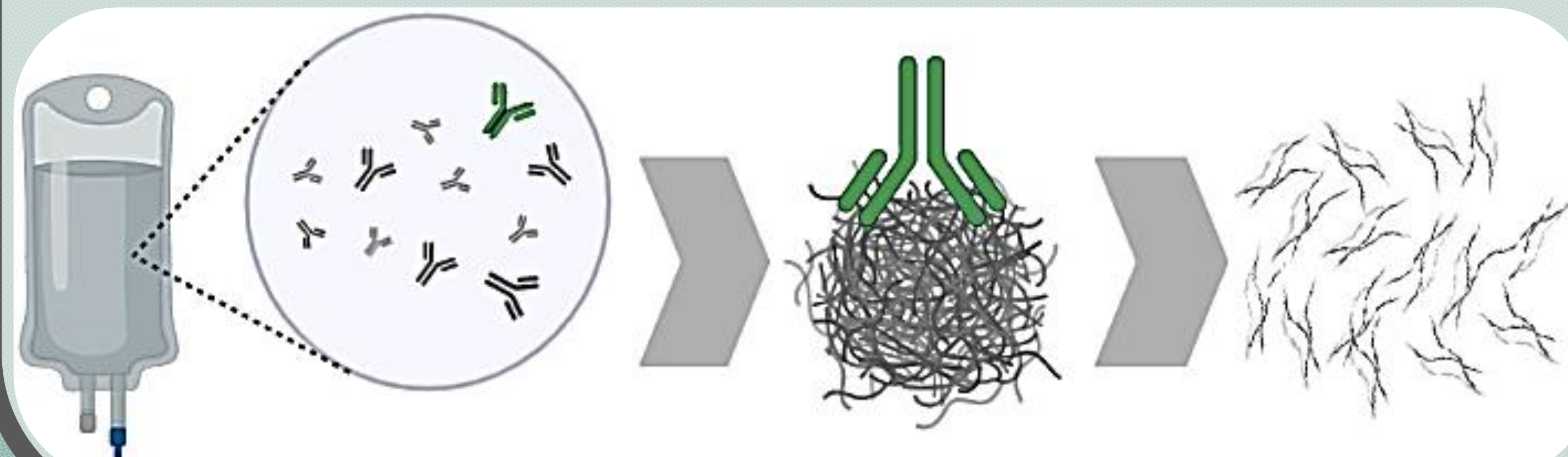
Neuropsychological Test: formal tests assessing episodic memory, executive function, language, visual and spatial skills, and attention

Other: Interviews with family and friends

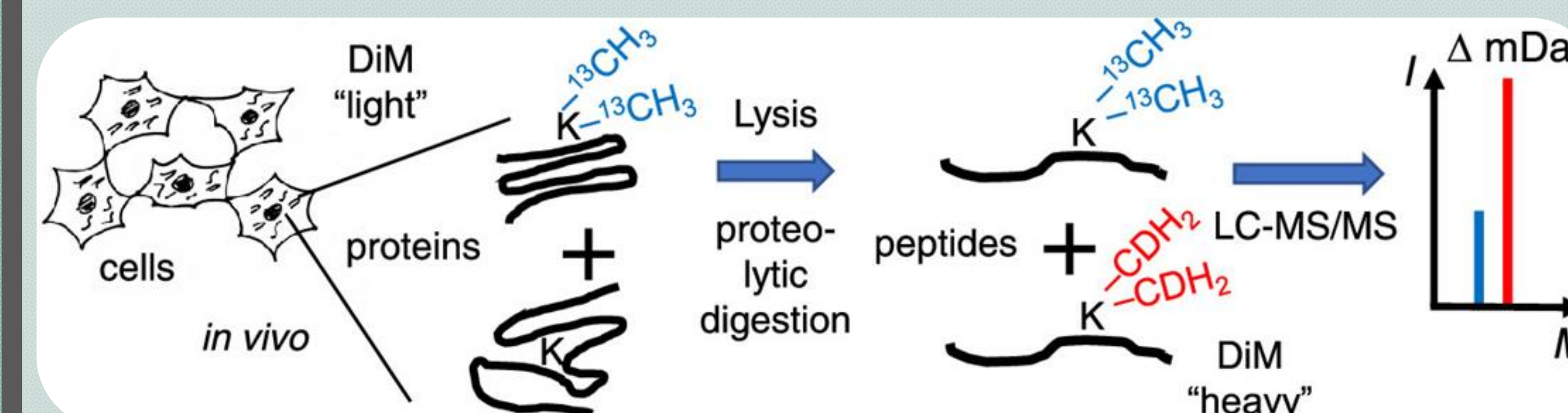
Monoclonal Antibody Treatment

Aduhelm (aducanumab): IV infusion

amyloid beta-directed antibody which targets and breaks apart plaque buildup



What is Covalent Protein Painting (CPP)?



A multi-step labeling process which allows for the shape of the protein to be elucidated based on the patterns of labeling shown on LS-MS/MS data.

| Diagnosis | AB#K28 | | | |
|-----------|--------|------|--------|------|
| | Lysate | | Pellet | |
| | SpC | %acc | SpC | %acc |
| AD | 2 | 89 | 2 | 99 |
| AD | 4 | 79 | 7 | 92 |
| AD | 7 | 65 | 5 | 92 |
| AD-dLBD | 4 | 75 | 5 | 94 |
| AD-dLBD | 7 | 84 | 6 | 94 |
| AD-dLBD | 6 | 51 | 7 | 86 |
| AD-dLBD | 6 | 49 | 5 | 82 |
| AD-dLBD | 7 | 48 | 8 | 51 |
| AD-dLBD | 6 | 62 | 5 | 84 |
| LBD | 0 | n.d. | 0 | n.d. |
| Normal | 0 | n.d. | 0 | n.d. |
| Normal | 0 | n.d. | 0 | n.d. |
| Normal | 0 | n.d. | 0 | n.d. |
| Normal | 0 | n.d. | 0 | n.d. |
| Normal | 0 | n.d. | 0 | n.d. |
| Normal | 0 | n.d. | 0 | n.d. |
| Normal | 0 | n.d. | 0 | n.d. |
| Normal | 0 | n.d. | 0 | n.d. |
| Normal | 3 | 7 | 1 | 4 |

Data Analysis:

%acc: shows how often the residue (Lysine #28) was labeled in the 1st step. In AD patients, this shows a misfolding of the amyloid-β protein.

Acknowledgements and References

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