



Brain donation: Final diagnosis and relevance

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Why is brain donation important?

Diagnosis, Research, Education



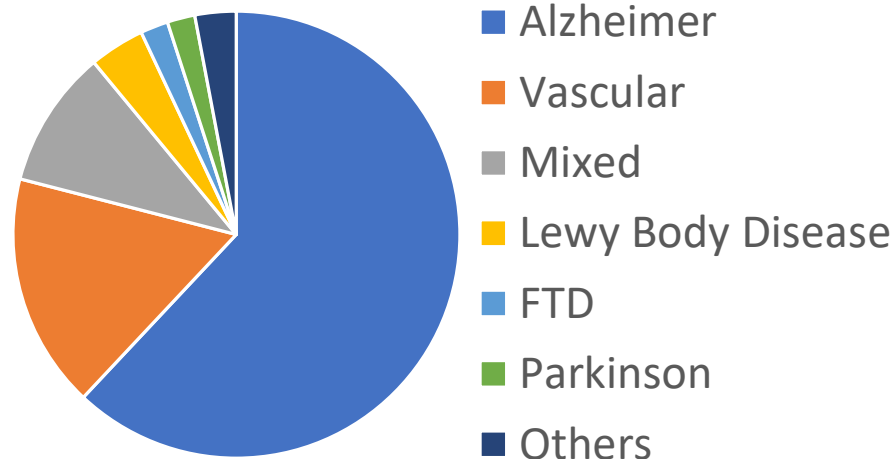
Brain donation: Final diagnosis

- Make a **definitive diagnosis** of neurodegenerative disease with 100% certainty
- **Grade the severity** of the neuropathological changes
- In most cases, reveal **mixed pathologies** and comorbidities



Brain donation: Final diagnosis

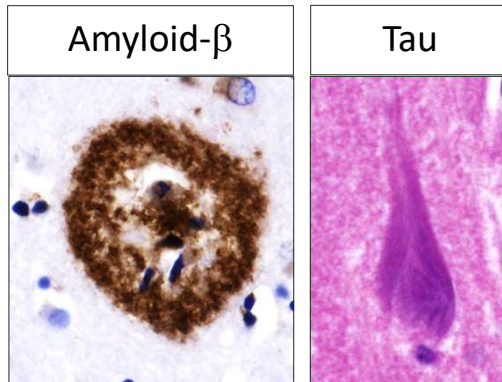
Causes of dementia



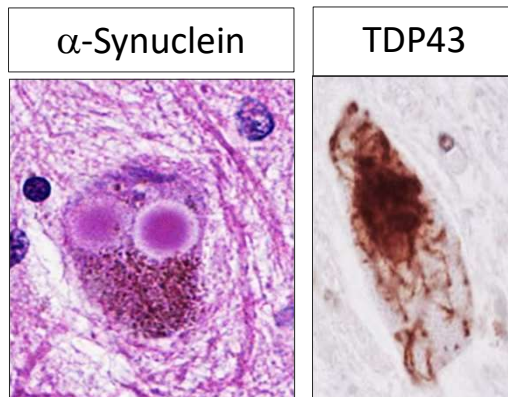
Mixed pathologies in brains with dementia are more prevalent than we thought:

- Vascular + Neurodegenerative
- Mixed Neurodegenerative

Alzheimer's disease



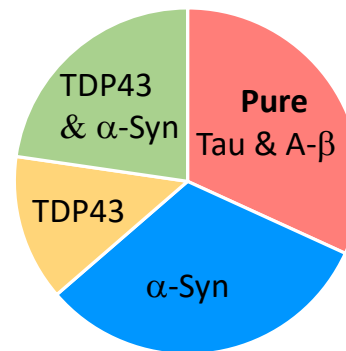
Lewy Body Disease



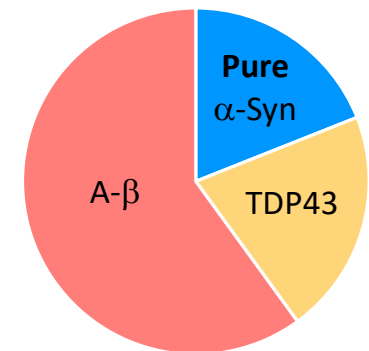
Mixed pathologies: Prevalence

- Increasingly recognized to be frequent, particularly in **older people**

Alzheimer

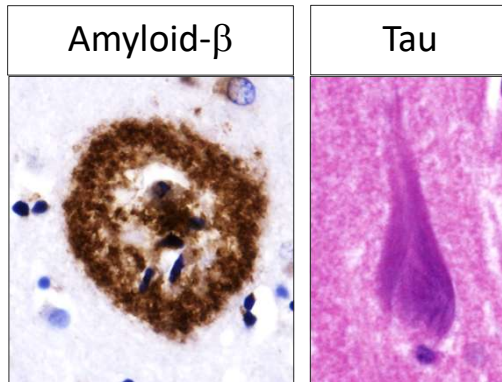


Lewy Body Disease

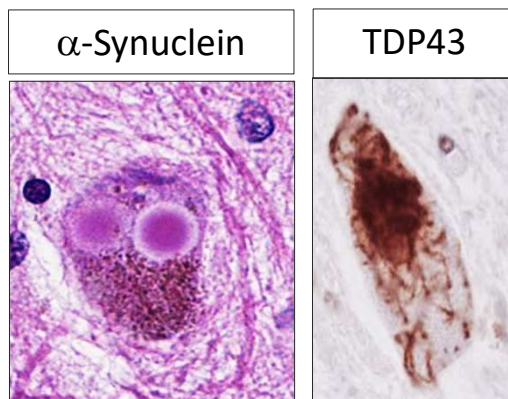


Robinson *et al.*, Brain 2018

Alzheimer's disease



Lewy Body Disease



Mixed pathologies: Relevance

- Can impact the progression of disease (more **rapid course**)
- Knowledge needed to evaluate the efficacy of clinical trials and the **response to therapies**



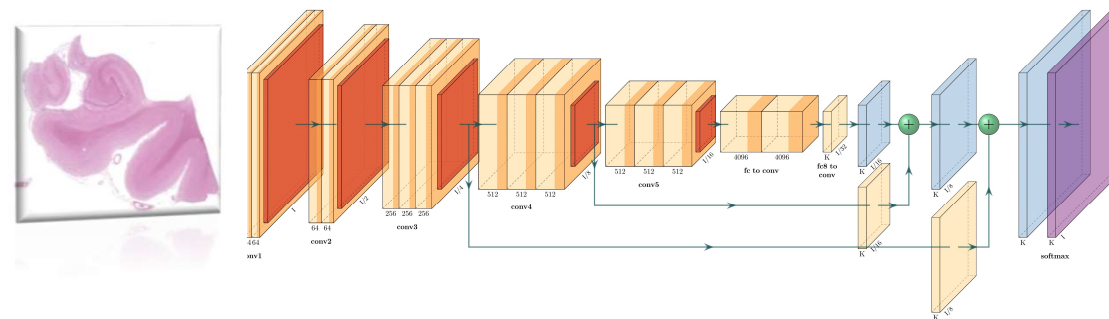
Brain donation: Healthy individuals

- Healthy donors are needed to study **normal aging**
- **Resilience:** Brains of cognitively normal older people often have pathology. Why people with Alzheimer's disease pathology have no dementia?
 - Initial stages of the disease?
 - Slow progression?
 - Compensatory/adaptative mechanisms



Brain donations are helping dementia research

MARVL lab: We are using artificial intelligence and computer vision to improve pathology diagnosis and link the pathology to blood, CSF, and radiology images to allow earlier diagnosis.

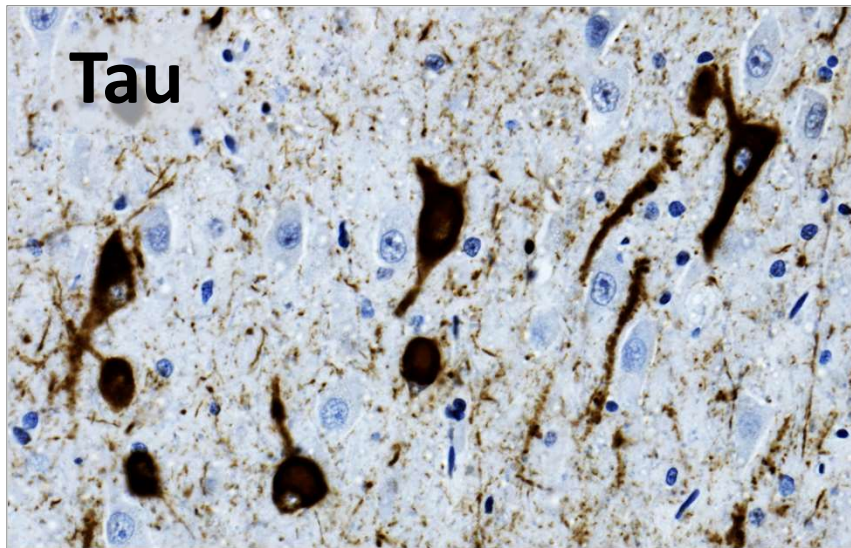


Hippocampus from patient with dementia (left) and schematic artificial neural network (right).





Brain donations are helping dementia research



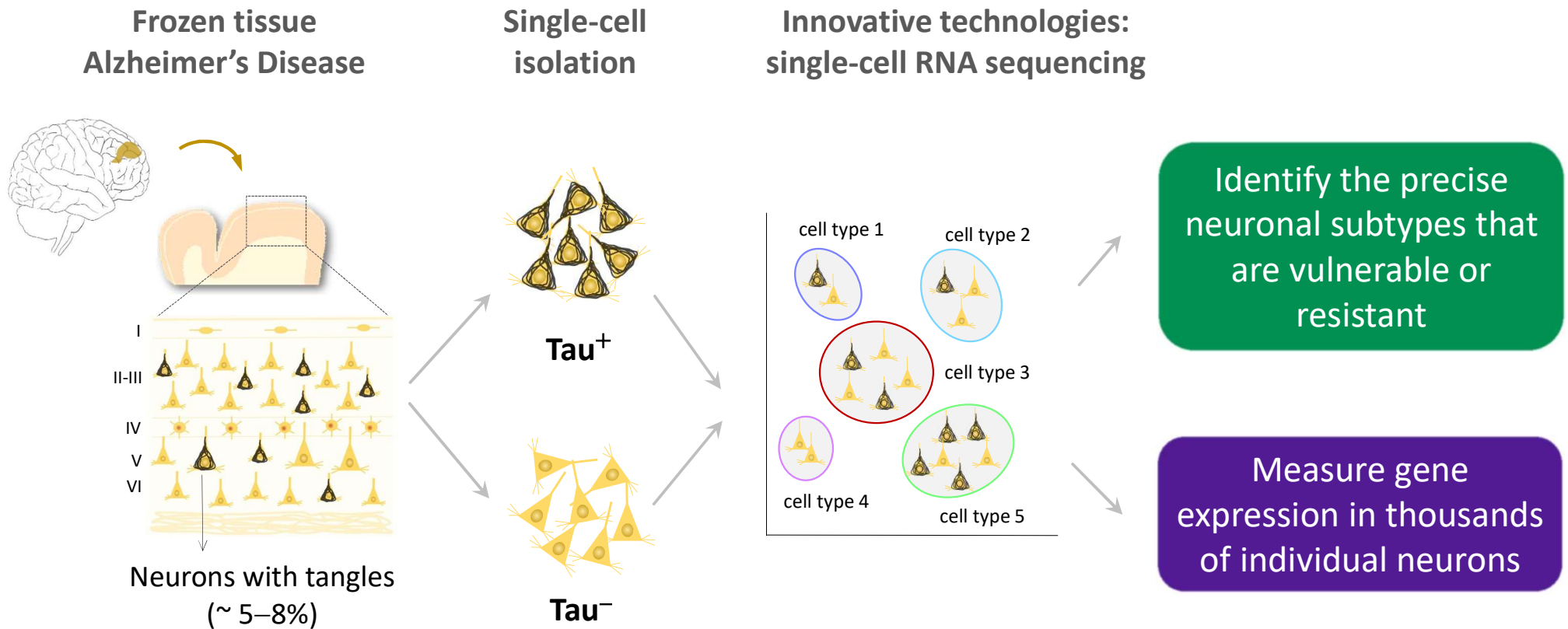
Neurons with and without tangles in advanced dementia

Cobos Lab: Why are some neurons more vulnerable or resistant to disease?

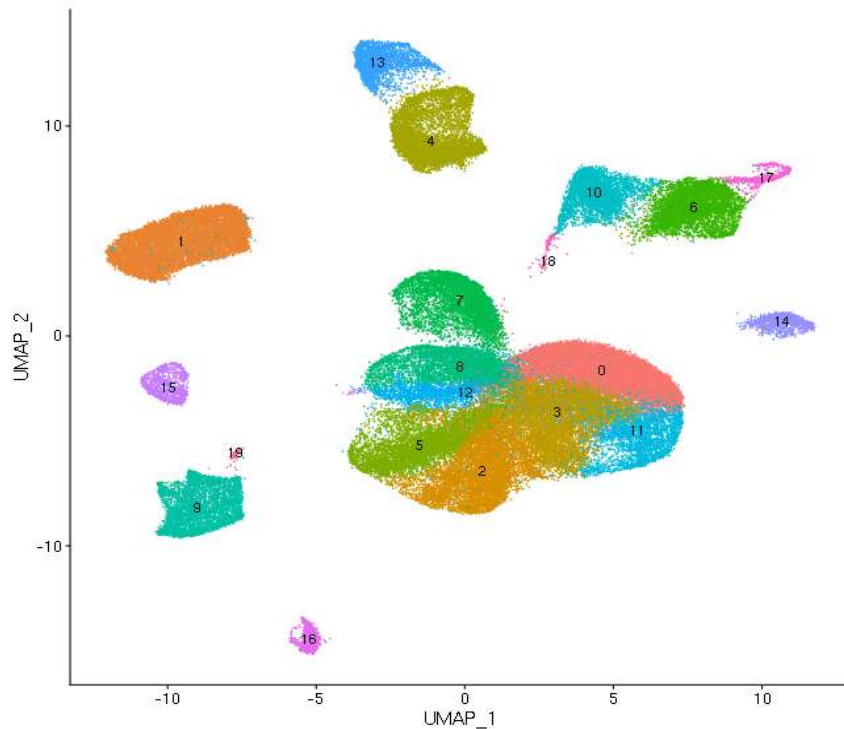
Cobos Lab

<https://med.stanford.edu/coboslab.html>

Studying neurons with and without tangles at single-cell resolution



Data analysis using bioinformatics



Combined data from 29 donors
(healthy controls and full spectrum of AD)
~ 90,000 cells

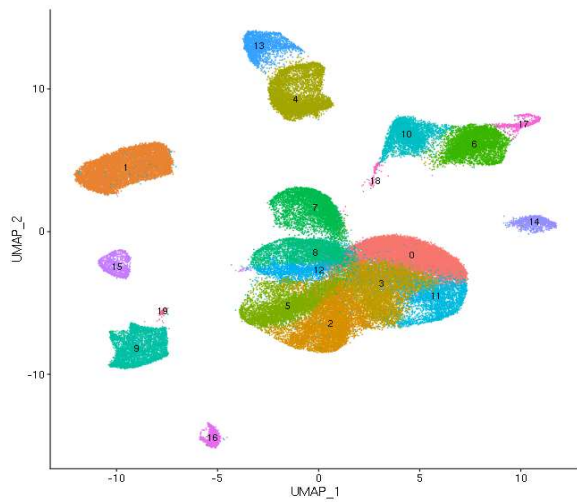
Each dot: one cell

Each color: one type of cell

Data available for each cell:

- Demographic (age, sex, race)
- Clinical data
- Neuropathologic data
- Gene expression levels

Inma Cobos, MD, PhD



Single-cell studies in human brains can help us to:

- **Identify the earliest pathogenic events in dementia**
- **Identify mechanisms that can contribute to the protection and repair of neurons**
- **Identify novel therapeutic strategies**

Inma Cobos, MD, PhD

Thank you!



Brain donor program at Stanford:

Christina Wyss-Coray, RN, BSN, PHN

Divya Channappa, MS

Syed Bukhari, MS

Tom Wyss-Coray, PhD

Birgitt Schuele, PhD

Donald Born, MD, PhD

Thomas Montine, MD, PhD

Inma Cobos, MD, PhD



Educational Conference on Healthy Brain Aging
Research Participant Appreciation Day
November 2, 2022

