Alzheimer's disease in 2025:
Early Detection & Blood Tests in a New Treatment Era

Sarah Ocañas, PhD

Assistant Professor

Genes and Human Disease Research Program

Oklahoma Medical Research Foundation

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Neuroscience Program

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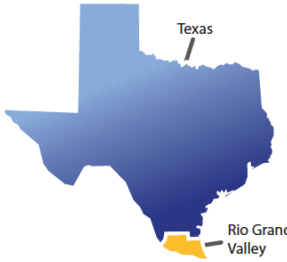
Dr. Ocañas background



Teaching HS Mathematics

B.S Biology & Mathematics

M.S. Mathematics

Ph.D. Physiology

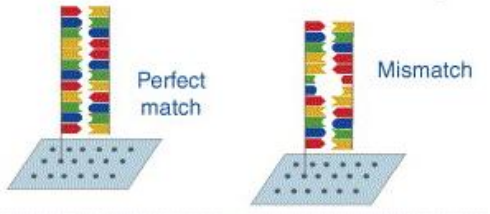
Ocañas Lab GHD, OMRF Nov. 2022

Grant Oct. 2023

2006 2010 2013 2015 2017 2022

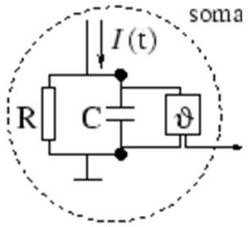
Biology & Math, B.S.

"Group testing to determine the presence of cross-hybridized duplexes of DNA within pools"



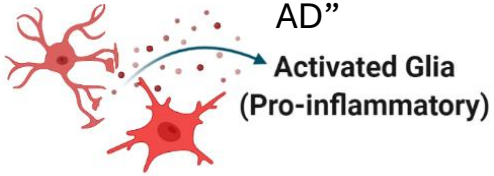
Mathematics, M.S.

"Mathematical Models of Electrical Neuron Activity"



Physiology Ph.D.

"Epigenetic regulation of sexually divergent neuroinflammation with brain aging and AD"



Postdoctoral Fellow

Reproductive Aging

Jillian Cox, B.S.

Ph.D. Candidate

Neuroscience

My background

Born & Raised
Newcastle, OK

2017
CNA & Phlebotomy
Wayne, OK

2019
Graduated HS

Cox Academy
Newcastle, OK

2021
B.S. Biology
OKC, OK

Lab Intern
2021

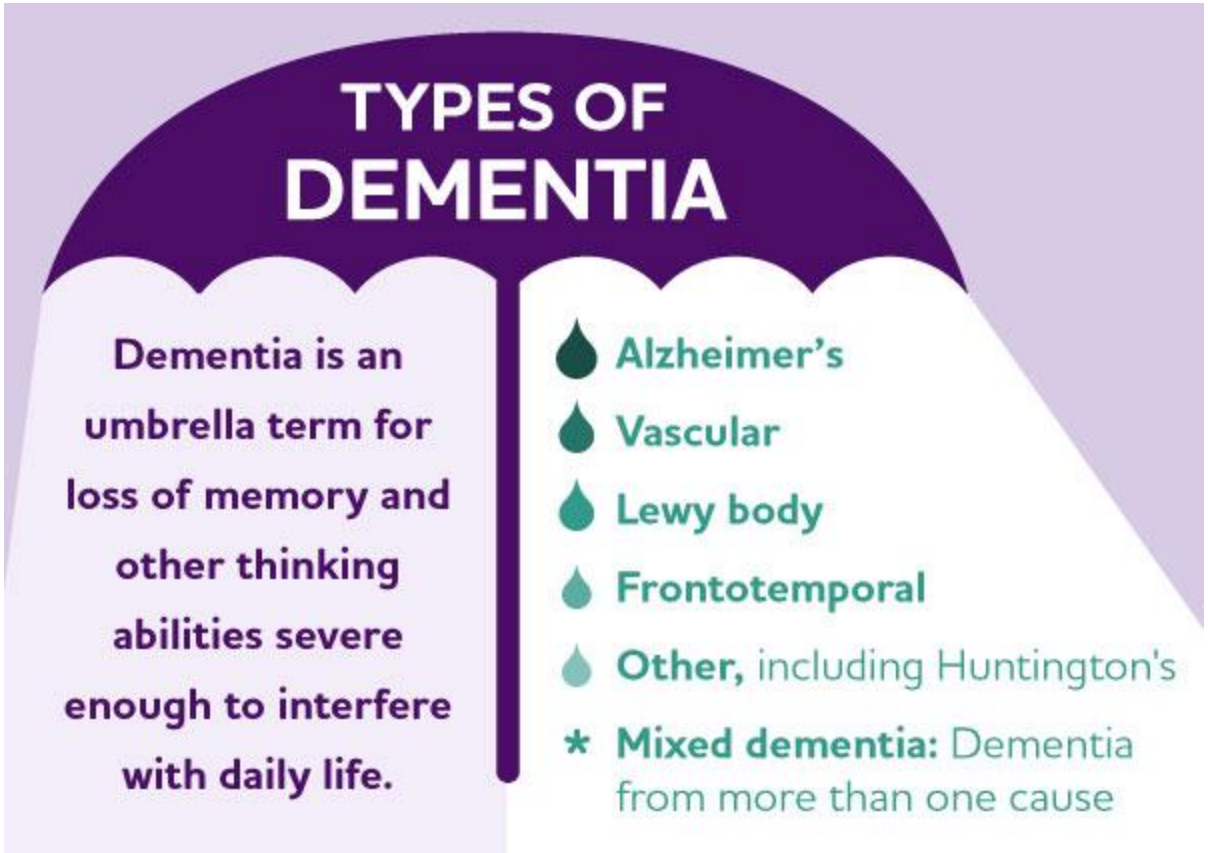
2022
Ph.D.
Neuroscience
(2027)

2023

2025
Science
Advocacy
Fellow

Ocañas Lab

What is Alzheimer's Disease?



- **Most common form of dementia**

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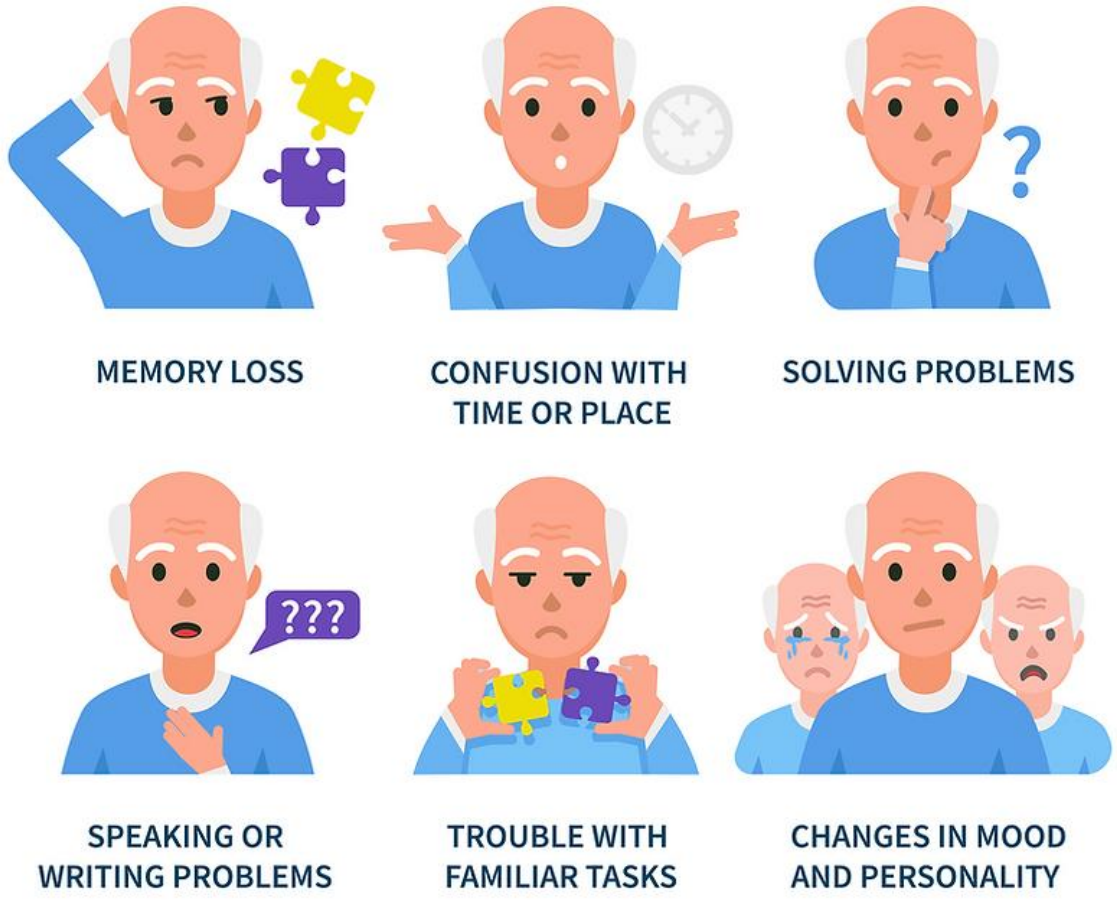
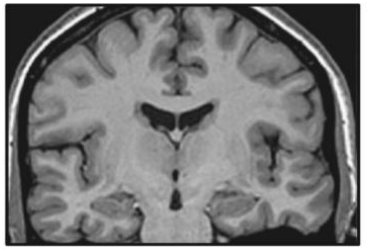
What is Alzheimer’s Disease?



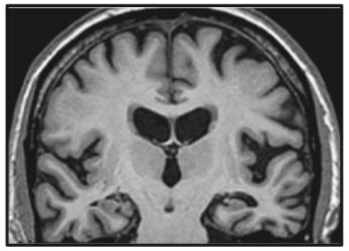
- **Most common form of dementia**
- **Results in memory loss, confusion, personality changes**

What is Alzheimer’s Disease?

Healthy brain

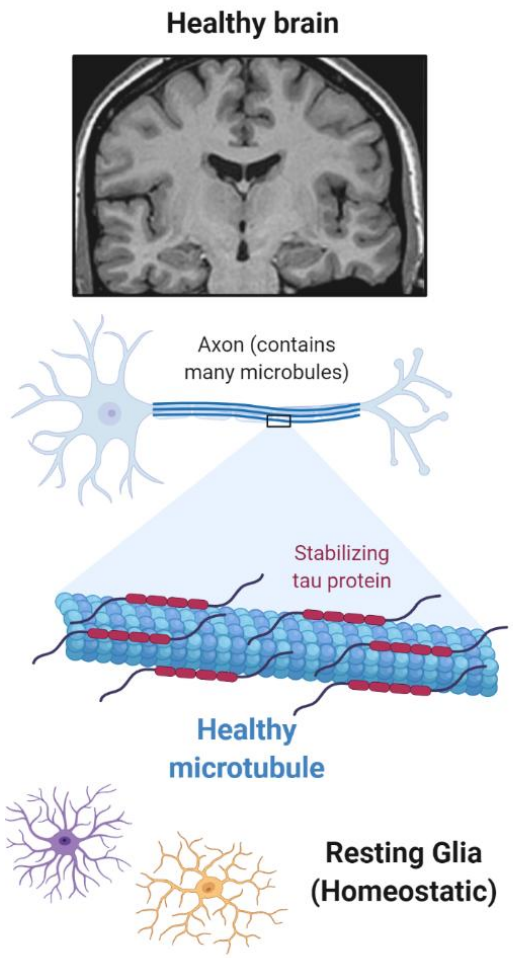


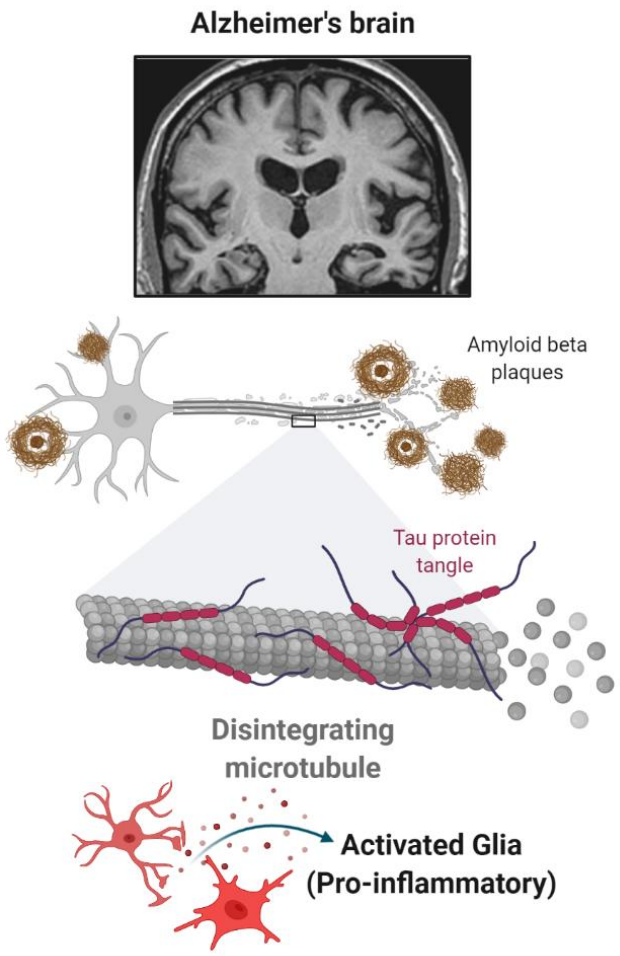
Alzheimer's brain



- Most common form of dementia
- Results in memory loss, confusion, personality changes
- Brain volume decreases

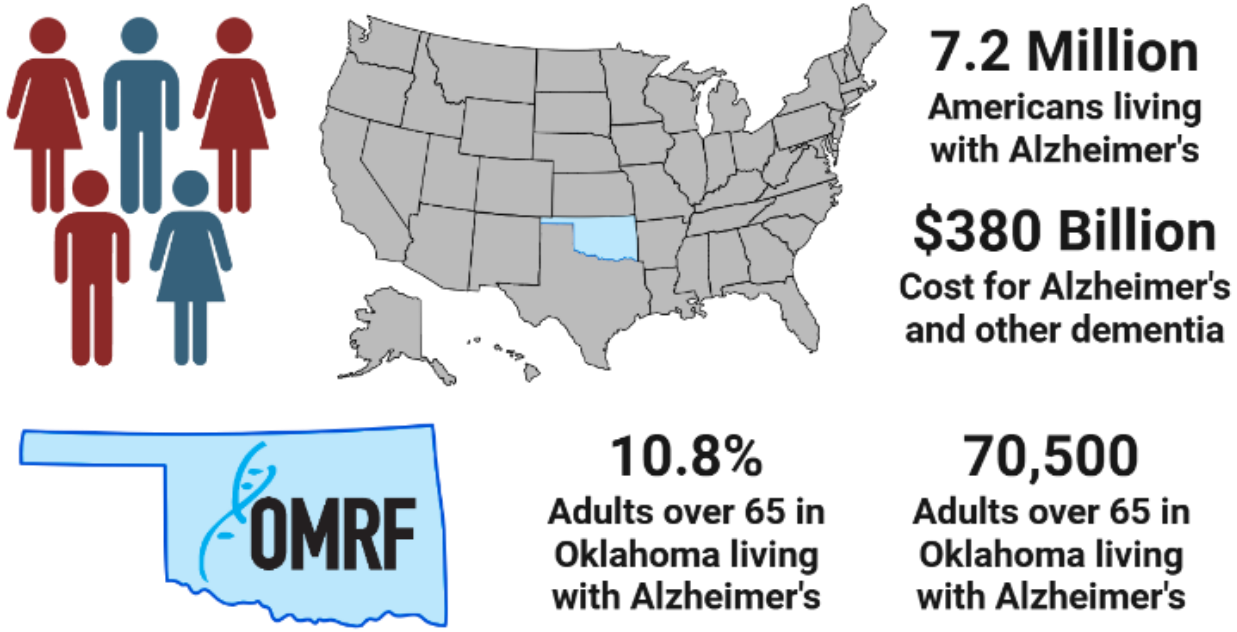
What is Alzheimer’s Disease?





- Most common form of dementia
- Results in memory loss, confusion, personality changes
- Brain volume decreases
- Pathological hallmarks:
  - Amyloid plaques
  - Tau tangles
  - Inflammation

Who is affected by Alzheimer's disease?



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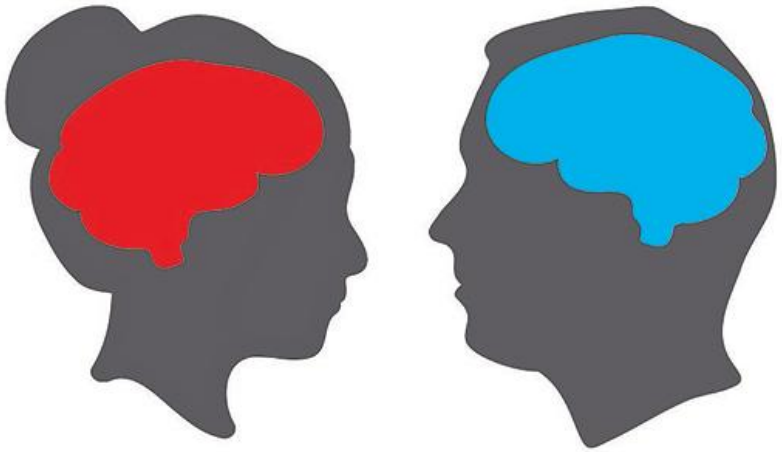
- More than 7 million Americans live with Alzheimer's disease
- 11 million nationwide provide unpaid care
- Huge economic cost, but much greater personal cost
- In Oklahoma
  - ~10% of adults >65 have Alzheimer's
  - 108,000 unpaid caregivers

Who is affected by Alzheimer's disease?



1 in 6 **1 in 11**

chance of developing Alzheimer's disease during the remainder of their lives at age 65

- More than 7 million Americans live with Alzheimer's disease
- 11 million nationwide provide unpaid care
- Huge economic cost, but much greater personal cost
- In Oklahoma
  - ~10% of adults >65 have Alzheimer's
  - 108,000 unpaid caregivers
- Women are at higher risk for Alzheimer's disease

What does the Ocañas lab study?

Goal: Find new ways that the brain's immune system can be targeted to treat Alzheimer's disease - using sex differences as a guide

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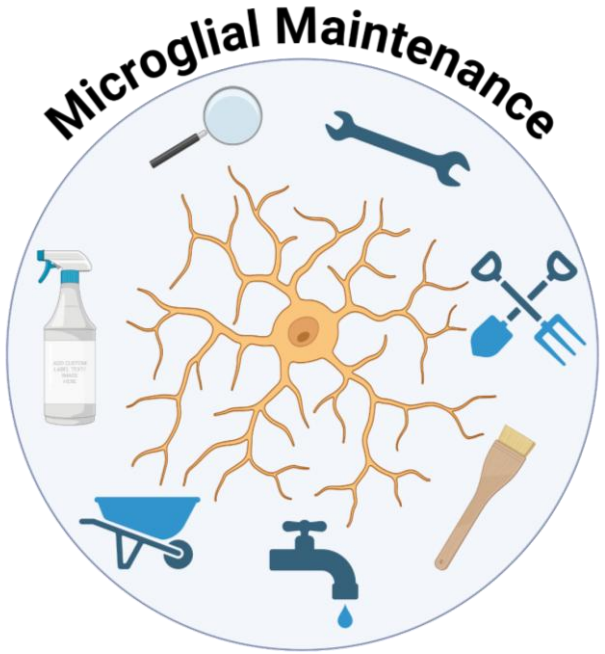

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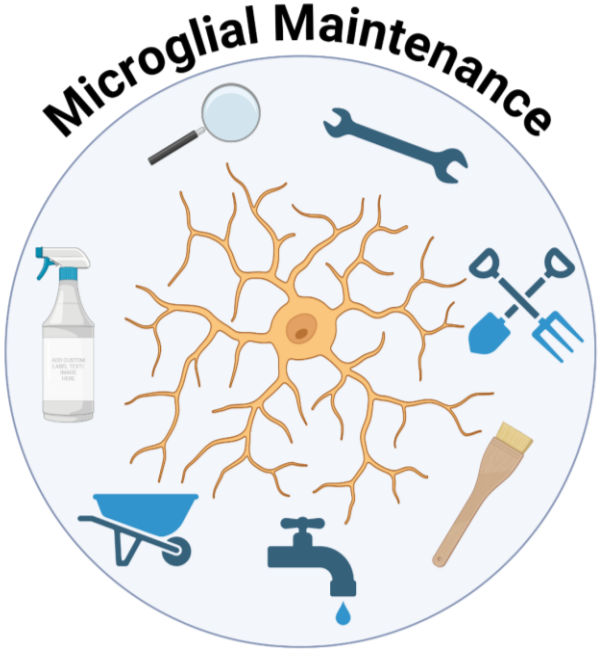

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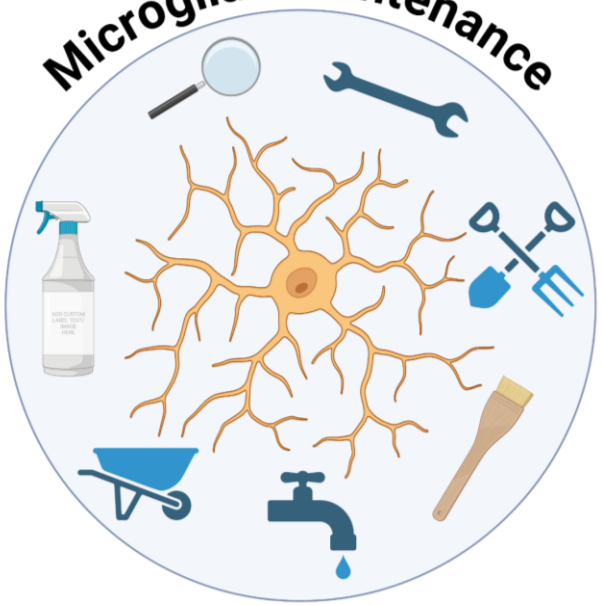

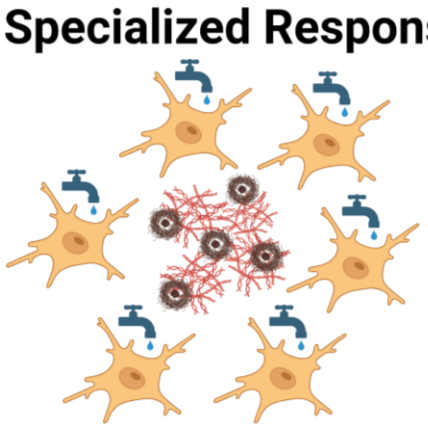

What if issue never resolves? What if the cells "forget" how to do other tasks?

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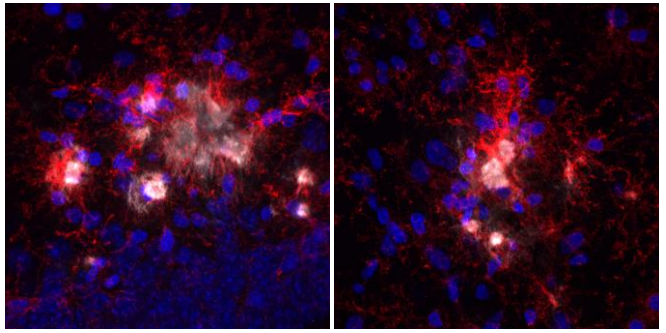
Microglia: Red, Plaques: White

♀



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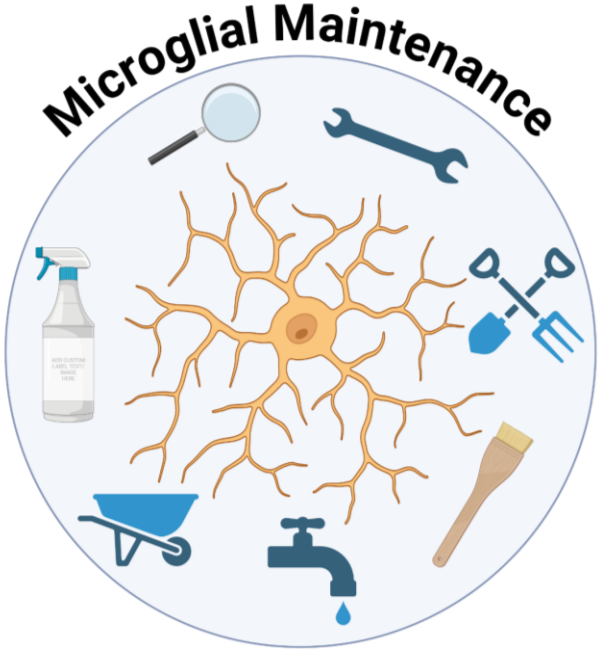

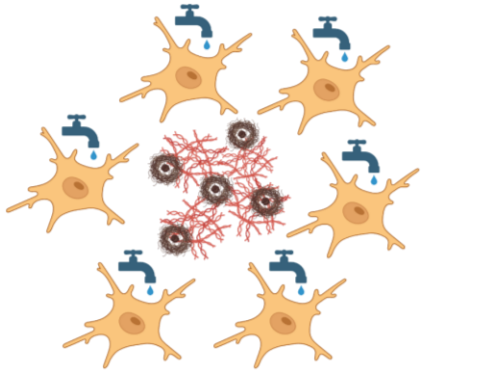

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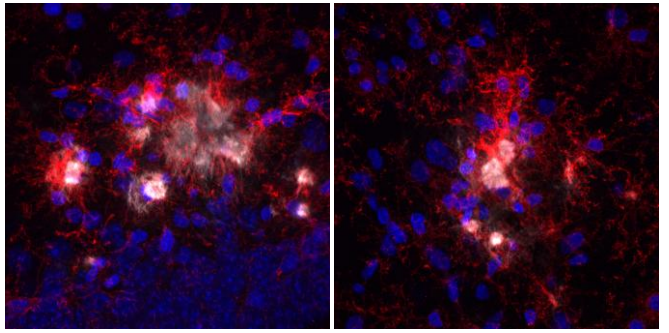

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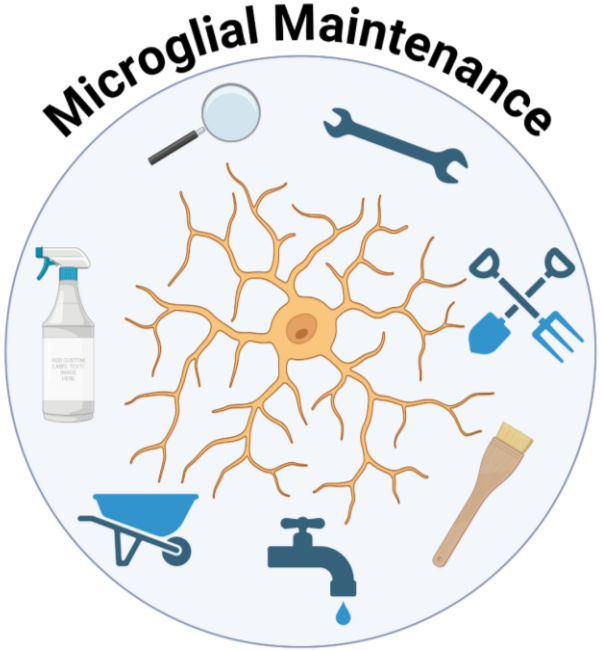

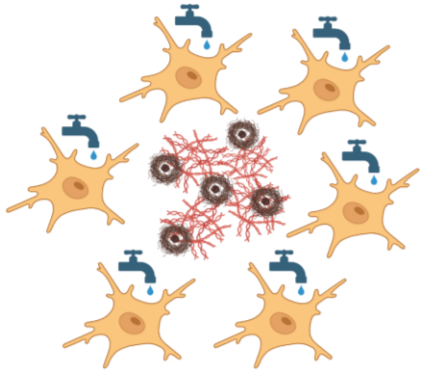

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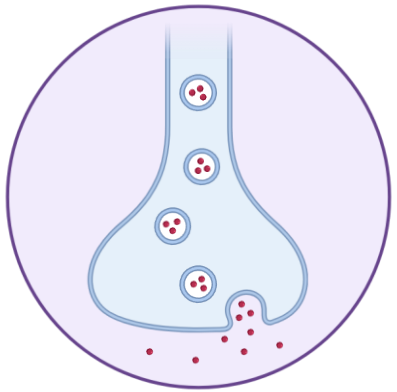
Where do therapeutics stand?



- **Symptomatic Therapies:**
- These help temporarily improve symptoms (memory, thinking, language), but **do not alter disease progression**
  - These drugs **compensate for lost brain chemicals** to make remaining neurons work better
  - Cholinesterase Inhibitors: Donepezil (Aricept), Galantamine (Razadyne), Rivastigmine (Exelon)
  - NMDA Receptor Antagonist: Memantine (Namenda)

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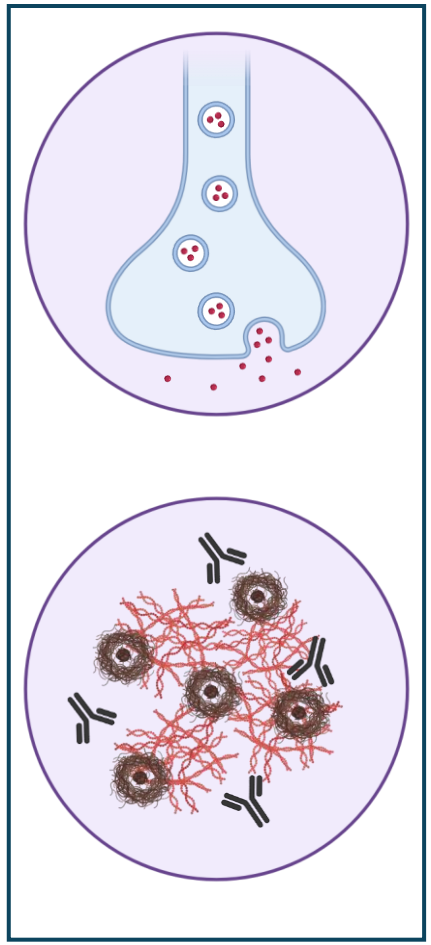
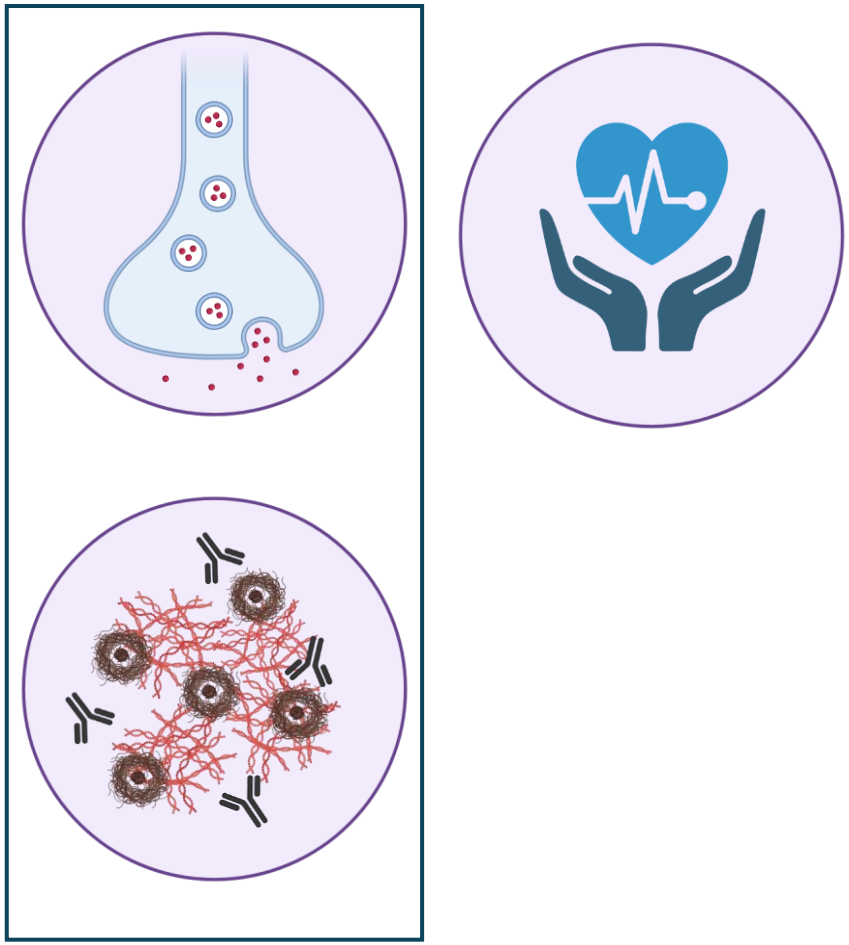


Approved

2021
First disease-modifying therapy for Alzheimer's approved by FDA

- Symptomatic Therapies
- **Disease-Modifying Therapies:**
- These **target amyloid plaques** to try to **slow disease progression**:
  - **Aducanumab (Aduhelm) –** FDA approval (2021), **DISCONTINUED**
  - **Lecanemab (Leqembi) –** FDA approval (2023)
  - **Donanemab (Kisunla) –** FDA approval (2024)

Where do therapeutics stand?



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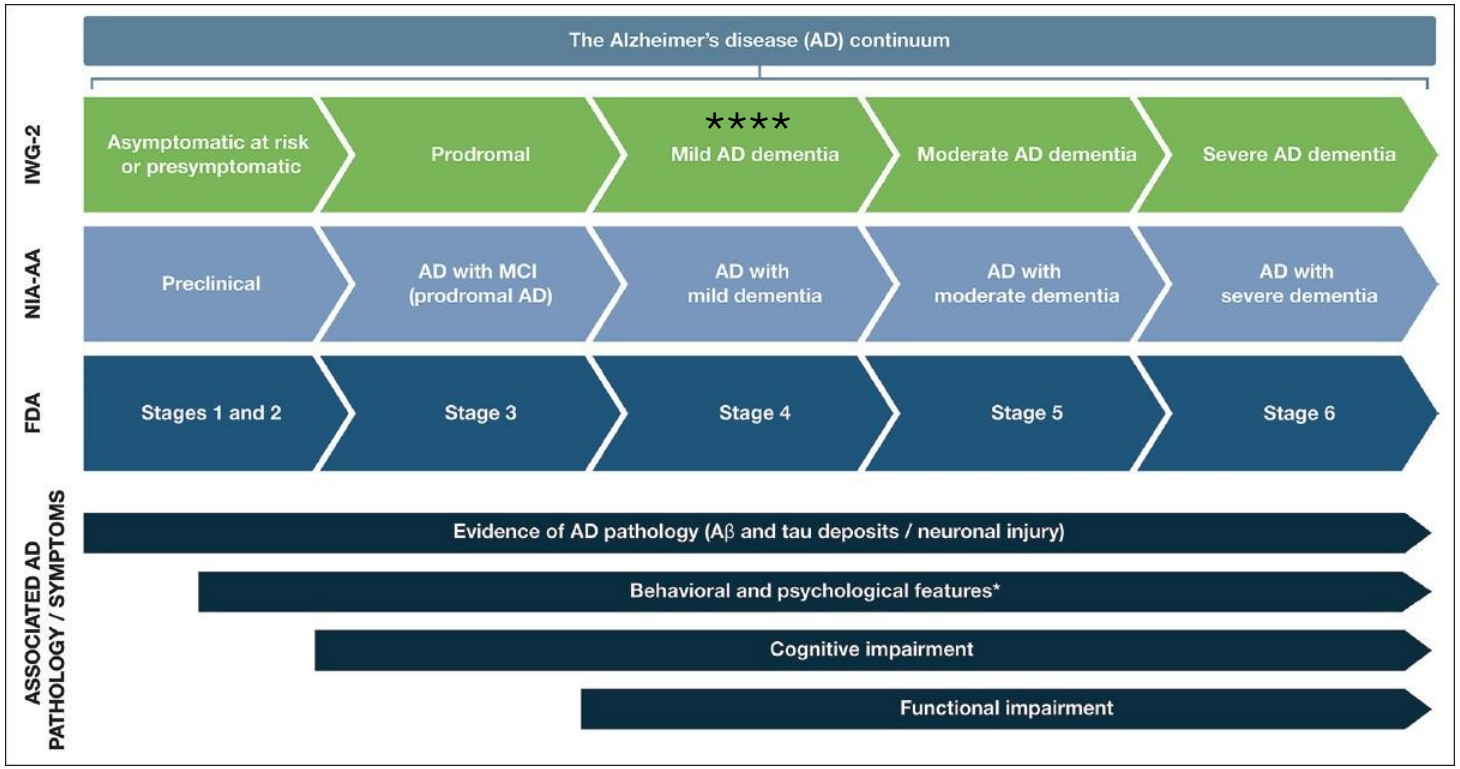
- Symptomatic Therapies
- Disease-Modifying Therapies
- **Preventative and Early Intervention Trials:**
  - **AHEAD Study (Leqembi)**
  - **Treatment before the onset of symptoms in people with higher risk of developing the disease later in life (APOE4)**
  - **Still must show evidence of amyloid buildup in the brain**

Who is eligible for approved disease-modifying therapies treatments?



- **Early Alzheimer's**
  - **Mild cognitive impairment**
- **Confirmed amyloid plaque pathology in their brains**
  - **Amyloid PET scan**
  - **Lumbar puncture (CSF)**
- **Often <u>diagnosis takes too long</u> and patients are no longer eligible for treatment**
  - **Average of 3.5 years from noticing symptoms to diagnosis**

Why does diagnosis take so long?

- **Denial about symptoms**
- **Often symptoms are excused as signs of healthy aging**
- **Difficulty in getting appointment with qualified doctor**
- **Lack of expertise within rural areas – difficulty in traveling**
- **Inaccessibility of current diagnostic tests**
  - **Expensive brain imaging tests**
  - **Invasive CSF collection**
  - **Out-of-pocket costs**

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2025

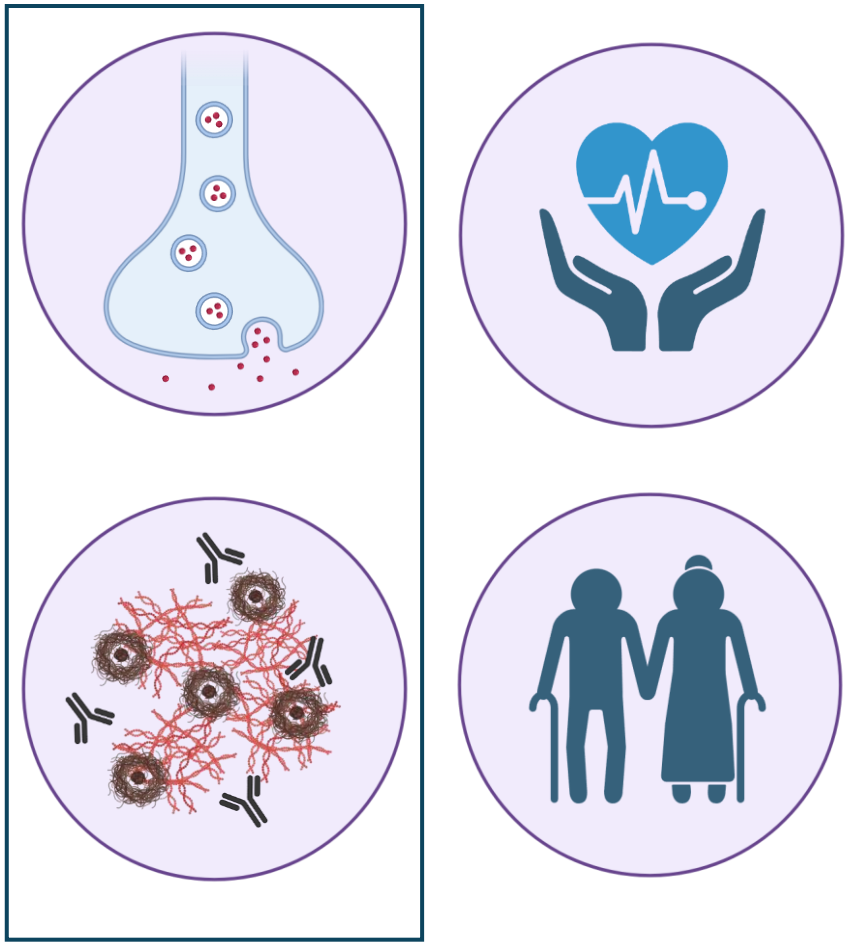
FDA approves first blood diagnostic for Alzheimer's

- **First blood-based diagnostic test for Alzheimer's disease approved this year!**
  - Lumipulse G pTau217/ß-Amyloid 1-42 Plasma Ratio

Accurate, Early, Accessible Screening Tools

- Lumipulse G pTau217/ß-Amyloid 1-42 Plasma Ratio (BLOOD TEST)
  - 91.7% of individuals positive results had the presence of amyloid plaques by PET scan or CSF test result
  - 97.3 % of individuals with negative results had a negative amyloid PET scan or CSF test result.
- Genetic Screening
  - 23andMe PGS Genetic Health Risk Report for Late-onset Alzheimer Disease
    - Primarily screening for APOE4 (strongest risk factor for late-onset Alzheimer's)
    - Not a diagnostic test, but determines risk
    - Can also screen for familial, early-onset Alzheimer's

Where do therapeutics stand?



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- Symptomatic Therapies
- Disease-Modifying Therapies
- Preventative and Early Intervention
- **Anti-Aging Intervention Trials**
  - **Metformin**
  - **Rapamycin**
  - **Senolytics**

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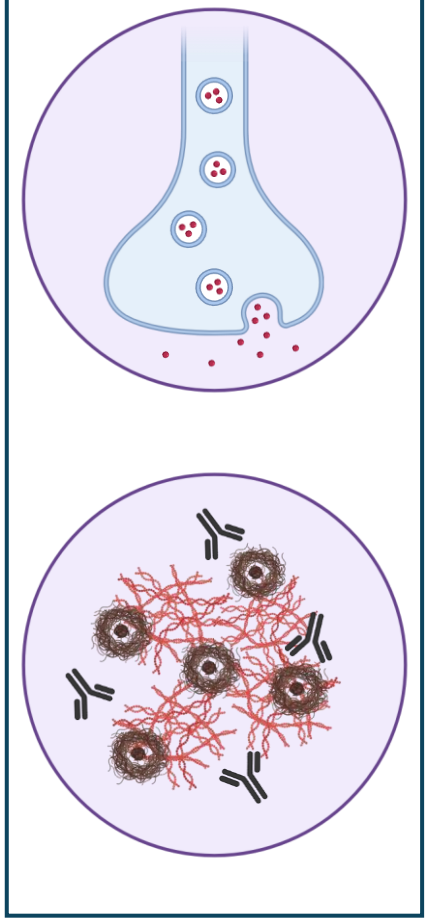

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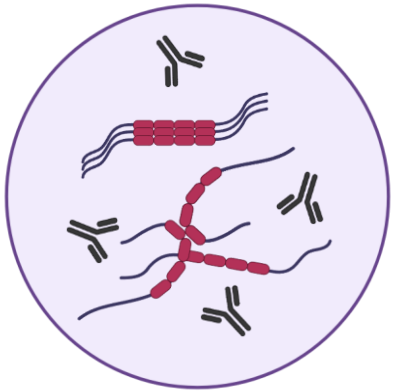

- Symptomatic Therapies
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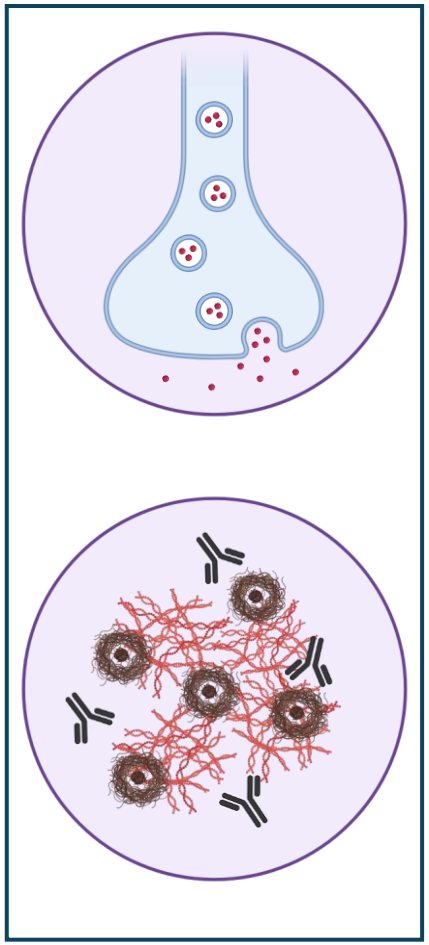
- Anti-Aging Intervention Trials
- **Tau-targeting Intervention Trials**

Where do therapeutics stand?



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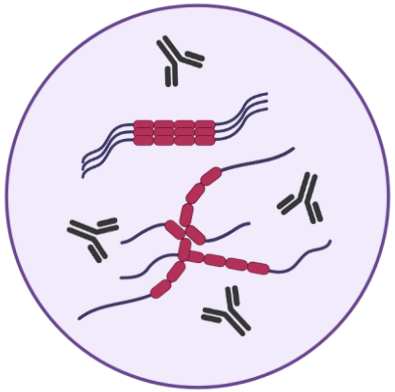

- Symptomatic Therapies
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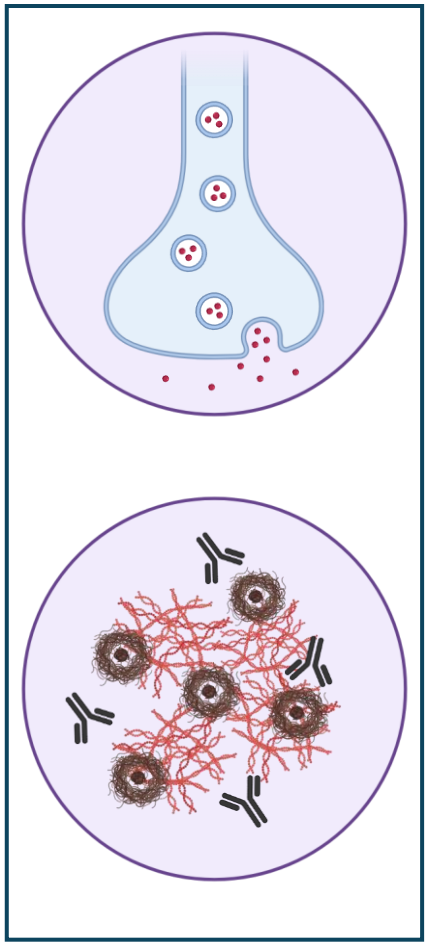
- **Lifestyle Interventions**

Where do therapeutics stand?



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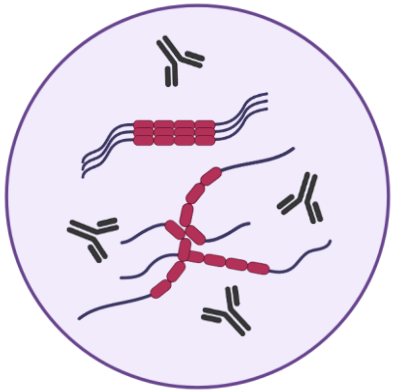

- Symptomatic Therapies
- Disease-Modifying Therapies
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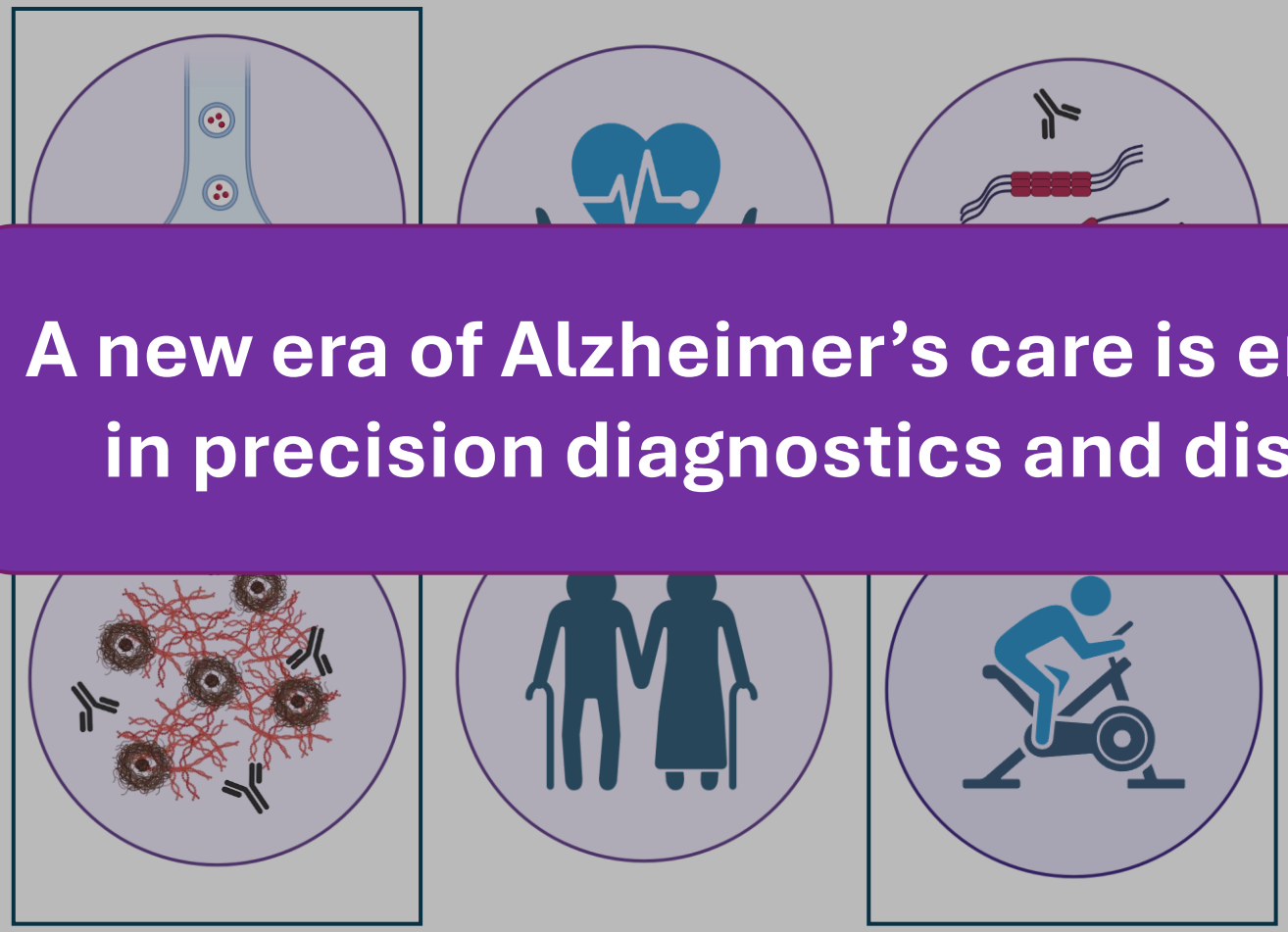
- Lifestyle Interventions
- **New & Exciting possibilities:**
  - **Cell based therapies**
  - **Gene therapies**

Where do therapeutics stand?



Approved

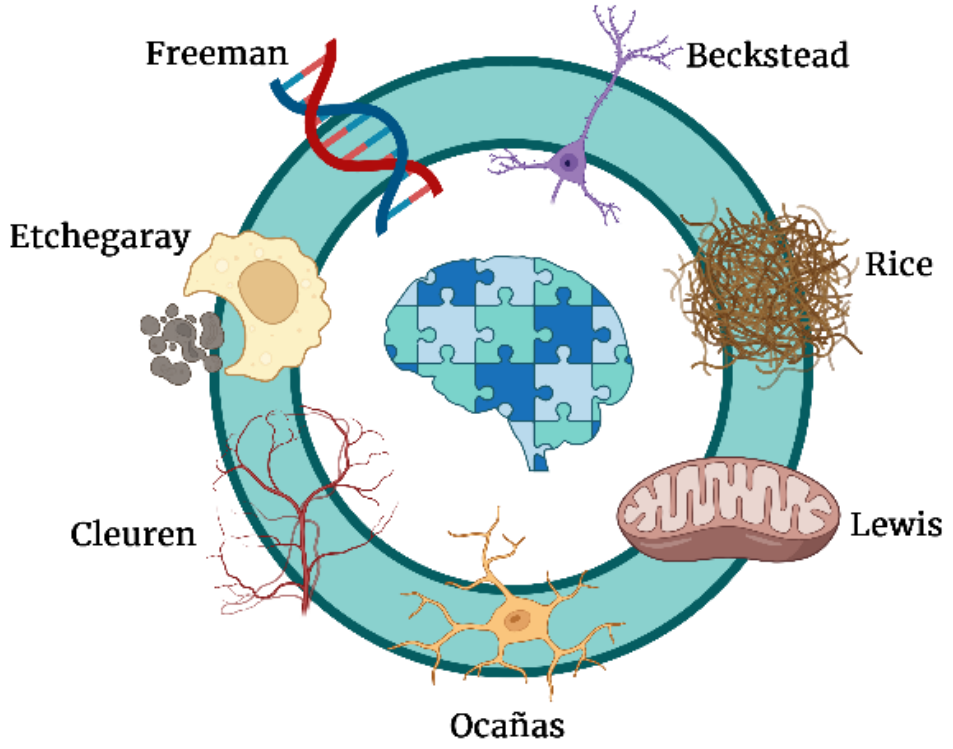
- Symptomatic Therapies
- Disease-Modifying Therapies
- Preventative and Early Intervention

A new era of Alzheimer's care is emerging, fueled by advances in precision diagnostics and disease-modifying therapies.

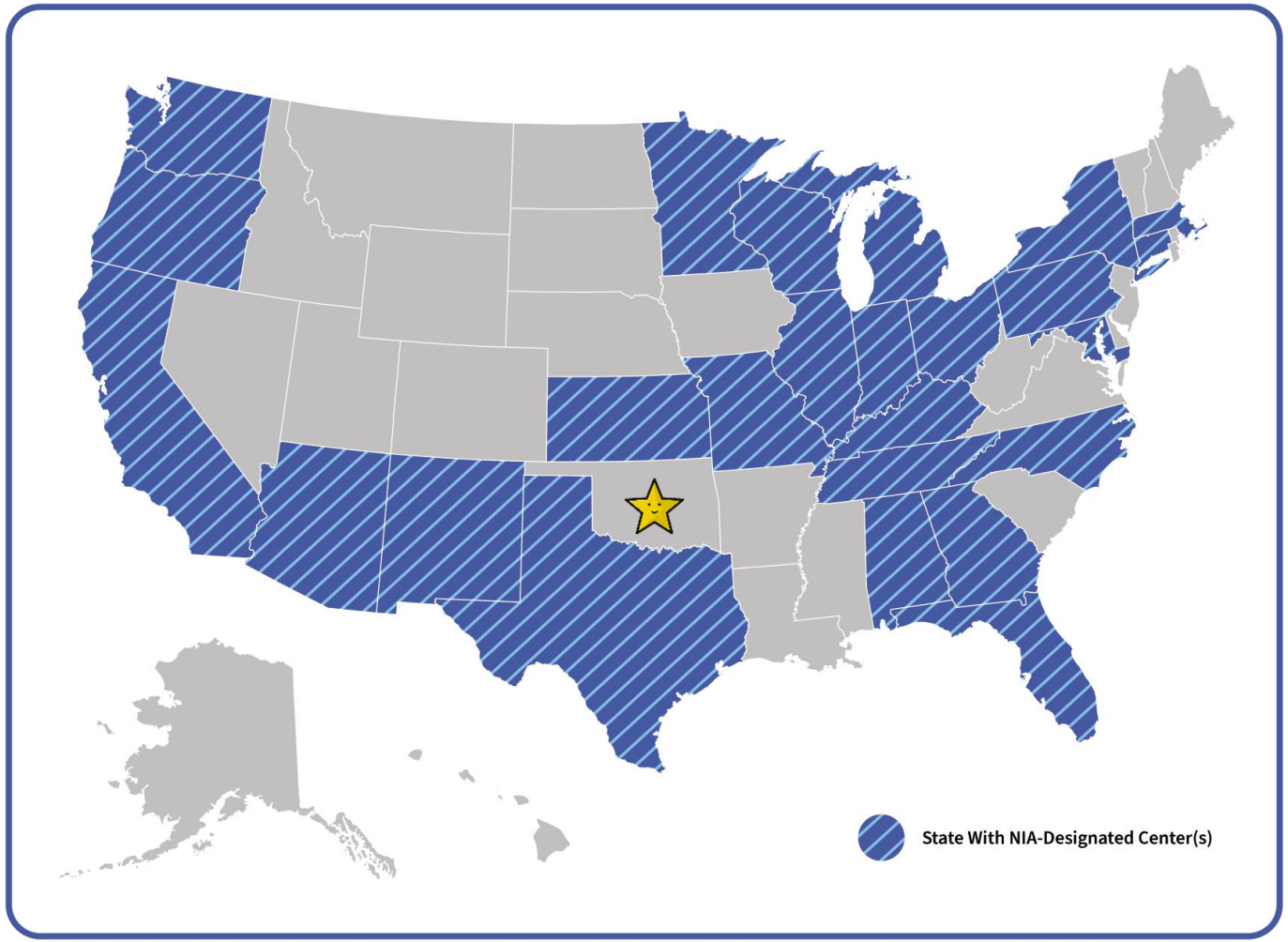
- **New & Exciting possibilities:**
  - **Cell based therapies**
  - **Gene therapies**

OMRF is on the forefront of Alzheimer's research

OMRF
Oklahoma Medical
Research Foundation



Goal for Future: NIH Alzheimer's Disease Research Center in Oklahoma



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Acknowledgments

Ocañas Lab

**Former Lab Member*

Jillian Cox
Sunghwan ‘Justin’ Ko
Sarai Badillo
Ewa Poljanska

Aldona Szewczyk
Lakshmi Birasam
Hana Kilani
**Alex Keck*
**Manu Thomas*
**Zsabre Wright*

Bill Freeman Lab
Dr. Ana Chucair-Elliott
Dr. Walker Hoolehan
Kevin Pham
Adeline Machalinski

Mike Stout Lab
Dr. Jose Isola
Dr. Subhasri Biswas
Chase Hubbart

Lindsay Hayes Lab
Abril Gamboa Gaona

Heather Rice Lab
Charles ‘Ike’ Lacy
Samah Houmam
Kriti Shukla

Core Facilities (OMRF)
Clinical Genomics Center
Imaging Core
Flow Cytometry Core
Center for Biomedical Data Sciences

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Presbyterian Health Foundation

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GLOBAL CONSORTIUM FOR REPRODUCTIVE LONGEVITY & EQUALITY

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