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TAKE-HOME MESSAGE



A simple tear test may enable identification of Alzheimer's disease risk decades before clinical diagnosis, providing an opportunity for preventative lifestyle interventions.



Non-invasive & Accessible
Tear fluid collection is simple, painless and suitable for large-scale screening



Early Detection in Midlife (40+ years)
Mature miRNA panel can detect risk even before noticeable symptoms appear



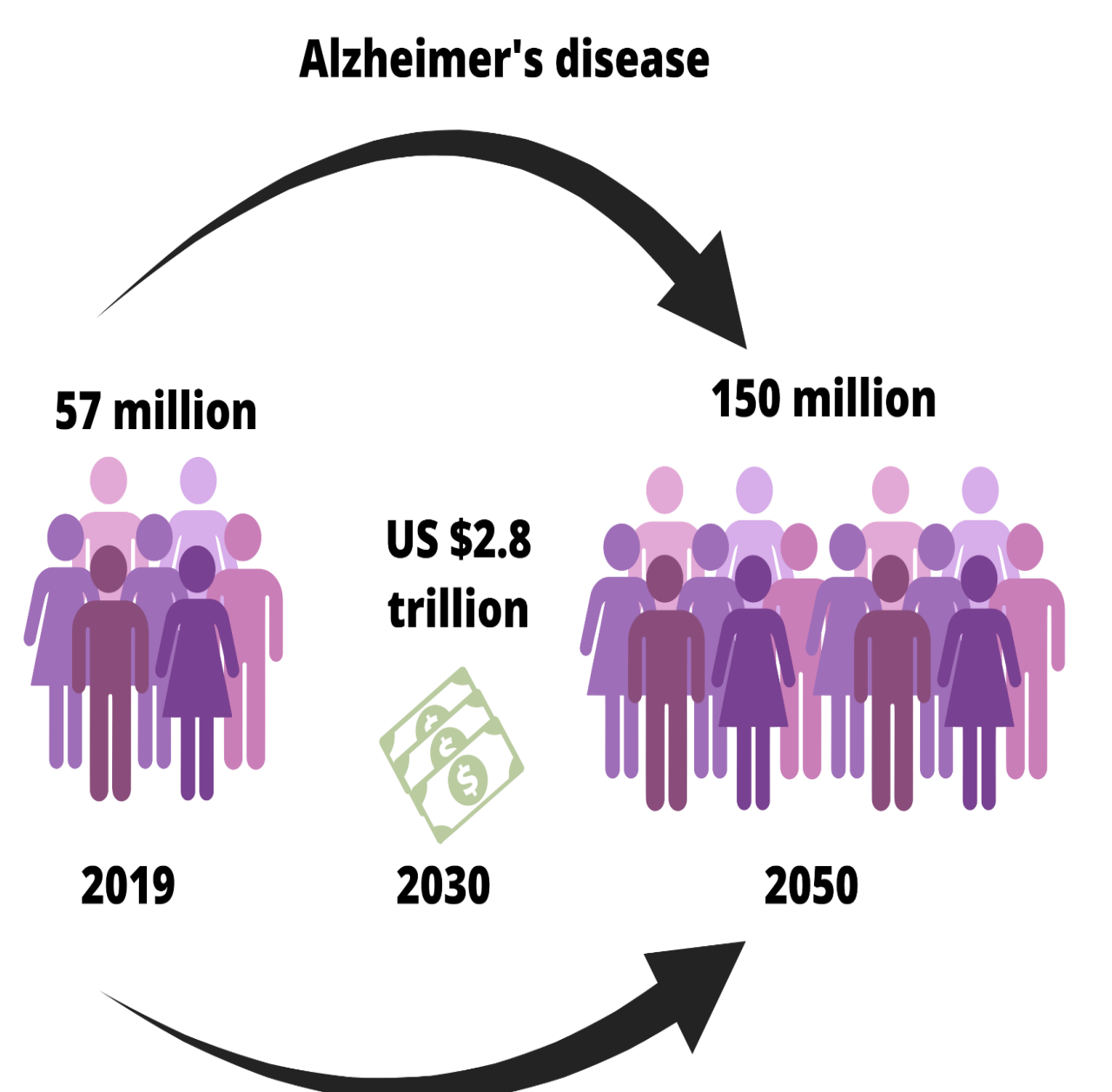
Enables Timely Preventative Strategies
Early risk identification empowers individuals to adopt healthy habits and reduce future risk



EARLY KNOWLEDGE TODAY, BETTER BRAIN HEALTH TOMORROW

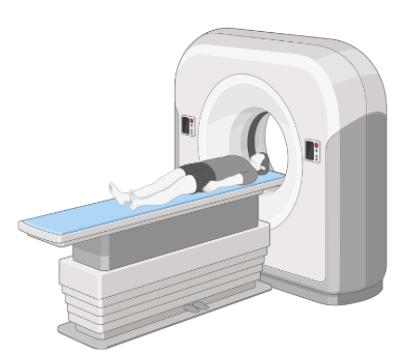
A non-invasive tear miRNA test to identify Alzheimer's risk early and guide a healthier, longer life.

Background



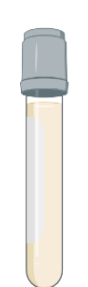
Major concerns associated with current diagnostic tools

PET Scan



- Expense & Availability
- Radiation Exposure

CSF biomarkers



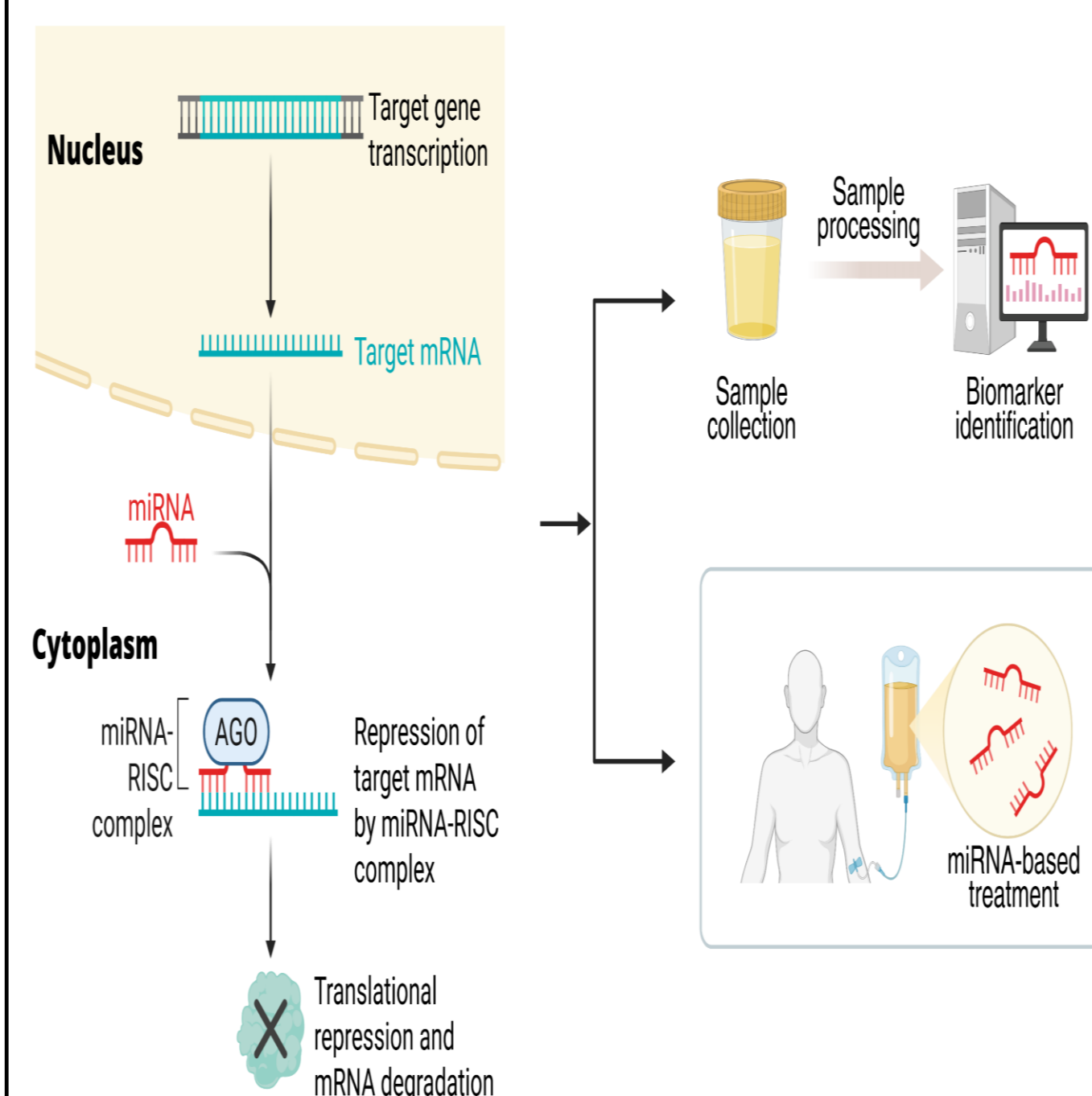
- Highly invasive
- Generally expensive
- Lack of uniform cut-off values
- Handling protocols

Plasma biomarkers

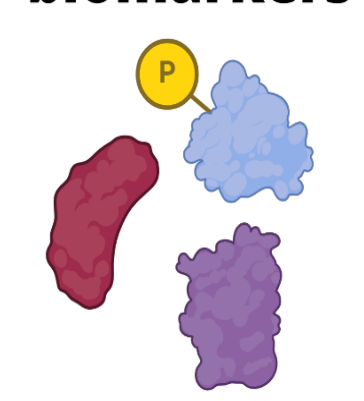


- Universal body fluid
- Confounding physiological and biological factors
- Lack of standardized thresholds

MicroRNAs

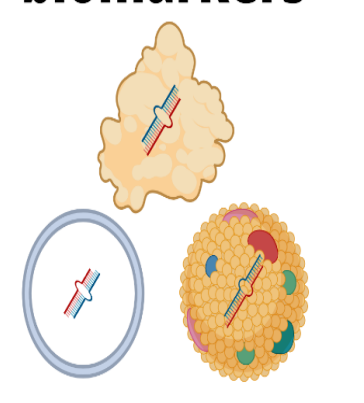


Protein biomarkers



- Structurally vulnerable to denaturation due to
 - pH changes
 - Clearance mechanisms
 - Circulating proteases
- Abnormal downstream accumulation - late mechanism

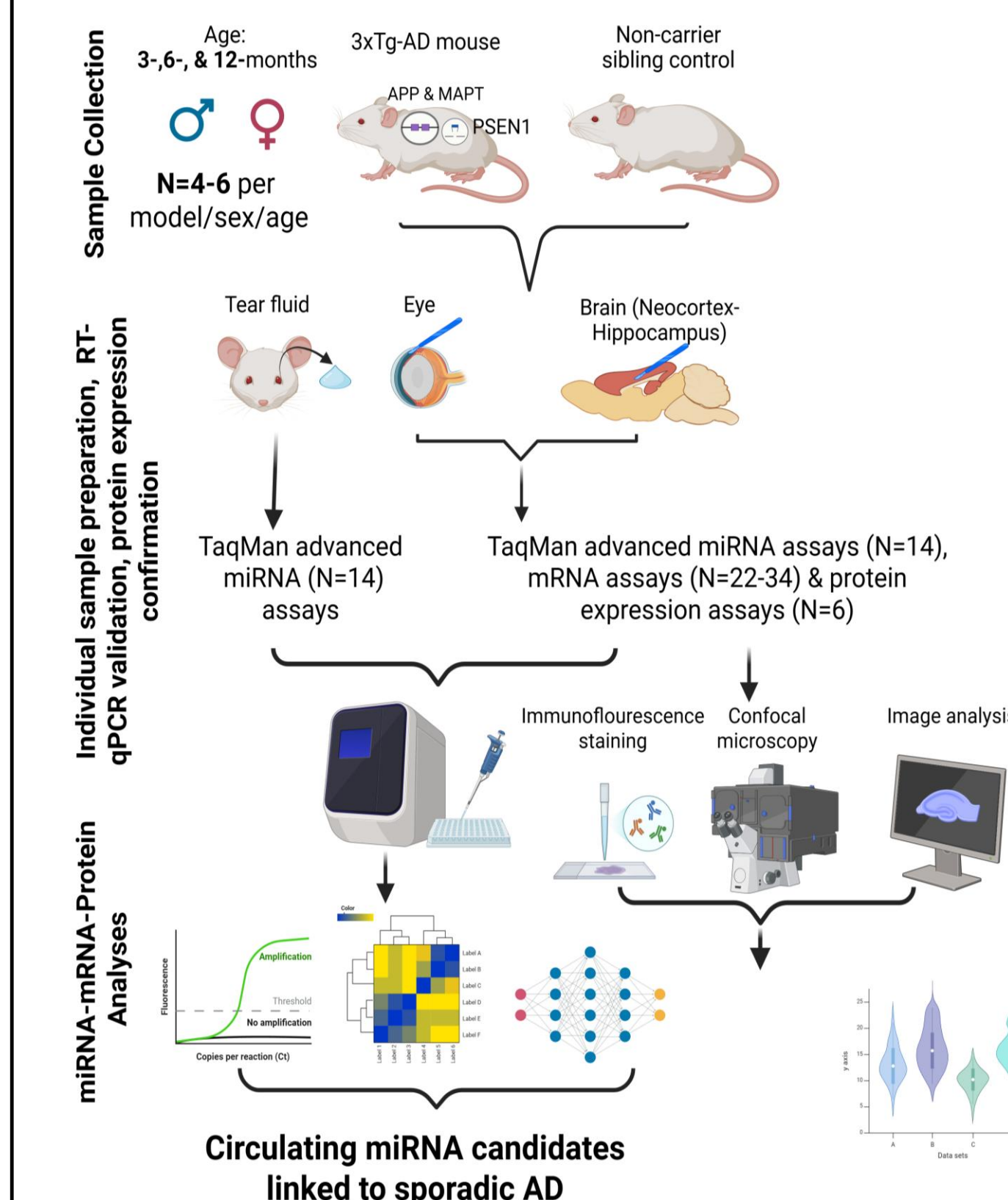
MicroRNA biomarkers



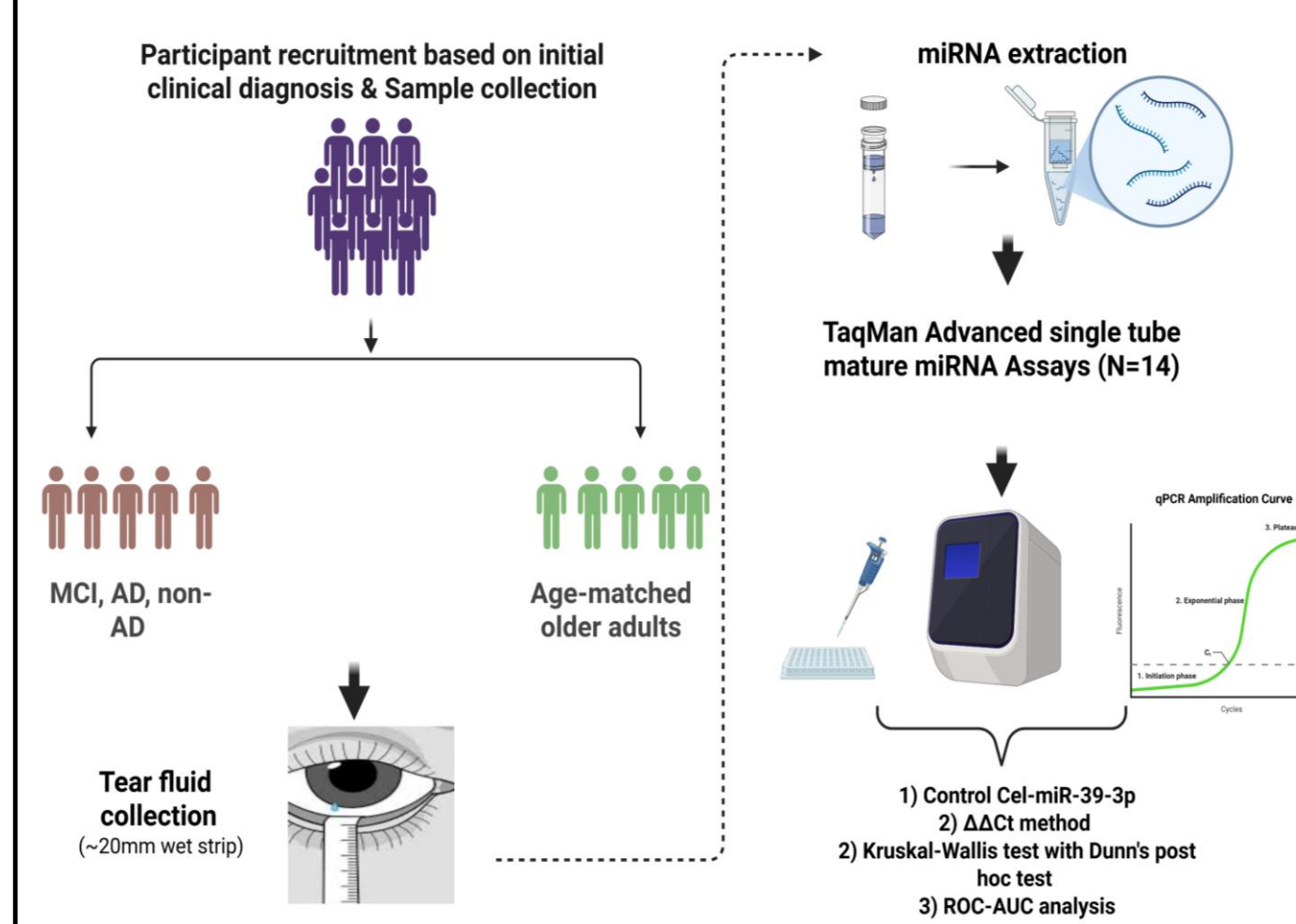
- Highly stable in the extracellular environment as they are
 - bound to protective RNA-binding proteins (AGO-2) or HDL
 - Encapsulated within the EVs
- Abnormal upstream dysregulation - early mechanism

Methods

Aim 1: Preclinical studies

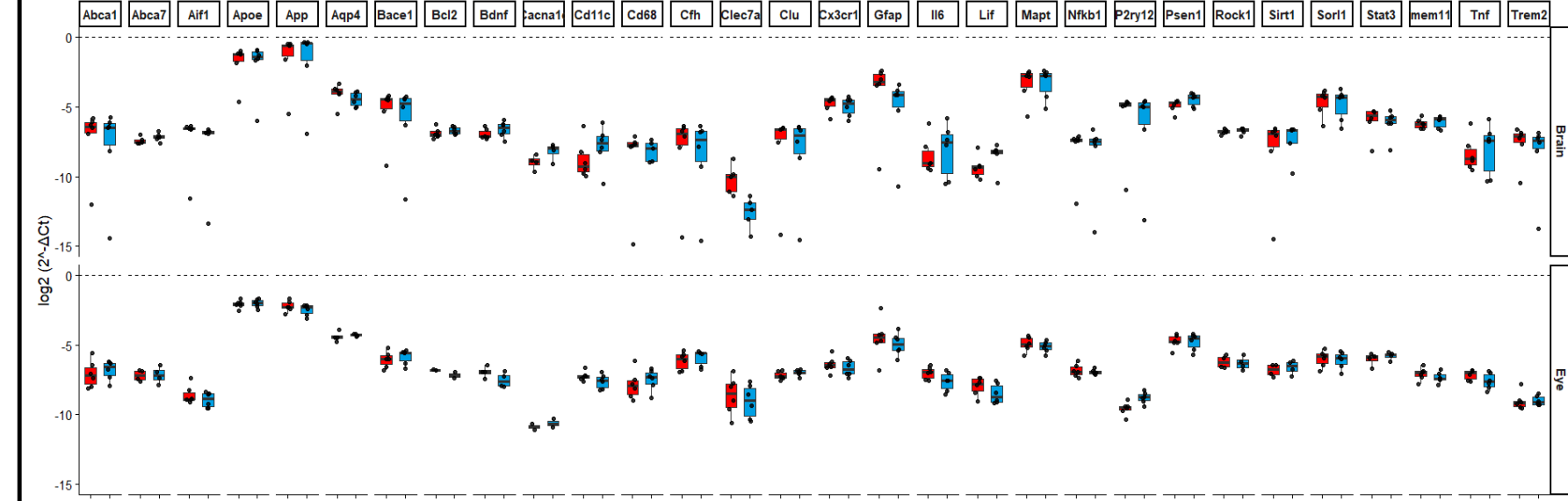


Aim 2: Clinical translation



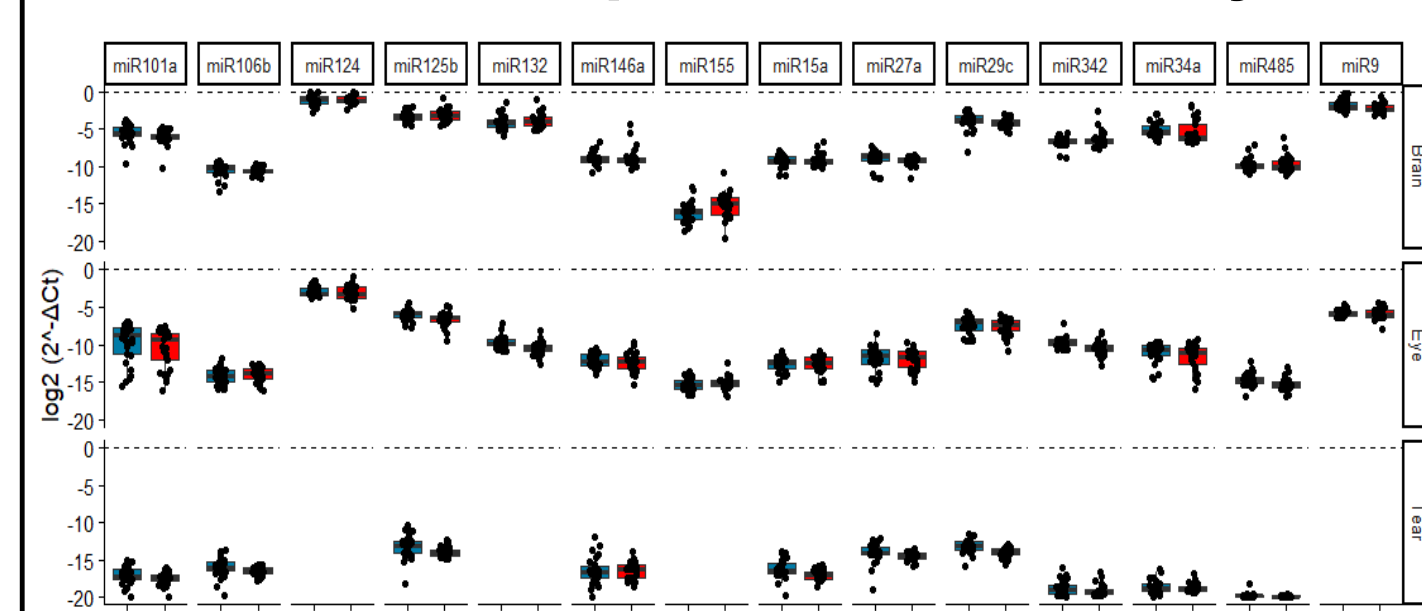
Results

1. Gene expression: Brain-Eye axis

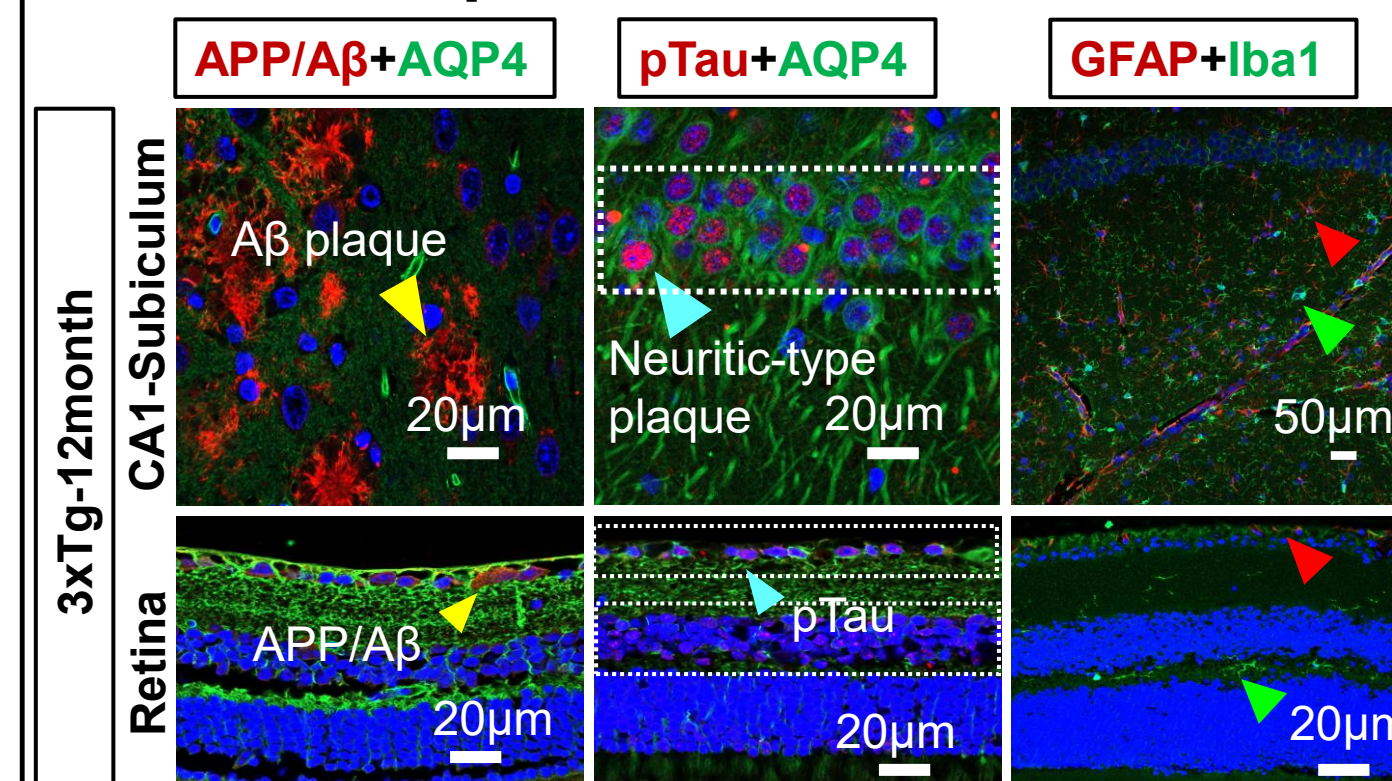


❖ **Transcript alignment** - AD and immune genes remained strongly concordant across brain and eye.

2. MicroRNA expression: Brain-Eye-Tear axis



3. Hallmark proteins: Brain- Retina axis

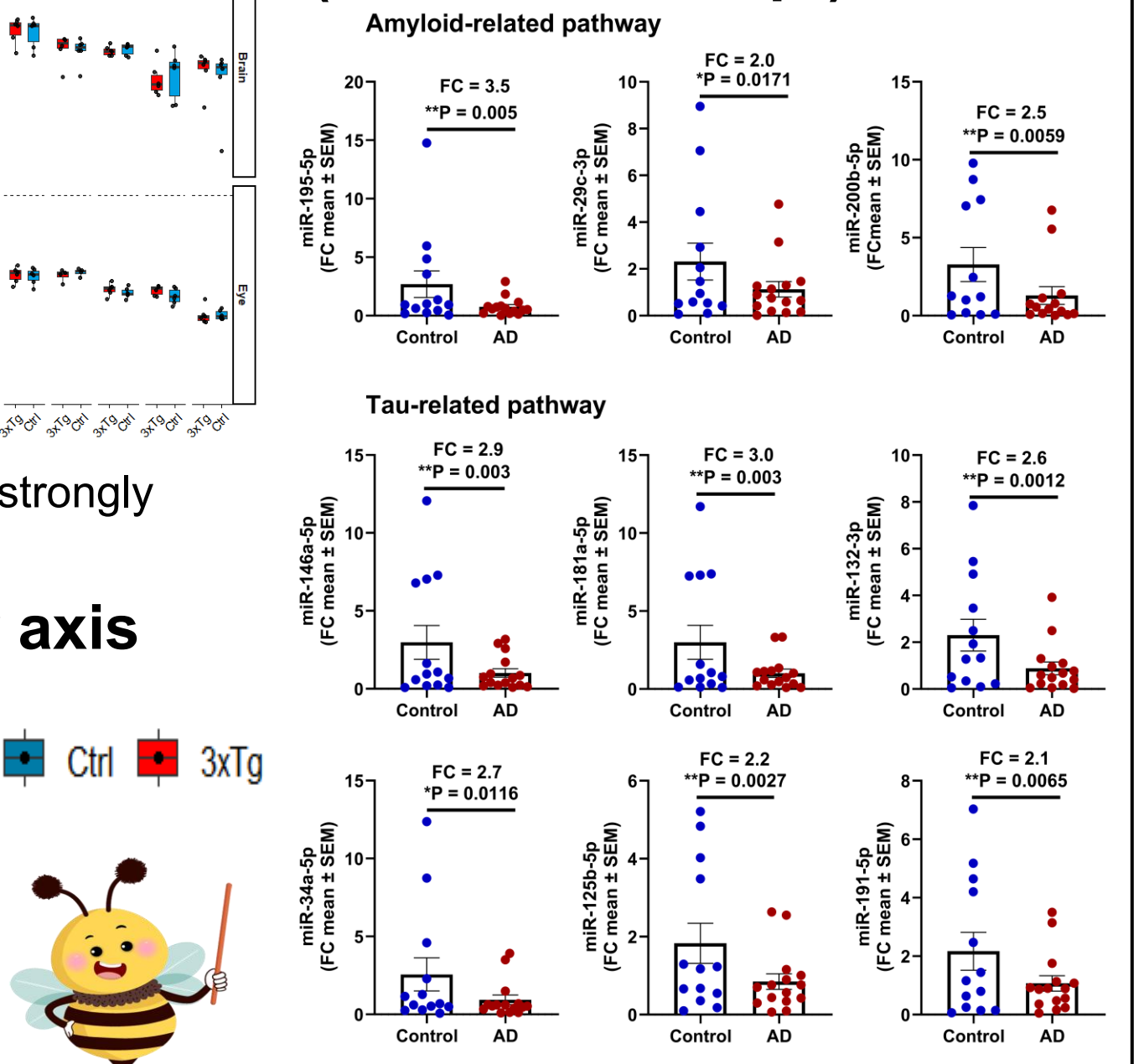


❖ **Amyloid coupling** - APP/Aβ increased in brain and retina with strong mid-/late-stage cross-tissue links.

❖ **Tau divergence** - pTau separated early between brain and retina, later becoming brain-dominant.

❖ **Inflammatory drift** - Early Iba1/GFAP coupling weakened with age.

4. Tear miRNAs - Clinical validation (Proof of concept)



Conclusions

- ❖ **miRNA patterning:** Conserved miRNA structure across brain-eye-tear, with brain-tear most similar.
- ❖ **Tear miRNAs:** miRNAs decreased in CSF-positive AD, forming a strong tear-based classifier.
- ❖ **Overall:** Early brain-eye-tear coupling gives way to divergence; retina reflects CNS pathology, and tear miRNAs show biomarker promise.

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