



4th Commonwealth Chemistry Posters

H₂S-releasing peptide frameworks: a multifaceted therapeutic approach to Alzheimer's disease

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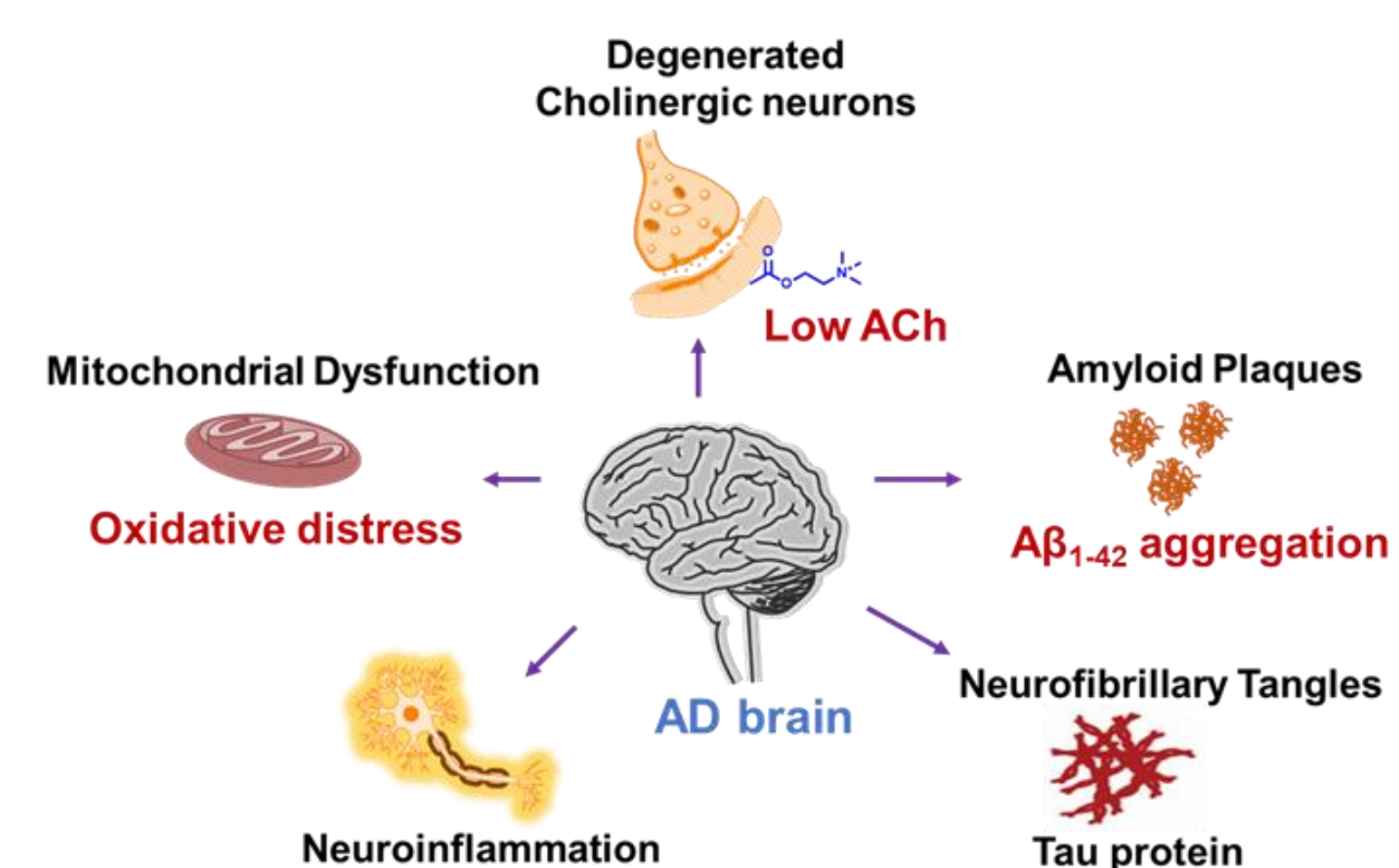
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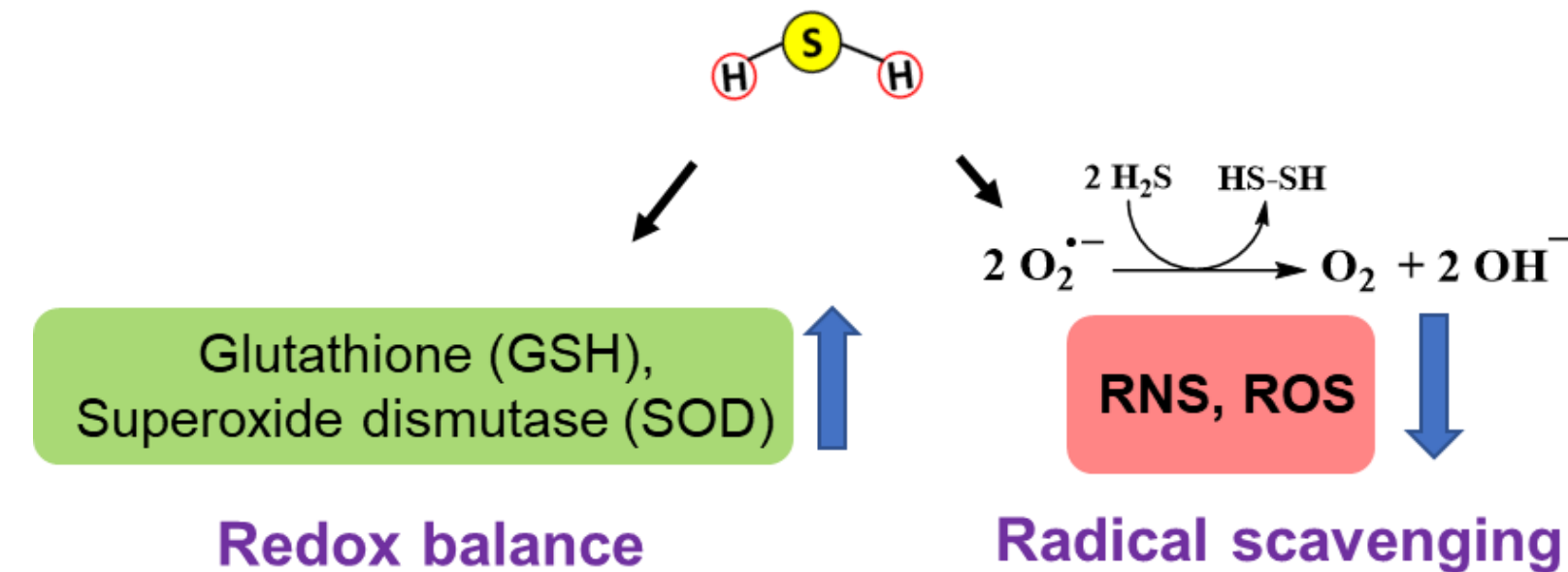


Alzheimer's: a multifactorial disease

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that slowly destroys memory and thinking skills. Generally incurable due to its multifactorial nature.

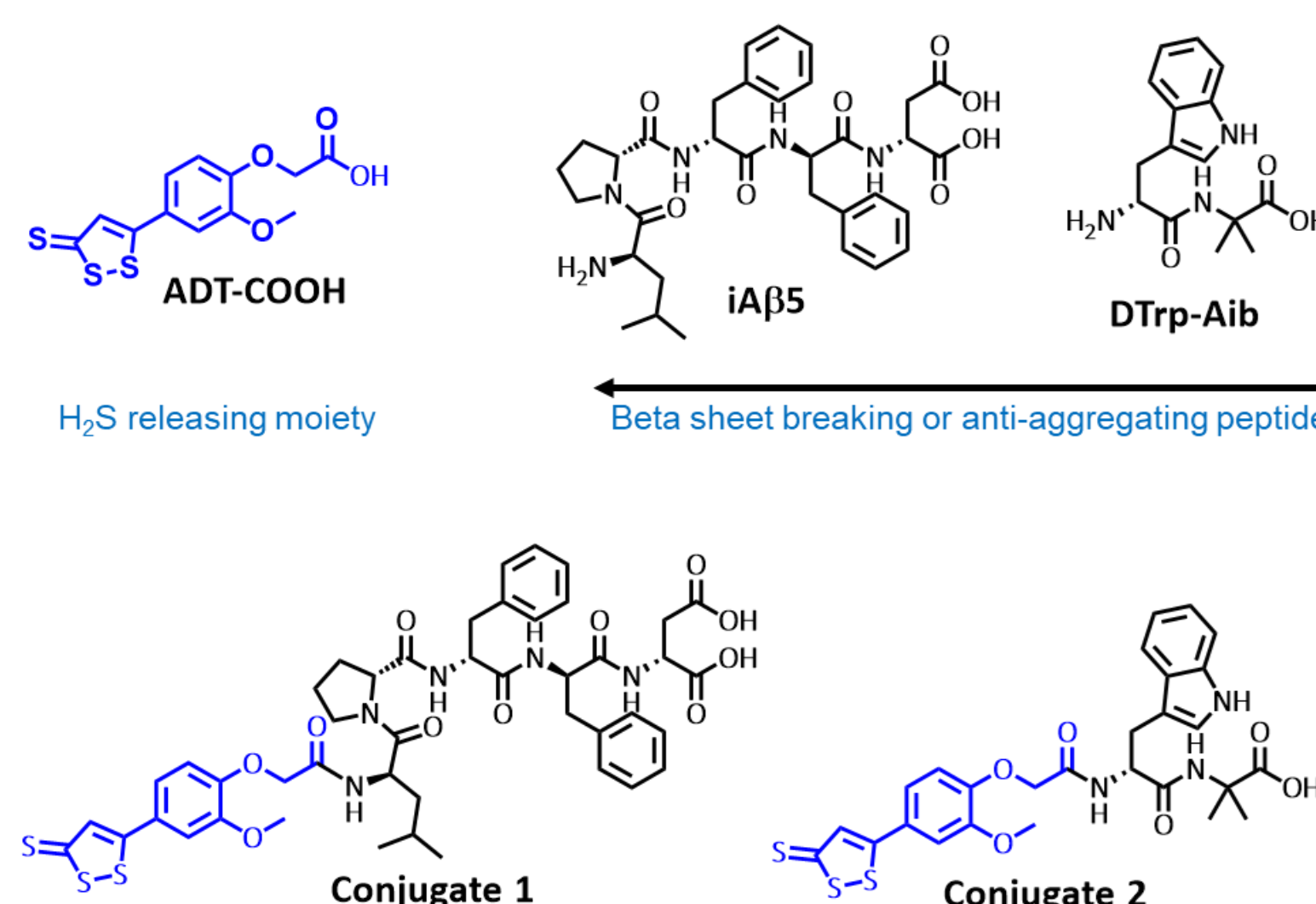


H₂S: an important player in AD



- H₂S display **antioxidant** and **neuroprotective** properties in human body.
- Low concentration of H₂S in AD patients.

H₂S releasing peptides: Design



Peptide Self assembly

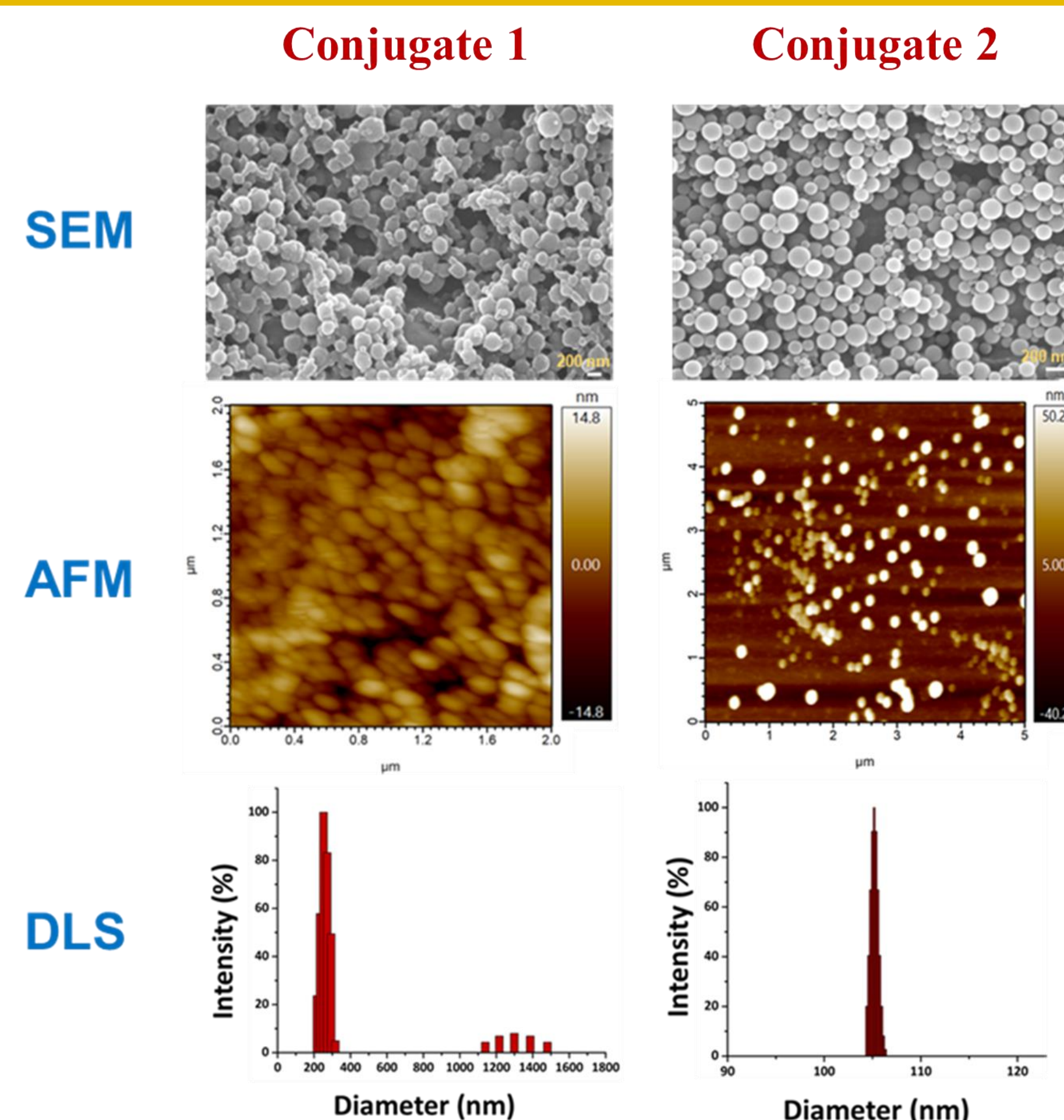


Figure 1: Self-assembly of peptide conjugates (100 μM) in aqueous solution

H₂S release kinetics

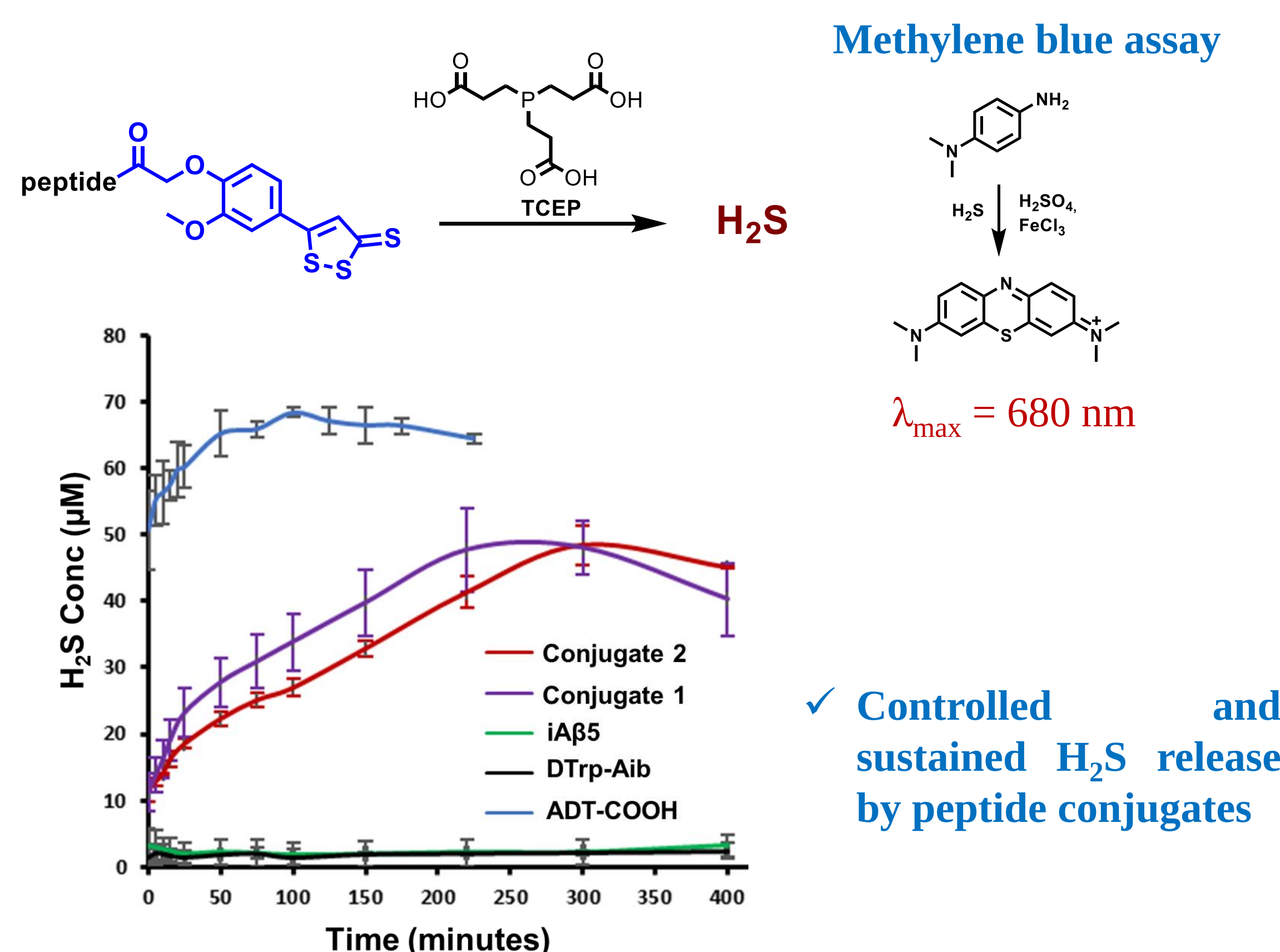


Figure 2: H₂S releasing kinetics of peptide conjugates (100 μM) on co-incubation with TCEP (1 mM) at 37 °C

Averting Aβ₁₋₄₂ aggregation

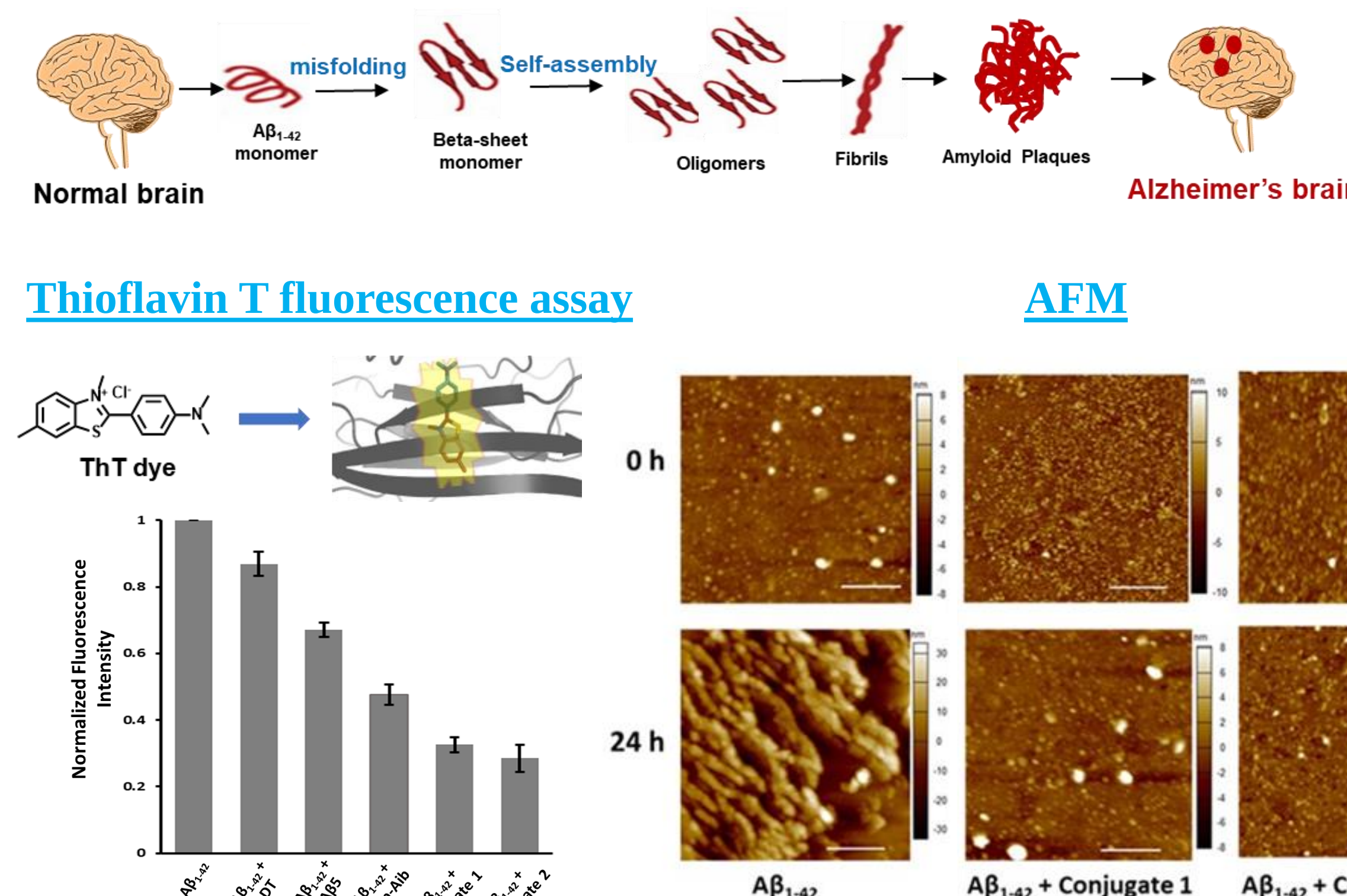


Figure 3: ThT assay showing Aβ₁₋₄₂ (10 μM) aggregation and their inhibition by peptide conjugates (10 μM) on 24 h incubation at 37 °C

Figure: AFM images of incubated Aβ₁₋₄₂ alone and in presence of peptide conjugates at 37 °C after 0 h and 24 h time intervals. Scale bar = 500 nm

H₂S delivery inside *C. elegans*

- We use *C. elegans* as an in-vivo system for our study.
- Have cytochrome P450 genes as well as NADPH/NADP⁺ machinery, thus providing suitable conditions required for H₂S release from these conjugates

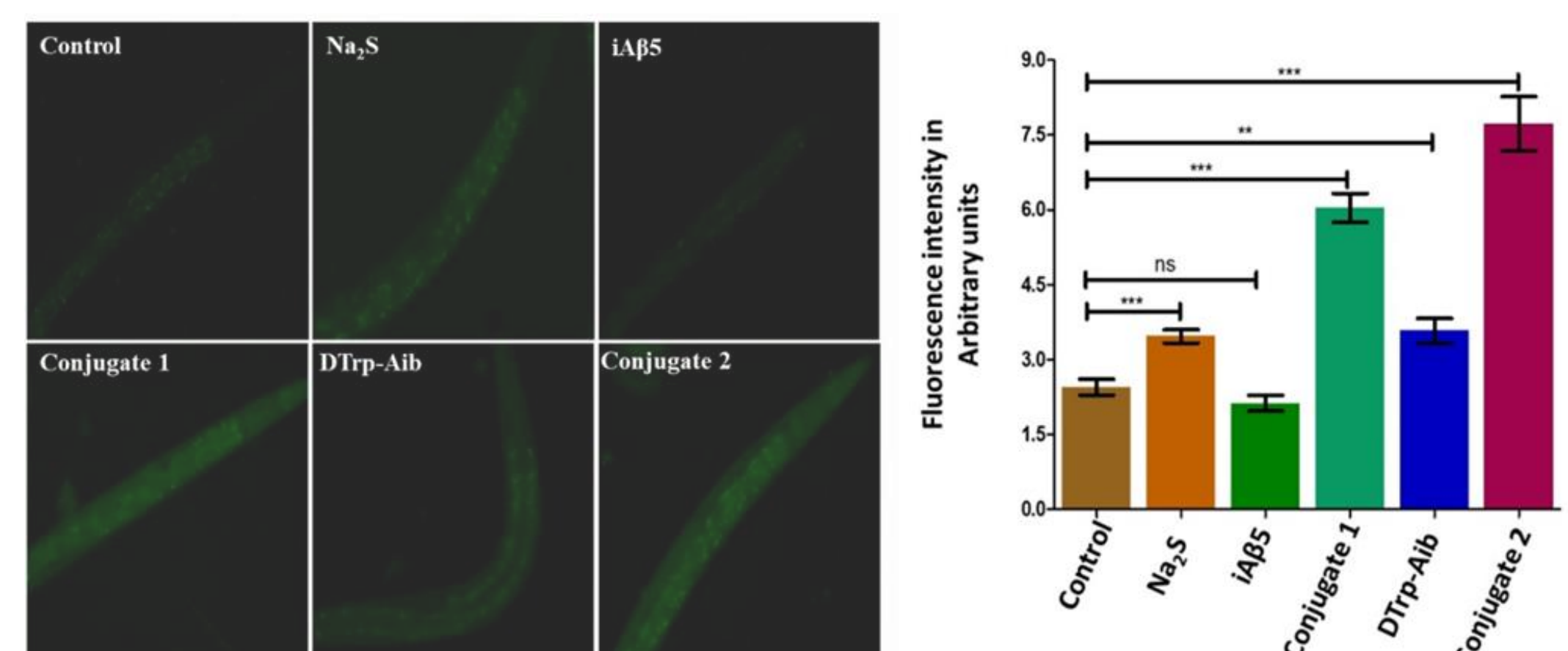
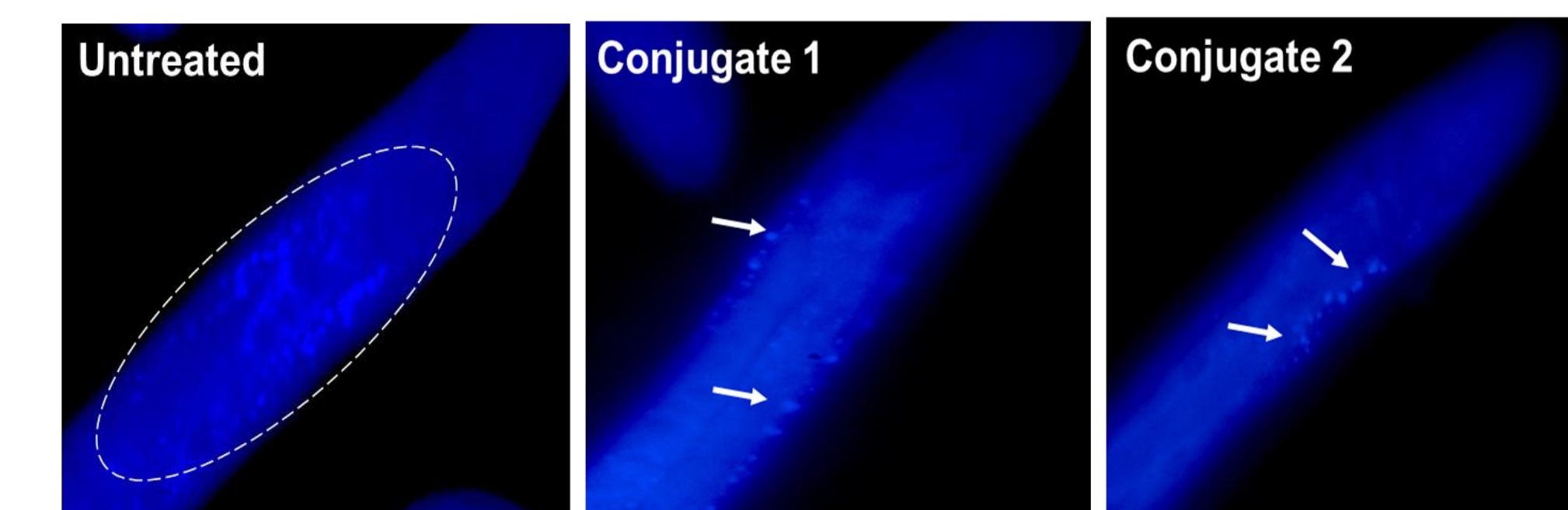


Figure 4: Fluorescent micrographs of the *C. elegans* N2 strain (wild type) showing the delivery of H₂S inside the worm by the peptide conjugates as detected via the AzMC dye.

Inhibit Aβ₁₋₄₂ fibrillation in *C. elegans*



Decreases ROS and increases in *C. elegans*

- High level of ROS in AD.
- Irreversible damages to biomolecules (Lipid peroxidation, protein carbonylation, nucleobase hydroxylation).



Reactive oxygen species (ROS)

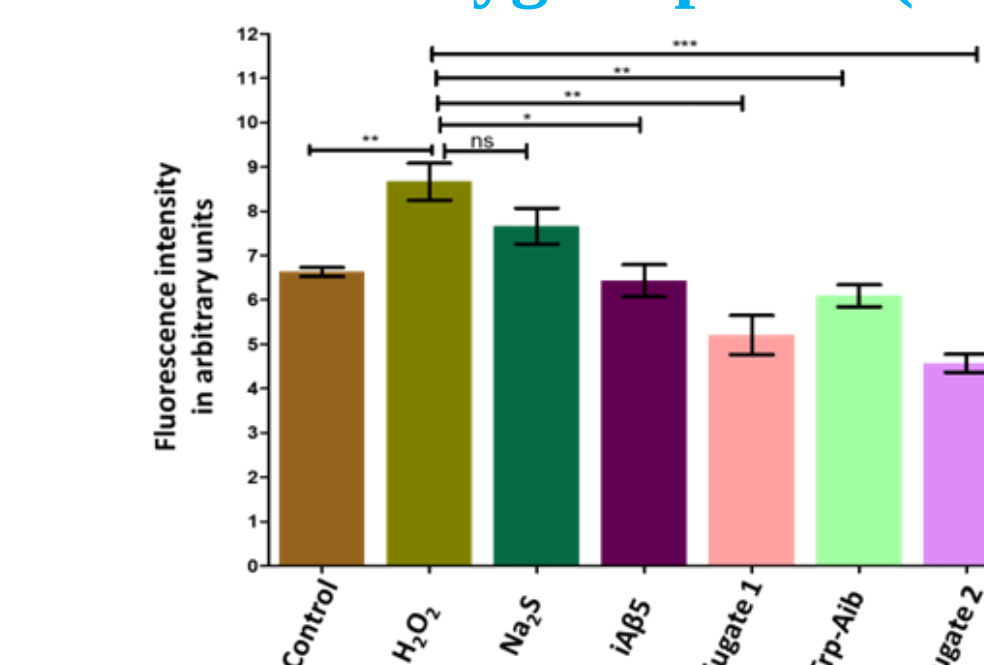


Figure 5: ROS estimation using the DCFDA assay in the N2 strain of *C. elegans*.

Significant increase in Acetylcholine in *C. elegans*

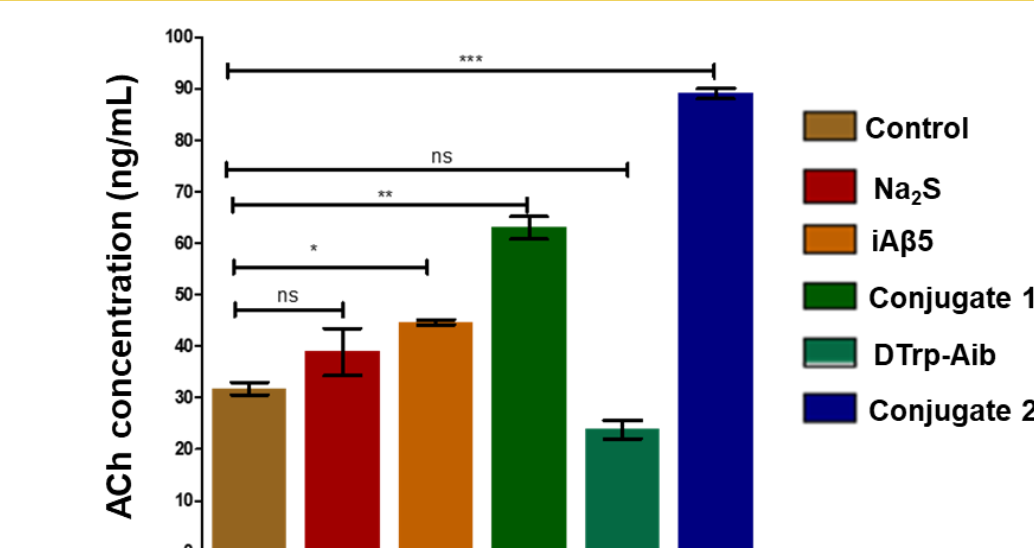
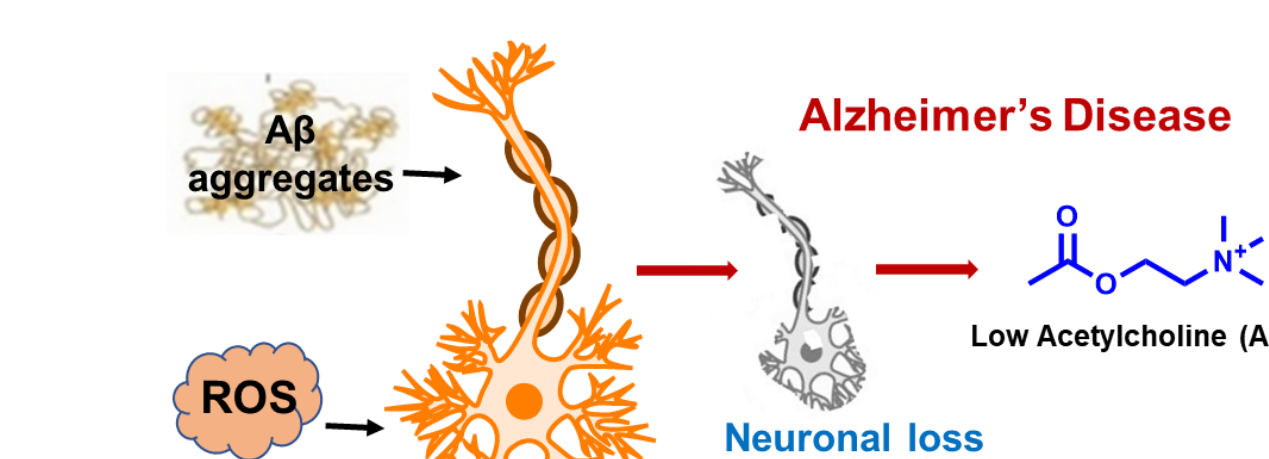
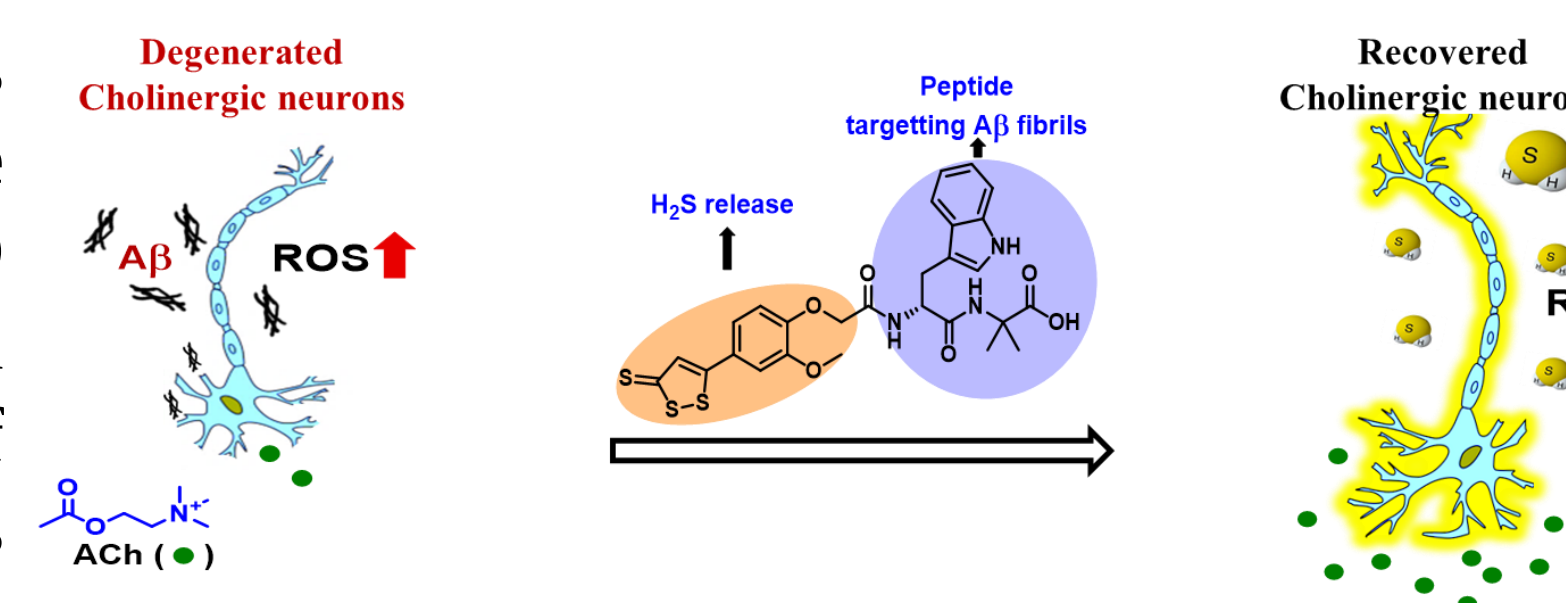


Figure 6: Estimation of ACh levels in the transgenic CL2006 strain of *C. elegans* (expressing human Aβ₁₋₄₂ peptide) via LC/MS-MS. The number of worms in each set is 3000.

Conclusions

This newly developed class of peptide conjugates ameliorates the **multiple factors** associated with AD and may play a beneficial role in the development of new therapeutics for this debilitating ailment.



References

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- Ali, R.; Pal, H.A.; Hameed, R.; Nazir, A.; Verma, S. ChemComm. 2019, 55, 10142–10145.