# Rhodanine Linker Compounds for Inhibiting IAPP, $\alpha$ Synuclein, and Tau Aggregation with Fluorescent Probing of IAPP Fibrils

Rhodanine derivatives both inhibit amyloid aggregation and fluoresce upon IAPP binding for diagnostics.

Alzheimer's Disease (AD) and Parkinson's Disease (PD) are the most prevalent neurodegenerative disorders characterized by continuous loss of functional neurons. Researchers at Purdue University have discovered a method by using rhodanine-based compounds that are designed and synthesized to target the oligomers and protofibrils related to neurodegenerative disease. The early-stage oligomers and protofibrils of tau are believed to be strongly linked to human cognitive impairment while the toxic  $\alpha$ -syn oligomers are associated with behavioral motor deficits. With this technology, concurrent targeting of both proteinaceous aggregates and their lower dense oligomers can be possible, which is believed to have great potential towards AD and PD therapeutics.

These rhodanines fluorescence upon binding with islet amyloid polypeptide (IAPP) fibrils. In addition, these rhodanines slow down the aggregation of IAPP. IAPP aggregate in the pancreas of type 2 diabetes in humans and cats. IAPP aggregates contribute to the progression of the disease. These rhodanines will be developed further for application in diagnostic of amyloidosis in cats and humans associated with type 2 diabetes.

## **Technology Validation:**

The indole-containing rhodanines 5l and 5r displayed significantly high antiaggregation activity towards  $\alpha$ -syn fibrils by reduction of the thioflavin-T (ThT) fluorescence to lower than 5%.

In the presence of IAPP aggregates, 5I demonstrated fluorescence enhancement. Fluorescence enhancement was not observed with 5I treated  $\alpha$ -syn and tau aggregates.

### **Technology ID**

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### Advantages:

- -Concurrent targeting of both proteinaceous aggregates and their lower dense oligomers
- -Can be used as an imaging agent as well

# Applications:

- -Alzheimer's Disease
- -Parkinson's Disease
- -Neurodegenerative disorders
- -Inhibit alpha-synuclein (α-syn) protein fibril formation
- -Inhibit tau 2N4R oligomer formation
- -Inhibit Aβ-plaques or their density
- -Inhibit Islet amyloid polypeptide (IAPP) fibril formation
- -Pancreatic amyloidosis diagnosis
- -Detection of islet amyloid polypeptides which indicate pancreatic amyloidosis

# Publication:

Exploring the rhodanine universe: Design and synthesis of fluorescent rhodanine-based derivatives as anti-fibrillar and anti-oligomer agents against  $\alpha$ -synuclein and 2N4R tau

https://www.sciencedirect.com/science/article/pii/S0968089624004048

**TRL:** Pharmaceuticals

# **Intellectual Property:**

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PCT-Patent, 2025-08-21, WO

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