

# Development of a safe and efficient near-infrared diagnostic method for Alzheimer's disease

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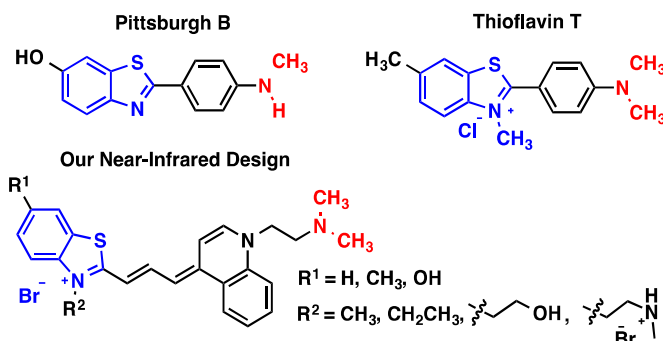
## Introduction

Alzheimer's Disease (AD) is an extremely debilitating neurodegenerative disease that causes progressive and substantial memory loss, as well as the loss of other necessary cognitive functions. Despite recent advances in medicine that have led to the decrease in death from several other diseases, the death toll for Alzheimer's continues to rise at an alarming rate. Researches currently consider the pathological trademark of AD to be the extracellular aggregation of Amyloid- $\beta$  peptides and intracellular neurofibrillary tangles in the human brain. The clinical demand for safe and efficient brain imaging capabilities continues to unfold, and in response, we report the synthesis of various unsymmetrical fluorophores that show strong potential for being used as tools to successfully diagnose AD. We have taken the current industry standards for AD diagnostics, Pittsburgh-B and Thioflavin T, and modified them such that they exhibit near-infrared fluorescence capabilities as opposed to the current methods that require PET imaging and emit harmful ionizing radiation.

**Key words:** Alzheimer's, near-infrared, Amyloid- $\beta$  peptides, intracellular neurofibrillary tangles, fluorescence, organic chemistry.

## Method

The primary backbone of these compounds is a substituted benzothiazole (Figure 1). To achieve NIR fluorescence capabilities, we utilized various systems of conjugation bridging a dimethylamino substituent with the benzothiazole core using phenyl, thiophene (data not shown here), and 4-methylquinoline (Figure 1). The compounds were injected into CD-1 mice and imaged using the FLARE imaging system to determine their localization and excretion patterns.



**Figure 1:** Pittsburgh B and Thioflavin T (top left and right respectively). Our proposed synthetic design of a NIR compound modified based on Pittsburgh B and Thioflavin T design (Bottom)

## Results

The proposed compounds were successfully synthesized and purified as determined by UV spectrophotometry, <sup>13</sup>C and <sup>1</sup>H NMR, HPLC and mass spectrometry. As research progresses, additional compounds with a wide array of substituents will be synthesized based on biological feedback.

## Discussion/Conclusion

As the harsh effects of Alzheimer's continue to take its toll, the need for a method of diagnosis becomes of the utmost importance. Unsymmetrical fluorophores derived from benzothiazole analogs have been successfully synthesized and show great promise in initial biological studies. In the future, our collaborators at Beth Israel Deaconess Medical Center at Harvard Medical School will test their efficacy in both *in vitro* and *in vivo* animal models.