

Development of a Clickable Probe for Imaging Hydrogen Peroxide in the Bilayer

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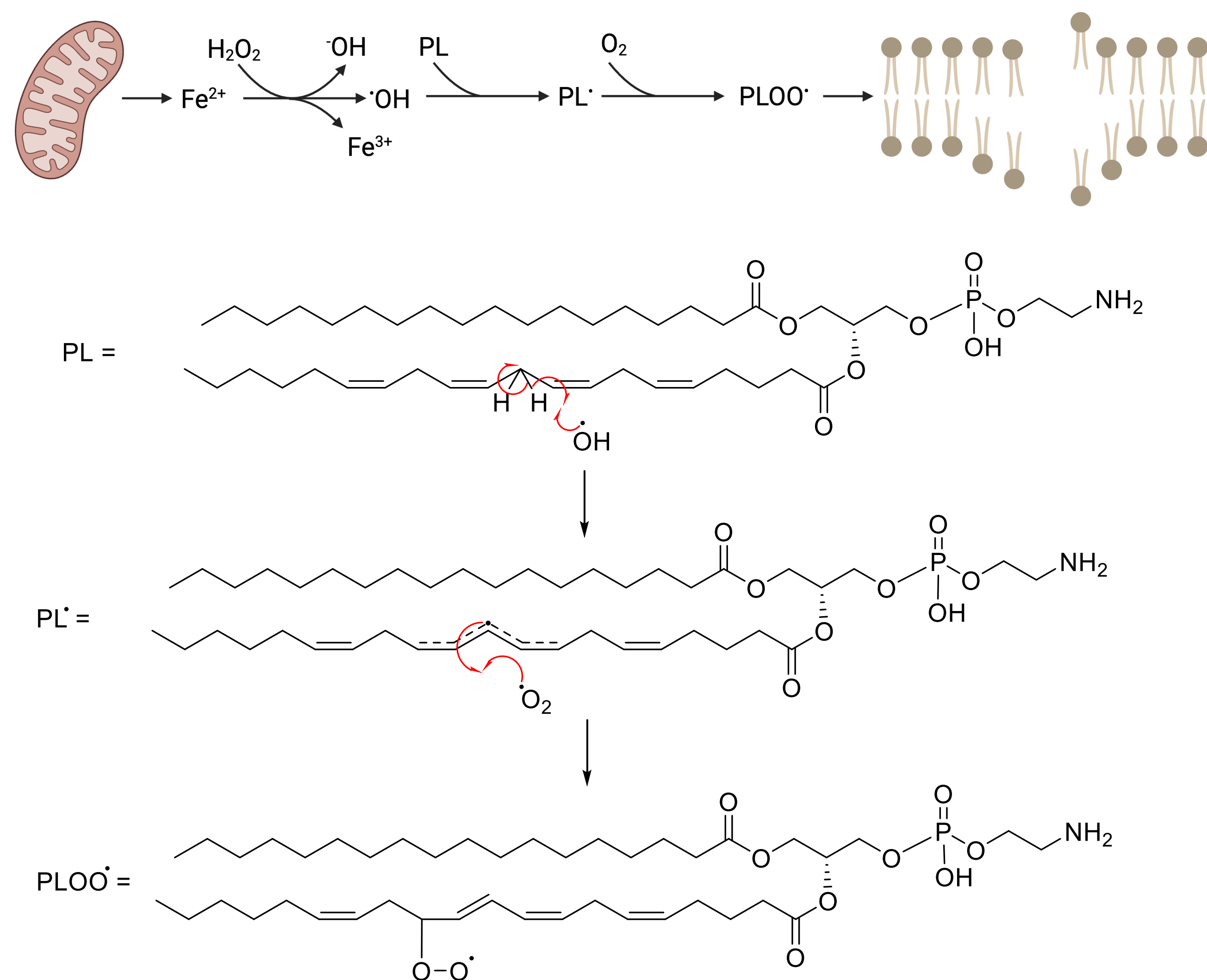
Background

Ferroptosis is a complex and regulated form of cell death. Ferroptosis is triggered when reactive oxygen species (ROS) react with iron released from mitochondria.

- During ferroptosis, phospholipids are destroyed, resulting in membrane damage and cell death.

Ferroptosis may play a role in diseases like **Dementia, Alzheimer's, and cancers**, opening doorways for further investigation of treatments.

Despite its importance to cellular and organismal health, **ferroptosis isn't well understood**, and more investigation is needed to understand the role of membranes in this form of cell death.



Project Introduction

This project aims to synthesize compounds to attach an H_2O_2 sensor to the inside of lipid membranes to **visualize the effects of ferroptosis**.

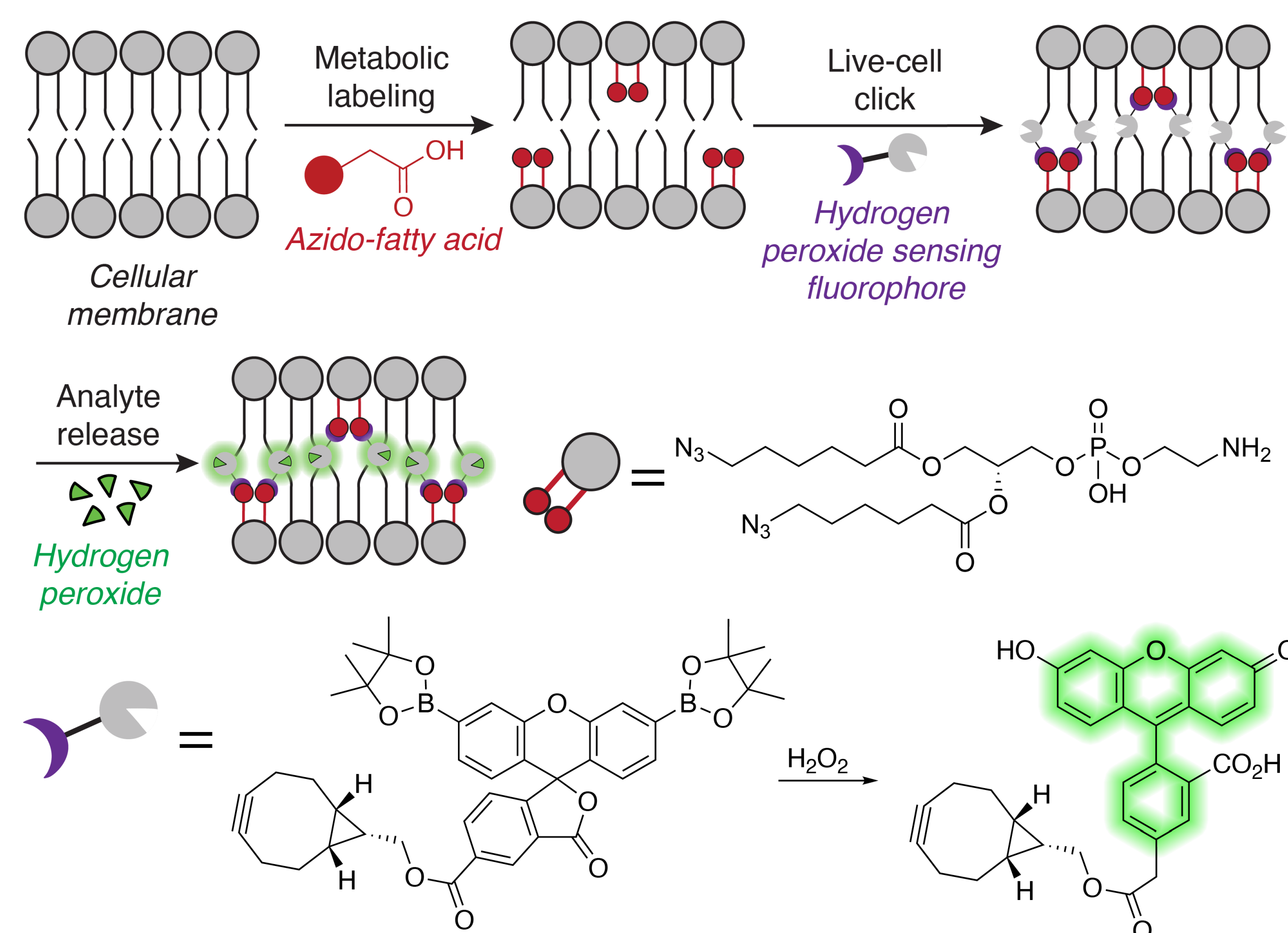
Goal: Investigate the role of membranes in ferroptosis by visualizing membranes when hydrogen peroxide is produced.

Aim 1: Synthesize molecules that can anchor a fluorophore inside of membranes.

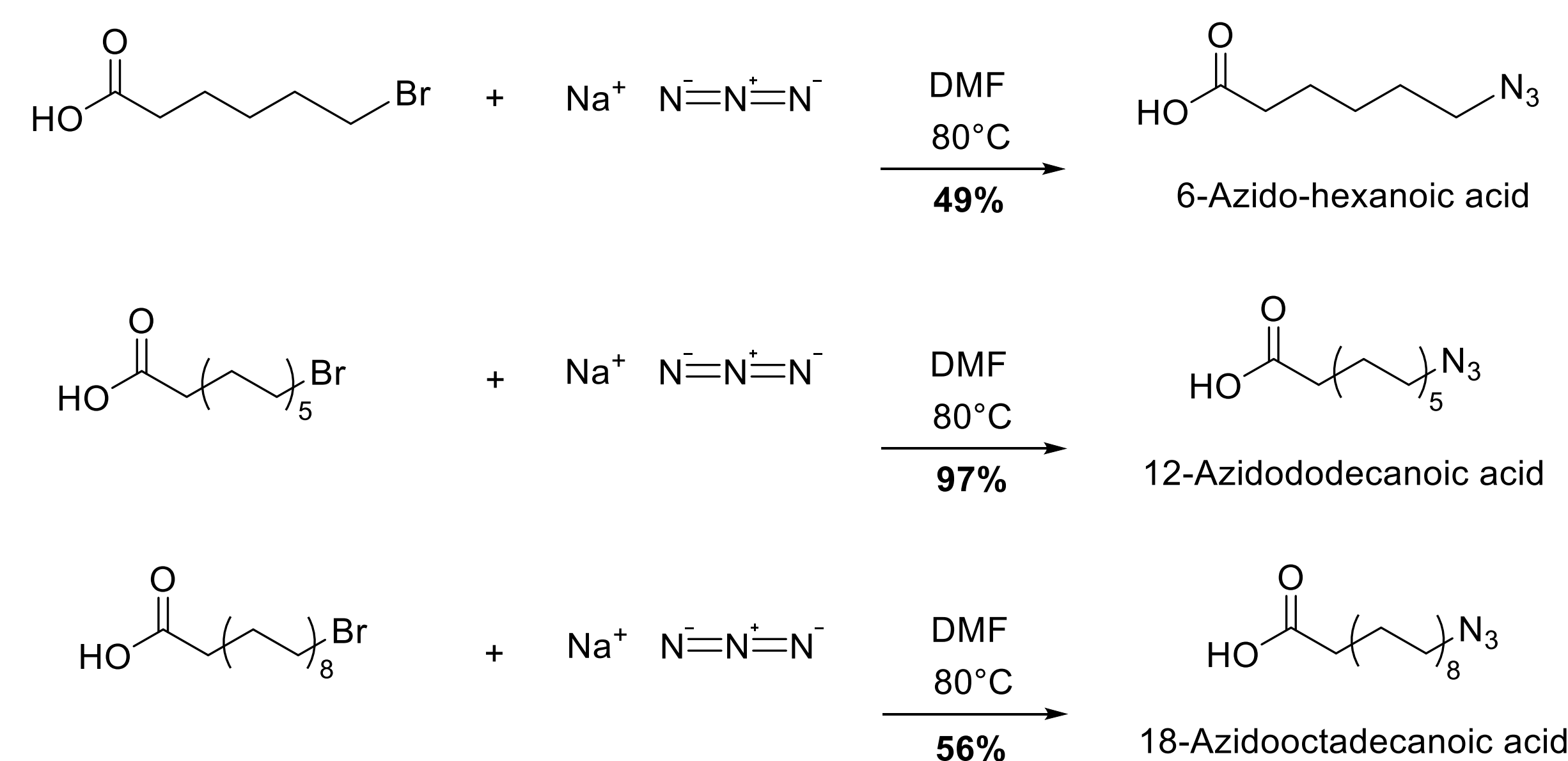
Aim 2: Synthesize a probe that will fluoresce in the presence of H_2O_2

Aim 3: Incorporate the compounds into live cells to track production of H_2O_2 and to observe changes in membrane morphology.

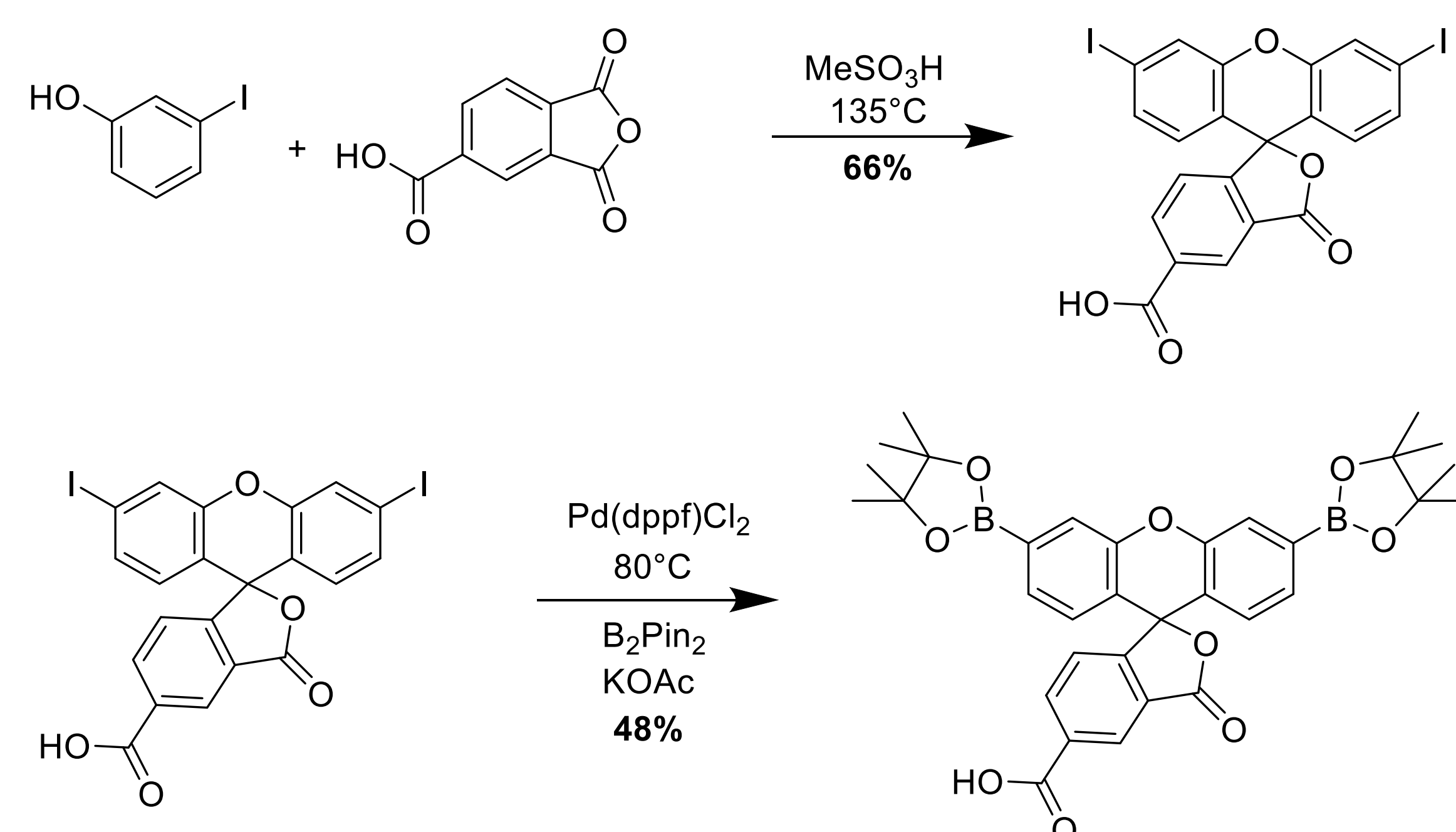
Methodology



Azido Fatty Acid Synthesis



PF1 Analogue Probe Synthesis



Current and Future Work

Current work focuses on the final purification of the PF1 H_2O_2 probe analogue after attaching it to the BCN anchor via EDC coupling.

Initial cell studies with the azido fatty acids have begun to test for live membrane incorporation in live cells.

Next steps include tests to ensure the specificity of the H_2O_2 probe. After fatty acid incorporation, the probe will be delivered to the cells.

Ferroptosis will be initiated, and confocal imaging will elucidate membrane morphology changes.

Applications

This foundational research will provide insight into the fundamental mechanism of ferroptosis.

- Investigational research is invaluable to our medical systems and our understanding of life.
- This research will provide a scaffold for countless further probes and investigations.**

This technique is not limited to sensing analytes involved in ferroptosis; **the method developed in this research will provide an improved tool for tracking a variety of analytes.**

References

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Acknowledgements

The White-Mathieu lab

Dr. Brittany White-Mathieu
Dr. Aakriti Garg

Paige Ring
Saghar Jarollahi
Thomas DiPhilippo
Matthew Fisk

Nicholas Mixon
Taylor Stock
Kylie Armor
Muriel Lubelczyk
Madison Pageau

Funding

