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Genetically Incorporated Vinyl Sulfide for Various Bioorthogonal Reactions

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Background

What does bioorthogonal mean?

The incorporation of organic chemistry reactions into biological processes.

Significance

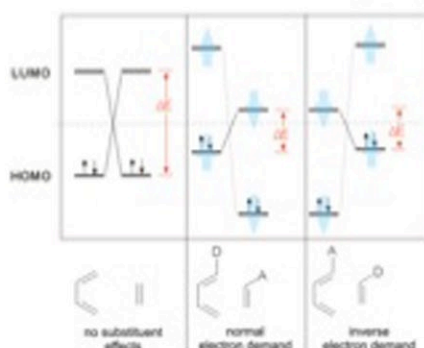
Bioorthogonal reactions have become extremely useful to further study the specific structure and functionality of various biomolecules such as amino acids, sugars, lipids, etc.; they heavily rely on a covalent attachment of a probe to a specific target biomolecules.

Features

- Reactivity at neutral pH
- High yields & fast rates
- No cross reactions with other cellular processes
- Thermal & metabolic stability
- Stable reaction products

Experimental Design

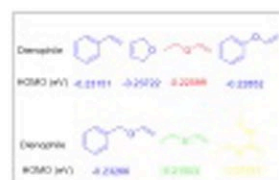
Inverse electron-demand Diels-Alder (IEDDA)



Proposed tetrazine-alkene mechanism

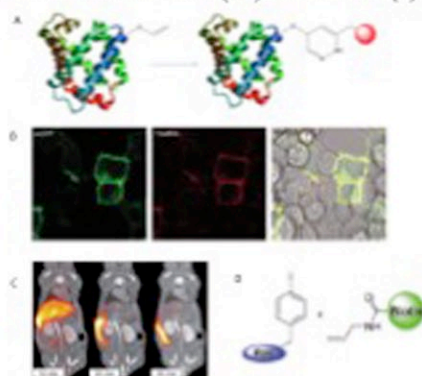


Various reactivity's for different dienophiles

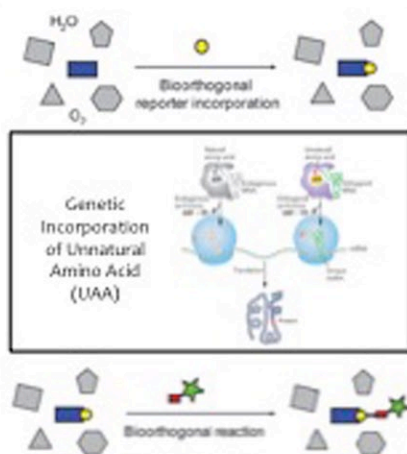


Future Plans

Reactions: Tetrazine-alkene (A-C) & Alkene-homo (D)

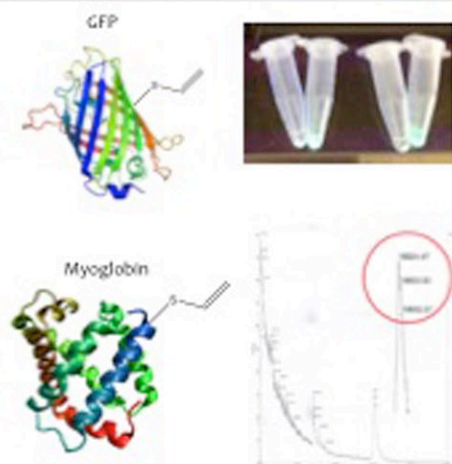


Introduction: Two Steps



Synthesis and Incorporation of EVSI

Ethyl vinyl sulfide derived lysine (EVSI) has been synthesized as a bioorthogonal reporter molecule and incorporated into various model proteins via genetic UAA incorporation technique. GFP and myoglobin (shown on the right) are two specific examples.



Summary

Overall, bioorthogonal reactions can be very useful when combining organic chemistry with biological systems. We have successfully incorporated unnatural lysine with promoted HOMO into proteins which will have a better reactivity in IEDDA reactions. Future research will focus on properly reacting labeled tetrazine with alkene incorporated proteins in vitro and eventually in vivo. Other reactions like the alkene-homo pair will be further investigated to incorporate a S-allylcysteine (SAC) tag onto alkenes which will lead to broader applications.

References:

- <http://wang.salk.edu/research.php>
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 U.S. ChemComm., 2010, 46, 1589-1600