

Protein Engineering with Phosphorus Fluoride Exchange (PFEx): A Novel Click Chemistry Approach for Biotherapeutics and Proteomics

Tech ID: 34567 / UC Case 2024-080-0

TECHNOLOGY DESCRIPTION

UCSF inventors have developed a groundbreaking technology using genetically facilitated click chemistry based on Phosphorus Fluoride Exchange (PFEx) to covalently link proteins with high precision and specificity. Traditional protein engineering methods often struggle to achieve stable covalent linkages, limiting their ability to produce durable and precise therapeutic modifications. This method addresses the unmet need for creating covalent protein modifications, which could enable stronger and more durable interactions in therapeutic applications. The innovation lies in the development of unnatural amino acids (PFY and PFK) that can be incorporated into proteins in vitro and in living cells, facilitating selective covalent linkages without requiring incompatible reagents. Currently in the development stage, this technology offers versatile capabilities for modifying proteins for use in proteomics, biotherapeutics, and drug development, such as antibody-drug conjugates (ADCs) and radiopharmaceuticals. By expanding the bioreactive arsenal for protein engineering, PFEx has the potential to transform biological research and therapeutic design, creating new avenues for oncology treatments and other biomedical applications.

RELATED MATERIALS

- ▶ [Genetically Enabling Phosphorus Fluoride Exchange Click Chemistry in Proteins, PMID: 38975291](#)
[PMCID: PMC11225796 DOI: 10.1016/j.chempr.2024.02.010 - 06/13/2024](#)

PATENT STATUS

Patent Pending

CONTACT

Catherine Smith
Catherine.Smith2@ucsf.edu
tel: 510-646-0631.



OTHER INFORMATION

KEYWORDS

Click Chemistry,
Biotherapeutics
Development, Antibody-Drug
Conjugates (ADCs),
Oncology Therapeutics, Drug
Development,
Radiopharmaceuticals,
Phosphorus Fluoride
Exchange (PFEx), Unnatural
Amino Acids, Covalent
Protein Engineering

CATEGORIZED AS

- ▶ **Medical**
 - ▶ [Disease: Cancer](#)
 - ▶ [Therapeutics](#)
- ▶ **Research Tools**
 - ▶ [Antibodies](#)

RELATED CASES

ADDRESS

UCSF

Innovation Ventures

600 16th St, Genentech Hall, S-272,
San Francisco, CA 94158

CONTACT

Tel:

innovation@ucsf.edu

<https://innovation.ucsf.edu>

Fax:

CONNECT

 Follow  Connect

© 2026, The Regents of the University of
California

[Terms of use](#) [Privacy Notice](#)