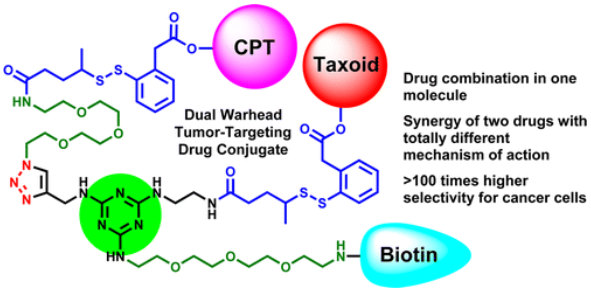
R-7694/8613

Novel Tumor-Targeted Drug Delivery System

A novel approach to release the original and most active form of the drug inside the targeted cells and therefor retain the efficacy of an anti-cancer drug in its conjugated form

Background

Drug selectivity, the ability to preferentially affect a particular cell population, is important because it may have a dramatic result when there is a single agent that can be targeted against the appropriate molecular-driver involved in the pathogenesis of a disease. A notable example is chronic myeloid leukemia (CML), which has a specific chromosomal abnormality that results in a single gene that produces an abnormal protein. While activity in this area of research is growing, binding drugs (or pro-drugs) to a biomarker has not always been feasible and may result in reducing the efficacy of the drug.



Technology

Dr. Iwao Ojima, Distinguished Professor of Chemistry and director of the Institute for Chemical Biology and Drug Discovery (ICB &DD) at Stony Brook University, has invented an elegant approach to reduce the loss of efficacy of an anti-cancer drug in its conjugated form. A linker drug conjugate binds to a cell via the attachment of the specific binding agent. The linker drug conjugate is then internalized into the cell where the disulfide bond of the linker drug conjugate undergoes cleavage by an endogenous peptide e.g. glutathione (GT), found in most mammalian cells and elevated in tumor cells. The cleavage of the disulfide bond causes the release of the specific binding agent and a thiolactonization process occurs between the remaining sulfur atom and the ester, thioester or amide linkage of the drug. The result of the thiolactonization process is the release of the original and the most active form of the drug inside of the targeted cells.

The technology has been further improved to enable attachment of a targeting module and "dual warheads" and/or imaging agents, using a 1,3,5 – triazine as the key tripod splitter module, self immolative linkers with oligoethyleneglycol diamine spacers to improve water solubility and an omega-alkylnylamine arm for the attachment of tumor-targeting module, drug-war-head and/or an imaging modules.

Patent number/Publication:

- Issued Patents US (7,282,590; 7,847,119) and International patents; Additional patents pending
- Seitz et al Bioorg Med Chem. 2015 May 1;23(9):2187-94
- Vineberg et al J Med Chem. 2014 Jul 10;57(13):5777-91; Vineberg et al J Med Chem. 2015 Mar 12;58(5):2406-16

Advantages

- **Enhances drug selectivity, while maintaining its efficacy**
- **Enables multiple functionalities, including targeting, multiple drug payloads, and imaging moities**

Applications

- **Enables tumor targeting for drug delivery and imaging**

Sean Boykevisch, PhD
Assistant Director

Office of Technology Licensing and Industry Relations
N5002 Melville Library
Stony Brook University
Stony Brook, NY 11794-3369
631-632-6952
Sean.boykevisch@stonybrook.edu
www.stonybrook.edu/research/otlir

Stony Brook University

SUNY RF The Research Foundation for The State University of New York