Drug Conjugates for More Potent Cancer Treatment

“We have invented an elegant approach to reduce the loss of efficacy of an anti-cancer drug in its conjugated form. The result of the process is the release of the original and the most active form of the drug inside of the targeted cells.”
— Iwao Ojima, Ph.D., Distinguished Professor of Chemistry, Director of the Institute for Chemical Biology and Drug Discovery (ICB &DD), Stony Brook University

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 Description:
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. He uses a linker drug conjugate that binds to a cell via the attachment of the specific binding agent. The linker drug conjugate is then internalized into the cell through, for example, endocytosis. Once inside the cell, the disulfide bond of the linker drug conjugate undergoes cleavage by an endogenous peptide. For example, glutathione (GT) is found in most mammalian cells and its level is considerably elevated in hypoxic cells such as tumor cells. The cleavage of the disulfide bond causes the release of the specific binding agent. Meanwhile, 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.

Advantages
- The linker drug conjugate formulation enhances drug selectivity while maintaining its efficacy.
- The linker drug conjugates may be administered alone or as an adjunct with other conventional drugs for treating conditions or diseases.

Applications
- Selective drug design

Patents / Publications:
- Patent Pending