“We have developed new compounds that show great promise for clinical use in chemotherapy against tumors with fewer side effects. The new compounds exhibit higher potency against drug-sensitive and drug-resistant tumors compared to paclitaxel, provide better tumor-targeting selectivity and use lower doses compared to unconjugated taxoids that minimize dose-dependent toxicity.”

— Iwao Ojima, Ph.D., Distinguished Professor of Chemistry, Director of the Institute for Chemical Biology and Drug Discovery (ICB & DD), Stony Brook University

Background:
Paclitaxel (Taxol®) and docetaxel (Taxotère®) are two first-generation taxanes used in chemotherapy against tumors. Paclitaxel is a naturally occurring taxane, and docetaxel is a semi-synthetic congener of paclitaxel and the first Taxol-like compound approved by the U.S. Food and Drug Administration for clinical use. Both compounds are effective against various tumors, but they are subject to undesirable side effects, as well as multidrug resistance upon treatment. Cytotoxic agents, such as modified taxoid anti-tumor agents, are needed to selectively target tumor cells instead of healthy cells.

Tumors are shown to voraciously take up natural fatty acids for use as biochemical precursors for metabolic and biochemical pathways. These fatty acids include omega-3 fatty acids — docosahexanoic acid (DHA), eicosapentaenoic acid (EPA) and α-linolenic acid (LNA). Research suggests that fatty acid-conjugated taxoids reduce undesirable side effects due to elective targeting of the conjugates to tumor cells, which could result in the use of lower doses compared to unconjugated taxoids.

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 developed an improved conjugate made up of a second-generation taxoid and an omega-3 fatty acid. He's discovered that by incorporating a simpler alkyl or alkenyl substituent at C-3’, he can considerably increase the activity against drug-sensitive and drug-resistant cancer cell lines. More importantly, appropriate modifications at the C-10 and C-3’ positions have led to the development of second-generation taxoid anticancer agents. Dr. Ojima’s series of taxoids display substantially higher potency against drug-sensitive and drug-resistant cell lines, expressing multidrug resistant (MDR) phenotypes. (For example: IC50 =2.1-9.1 nM; paclitaxel IC50=300-800 nM against human breast cancer cell line MCF7-MDR).

Advantages
- New generation of taxoids that exhibit higher potency against drug-sensitive and drug-resistant tumors compared to paclitaxel.
- Fatty acid-conjugated taxoids provide better tumor-targeting selectivity and use lower doses compared to unconjugated taxoids, which minimize dose-dependent toxicity.

Applications
- Cancer chemotherapy

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Patents / Publications:
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