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Novel Azapodophyllotoxin Derivatives for Treatment of Lymphoma and Kidney Cancer

Researchers at Stanford have developed synthetic derivatives of a natural product, azapodophyllotoxin (AZP), that exhibit remarkable anticancer activities. In vitro and in vivo studies show that the AZP derivatives cause lymphoma and kidney cancer regression by a dual mode of action: tubulin polymerization disruption and monoglycerol metabolism inhibition. Currently there is no cure for kidney cancer and only a handful of known cures for specific types of lymphomas. Advantageously, the AZP derivatives are structurally simpler than podophyllotoxin (a natural product from which clinically important anticancer drugs have been derived) and were synthesized in a single step in good yields from commercially available starting materials.

Stage of Development
The researchers have identified anticancer natural compounds and improved upon them to develop a potentially potent small molecule.

Applications

- Treatment of lymphomas and kidney cancer

Advantages

- Suppresses proliferation of mouse and human lymphoma and kidney cancer cell lines
- Suppresses growth of human xenografts of lymphoma and kidney tumors in vivo

- Prevents tubulin polymerization, thus reducing total tubulin levels both in vitro and in vivo
- Prevents monoglycerol breakdown causing depletion of fatty acids

Patents

- Published Application: WO2021091869
- Published Application: 20230003715

Innovators

- Arvin Gouw
- Sanjay Malhotra
- Dean Felsher

Licensing Contact

Sam Rubin

Licensing Associate, Life Science

Email