MedicalXpress

Scientists identify key structural qualities that distinguish novel anticancer agent

January 2 2014

A team led by Fengzhi Li, PhD, of Roswell Park Cancer Institute has reported significant new findings regarding the chemical structure of the novel anticancer agent FL118. The research, which included comparative analysis of the agent and several similar compounds, confirms the broad, superior antitumor activity of FL118 and suggests promising directions for further studies.

In September 2012, Dr. Li and colleagues published their first findings identifying FL118 as a promising anticancer agent with unique mechanisms of action and favorable toxicity profiles. The small molecule is structurally similar to camptothecin, a component in the bark and stem of a tree native to China that has long been a traditional Chinese remedy for cancer. While thousands of agents based on camptothecin have been synthesized, and two of these analogs—irinotecan and topotecan—have been approved for treatment of many solid-tumor cancers, these compounds typically are highly toxic to healthy cells, and not all of them have proven effective as anticancer agents.

These latest findings, published in *Molecular Pharmaceutics*, a journal of the American Chemical Society, report on the structure-activity relationship (SAR) of the hydroxyl group within the agent's lactone ring. The research team, which included scientists from the School of Medicine and Pharmacy at the Ocean University of China, assessed the relative efficacy of FL118 and seven new compounds derived from FL118 or a sister molecule, FL113. Consistently, FL118 was

significantly more effective in inhibiting cancer-survival proteins, both in vitro and in vivo, than those analogs.

"We learned that the steric configuration of FL118, the way the atoms are arranged within the molecule, is critically important to its effectiveness as an anticancer agent," said Dr. Li, an Associate Professor of Oncology in RPCI's Department of Pharmacology and Therapeutics. "Specifically, we now know that a free hydroxyl group is a key component for any FL118 analogs we develop, and we'll apply that finding as we move forward with subsequent studies. It appears that FL118 will be an outstanding model on which to base new analogs that will represent even more promising investigational therapies for personalized cancer treatment."

More information: *Mol. Pharmaceutics*, Just Accepted Manuscript
DOI: 10.1021/mp4004282

Provided by Roswell Park Cancer Institute