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Scientists advance findings about novel, low-toxicity anticancer agent

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(Medical Xpress)—Researchers at Roswell Park Cancer Institute (RPCI) have found that a new formulation of a promising anticancer agent, the small chemical molecule FL118, is even more effective in controlling two types of cancer than a version reported in *PLOS ONE* six months earlier proved to be. Additional evidence also suggests that the agent may successfully treat other solid tumors as well.

In their previous research, a team led by Fengzhi Li, PhD, Associate Professor of Oncology in RPCI's Department of Pharmacology and Therapeutics, demonstrated that FL118 eliminated human colon and head-and-neck tumors in animal models without relapse but was limited in that it could be delivered only by intraperitoneal (IP) administration. This new study, to be published in the April 8 issue of the *American Journal of Translational Research*, compares the earlier formulation of the agent to a new version that can also be administered intravenously, translating to much wider potential clinical application.

Comparing the antitumor efficacy and therapeutic index, or relative toxicity, of FL118 in its new intravenous (IV) formulation with the earlier form, the researchers found that maximum tolerated dose increased three- to seven-fold, depending on dosing schedule. While the original formulation contained Tween 80 or polysorbate 80, a solvent commonly included in drug formulations, the agent in its new composition is free of Tween 80, resulting in significantly lower toxicity.

FL118 is a targeted therapy that selectively inhibits the expression of

four major cancer-survival gene products: survivin, Mcl-1, XIAP and/or cIAP2. While both studies tested the agent's effectiveness against models of head-and-neck and colon tumors, other research from Dr. Li's lab suggests that mesothelioma, ovarian and pancreatic cancers, and potentially other solid tumors, may also be good targets for treatment with FL118.

"This work represents a significant move forward," notes Dr. Li, senior author on the study. "We're targeting four of the most resilient and pervasive cancer survival mechanisms, and because the findings from preclinical testing have been so striking, we're anxious to see FL118 tested in the clinical setting."

Xiang Ling, MD, PhD, a senior scientist in RPCI's Department of Pharmacology & Therapeutics, is co-author of the paper, "An intravenous (i.v.) route-compatible formulation of FL118, a survivin, Mcl-1, XIAP, and cIAP2 selective inhibitor, improves FL118 antitumor efficacy and therapeutic index (TI)." The study was e-published today and is available at goo.gl/y0oZy.

More information: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0045571

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