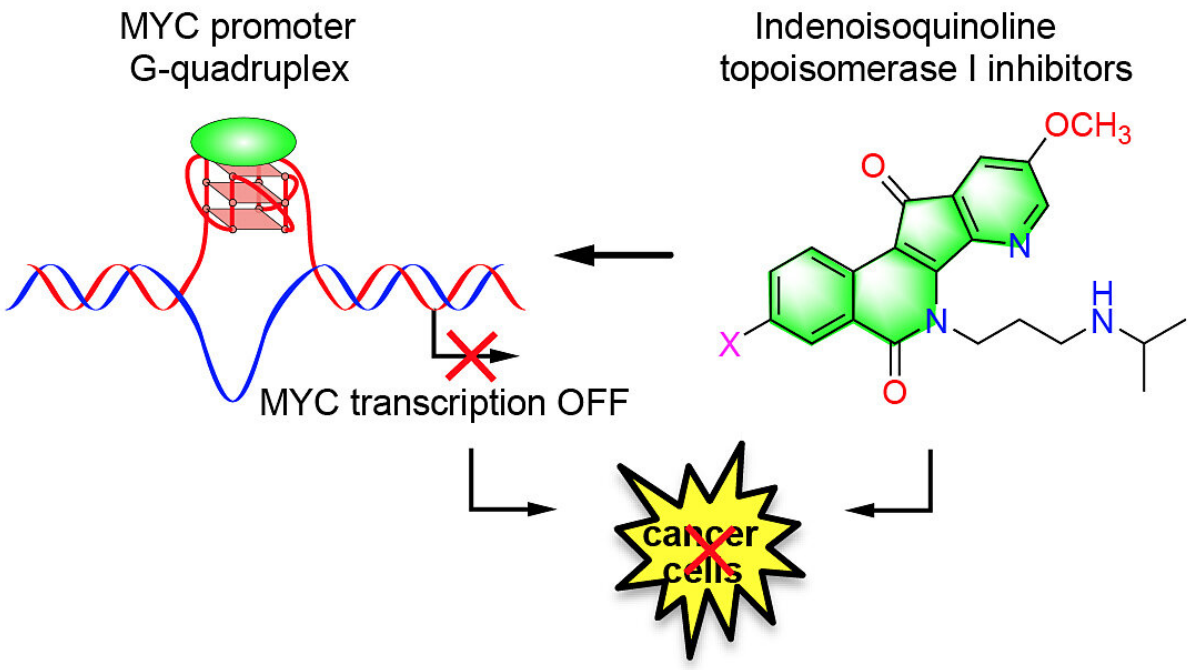
New anticancer agents may better control tumor growth in nearly every cancer type

July 8 2019, by Chris Adam



Purdue University researchers have discovered potential anticancer agents that stabilize the MYC promoter G-quadruplex and downregulate the expression of the MYC oncogene. Credit: Purdue University/Danzhou Yang

A gene called MYC has become one of the hottest targets for cancer researchers around the world. MYC is known to drive tumor growth in nearly all cancer types—but successfully targeting the gene has proven to

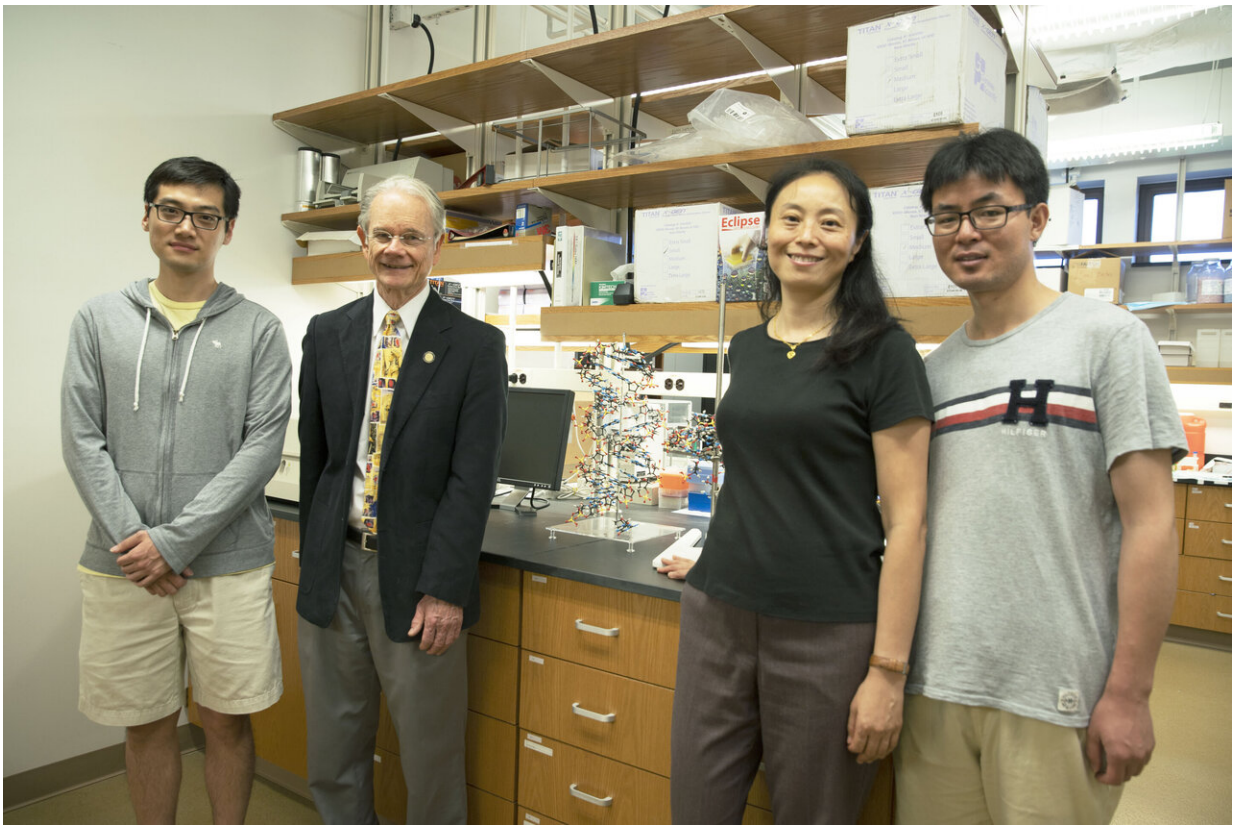
be a challenge. One that has been baffling researchers for more than three decades.

Now, researchers at Purdue University have discovered a novel set of MYC promoter G-quadruplex stabilizers that have demonstrated anticancer activity in human cancer cell cultures. The discovery is published in the July 8 edition of the *Journal of the American Chemical Society*.

"We are striving to discover effective anticancer agents," said Mark Cushman, a distinguished professor of medicinal chemistry in Purdue's College of Pharmacy, who helps lead the research team. "The ability to incorporate MYC promoter G-quadruplex stabilizing activity into existing topoisomerase I inhibitors has shown promise in making them more potent as anticancer agents and in making cancer cells less likely to become resistant to them."

The Purdue team discovered potential anticancer agents that target the MYC promoter G-quadruplex and downregulate the expression of the MYC oncogene, which is overexpressed in cancer and is associated with almost all aspects of cancer development. The work has been supported by the National Cancer Institute and the National Institutes of Health.

Cushman, whose cancer research work contributed to his election as a fellow of the National Academy of Inventors, said they discovered a novel class of indenoisoquinoline MYC promoter G-quadruplex stabilizers in collaboration with Danzhou Yang. Some of them also inhibit topoisomerase I, an enzyme that facilitates DNA replication and is produced in greater amounts in cancer cells.



Purdue University cancer and pharmacy researchers have discovered a novel set of MYC stabilizers that have demonstrated anticancer activity in human cancer cell cultures. Pictured are Guanhui Wu, a doctoral student, Mark Cushman, Danzhou Yang and Kaibo Wang, a postdoctoral research associate. Credit: Purdue Research Foundation/Hope Sale

"Targeting promoter G-quadruplexes offers a relatively new and exciting strategy to inhibit the critical oncogene expression in cancer cells," said Yang, the Martha and Fred Borch Chair of Cancer Therapeutics in Purdue's College of Pharmacy, who led the research with Cushman. "We hope to combine the potency of the DNA-targeted drugs and selectivity of molecular-targeted approaches for new cancer therapeutics."

Yang and Cushman, both members of the Purdue University Center for

Cancer Research, said the agents they discovered could be used in helping to treat nearly every type of cancer. Some of the technology from their work has been licensed to Gibson Oncology LLC through the Purdue Research Foundation Office of Technology Commercialization.

Some of the work Cushman and his team previously developed led to three anticancer agents that are in clinical trials. The MYC innovation will greatly enhance interest in these anticancer agents within the scientific community and will also contribute to the understanding of how they work.

More information: Kai-Bo Wang et al. Indenoisoquinoline Topoisomerase Inhibitors Strongly Bind and Stabilize the MYC Promoter G-Quadruplex and Downregulate MYC, *Journal of the American Chemical Society* (2019). DOI: 10.1021/jacs.9b02679

Provided by Purdue University