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## Researchers discover potential candidates for development of novel targeted therapies for blood cancers

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A research team from the Department of Pharmacology and Therapeutics at Roswell Park Cancer Institute (RPCI) has discovered a new class of small-molecule compounds that are good candidates for development of novel targeted therapies in the treatment of leukemia and lymphoma. This new class of compounds drives cancer cells to suicide, the researchers report in the peer-reviewed journal *Cell Death and Disease*.

"We are excited about the unique activities of these compounds and will continue to focus our research efforts on development of their clinical potential," says the study's senior author, Xinjiang Wang, PhD. "These compounds kill cancer cells, not just stop cancer cell growth temporarily. These types of agents offer the promise of therapeutic benefit."

The researchers demonstrate that the small-molecule MMRi compounds have an advantage over p53-activating agents in current use as cancer therapies. MMRi compounds, they found, activate the pro-death function of the p53 pathway, whereas current p53-activating agents are effective in temporarily preventing cancer growth, but do not damage existing cancer cells or prevent cancer growth long-term. MMRi inhibits Mdm2-MdmX function, the research team reports, and eliminates the two cancer-causing proteins in cells — mechanisms potentially responsible for MMRi's death-promoting effect in cancer. Dr. Wang and team report that MMRi64 is the first-in-class inhibitor of RING domain function of Mdm2-MdmX E3 ligase.

"This study opens a new area for anticancer drug development. MMRi compounds also can be used as a tool for better understanding the anti-death mechanisms developed by cancer cells," continues Dr. Wang. "We are moving the research of MMRi compounds forward using both preclinical models and human cancer cell lines. Our hope is that further development of clinically useful MMRi will eventually provide a new treatment option for cancer patients."

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Source:

Roswell Park Cancer Institute (RPCI)

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