

New drug combination brings 1-2 punch against acute leukemia



Scientists in lab. Credit: M. D. Anderson Cancer Center

Researchers at The University of Texas M. D. Anderson Cancer Center have discovered a drug combination that kills leukemia cells by shutting down their energy source and hastening cell starvation.

In a preclinical study, Lauren Akers, D.O., postdoctoral fellow from the Children's Cancer Hospital at M. D. Anderson, found that combining a novel glycolysis inhibitor, 3-BrOP, with mTOR inhibitor, rapamycin, induced more than 90 percent cell death in human tissue cultures of acute lymphocytic leukemia. She presented her study at the American Society of Pediatric Hematology/Oncology annual conference on May 16.

"We already knew that 3-BrOP was effective in preclinical research of glioblastoma, colon cancer and lymphoma, and most recently acute leukemias" says Akers, lead investigator on the study. "We also knew that mTOR inhibitors intensify cellular starvation. This study showed that the two together have a more powerful impact on treating acute lymphocytic leukemia, which is the most common childhood cancer."

Glycolysis is a process that turns glucose into energy for cells. Unlike healthy cells that get their energy for growth from both glycolysis and respiration, cancer cells are highly dependent on glycolysis. Using the M. D. Anderson-developed drug, 3-BrOP, researchers inhibited glycolysis, thus starving the leukemia cells from their energy source while leaving healthy cells free to get their energy from respiration.

Rapamycin is an mTOR inhibitor that keeps cancer cells from coping with stress, thus resulting in cell death. When researchers on the study combined the two drugs, they discovered a synergistic effect.

"We found that a lower dosage of 3-BrOP with rapamycin created the same results of more than 90 percent tumor cell death," says Akers. "Theoretically, we believe that patients will better tolerate the therapy by lowering the dosage of 3-BrOP and combining it with rapamycin."

Other researchers on the study include senior investigator Patrick Zweidler-McKay, M.D., Ph.D., Anna Franklin, M.D. and Wendy Fang, M.D., all from the Children's Cancer Hospital at M. D. Anderson. Peng Huang, M.D., Ph.D., from the Department of Molecular Pathology at M. D. Anderson was also an investigator and was responsible for the development of 3-BrOP.

The team of researchers plans to conduct additional mouse studies, which could lead to a Phase I clinical trial some time in the future.

Source: University of Texas M. D. Anderson Cancer Center

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