MedicalXpress

Scientists devise new strategy to destroy multiple myeloma

August 14 2012

Researchers at Virginia Commonwealth University Massey Cancer Center are reporting promising results from laboratory and animal experiments involving a new combination therapy for multiple myeloma, the second most common form of blood cancer.

The study published online in the journal Cancer Research details a dramatic increase in multiple myeloma cell death caused by a combination of the drugs obatoclax and flavopiridol. The researchers, led by Steven Grant, M.D., Shirley Carter Olsson and Sture Gordon Olsson Chair in Oncology Research, associate director for translational research, program co-leader and member of Developmental Therapeutics and member of the Cancer Cell Signaling program at VCU Massey Cancer Center, found that the two drugs worked together through different mechanisms to promote a form of cell suicide known as apoptosis.

"There is an urgent need for curative therapies for multiple myeloma," says Grant. "Our hope is that this research will lay the foundation for new and more effective treatments for patients with multiple myeloma and potentially other blood cancers for which adequate therapies are lacking."

Obatoclax is an experimental agent currently being investigated in various forms of blood cancers. It works by disabling proteins that prevent cancer cells from undergoing apoptosis. Flavopiridol is a member of a class of agents known as a cyclin-dependant kinase (CDK)

inhibitors, and blocks the growth of cancer cells in addition to reducing levels of anti-apoptotic proteins.

In laboratory experiments, the novel drug combination dramatically increased multiple myeloma cell death. These results were confirmed in animal models where the drugs significantly improved the survival of immune-compromised mice with human multiple myeloma. An unexpected effect was also observed – flavopiridol, in addition to reducing levels of anti-apoptotic proteins, significantly increased the expression of apoptosis-inducing proteins such as Bim, a protein shown in previous studies to trigger cell death.

"This research builds on nearly a decade of work carried out by our laboratory that focuses on manipulating mechanisms that lead to apoptosis in hematological malignancies," says Grant. "Our findings could have immediate implications for the design of clinical trials using combinations of these types of drugs. In fact, plans to develop such a trial at Massey are currently underway."

Because the findings showed synergism between these two classes of drugs, the researchers plan to test other clinically-relevant CDK inhibitors in combination with obatoclax for multiple myeloma.

More information: cancerres.aacrjournals.org/con … 472.CAN-12-1118.long

Provided by Virginia Commonwealth University