MedicalXpress

Study IDs potential treatment for deadly, HIV-related blood cancer

June 25 2013

Researchers at the USC Norris Comprehensive Cancer Center have discovered a promising new way to treat a rare and aggressive blood cancer most commonly found in people infected with HIV.

The USC team shows that a class of drugs called BET bromodomain inhibitors effectively targets primary effusion lymphoma (PEL), a type of cancer for which those drugs were not expected to be effective.

"It's a reversal of the paradigm," said Preet Chaudhary, MD, PhD, chief of the Nohl Division of Hematology and Blood Diseases at the Keck School of Medicine of USC and principal investigator of the study. "Our results suggest that this new class of drug may be an effective treatment for a wider range of cancers than previously thought."

PEL is caused by infection with Kaposi's sarcoma-associated herpes virus, the most common cause of cancer among patients with AIDS. The prognosis for PEL is poor, with a median survival of three to six months. Thus, there is a critical need for new therapies for the disease.

Chaudhary and his colleagues show that inhibitors targeting the BRD4 protein blocked growth of PEL cells in a test tube and in a mouse model. The results were surprising because BET inhibitors were thought to be only effective against cancers linked to an overexpression of the Myc gene.

"We actually found that cancers that overexpress Myc are not as

responsive to BRD4 inhibitors. PEL is more responsive," Chaudhary said.

Cancers like multiple myeloma and Burkitt's lymphoma overexpress the Myc gene and have been shown to respond to BRD4 inhibitors. In PEL, the Myc gene is moderately expressed and there is no chromosomal translocation as is seen in multiple myeloma or Burkitt's.

More research is needed to create compounds ready for testing in people. Once those drugs are ready for clinical trial, data from this study suggest that they may treat a wide range of cancers. Chaudhary anticipates testing them alone and in combination with other drugs.

The study, "Targeting Myc in KSHV-associated primary effusion lymphoma with BET bromodomain inhibitors," appears in *Oncogene*, a peer-reviewed scientific journal from the Nature Publishing Group.

More information: Tolani, B., Gopalakrishnan, R., Punj, V., Matta, H., & Chaudhary, P.M. (2013). Targeting Myc in KSHV-associated primary effusion lymphoma with BET bromodomain inhibitors. *Oncogene*. Published online June 24, 2013; doi:10.1038/onc.2013.242

Provided by University of Southern California

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