



## SYRACUSE UNIVERSITY

### TECHNOLOGY TRANSFER AND INDUSTRIAL DEVELOPMENT

#### **Cosgrove Lab Creates New Approach to Leukemia Treatment**

*Synthetic peptide may disrupt production of immature white cells*

A team led by Professor Michael Cosgrove has discovered a promising lead for disrupting the protein switch that is a critical component of the process for creating white blood cells. This new approach may lead to more effective treatment of several forms of Leukemia and potentially revolutionize the fight against other cancers.

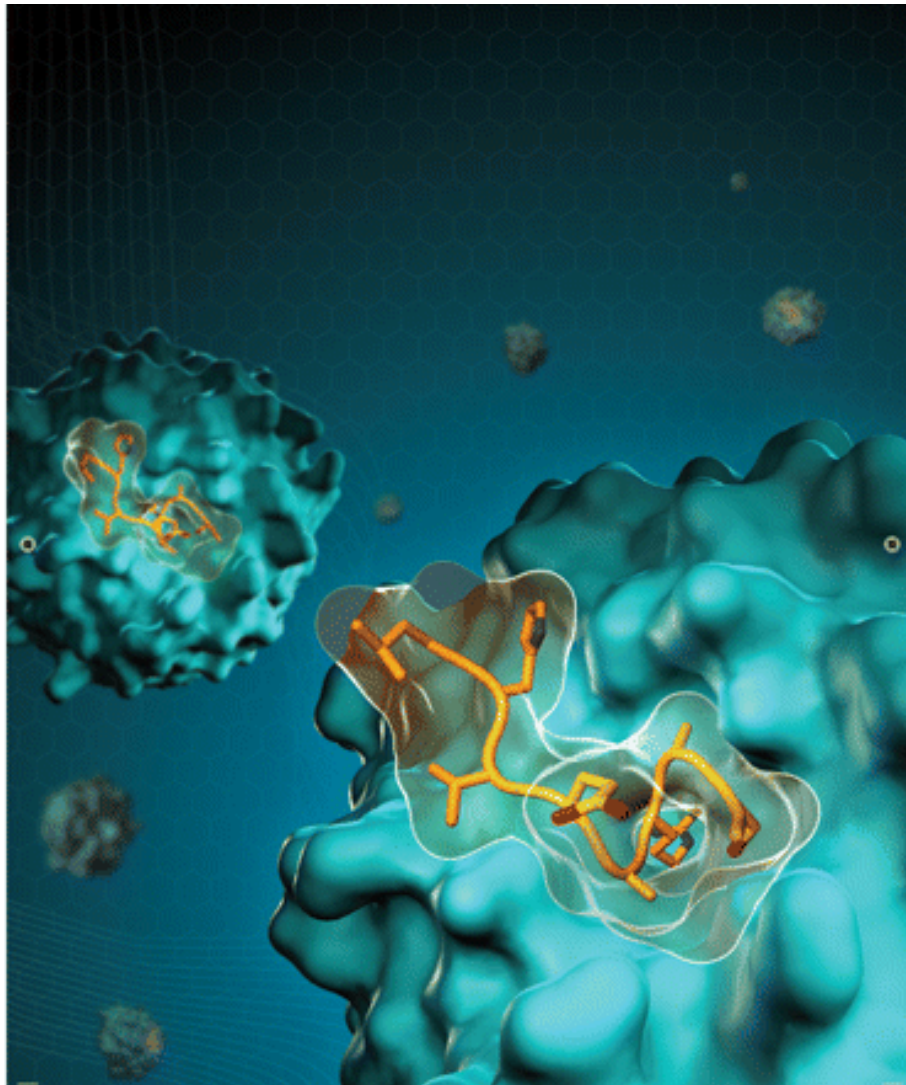
The team has spent three years studying the Mixed Lineage Leukemia (MLL) protein that regulates the way DNA is packaged when white blood cells are formed. In normal cells, that protein combines with three others to create a molecular switch that controls the formation of white blood cells. In some types of leukemia, that switch is broken, preventing the white blood cells from maturing and resulting in a deadly proliferation of immature cells.

The Cosgrove team identified a tiny component of the MLL protein called the WIN motif, a peptide sequence that is responsible for assembling the molecular switch in normal cells.

They discovered that a synthetic version of the peptide acts like a drug that breaks apart the molecular switch and interrupts a process that is required for production of white blood cells. When used against a faulty switch that is working too fast the peptide drug attacks the protein switch and breaks it apart, which may slow or stop production of the abnormal white cells.

With this approach working well in vitro, the team is moving to design drugs that may be useful for treating leukemias caused by increased MLL activity and to seek other compounds that may be active against this or other cancers.

“It is our hope,” said Professor Cosgrove, “that as we build our understanding of how these DNA packaging proteins work we will find new ways to treat all types of leukemia as well as other diseases.” A report of the research was recently published online in The Journal of Biological Chemistry.



The WDR5 component of the mixed lineage leukemia (MLL) core complex recognizes a conserved arginine-containing motif in MLL1 called the *Win* motif. The crystal structure of WDR5 (*teal*) bound to a peptide (*orange*) derived from the human MLL1 *Win* motif. The structure gives insight into an interaction that is required for the assembly and histone H3 lysine 4 methyltransferase activity of the human MLL1 core complex.

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