Team uncovers new insight into cell development and cancer

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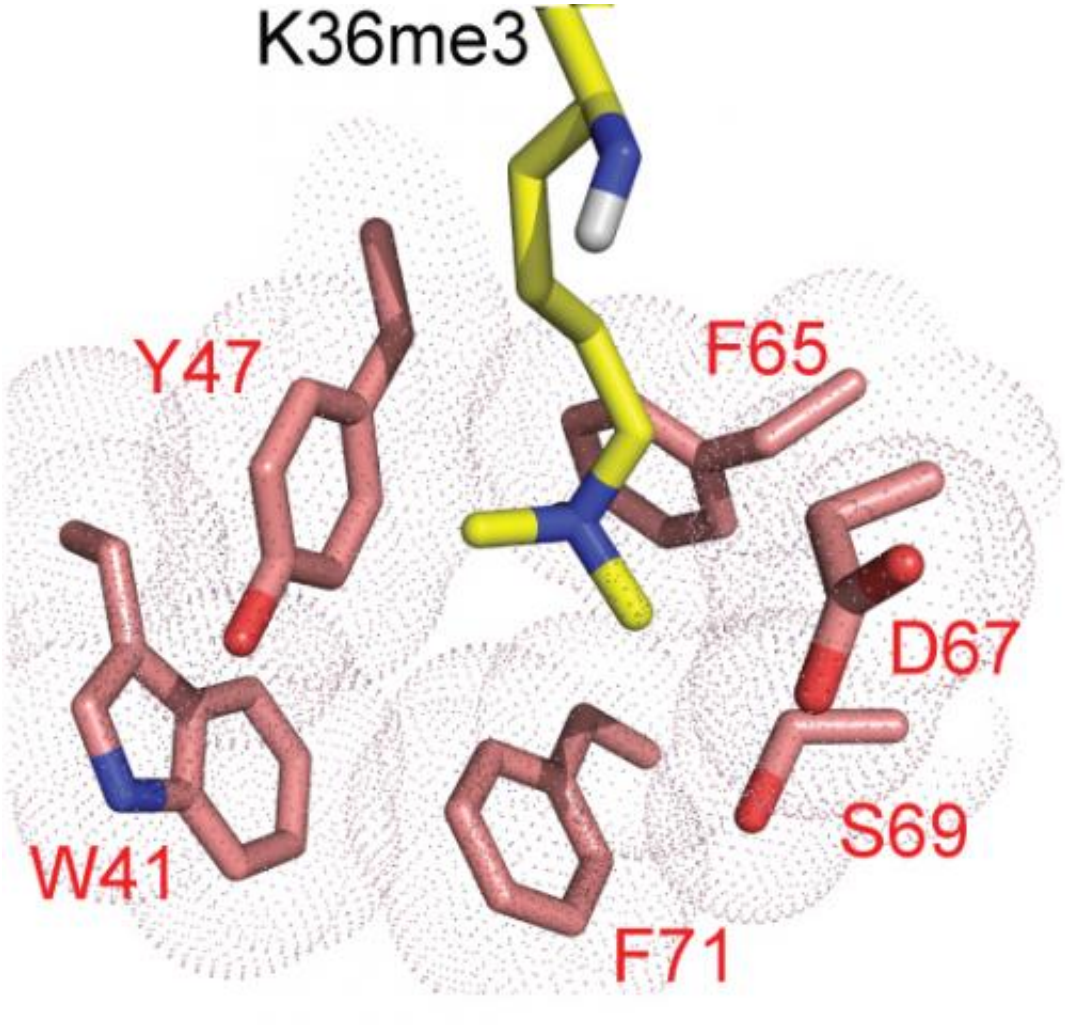

PCLs utilize an amino acid group to engage with a chemical marker that signals gene activation. Credit: University of North Carolina

Long-standing research efforts have been focused on understanding how stem cells, cells capable of transforming into any type of cell in the body, are capable of being programmed down a defined path to contribute to the development of a specific organ like a heart, lung, or kidney. Research from the University of North Carolina at Chapel Hill School of Medicine has shed new light on how epigenetic signals may function together to determine the ultimate fate of a stem cell.

The study, published December 27, 2012 by the journal *Molecular Cell*, implicates a unique class of proteins called polycomb-like proteins, or PCL's, as bridging molecules between the "on" and "off" state of a gene. While all of these specialized types of cells share the same genetic information encoded in our DNA, it is becoming increasingly clear that information outside the genome, referred to as epigenetics, plays a central role in orchestrating the reprogramming of a stem cell down a defined path.

Although it is understood that epigenetics is responsible for turning genes "on" and "off" at defined times during cellular development, the precise mechanisms controlling this delicate process are less well understood.

"This finding has important implications for both stem cell biology and cancer development, as the same regulatory circuits controlled by PCL's in stem cells are often misregulated in tumors," said Dr. Greg Wang, senior author of the study and Assistant Professor of Biochemistry and Biophysics in the UNC School of Medicine and a member of UNC Lineberger Comprehensive Cancer Center.

The study, led by postdoctoral research fellows Drs. Ling Cai and Rui Lu in the Wang lab, and Dr. Scott Rothbart, a Lineberger postdoctoral fellow in the lab of Dr. Brian Strahl, Associate Professor of Biochemistry and Biophysics in the UNC School of Medicine and a

member of UNC Lineberger Comprehensive Cancer Center, identified that PCL's interact with an epigenetic signal associated with genes that are turned on to recruit a group of proteins called the PRC2 complex which then turn genes off.

"In stem cells, the PRC2 complex turns genes off that would otherwise promote reprogramming into specialized cells of organs like the heart or lungs," said Wang.

In addition to its fundamental role in cellular development, elevated levels of PRC2 have been found in cancers of the prostate, breast, lung, and blood, and pharmaceutical companies are already developing drugs to target PRC2. Wang and colleagues determined that the same mechanisms controlling PRC2 function in stem cells also applies in human cancers.

"The identification of a specific PCL in controlling PRC2 in cancer cells suggests we may be able to develop drugs targeting this PCL to regulate PRC2 function in a more controlled manner that may maintain PRC2 function in stem cells while inhibiting it in the tumor," said Wang.

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