

Cancer-killing cells controlled by epigenetic process, new study shows

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Natural killer (NK) cells in the human body can kill and contain viruses and cancerous tumors, and a new study from the University of Southern California (USC) describes for the first time how those cells can be manipulated by epigenetics. The discovery, detailed in the *Proceedings of the National Academy of Sciences*, paves the way for developing more effective cancer drugs.

"Natural killer cells are very attractive targets for immunotherapy because they are able to kill tumor cells," said Si-Yi Chen, M.D., Ph.D., a faculty member of the USC Norris Comprehensive Cancer Center and senior author of the study. "While scientists all around the world are working on developing new drugs using NK cells, none of the drugs in development focuses on epigenetic regulation of the cells. Our study describes how an epigenetic process involving the enzyme MYSM1 plays a critical role in the development of natural killer cells."

Epigenetics involve biochemical changes in the body that directly affect DNA, turning some genes on and turning others off. MYSM1 is an enzyme in the body's immune system that turns genes on and off by modifying proteins called histones embedded in DNA.

Through a series of experiments in mice, Chen and his colleagues demonstrate that MYSM1 is required for natural killer cells to mature and function properly.

"We found that MYSM1 creates access to proteins that enhance gene transcription and, ultimately, the maturation of natural killer cells themselves," said Vijayalakshmi Nandakumar, a Ph.D. student at the Keck School of Medicine of USC and the study's first author. "To date, there are no elaborate reports linking an epigenetic phenomenon to natural killer cell development. More importantly, unlike conventional therapies, NK cell-based therapies have shown to be more

effective against metastasis. We believe <u>cancer</u> <u>drugs</u> targeting this pathway could be a viable option for future immunotherapies."

More information: Nandakumar, V., Chou, Y.C., Zang, L., Huang, X.F., & Chen, S.Y. (2013). Epigenetic control of NK cell maturation by histone H2A deubiquitinase MYSM1. *Proceedings of the National Academy of Sciences* Early Edition, 1-11. Published online Sept. 23, 2013; DOI: 10.1073/pnas.1308888110

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