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Fighting cancer with the immune system

June 11 2012

The human immune system has a natural ability to identify and attack tumor cells. Natural killer (NK) cells are innate immune cells that are particularly effective at killing tumor cells due to their ability to secrete cytotoxic enzymes. However, mutations have allowed many types of tumors to develop a resistance to NK-mediated killing through ill-defined mechanisms.

Dr. Jerome Ritz and colleagues at the Dana-Farber Cancer Institute in Boston sought to pinpoint some of these mechanisms using a library of short hairpin RNAs (shRNA), a type of RNA that binds complementary RNA sequences in the cell and prevents their transcription into proteins.

His group used a multiple myeloma cell line to screen for genes whose reduced expression increased susceptibility of the cancer cells to NK-mediated death. They identified dozens of genes that, when shut down by shRNA, allowed increased tumor cell killing by NK cells. The strongest effect was induced by silencing proteins called JAK1 and JAK2, kinases important for integrating signals from many membrane receptor proteins. In addition to targeting these kinases by shRNA, the research team showed that pharmacological inhibition of JAK1 and 2 also increased tumor cell killing. Many kinase inhibitors being used or tested today target genes identified in this screen.

The researchers suggest that targeting the JAK1 and 2 pathways in particular may aid in eradicating tumors that have developed mechanisms to escape NK cell killing.

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More information: Tyrosine kinase pathways modulate tumor susceptibility to natural killer cells, *Journal of Clinical Investigation*, doi:10.1172/JCI58457 .

Provided by Journal of Clinical Investigation

Citation: Fighting cancer with the immune system (2012, June 11) retrieved 4 May 2024 from https://medicalxpress.com/news/2012-06-cancer-immune.html

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