

# Key immune cell may play role in lung cancer susceptibility

September 21 2012, by Caroline Arbanas

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(Medical Xpress)—Why do many heavy smokers evade lung cancer while others who have never lit up die of the disease? The question has vexed scientists for decades.

Now, new research at Washington University School of Medicine in St. Louis suggests a key immune cell may play a role in lung cancer susceptibility. Working in mice, they found evidence that the [genetic diversity](#) in [natural killer cells](#), which typically seek out and destroy tumor cells, contributes to whether or not the animals develop lung cancer.

The research is published in September in [Cancer Research](#).

"Overall, humans are genetically very similar but their immune systems are incredibly diverse," explains senior author Alexander Krupnick, MD, a thoracic surgeon at the Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine. "Our findings add to the growing body of evidence suggesting that innate differences in immunity may determine not only a person's susceptibility to colds but also to lung cancer."

Based on the findings in mice, Krupnick says he and his colleagues now are studying whether humans have a similar genetic diversity in their [natural killer](#) cells. As part of a new clinical study, they're analyzing the blood of heavy smokers with and without lung cancer and never-smokers with and without lung cancer to look for differences.

"We want to know whether [heavy smokers](#) who don't get lung cancer have natural killer cells that are somehow better at destroying newly developing [lung cancer cells](#)," says Krupnick, associate professor of surgery. "And, by comparison, do patients who have never smoked but develop lung cancer have weak natural killer cells?"

For the mouse study, the scientists evaluated three groups of mice with varying susceptibilities to [lung tumors](#). After the mice were exposed to a carcinogen that causes lung cancer, one group readily developed the disease while another showed little evidence of the tumors. A third group experienced moderate tumor growth.

When the researchers depleted natural killers cells from the mice using an antibody, those that had been resistant to lung cancer developed large, aggressive tumors.

Further, in mice susceptible to lung cancer, the scientists showed that manipulating the immune system with a bone marrow transplant could significantly block the development of lung cancer. Their studies indicate that natural killer cells, not other types of [immune cells](#) like T cells or inflammatory cells, are responsible for this phenomenon.

In other types of cancers, including those of the breast, colon and prostate, T cells are capable of destroying [tumor cells](#). But in lung cancer, scientists suspect that T cells become inactivated, which may give natural killer cells a more prominent role.

The researchers also traced the genetic diversity of the natural killer cells in the mice to a region of chromosome 6, which includes numerous genes that influence the effectiveness of these cells.

Moving forward, Krupnick and his team want to learn whether natural killer cells influence lung cancer susceptibility in people. "We need to

identify those patients who are resistant to lung cancer and ask, 'What is unique about their natural killer cells – are they more potent or do they produce more of them than people with [lung cancer](#)?' The answer will determine our next steps."

**More information:** Kreisel D, Gelman AE, Higashikubo R, Lin X, Vikis HG, White JM, Toth KA, Deshpande C, Carreno BM, You M, Taffner SM, Yokoyama WM, Bui JD, Schreiber RD, Krupnick AS. Strain-specific variation in murine natural killer gene complex contributes to differences in immunosurveillance for urethane-induced lung cancer. *Cancer Research*. September 2012.

Provided by Washington University School of Medicine in St. Louis

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