

Some immune cells defend only one organ

April 17 2014, by Michael C. Purdy



Postdoctoral research fellow Dorothy K. Sojka, PhD, prepares for an experiment involving immune cells known as natural killer cells.

(Medical Xpress)—Scientists have uncovered a new way the immune system may fight cancers and viral infections. The finding could aid efforts to use immune cells to treat illness.

The research, in mice, suggests that some organs have the immunological equivalent of "neighborhood police" – specialized squads of defenders that patrol only one area, a single organ, instead of an entire city, the

body.

Scientists at Washington University School of Medicine in St. Louis have shown that the liver, skin and uterus each has dedicated immune cells, which they call tissue-resident [natural killer cells](#). Other organs may have similar arrangements.

Their study, published in eLife, disproves the long-held assumption that all [natural killer](#) cells roam the body to provide the first line of defense against cancers and viruses.

"If, for example, we can use specialized medications to activate only these organ-specific cells, they could provide powerful and selective weapons against infections and tumors in the organs where they reside," said senior investigator Wayne M. Yokoyama, MD, the Sam and Audrey Loew Levin Professor of Medicine. "Cells that only defend one organ may be much better equipped than the roaming immune cells to mount an attack and limit collateral damage to healthy tissue."

Scientists have thought that mature natural killer cells circulate through the body looking for viruses and cancers. When these [immune cells](#) identify a threat, they attack. Scientists also thought that natural killer cells that stayed in the liver instead of circulating were immature or inactive and eventually would become like other natural killer cells, leaving the liver and moving through the body.

In the new study, lead author Dorothy K. Sojka, PhD, a postdoctoral research fellow in Yokoyama's laboratory, showed that some natural killer cells never leave the liver. She identified additional tissue-resident natural killer cells in the skin and uterus.

Sojka also experimented with [transcription factors](#)—molecular switches that turn a number of genes on and off. Among other results, she found

that disabling one of these switches could prevent circulating natural killer cells from developing without affecting tissue-resident natural killer cells in the liver, skin and uterus. Disabling another transcription factor wiped out the liver and skin tissue-resident natural killer cells while having little effect on the circulating and uterus tissue-resident natural killer cells.

"If one group of cells absolutely needs a specific transcription factor to exist, while another group of cells doesn't care if that factor is gone, that strongly suggests the two groups of cells use distinct developmental pathways and are therefore different," Sojka said.

Her results point to at least four types of natural killer cells rather than just the one major type long recognized by immunologists. She is looking for groups of resident natural [killer cells](#) in other organs and investigating the origins and functions of those she already has identified.

"Conceptually, this is very different, a significant change in our thinking about how a very important part of the immune system works," said Yokoyama, a Howard Hughes Medical Institute Investigator.

More information: Sojka DK, Plougastel-Douglas B, Yang L, Pak-Wittel MA, Artyomov MN, Ivanova Y, Zhong C, Chase JM, Rothman PB, Yu J, Riley JK, Zhu J, Tian Z, Yokoyama WM. "Tissue-resident natural killer (NK) cells are cell lineages distinct from thymic and conventional splenic NK cells." *eLife*, April 8, 2014. DOI: [dx.doi.org/10.7554/eLife.01659](https://doi.org/10.7554/eLife.01659)

Provided by Washington University School of Medicine in St. Louis

Citation: Some immune cells defend only one organ (2014, April 17) retrieved 27 April 2024 from <https://medicalxpress.com/news/2014-04-immune-cells-defend.html>

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