

Scientists discover trained immune cells are highly effective against cancer

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Sophie Poznanski, lead author of the paper and Ali Ashkar, professor of medicine Credit: McMaster University

Modified immune cells that ruthlessly kill cancerous tumors may prove a game-changer for people living with late-stage cancer.

McMaster University researchers Ali Ashkar and Sophie Poznanski have uncovered that changing the [metabolism](#) of natural killer (NK) immune [cells](#) allows these cells to overcome the hostile conditions found inside tumors and destroy advanced ovarian and [lung cancer](#).

In the past decade cancer immunotherapy has achieved tremendous therapeutic effects in patient with blood cancers. However, the immunosuppressive conditions found inside solid tumors, whose aggressive growth starves surrounding healthy tissues of energy, have until now remained a formidable barrier for immune cell therapies.

"In this study, we discovered that the metabolism, or energy 'hub,' of NK cells is paralyzed by tumors, causing the NK cells to undergo an energy crisis

and lose their tumor killing functions," said Poznanski, a McMaster Ph.D. student.

"With that understanding, we were able to reverse the dysfunction of NK cells by repurposing a pre-existing metabolism drug that restored their energy production," she added.

Poznanski is lead author of the paper published this week in the journal *Cell Metabolism* and a Vanier Scholar.

While these findings answered the decades-old question of how it is that NK cells are suppressed by tumors, the study has another major discovery.

"Drawing on the old adage 'To defeat your enemy, you have to think like your enemy', we additionally discovered that NK cells can be modified to mimic the metabolism of tumors," Poznanski said.

She added that the modified NK cells proved to be far better adapted for the hostile tumor environment.

"We were just hoping that the modified NK cells would better resist suppression in tumors. We were astounded to see that not only did they show no suppression, but they paradoxically functioned better inside of the tumor than outside of it."

"This is the first report of an anti-tumor immune cell that exploits the hostility of tumors for their own advantage" said senior author Ashkar, professor of medicine and the Canada Research Chair in Natural Immunity and NK Cell Function.

"Generating cytotoxic [immune cells](#) to have tumor-like metabolism is key for their anti-tumor functions in a very hostile environment of a solid tumor. This could be a [paradigm shift](#) for immune cell-based cancer immunotherapy."

So far, NK cells have only proven effective against

blood cancers, he said. "The re-programmed and trained NK cells could mean patients with otherwise terminal cancers may have a safe and an effective treatment option. Lung and [ovarian cancer](#) are two examples of cancers whose survival rates have remained low over the last 30 or so years."

He added that immunotherapy with NK cells has already proven safe with few, if any, side effects.

Hal Hirte agrees. He is an associate professor of oncology at McMaster, an author of the study and a medical oncologist for Hamilton Health Sciences.

"This could have real potential for the treatment of ovarian cancer, lung cancer, and other poor prognosis tumors.

"Ovarian cancer, in particular, is one of the most immunosuppressive tumor types which is a major reason survival rates have not improved. The therapeutic effects observed in preclinical models in this study presents a major breakthrough for the field.

"Certainly, the next step is to move this promising therapy to [clinical trials](#) in patients, and we plan to have the trials underway soon to test this approach in patients with recurrent ovarian [cancer](#)."

More information: Sophie M. Poznanski et al. Metabolic flexibility determines human NK cell functional fate in the tumor microenvironment, *Cell Metabolism* (2021). [DOI: 10.1016/j.cmet.2021.03.023](#)

Provided by McMaster University

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