Medical Xpress

Bladder cancer discovery leads to potential new treatment pathway

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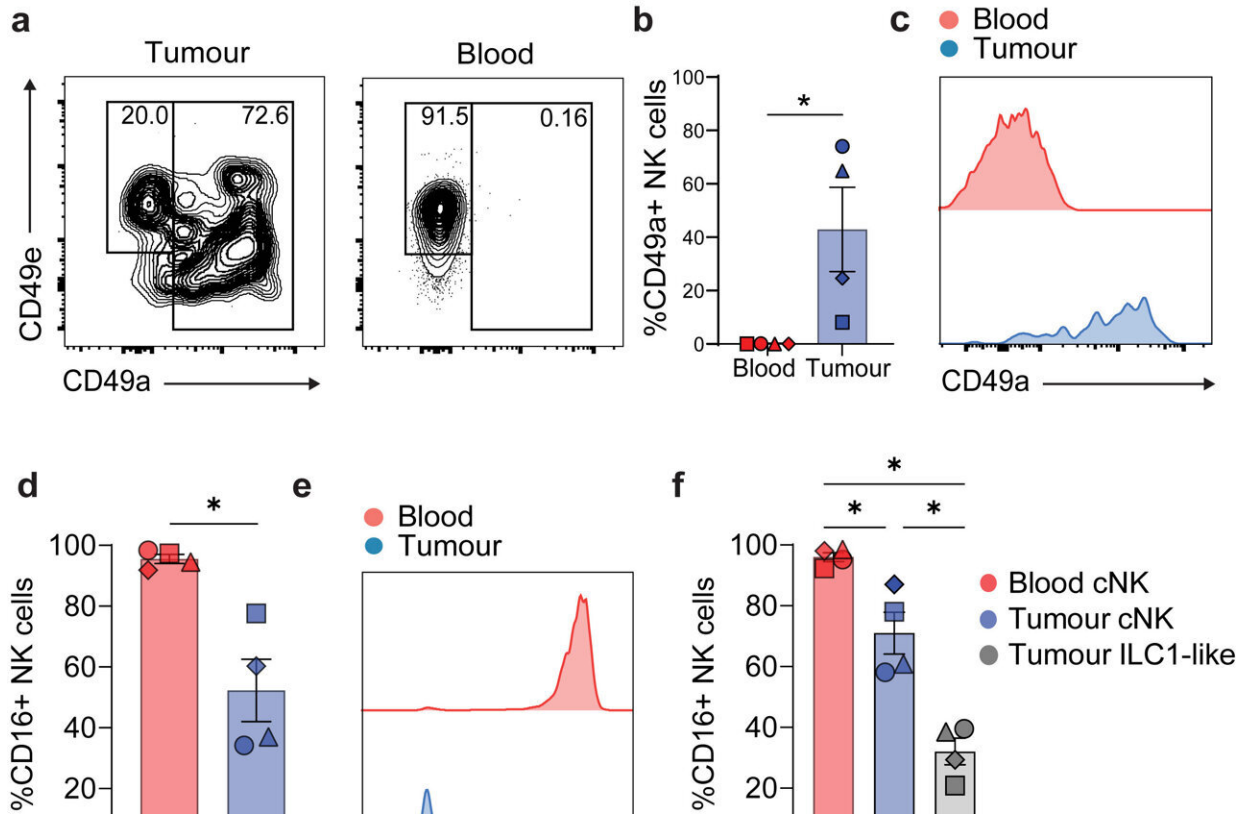

Validation of CD16 downregulation on NK cells within bladder tumors. CD16 marker expression on NK cells from human bladder tumors and matched blood was analyzed by multiparametric flow cytometry. Credit: *eBioMedicine* (2024). DOI: 10.1016/j.ebiom.2024.105176

Researchers from University of Queensland's Frazer Institute have

discovered the mechanism that bladder cancer uses to suppress the immune system's natural killer (NK) cells.

The discovery could see researchers apply existing drugs to target and neutralize the mechanism, allowing the NK immune cells to kill the cancer.

The TRI-based team led by Associate Professor Fernando Guimaraes said the research, published in the journal *eBioMedicine*, could lead to new bladder cancer therapies within three to five years.

"For us, it is all about unlocking the power of immunotherapy," Guimaraes said. The team found that bladder cancer suppresses immune cells by releasing a protein called TGF-β and blocking that protein may offer a new therapy for some of the worst types of the cancer.

"Our research is a step towards clinical trials to explore the effectiveness of TGF-β inhibitors combined with NK cell-based therapies," Guimaraes adds.

Bladder cancer is the ninth most common malignancy in the world, with more than 3,000 people diagnosed in Australia and more than 1,000 dying in 2023. It occurs when cells in the lining of the bladder grow and divide in an abnormal, uncontrolled way.

The bladder cancer immune suppression mechanism was discovered by Guimaraes' Ph.D. candidate Joshua Wong.

"It really was a eureka moment and it's extremely motivating to come in here every day and do your best work, because ultimately we are trying to find a cure for cancer," Wong said.

Bladder cancer patient Mr. Gary Horay said the discovery gave him hope

of more effective treatment options. "This research is just amazing and for those of us living with bladder cancer, it's discoveries like this that give us hope. It's the hope that keeps you going," he said.

Gary's prognosis is good because his cancer was caught early. He felt generally unwell and had difficulty passing urine, so he went to the doctor and tests revealed the cancer. "The lesson from my case is, get checked. If you think there is something wrong, get it checked," Horay said.

The standard treatment for early-stage bladder cancer is endoscopic surgery, occasionally combined with chemotherapy or immunotherapy.

For advanced disease, more invasive surgery or radiotherapy is combined with chemotherapy or immunotherapy, which are associated with significant ill health and life-long impacts on quality of life.

Guimaraes said NK cells are components of the immune system that naturally attack cancer cells and are a focus of emerging cancer treatments, including antibody-based immunotherapies. The side-effects of immunotherapy for cancer are generally less severe than chemo and radio therapy.

His team has used patient samples, as part of a collaboration with UQ researchers and Princess Alexandra Hospital urologists, including Dr. Handoo Rhee, Professor Eric Chung and Dr. Alice Nicol.

More information: Joshua K.M. Wong et al, TGF-β signalling limits effector function capacity of NK cell anti-tumour immunity in human bladder cancer, *eBioMedicine* (2024). DOI: 10.1016/j.ebiom.2024.105176

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