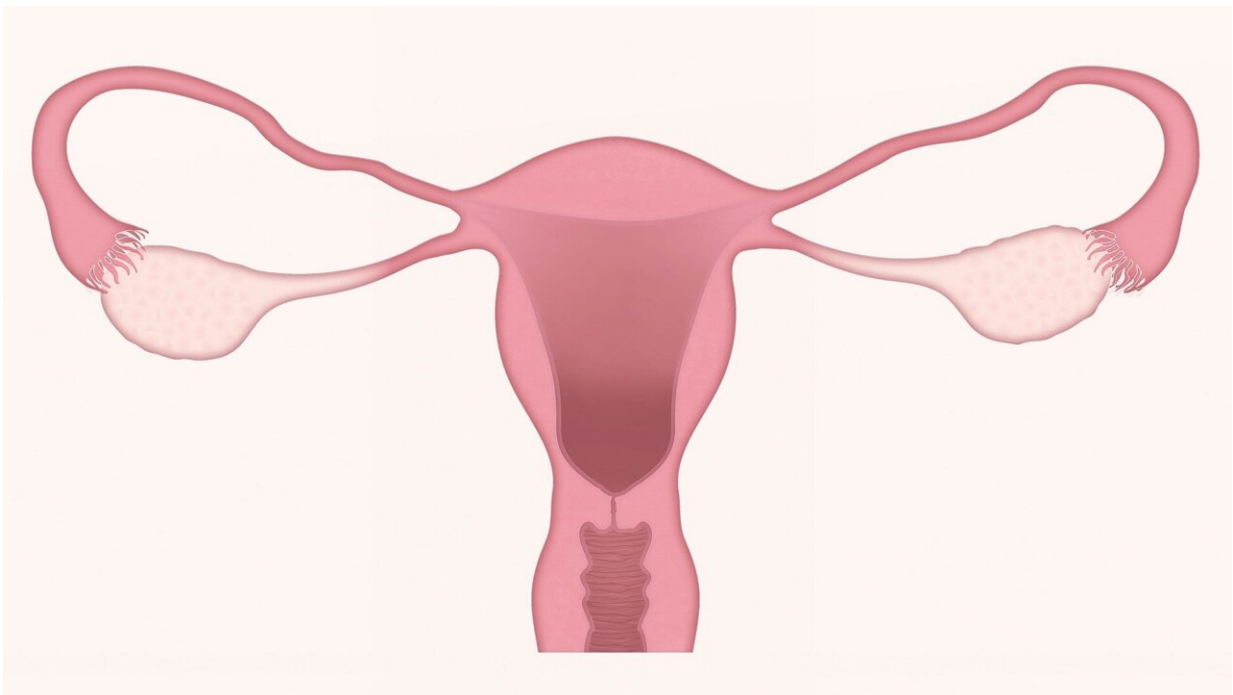


Cancerous uterine tumors found to be more aggressive in Black patients than white patients

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Northwestern Medicine investigators have discovered that uterine serous carcinoma (USC) tumors in Black patients express more aggressive and immunosuppressive features than tumors in white patients, according to a new study [published](#) Aug. 12 in the *Proceedings of the National*

Academy of Sciences.

USC is a rare and aggressive type of endometrial cancer, constituting up to 10% of all primary endometrial cancer cases, according to the Foundation for Women's Cancer. The five-year survival rate for patients with advanced cancer is about 30%.

The cancer also disproportionately affects Black women, with previous research that shows differences in cancer driver mutations in tumors from Black patients compared to [white patients](#).

"Our environment, [socioeconomic status](#) and societal stressors can all impact us psychologically," said senior author Julie Kim, the Susy Y. Hung Research Professor of Obstetrics and Gynecology at Northwestern Feinberg School of Medicine.

"If the environmental insults are chronic, they can have an impact on health. We are seeing differences in these tumors in terms of the genes that they express, in terms of the immune system and the [immune response](#)."

Alongside senior author Kim, the lead author is Grace Foley, a student in the Driskill Graduate Program in Life Sciences. Mazhar Adli, the Thomas J. Watkins Memorial Professor of Tumor Genomics and an assistant professor of obstetrics and gynecology, was a co-author of the study.

Kim and Adli are also members of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

The scientists investigated the molecular and genomic differences in USC tumors between Black patients and white patients by performing single-nuclei RNA sequencing of USC [tumor](#) samples from four white

patients and nine Black patients.

"These tumors are very rare, and so it's difficult to get samples," Kim said. "We had to rely on tumor banks that have been established to obtain these samples."

From these samples, the investigators discovered that tumors from Black patients demonstrated increased expression of genes associated with tumor aggressiveness—notably PAX8, which is commonly increased in other endometrial cancers and in [ovarian cancer](#)—compared to white patients.

Patients with tumors with increased PAX8 expression also had worse overall survival compared to patients with low PAX8 expression, according to the authors.

Furthermore, they discovered that PAX8 directly influences the activity of macrophages—specialized white blood cells that kill [cancer cells](#) and stimulate other [immune cells](#)—within the USC tumor microenvironment to suppress anti-tumor immune responses, and that this was more prevalent in tumors from Black patients.

"This is the first time PAX8 has been investigated for its involvement with immune signaling," said Foley. "Hopefully, this work can contribute to our understanding of endometrial cancer and improve survival for these patients."

The findings may inform new strategies to improve disparities in patient outcomes, according to Kim. They underscore the clinical relevance of increased PAX8 in USC, especially in Black patients, which may serve as a potential therapeutic target, Kim said.

The next steps for the research include duplicating their findings in a

larger patient cohort and identifying current drugs that may help tumors with increased PAX8 expression better respond to the immune system.

"It'll be important to test what we found in a larger cohort to make sure that this is indeed something that is fundamentally different between Black and white women," Kim said. "We want to gather more data so that we can be confident in potentially testing compounds in preclinical studies before going towards clinical trials."

More information: K. Grace Foley et al, Single-nuclei sequencing of uterine serous carcinoma reveals racial differences in immune signaling, *Proceedings of the National Academy of Sciences* (2024). [DOI: 10.1073/pnas.2402998121](https://doi.org/10.1073/pnas.2402998121)

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