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Study: The immune effects of seclidemstat in aggressive ovarian cancer striking young women

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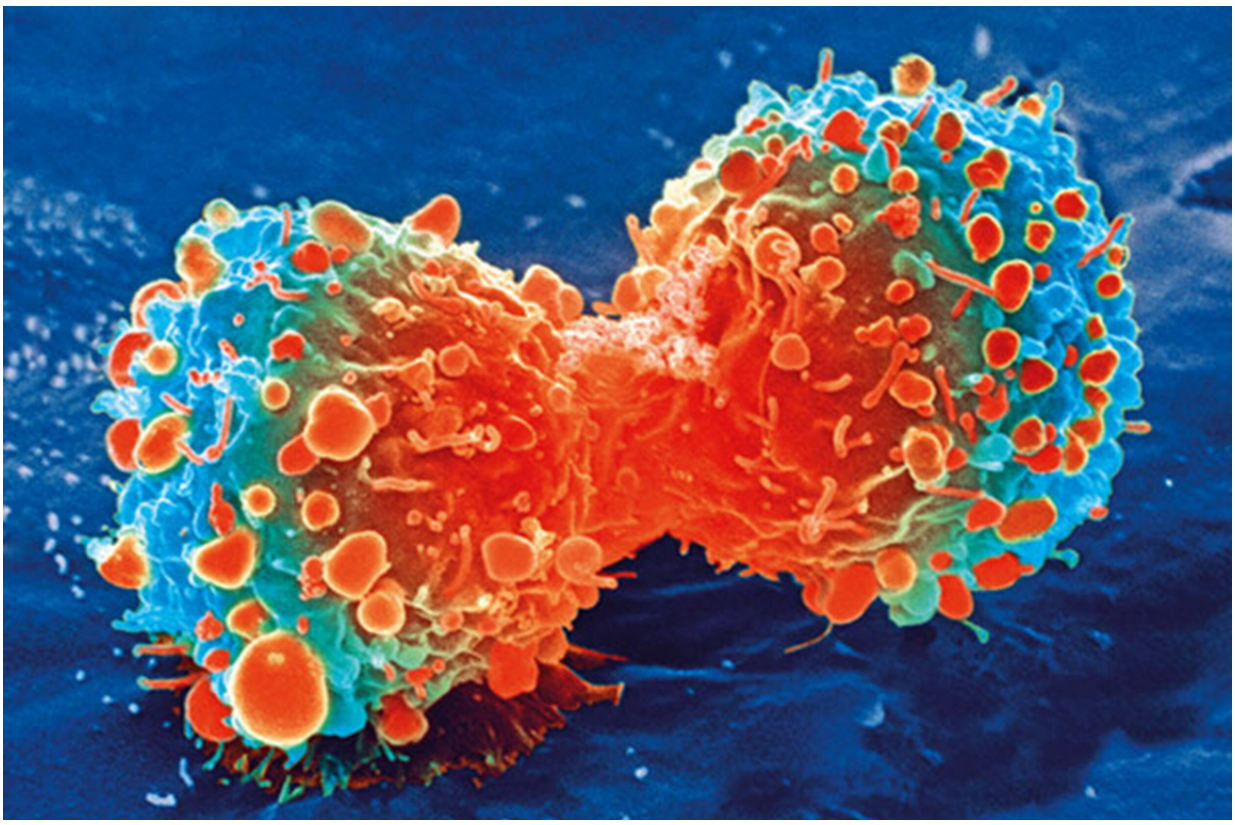

Cancer cell during cell division. Credit: National Institutes of Health

A drug known as SP-2577 could help enable the body's own immune system to attack ovarian cancer, according to a study led by the

Translational Genomics Research Institute (TGen), an affiliate of City of Hope.

Published today in the scientific journal *PLOS ONE*, the study builds on years of research led by Dr. Jeffrey Trent, TGen President and Research Director, into a type of ovarian cancer known as small cell carcinoma of the ovary, hypercalcemic type (SCCOHT), an aggressive and deadly cancer that usually strikes girls and young women.

Clinical trials already are on the horizon to test SP-2577 in combination with another proven immunotherapeutic compound for the first time in patients with SCCOHT.

"Immunotherapy is the future of cancer treatment. Our combination of drugs should promote an immune response in an ovarian cancer that usually does not respond well to immunotherapies," said Dr. Raffaella Soldi, a TGen Research Associate Professor and the lead author of the study. "One drug opens a biological gate, while the other drug helps push immune cells through the gate to attack the cancer."

SP-2577, also known as seclidemstat, was developed in the laboratory of Dr. Sunil Sharma, TGen Deputy Director of Clinical Sciences, and senior author of the study. Seclidemstat has already shown to be a promising drug in clinical trials against a bone cancer known as Ewing sarcoma.

Dr. Sharma, who also is Director of TGen's Applied Cancer Research and Drug Discovery Division, explained that Seclidemstat works by inhibiting LSD1, a protein that is abundant in SCCOHT ovarian cancer. LSD1 also is implicated in initiating and aggressively accelerating many other types of cancer.

"We suggest in this paper that LSD1 inhibition should improve the

immune-therapy response in these tumors," Dr. Sharma said. "This treatment is exquisitely dependent on the mutation found by Dr. Trent and his group. Without that mutation, this treatment would not work."

In 2014, Dr. Trent led and international team of investigators discovered that a single mutation in a gene called SMARCA4 triggered SCCOHT. The SMARCA4 gene—previously associated with lung, brain and pancreatic cancer—was the only recurrently mutated gene in the study's ovarian cancer samples, a finding that at the time Dr. Trent likened to "a genetic superhighway."

"Many genetic anomalies can be like a one-lane road to cancer; difficult to negotiate. But these findings indicate a genetic superhighway that leads right to this highly aggressive disease," Dr. Trent said at the time of his team's discovery. "The correlation between mutations in SMARCA4 and the development of SCCOHT is simply unmistakable."

The study published today in *PLOS ONE*—The novel reversible LSD1 inhibitor SP-2577 promotes anti-tumor immunity in SWItch/Sucrose-NonFermentable (SWI/SNF) complex mutated ovarian cancer—is based on TGen laboratory findings.

In an upcoming clinical trial for those with SCCOHT ovarian cancer, patients will receive Seclidemstat plus another drug, Pembrolizumab, a proven immunotherapy treatment that prevents cancer from hiding from the body's immune system. It uncloaks the tumor so immune cells can see the cancer and attack it.

More information: Raffaella Soldi et al, The novel reversible LSD1 inhibitor SP-2577 promotes anti-tumor immunity in SWItch/Sucrose-NonFermentable (SWI/SNF) complex mutated ovarian cancer, *PLOS ONE* (2020). DOI: 10.1371/journal.pone.0235705

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