

# T-cells can be directed to treat a variety of ovarian cancers

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Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. H&E stain. The micrograph shows: Simple mucinous epithelium (right) and mucinous epithelium that pseudo-stratifies (left - diagnostic of a LMP tumour). Epithelium in a frond-like architecture is seen at the top of image. Credit: Nephron /Wikipedia. CC BY-SA 3.0

With only incremental improvements in ovarian cancer survival over the last 40 years, there is a clear need for new treatment options with long-lasting results. Many researchers have turned toward the development of

immunotherapies that direct T-cells to selectively eliminate ovarian tumor cells, but an appropriate therapeutic target for ovarian cancers has remained elusive.

Now, scientists at The Wistar Institute have discovered a receptor-protein that is expressed on the surface of different types of ovarian tumor cells, including clear cell and mucinous ovarian tumors, two of the most aggressive subtypes of the disease. The protein is not found on non-ovarian healthy tissues in adult women, meaning that this protein could represent a highly specific therapeutic target in a range of ovarian tumors. Additionally, T-cells could be directed to treat these tumors with almost no adverse effects observed. The findings were published in the journal *Clinical Cancer Research*.

"We began this research almost four years ago with the goal of finding a safe and effective immunologic approach to the treatment of epithelial [ovarian tumors](#)," said José R. Conejo-Garcia, M.D., Ph.D., professor and program leader of the Tumor Microenvironment and Metastasis Program at Wistar and lead author of the study. "Finding a receptor expressed exclusively on ovarian cells allows us to utilize groundbreaking targeted T-cell technology to potentially eliminate cancerous cells in patients."

The researchers showed that the follicle-stimulating hormone receptor (FSHR) is expressed on the surface of tumor cells in approximately 50 to 70 percent of serous ovarian carcinomas. It was expressed in 70 percent of endometrioid carcinomas, 67 percent of mucinous ovarian carcinomas, and 33 percent of clear cell ovarian carcinomas. While the receptor is expressed in non-cancerous ovarian cells, it is not expressed in any other tissue in the body and targeted treatment would only affect the ovaries while eliminating [cancerous cells](#).

When it comes to potential targeted treatments, one of the more promising developments in immunotherapy in the past few years has

been the use of chimeric antigen receptor (CAR) T-cell technology. CARs are proteins that allow T cells to recognize specific antigens found on tumors and eliminate them. This has resulted in remarkable results in cancer patients, but so far it has been limited to B-cell blood cancers like chronic lymphocytic leukemia.

Conejo-Garcia and his team developed a modified version of CAR technology they refer to as chimeric endocrine receptor-expressing T-cells (CER-T). These T-cells are directed to [ovarian cancer cells](#) expressing FSHR with the full-length sequence of the FSH hormone rather than the antibody fragment typically used in CAR-T cells. They were able to induce the rejection of established tumors of human origin in immunodeficient mice. In addition, the researchers did not observe adverse effects when administering T-[cells](#) of mouse origin in tumor-bearing mice that otherwise had a normal immune response. There was no evidence of weight loss, signs of distress, no effect on healthy tissues, and levels of liver enzymes and glucose remained unaffected by the treatment.

"Ideally, we'd like to see this technology used after initial treatment with surgery and chemotherapy," said Alfredo Perales-Puchalt, M.D., Ph.D., a postdoctoral fellow in the Conejo-Garcia lab and first author of the study. "Recurrence remains a major concern in the treatment of ovarian cancer, and so we believe the method we studied could be used to rid the patient of residual disease and drastically reduce the chance of the cancer returning."

**More information:** A. Perales-Puchalt et al, Follicle-Stimulating Hormone Receptor Is Expressed By Most Ovarian Cancer Subtypes And Is A Safe And Effective Immunotherapeutic Target, *Clinical Cancer Research* (2016). [DOI: 10.1158/1078-0432.CCR-16-0492](https://doi.org/10.1158/1078-0432.CCR-16-0492)

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