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Wistar Scientists Develop DNA-delivered Immunotherapy that Targets Ovarian Cancer More Effectively

Novel DNA Delivery approach of Bispecific T Cell Engagers brings T cells to tumors, improving how they recognize and attack cancer

PHILADELPHIA — (JULY 21, 2026) — Wistar scientists have developed a new type of bispecific T cell engager, or BTE, that is effective against ovarian cancer in preclinical studies. It's a major development for this type of immunotherapy, which has been used successfully against blood cancers, but has so far been less effective in solid tumors.

The researchers developed a novel “knob-into-hole” platform to deliver BTEs whereby they engineer an antibody “knob” that is forced to match with an antibody “hole” resulting in an accurate fit—like two puzzle pieces locked together perfectly.

They showed that BTEs could be delivered with DNA-based technology, a powerful approach that could significantly reduce manufacturing costs and treatment burden on patients. They also developed a way to deliver two different antigen-targeting BTEs in a single dose, a key strategy to overcoming therapeutic resistance.

“I think it’s a major advancement for the field of bispecific antibodies,” said Pratik S. Bhojnagarwala, Ph.D., a postdoctoral fellow in the lab of [David B. Weiner, Ph.D.](#), at The Wistar Institute’s [Vaccine and Immunotherapy Center](#) and first author of the study. “It’s also significant for ovarian cancer, where there’s a real need for new therapeutic options, but there are likely broader applications for other solid tumors as well.”

Bispecific T cell engagers are a powerful immunotherapy that have seen a significant increase in clinical use over the past 10 years. They help the immune system fight cancer by physically grabbing cancer cells and disease-fighting T cells and bringing them together, which redirects the killing activity of T cells against cancer cells.

Existing BTEs have been ineffective against solid tumors like ovarian cancer in part because of their short half-life, which causes them to be rapidly cleared from the body. Solid tumors are also less uniform than blood cancer cells, making them better able to evade BTEs, which work by targeting a single antigen on the cancer cell’s surface. The new technology solves both problems.



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The first key innovation is using a DNA-based delivery platform to make the patient's own muscle tissue function like a "factory" that produces BTEs directly within the body. The knob-into-hole design adapted for DNA delivery by the researchers further improves the half-life of the BTEs, making them last longer. This approach is more affordable, easier to manufacture, doesn't require cold storage, and lasts longer with fewer doses, Bhojnagarwala explained.

Researchers also showed that they could use the platform to deliver two different BTEs at the same time, an approach that's more effective at targeting the diverse antigens found on solid tumors.

"Showing that we can deliver these really complex molecules in vivo in murine models was a very exciting achievement that demonstrates its potential as a next-generation tool to improve patient outcomes," Bhojnagarwala said. "The cost of therapy could become less expensive, and we could also require fewer doses, because the body's muscle cells keep producing it, instead of having to return for multiple doses."

In a preclinical model, researchers showed that the new BTE lasted longer in the body and was more effective at slowing tumor growth. They also conducted a study in the lab that showed that it worked on cells from human patients with ovarian cancer. Another experiment showed that it could be combined with an immune checkpoint blockade, an immunotherapy commonly used in solid tumors, to make the treatment more effective.

Next, researchers plan to test the therapy in more advanced models of human cells, taking it a step closer to human trials. They also hope to study it against other cancer targets.

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