New immunotherapy could treat cancer in the bone

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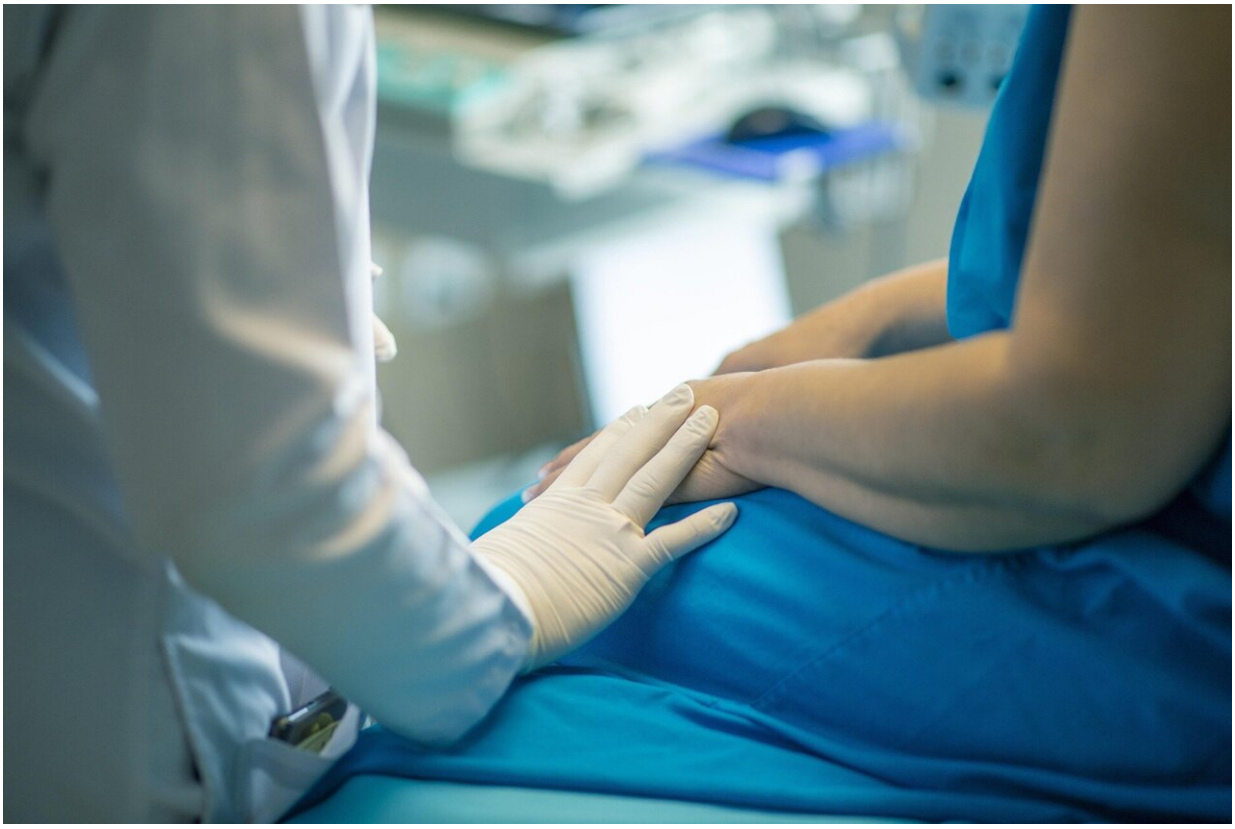

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A new type of immunotherapy, developed by UCL researchers, has shown promising preclinical results against a bone cancer called osteosarcoma, as part of a study in mice.

Osteosarcoma is the most common bone cancer in teenagers but is still relatively rare, with around 160 new cases each year in the UK. Meanwhile, more than 150,000 people suffer from cancer that has spread to the bones.

Cancer that starts in or spreads to the bones is particularly hard to treat, meaning that it is a leading cause of cancer-related death. It is also frequently resistant to chemotherapy, so new treatments are needed.

The results of the experiment, published in *Science Translational Medicine*, found that using a small subset of immune cells, called gamma-delta T cells (gdT cells) could provide an efficient and cost-effective solution.

gdT cells are a less well-known type of immune cell that can be made from healthy donor immune cells. They have strong innate anti-cancer properties, can kill antibody labeled targets and can safely be given from one person to another, without the risk of graft-versus-host disease.

In order to manufacture the cells, blood is taken from a healthy donor. The gdT cells are then engineered to release tumor targeting antibodies and immune stimulating chemicals called cytokines, before being injected into the patient with cancer in the bone. This new treatment delivery platform is called OPS-gdT.

The researchers tested the treatment on mouse models with bone cancer and found that OPS-gdT cells outperformed conventional immunotherapy when controlling osteosarcoma growth.

Lead author, Dr. Jonathan Fisher (UCL Great Ormond Street Institute of Child Health and UCLH), said, "Current immunotherapies such as CAR-T cells (another type of immunotherapy using genetically modified immune cells) use the patient's own immune cells and engineer them to

improve their cancer-killing properties. However, this is expensive and takes time, during which a patient's disease can get worse. And, while it is an effective treatment for leukemia, it has been found to be less effective against solid cancers.

"An alternative is to use an 'off the shelf' treatment made from healthy donor immune cells, but in order to do this, care must be taken to avoid graft-versus-host disease, where the donor immune cells attack the patient's body.

"The Fisher Lab discovered a way of engineering the previously under-utilized gdT cells, which have been clinically proven to be safe when made from unrelated donor blood. This offers a more cost-effective alternative to current per-patient manufacturing."

As part of the trial, researchers injected the mice with gdT cells that hadn't been engineered at all, an anti-tumor antibody, OPS-gdT cells alongside a bone sensitizing drug, and CAR T-cells.

They found that the OPS-gdT cells were most effective when partnered with the bone sensitizing drug—which has previously been used on its own to strengthen weak bones in patients with cancer. This treatment prevented the tumors from growing in the mice that received it—leaving them healthy three months later.

Dr. Fisher said, "Thousands upon thousands of people have cancer that spreads to the bones. There is currently very little that can be done to cure these patients. However, this is an exciting step forward in finding a potential new treatment.

"Our hope is that not only will this treatment work for osteosarcoma but also other adult cancers."

Following the successful preclinical trial, the team is now generating data on the effectiveness of OPS-gdT cells in secondary bone cancers and plan to move towards an early phase clinical trial using patients with secondary cancers within the next couple of years.

Sara Garcia Gomez, Senior Business Manager at UCLB, said, "We work closely with clinicians at the forefront of research to help them bring new treatments from the lab to the patient. With few treatment options out there for bone cancers, this study has shown encouraging potential for new therapies. We will continue to work closely with Dr. Fisher and his team through the next important stages of exploring the potential of this new approach."

More information: Daniel Fowler et al, Payload-delivering engineered γδ T cells display enhanced cytotoxicity, persistence, and efficacy in preclinical models of osteosarcoma, *Science Translational Medicine* (2024). DOI: 10.1126/scitranslmed.adg9814.
www.science.org/doi/10.1126/scitranslmed.adg9814

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