Killer cell immunotherapy offers potential cure for advanced pancreatic cancer

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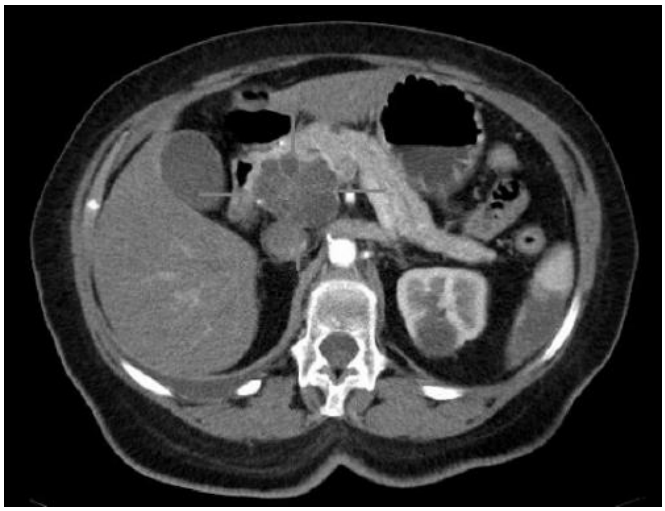

Axial CT image with i.v. contrast. Macrocystic adenocarcinoma of the pancreatic head. Credit: public domain

A new approach to treating pancreatic cancer using 'educated killer cells' has shown promise, according to a new study by UNSW medical researchers.

Researchers from UNSW Sydney and the California Institute of Biomedical Research (CALIBR) have demonstrated the success of a new, cell-based immunotherapy for pancreatic cancer. The treatment led to mice being completely cancer-free, including cancer cells that had already spread to the liver and lungs. The landmark study was recently published in top-tier academic journal *Gut*.

In the study, the team obtained pancreatic cancer cells from patients with late-stage disease, and transplanted them into mice. They then took the patients' immune cells and modified them to specifically identify and eliminate the cancer cells – which is why they're also called educated killer cells, or CAR-T cells.

"After injecting these CAR-T cells into mice, they were capable of finding any cancer cells in the body, stick to them via surface markers, and subsequently destroy the cancer cells. The treatment was so effective that the animals remained tumour-free," lead author Professor Chris Heeschen from UNSW Medicine says.

The researchers didn't just demonstrate the outstanding efficiency of their new CAR-T immunotherapy for the treatment of pancreatic cancer. They also introduced a new technology that allows them to completely control the activity of CAR-T cells.

Using so-called 'switchable CAR-T cells', the team used this new concept for the first time in pancreatic cancer, and divided cancer target recognition and subsequent killing of the cancer cells into two separate processes.

Dr. Alexandra Aicher, joint corresponding author, who recently moved to the School of Medical Sciences at UNSW Sydney, says CAR-T cells are very powerful therapies that need to be tightly controlled.

"Switchable CAR-T cells now allow us to stop the treatment, if required, thus making our therapy extremely safe. Switchable CAR-T cells will also ensure we can rapidly adapt our treatment target to another cancer surface marker, if resistance may occur."

The team now hopes to bring this promising therapy to the clinic, and is seeking funding to progress.

"This is the first time in my career that I have seen an actual cure for this very aggressive disease. The next step will be to combine CAR-T cells with treatments that make it easier for the CAR-T cells

to reach the cancer cells," Professor Heeschen says.

"Pancreatic cancer is known for its fortress-like structure that needs to be overcome in order for the CAR-T cells to reach their target cells and remain at maximum activity. We hope to have this new treatment strategy ready for the clinic within the next three years, pending funding."

More than 3,300 Australians will be diagnosed with pancreatic cancer in 2018. Pancreatic cancer is often diagnosed at a late and advanced stage, when the tumour has already spread to other organs. Current treatments only marginally extend the lifespan of pancreatic cancer patients, with five-year survival at just 7.7 percent.

More information: Deepak Raj et al. Switchable CAR-T cells mediate remission in metastatic pancreatic ductal adenocarcinoma, *Gut* (2018). DOI: 10.1136/gutjnl-2018-316595

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