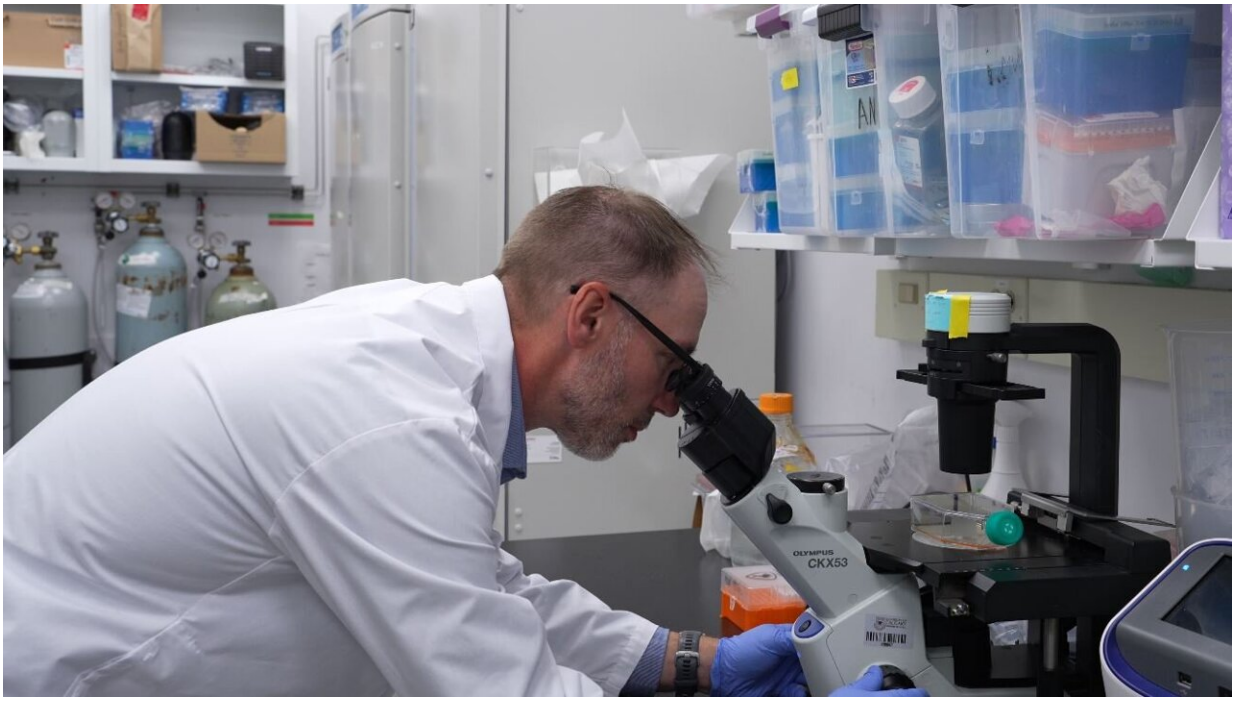
Researchers translate a hypothesis into a personalized treatment for cancer

December 1 2023



Franz Zemp designed a personalized CAR T-cell therapy for a Calgary teen. Credit: Arnie Charbonneau Cancer Institute, University of Calgary

Dr. Franz Zemp, Ph.D., gets chills talking about how his idea to target a specific cancer cell has evolved.

"I never thought I'd be that close to a patient. I never thought anything that I would build, or design would be in a clinical trial," says Zemp, an

adjunct assistant professor at the Cumming School of Medicine (CSM). "I would imagine it is every medical scientist's dream to build something or be part of something that could help somebody someday."

Zemp designed a chimeric antigen receptor (CAR) T-cell therapy to attack alveolar soft part sarcoma (ASPS) for Calgarian, Milan Heck. In 2015, Heck was a patient at the Alberta Children's Hospital. After undergoing the initial resection of the sarcoma in her hip, she was approached to donate samples of her cancer to the Clark H. Smith Tumor and Tissue bank at the University of Calgary.

"I had thought, why not? I'm not going to do anything with a bunch of tumor tissue. It was hard to imagine any kind of research development from just these few samples," remembers Heck, 14 at the time. "I thought it would just be frozen somewhere."

That donation would be one of many, because her cancer kept returning. During each surgery, some of the tissue removed would be sent to the biobank. Part of those samples was used by Drs. Donna Senger, Ph.D., and Jennifer Chan, MD, to develop a mouse model of Milan's cancer, which researchers say was a pivotal piece of the process.

"In 2021, I got an email from Dr. Douglas Mahoney and found out a project had been started that used my samples, and that it could have significant clinical potential," says Heck. "He said that a post-doc in his lab had developed a new CAR T-cell immunotherapy for my cancer that and that it was showing signs of working."

Finding a target for the immunotherapy

ASPS is a unique form of cancer affecting children and young adults which is driven by one molecular rearrangement. A chromosome breaks and reforms essentially creating a new gene that is not seen in nature.

Zemp suspected that the irregular chromosome would be driving changes within the cells that could be a potential target for CAR T-cell immunotherapy. He looked for proteins that were present in the cancer cells that were not found in normal cells.

"Our T-cells, one of our immune cells, are great at killing cancer cells—if they can see them," says Zemp. "This therapy works by genetically engineering a patient's T-cells to detect cancer-specific markers. We genetically engineered Milan's T-cells in the lab, and then gave them to the mouse model."

Zemp hoped the T-cells would do what they do in nature. He remembers the first time he checked back on the mice to see whether their modified immune system was responding.

"I was shocked to see such an immediate response in the mice. It was incredible! That, was a cool day, probably the best day of my career," says Zemp. "We couldn't have done it without her samples. And, not just to test the medicine we built. We also needed to test the hypothesis that the marker we chose to target would be consistently expressed In Milan's cancer over time, even after other forms of treatment. Everything went forward from there."

It moved quickly. Collaborations were formed at local, provincial and national levels. The local collaboration included scientists at the University of Calgary, biomanufacturing experts at Alberta Precision Labs, and clinicians at the Tom Baker Cancer Center and Alberta Children's Hospital.

"We needed to quickly understand whether this medicine that we built had any real-world potential. It wasn't easy. It took a lot of work. It took time to build the right team in the right way," says Mahoney, Ph.D., an associate professor at the CSM and associate director of basic and

translational research of the Arnie Charbonneau Cancer Institute.

Center for cancer immunotherapy created

Researchers quickly realized the learnings from Heck's cancer could also be applied to other people with ASPS and possibly other cancers.

"It is perhaps the thing that I'm most proud of. The entire effort from idea to first patient experience is less than three years. This is very unusual. It's because we've had lots of resources and lots of support at the university and Alberta Health Services (AHS) to try and accomplish this," Mahoney adds.

The UCalgary scientist says the astonishing timeline and discovery have also been powered by philanthropy.

"This type of research is impossible without philanthropy. It's that simple," says Mahoney. "It is expensive and resource intensive to drive a discovery or an invention into clinical translation."

The Riddell Center for Cancer Immunotherapy will encompass projects at several locations including the Arthur J. E. Child Comprehensive Cancer Center.

"We are very excited about the future of immunotherapy, as a pillar of cancer treatment," says Chan, director of the Charbonneau Institute.

"From cell-based therapies, like the CAR T-cells created for Milan, to the development of new antibodies, immune-modulating drugs, and cancer vaccines, we are innovating, collaborating, and leveraging new technologies every day in our labs and with our partners including AHS to find new ways to harness the body's immune system to treat cancer and ultimately improve outcomes."

The Riddell Center will allow for an expansion of the translational pipeline from discovery and invention in the research lab through to biomanufacturing and testing of clinical-grade cell and immune therapy products. Mahoney says having scientists and clinicians in the Arthur Child will increase the collaborative potential and the speed to drive ideas into clinical trials.

The potential of a new treatment option for her patients has Dr. Mona Shafey, MD, excited about being part of this scientific effort. She says immunotherapy is proving to be very effective in some of her patients with blood cancers, particularly those with an aggressive form of non-Hodgkin's lymphoma called diffuse large B-cell lymphoma.

"It can be quite dramatic. Sometimes you can see an impact within a week to a couple of weeks after the treatment," says Shafey, hematologist at Foothills Medical Center and clinical associate professor at the CSM. "And in fact, some patients have been demonstrated to have complete responses within a month of receiving the CAR T-therapy."

While results are promising and have created hope for a new treatment option for some cancer patients, Shafey says it is important to remember that we are still only scratching the surface of the potential of immunotherapy, and that at this point CAR-T cell therapy has been used to treat blood cancer patients who have failed other lines of treatment in hopes of putting them into remission.

She would like to see the Riddell Center become the place where new medicines are developed, including new CAR T therapies for a wide range of cancer types for many patients like Heck, who never imagined her donated tumor tissue would result in a personalized treatment, if or when she needs it.

"I can think back to my diagnosis at 14, with doctors telling me that this

cancer had no standard treatments, and that the best they could do was try radiation and surgery," says Heck. "My dream is that one day the CAR T therapy developed in the Mahoney lab becomes a standard of care. I cannot say enough about this team. They are absolutely brilliant people. It's not just research they do, it's the compassion they show and what they've been able to accomplish to actually develop something promising. I really am grateful with all of my heart for who they are as people."

Heck recently completed a Bachelor of Health Sciences degree at UCalgary and is now a research assistant in immunology at the CSM. She is planning to complete a master's degree and is considering a career in science translation. She knows, unequivocally, that what happens in the lab can translate to the real world and she wants to help others understand that.

Provided by University of Calgary

Citation: Researchers translate a hypothesis into a personalized treatment for cancer (2023, December 1) retrieved 28 April 2024 from https://medicalxpress.com/news/2023-12-hypothesis-personalized-treatment-cancer.html