The pandemic's silver lining? Widespread COVID immunity could provide platform for future cancer treatment

Steve McKinley

THE GOAL: To determine whether someone's immune response to the coronavirus can be repurposed to attack cancer tumours, given the premise that a large portion of the global population is expected to develop that immune response — through infection or potential vaccination — in the coming years.

THE TEAM: Dr. Shashi Gujar, a scientist in the Department of Pathology, Faculty of Medicine at Dalhousie University in Halifax, who is leading an international collaboration with partners in France, Denmark, Germany, the United States and India. Also on the team are Youra Kim, also with Dalhousie's Department of Pathology, and Jonathan Pol and Guido Kroemer, both of France.

THE TIMELINE: Using the immune response to COVID-19 to battle tumours is still many years down the line, but given the widespread distribution of the coronavirus, it's expected that hundreds of millions of people globally will have the immune response tools to be repurposed to fighting cancer. Cancer immunotherapy is already being used to treat melanoma, the deadliest form of skin cancer.

What brought on this idea?

Gujar's team has been working for several years on cancer immunotherapy as an alternative to chemical and radioactive treatments. He likes to refer to cancer immunotherapy as "retraining the immune system so it can go after cancer."

His work until now has been focused on using reoviruses for that purpose. Reoviruses are common RNA viruses that result in either asymptomatic infections or mild gastrointestinal symptoms in humans.

About 50 per cent of the human population has antibodies to the reovirus in their system. That means that at some point about 50 per cent of the world's population has been infected by a reovirus.

Those reovirus antibodies can be re-tasked to attack cancer cells, Gujar's team will argue in a soon-to-be-released paper. And if that can be accomplished using reovirus antibodies, it can likely be accomplished with coronavirus antibodies, too.

How would it work?

When the human body encounters an invader — called an antigen — it mounts an immune response. The response involves identifying the intruder, mounting a defence and killing the intruder.

T-cells are a major component in that process. The version that Gujar works with is

called the CD8+ T-cell — a cytotoxic, or "killer cell."

When an intruder is present, T-cells increase rapidly to fight the infection. When the fight is over, those numbers dwindle, but a small number of "memory" T-cells remain.

When a person encounters the same intruder again, the remaining T-cells recognize the antigen and produce more T-cells to attack the infection. With T-cells for that intruder already in place, the immune system mounts a defence far more rapidly than it was able to the first time.

This is the basis of immunity. If a person has had the measles, after they've fought off the infection — or received a measles vaccination — for many years afterward there remain some memory T-cells in the body.

If that same measles virus comes along again, those T-cells recognize it and mount a rapid response, stopping the disease in its tracks.

The T-cells can do that because they recognize a specific sequence of amino acids that the measles virus have. This is called an epitope.

Picture it like this: an epitope is like a hat the virus wears. If a T-cell sees an intruder with a blue hat, it recognizes it as a measles virus, mounts a response — producing more T-cells — and attacks it.

If it sees a red hat, or no hat at all, it ignores the intruder — it's somebody else's problem.

And it may well be. The body's immune system keeps all kinds of T-cells on hand from previous infections it has battled. There could easily be another T-cell that recognizes the red hat, and jumps into action.

That being said, why don't T-cells recognize cancer cells as intruders and mount an attack and kill them?

"Cancer is a process that takes a long time to develop inside your body. And the cancer cell is basically a mutated version of your cells," said Gujar. "So your T-cell, or your body, is used to looking at those normal cells day-in, day-out and ignoring them, because you don't attack your own, right?"

There is a hypothesis that the body is constantly attacking and killing cancer cells before they become problematic, he added, and it is only the occasional instance when a T-cell fails to recognize a cancer cell as a threat and the cancer begins to grow.

This is called "escape of immune recognition." And as the cancer continues to grow, the immune system continues to fail to recognize it as a threat.

"Cancer is very sneaky," adds Gujar. "(Cancers) also produce things that will dampen the functions of these T-cells and other immune cells.

"So it's a double whammy. Not only have they learned how to hide from the immune system to start with, but they also produce what we call immunosuppressive cytokines or an environment where most of the immune cells don't function properly."

So even a T-cell that recognizes a cancer cell may not be very effective in fighting it.

On the other hand, an antiviral T-cell is very potent.

So Gujar's research over the past several years has been about tricking those antiviral T-cells into thinking cancer cells are the viruses they usually attack.

He does this by attaching the epitope that the T-cell recognizes to a cancer cell — in essence, taking the blue hat that the T-cell recognizes on the virus it always attacks and putting it on the cancer cell.

That sounds easier than it is. In reality, T-cells in different humans may recognize different epitopes for the same virus. That is, one person's T-cells might recognize a virus by the fact it is wearing a blue hat. Another person's T-cells might recognize the same virus by the fact it is wearing red gloves.

That means that before Gujar can repurpose a particular person's T-cells into attacking a cancer cell, he has to figure out how that specific T-cell recognizes the virus it's meant to attack — which epitope it recognizes on the virus.

Once that has been accomplished, he can create that epitope in the lab, deliver it to the tumour and let the T-cells attack the tumour.

This same approach can be applied to the coronavirus, he believes.

"By the time it is all said and done in the next year or two, most of the world population will be either infected or vaccinated," he said. "So all these people will have anti-COVID immunity. And then, for better or for worse, there is just so much research that is going on right now in COVID, that the anti-COVID immune response will be very well characterized."

That means that, potentially, a large portion of the world's population may have, within themselves, the tools to battle cancer without radiation or chemotherapy.

What are the pressing questions that need to be answered?

Before that becomes common treatment though, there are still some problems that need to be ironed out. One of those problems is, once they've made the epitopes for a particular T-cell in the lab, how then do they deliver those epitopes to the tumour?

"We already have evidence in the lab that as soon as we put (epitopes) in tumours, they take it … this was something that wasn't really clear in the past," said Gujar.

One method is by direct injection. This is already being done with melanomas. But it's still unclear whether that epitope will spread throughout the tumour. Are repeated injections into the tumour in different areas necessary so the epitope is absorbed equally? And how long will those epitopes last anyway?

These are questions Gujar and his teams will be asking as they continue their research.

Additionally, at this stage of research, no one is sure how long memory T-cells for the coronavirus will last in the human body. That is, no one is yet sure how long an immunity to the coronavirus will last.

That is part of ongoing research, which will also provide Gujar's team with types and frequencies of the epitopes in the coronavirus that human T-cells recognize.

That will impact how widespread a coronavirus T-cell cancer treatment might be in the future, but not on the general principle itself.

A workable cancer immunotherapy treatment could potentially help millions battle cancers with few of the side effects of radiation or chemotherapy.

"When we were working on this, we always kept joking about the old saying, "If life gives you lemons …" said Gujar.

"It's the same thing — the whole world was thrown by this lemon. So how do we make the lemonade out of it? Because that's our reality, whether we like it or not. So how do you deal with it and can we make something positive out of it?"

COVID: Front-line thinkers is part of a regular series highlighting COVID-19 research in Canada.

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