

# New kind of homing beacon targets cancerous cells and other diseases

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The CD19 molecule on a leukemia cell is like a tiny radio broadcasting to the world, “I’m leukemia. Come and get me.” Credit: Kevin Craft

Leukemia is a deadly cancer in which rogue white blood cells roam the bloodstream, slowly killing the body that gave them life.

But this insidious killer has an Achilles' heel. Many [leukemia](#) cells are betrayed by a molecule on their exterior surfaces known as CD19.

When activated, CD19 will kill the [cancer](#) cell to which it is attached. To

cancer biochemists, CD19 is like a tiny radio signal broadcasting to the world, "I'm leukemia. Come and get me." But when a body is without the immune cells equipped to hear CD19's siren song, the leukemia is free to carry on its lethal business undeterred. So, researchers created leukemia-specific [human immune cells](#) that track down and kill any leukemia cell exhibiting the CD19 signal.

Developing better hunter-killer cells to target cancers is part of what goes on in the lab of Stanley Qi, assistant professor of bioengineering and of chemical systems biology. In a recent article in Nature Communications, Qi and his team explained how they used the CRISPR gene-editing technique to equip certain [immune cells](#) with a homing beacon to target leukemia.

Though this is still basic research, Qi's approach could one day lead to new ways to treat the roughly 170,000 Americans who were diagnosed leukemia and other blood-related cancers last year.

But leukemia is just the beginning. Cancers of the blood system account for a mere fraction of all cancers, most of which are solid tumors—clumps of cells that grow inappropriately in breasts, ovaries, lungs and prostate, for example. Solid tumors take refuge within a complex microenvironment of molecules, hormones and growth factors that help these unwanted cells spread and suppress the immune system agents that seek to kill the tumor.

Qi hopes to prove that his technique could work on all cancers because it targets a beacon found not just on leukemia, but on almost every type of cell in the body, including solid cancers. That is why Qi's team is so excited. By using CRISPR to hack ever more precisely into the genome, Qi believes it may one day be possible to bioengineer therapeutic agents to dial in on not just cancers, but other diseases that use the same radio-like signaling that has already used to attack leukemia.

## Hacking biochemical communications

Qi's team describes used the CRISPR gene-editing technique to modify cellular receivers known as G protein-coupled receptors—GPCRs for short.

One of the largest and most important families of chemical receptors in human physiology, GPCRs are like cellular antennae, constantly searching for biochemical signals that allow cells to communicate and to function together as tissues. When antennae molecules recognize a particular signal—a molecule like CD19, for instance—they initiate a cascade of cellular communications with the nucleus that triggers a broad array of genetic outcomes ranging from immune responses to chemical generation to cell reproduction.

When GPCRs detect opiates, for instance, they instruct cells to flood the body with pleasure-enhancing, painkilling dopamine. As such, GPCRs are the gateways—the input/output devices—by which various important hormones, proteins, fatty acids and drugs communicate on a cellular level.

GPCRs are found on the surface of almost every cell type in the body. Of the 20,000 or so genes that make up the human genome, 800 alone are dedicated to distinct GPCR variations. "That's a huge proportion of our genetic code," Qi says, noting that some 40 percent of all drugs already on the market today target GPCRs.

Therein lies the excitement in this research. By developing a technique that can turn the plethora of GPCRs into tattle tales for different illnesses and dysfunctions, Qi's team has developed a platform for hacking into the body's biochemical communications network to battle disease. In the cancer example described above, the team has been able to recalibrate the GPCR antennae to home in on key molecules present

in the tumor microenvironment.

## Doing the ChaCha

Qi has dubbed their variation of the CRISPR technique "ChaCha" for the way it involves a dance of two molecules to modify the genetic code of GPCRs. "With ChaCha we can now create GPCR antenna devices that recognize virtually any molecule imaginable, including hormones, cellular growth factors and synthetic drugs," he says.

While there are existing CRISPR techniques that target GPCRs, ChaCha has two key advantages. First, ChaCha is dose dependent. A GPCR trained to recognize a specific hormone, for instance, would be able to modulate its response based on the relative presence of that hormone—more hormone would mean a greater response, and vice versa. "This is a programmable logic by which cells can figure out what their charge is and when they have completed an assigned task," he notes. "We're trying to design smarter cells."

The second advantage is that ChaCha is reversible. A cell modified for a specific task could be returned to its normal state once its duty was complete.

Early clinical trials have been promising and are already leading to new leukemia therapies. What has been most revolutionary, however, is a growing ability to use living cells as therapies, opening a world beyond traditional chemotherapies.

Qi and collaborators are excited by the broader prospect of adapting their genetic approach to an array of diseases ranging from solid tumors to neurological disorders such as Parkinson's disease and autoimmune disorders like lupus.

Asked about next steps for ChaCha, Qi says he plans to continue to test the bounds of his technique to make it easier to create cells to attack disease or to conjure desirable chemicals in the body. There has already been commercial interest in the approach. "We are just at the beginning of a very exciting period in predictably designing living [cells](#) for medical uses," Qi says. "Now we're moving quickly and in the right direction."

Provided by Stanford University

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