T-cells trained to fight viruses offer hope for bone marrow transplant patients

Viruses are stubborn bastards. As creatures that exist on the line between life and death, they are very hard to kill. Most of time, it falls to our immune system to handle them with limited help from medications. Thankfully, most of the time the immune system wins.

In patients who have just received a bone marrow transplant, however, their immune system is essentially in the process of rebooting — and during this window, they are exceedingly vulnerable to viruses that might otherwise pose limited threat.

A recent clinical trial published in *Science Translational Medicine* describes a method of fighting viruses using killer T-cells (a type of white blood cell) cultured from the same donors who are providing bone barrow to both combat and prevent the viral infections that ravage patients after receiving a transplant. Using 'designer' T-cells in this way is not a new idea, but previous methods could take up to three months to yield the needed cells — far too long a wait for many post-transplant patients in serious condition. The new technique takes 10 days and avoids the use of live (and therefore biohazardous) viruses.

How to Train Your (Donor's) T-Cells

In essence, researchers from the Baylor College of Medicine in Texas 'trained' the donor T-cells to recognize five common and problematic viruses that are significant sources of morbidity and mortality after a bone-marrow transplant. These five viruses are adenovirus, BK virus, Epstein-Barr virus (EPV), Human Herpesvirus 6 (HHV6), and cytomegalovirus (CMV).

The Baylor team circumvented the use of live viruses by synthesizing inert versions of the proteins that characterize the outer shell of the target viruses — proteins that are the crux of how T-cells know what to find and kill. It's like giving the a bloodhound a scrap of cloth worn by a dangerous serial killer: you can give the dog the piece of information it needs (scent) without actually needing the cooperation of a dangerous agent. Chalk this up as another positive of modern synthetic biology. A similar "just the shell" technique was used to create preemptive vaccines for a new bird flu last year, which you can read about in this Gene-ius post.

Immunocompromise

Bone marrow transplant are a life-saving procedure that is often the last, best hope to treat serious immune system and blood-related diseases like leukemia, lymphoma, and sickle cell disease. Stem cells in your marrow are the source of all your red blood cells; replacing someone's marrow essentially replaces the faulty hardware that leads to these diseases.

Unfortunately, to prevent rejection of the new marrow by the patient's immune system, transplants have their immune systems heavily suppressed by medications. It can take up to three months after atransplant for the patient's immune system to come back to full function. This is the compromise thatdefines current transplant medicine of all sorts, not only bone marrow.

During this time, "Severe viral infections occur in the majority of patients and are fatal in 17 to 20 percent of cases," writes Gienna Picton in a release for the Baylor College of Medicine.

"Over the past 24 years, I've seen too many [transplant] patients losing their battle to adenovirus, BK virus, EBV, HHV-6 and CMV," Jose Montoya, professor of medicine at Stanford told The Scientist.

Of the 11 transplant patients they observed, 8 had up to 4 active infections from the above list. Three of the 11 received the same therapy as the rest, but in advance to act as a prophylactic. those three did not get sick.

It was a small clinical trial, but the percentage reported is impressive: 94 percent virological and clinical response, according to the authors. It seems like modified T-cells are out-and-out better than any medicines we've devised at combating viruses, the trick is just to give them ability to recognize their targets.

Kathryn Leung, one of the co-authors on the study, explains the faults in current antiviral treatments in the release: "[F]or adenovirus, the best medicine is only 50 percent effective; whereas, if you train cells to fight adenovirus directly, it's almost 100 percent effective."

This was also the first time designer T-cells were used to combat BK virus and HHV6. The Scientist's reporting, by Ruth Williams, captures the pragmatic significance of the results:

> "Making T cells for therapy has always been a nightmare," said John Barrett, an expert in allogenic stem cell transplants from the National Heart, Lung, and Blood Institute in Bethesda, Maryland, who was not involved in the study. "The importance of this [new] approach is that it is a little bit simpler and more rapid to generate these T cells . . . and that is actually a practical breakthrough," he said. "As a step towards making a product that could be widely available, it is very exciting."

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Additional Resources:

- “Immunotherapy hype: Are biotech companies overshooting clinical evidence?” Meredith Knight | Genetic Literacy Project
- “Human Antibodies Given Sharklike Armor to Fight Disease,” Josh Fischman | Scientific American
- “Genetically modified pig lungs or lab-grown lungs: Which is the future of our organ supply?” Kenrick Vezina | Genetic Literacy Project