REASONS FOR HOPE

The next step

The promise of immune-based therapies, those that help the body help itself, represents a new frontier in HIV/AIDS research

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by the Boston AIDS Writers Group

In this age of new and powerful antiviral combinations that lengthen lives, people living with HIV disease must focus on helping their immune systems to win the war against the virus. Immune-based therapies are the best hope for ensuring that the ultimate benefits of antiviral treatment are realized. In fact, some scientists believe that IBTs are a necessary part of a treatment plan geared toward curing the disease.

Health

Immune-based therapies have two distinct objectives for the treatment of HIV disease: They help the immune system fight the virus, and they modify immune systems damaged by the virus so that they can function properly again.

Overall, there has been less progress to report in the development of IBTs, as they have not been the focus of significant federal or pharmaceutical company efforts. However, limited research into this branch of treatment has already resulted in new therapies and a better understanding of the disease that should not be lost in the emerging world of viral load tests and protease inhibitors. IBTs now need the kind of focused effort that antivirals have benefited from for the past 10 years.

What Is an Immune-Based Therapy?

Immune-based therapies are a response to the fact that HIV disease is an illness of the immune system. Although HIV disease is caused by a virus and might be cured by eradicating the virus, people living with the disease are most disabled by the way that HIV affects the immune system. IBTs are different from antivirals in that they do not directly attack HIV. Rather, IBTs try to give the immune system an edge in its war against the virus.

An immune-based therapy is any treatment geared toward re-establishing proper functioning of the immune system or directly helping the immune system fight HIV. Whether it be drugs, vaccines or even substances that the body produces naturally, many of the IBTs in development look promising. Other everyday immune-based therapeutic approaches include proper nutrition, sleep, exercise and stress reduction. All of these methods aid the immune system to function properly.

The theory behind IBTs is based upon a new understanding of HIV disease. The battle between the virus and the immune system is ferocious. Cells infected by HIV produce billions of new viruses every six hours, and the immune system kills off those new viruses and clears out hundreds of millions of infected cells at almost the same rate. Over many years of fighting this daily battle, the immune system slowly wears out and is eventually crippled by HIV. However, it is clear that the body's natural defenses are better than any antiviral that has ever been developed by a scientist in a laboratory. Therefore, IBTs give those powerful natural defenses an extra push to help the immune system fight the war against HIV.

Regulating the Immune System

Over time, the human immunodeficiency virus throws the immune system into a state of chaos. The immune system begins to overproduce some chemicals and underproduce others. In particular, the body stops making antibodies and other chemicals, called cytokines, that specifically control the immune response. Immune-based therapies that reorganize how the immune system recognizes and attacks HIV could be extremely useful.

One such treatment is a therapeutic vaccine (a vaccine used for treatment as opposed to prevention) called Remune. This treatment reportedly increases those antibodies and chemicals that help stop HIV. Results from early testing are enough to warrant a larger study to ensure that the therapy does help people with the disease.

Therapeutic approaches have also been developed to cope with dysfunctional immune systems that don't work properly because they overproduce some substances. For example, tumor necrosis factor, a significant participant in the immune response, is often overproduced by the immune systems of people with HIV illness. High levels of this cytokine in the body can lead to wasting syndrome, a life-threatening condition. Thalidomide is one immune-based therapy that acts as an immunosuppressant, regulating the immune response by reducing the amount of tumor necrosis factor in the body and effectively preventing wasting syndrome. (Although technically it is not an IBT, another effective treatment for wasting syndrome, Serostim, was recently approved by the FDA and will be available by prescription in the upcoming weeks.)

Helping the Immune System Fight HIV

Over the course of HIV disease the body's supply of T cells, which are needed to fight illness, is constantly depleted. The immune system eventually runs out of T cells to fight the virus and other infections. Researchers have already started exploring ways to help the immune system better fight HIV by increasing the number and quality of T cells in the body.

One effective effort has been the therapeutic use of a chemical that the body naturally produces, interleukin-2, known as IL-2. In the body, one function of this substance is to tell T cells to multiply. For the past two years scientists have used IL-2 as a therapy to produce astonishing increases in T cells for some people. Most people starting with more than 250 T cells have been able to boost their T cells up to normal levels for years. Scientists hope that by doing this, not only will the immune system be better at fighting HIV, but it will continue to have enough T cells to protect itself from opportunistic infections.

Unfortunately, IL-2 sometimes temporarily increases viral load (the amount of virus in the bloodstream), since it makes infected T cells multiply, too. This means IL-2 is most useful when T cells are high and viral load is low. However, last year scientists began using this IBT along with protease inhibitors, and discovered that this combination prevents viral increases and still boosts T cell levels up to the normal range (800 to 1,200). These results were even better than when using IL-2 or protease inhibitors alone.

Theoretically, another prospect for IL-2 therapy is to clear the virus from the body much more quickly than by using antivirals alone. It is known that—if even it is possible—it will take a long time for the body to get rid of cells infected with HIV while using powerful antiviral combinations to stop the virus from infecting new cells. Although most infected cells are cleared quickly, as much as 1 percent of virus-producing cells are much harder to eliminate. These cells are not cleared out because the immune system cannot tell that they are infected with HIV. For the immune system to know that they are infected the cells must be "activated" and produce new viruses. Using IL-2 to activate all of the infected T cells in conjunction with powerful antiviral combinations could be part of this possible solution for positively curing HIV disease.

Another way to help the immune system fight HIV is T cell expansion. This process involves taking T cells from the body and making billions of copies of them. These cells are then taught to kill HIV by exposing them to the virus. The cells that fight HIV energetically are then selected and put back into the body in hopes that they will keep the disease under control. For one type of T cells, CD4s, this procedure is still in the experimental phase. For another type, CD8s, preliminary results are promising enough to warrant a larger study of this type of therapy.

The Future for IBTs

It will soon be known whether or not therapeutic vaccines might help slow progression to AIDS and help antivirals do their job. There is also reason to hope that a preventative vaccine can be created.

There are other efforts underway to rebuild the immune system. These include the famous transplant of a baboon's immune system into a human, efforts at gene therapy, and a fascinating new method of treating T cells that might make them very difficult to infect. Unfortunately, these therapies have not been studied sufficiently to predict much about their potential usefulness.

For those people with immune systems which have been damaged so severely that stopping the virus will not be enough to stop opportunistic infections, scientists are optimistic about the possibility of rebuilding the immune system by teaching T cells how to fight illness.

IBTs are at an early stage of development, but they have already shown tremendous promise. It took over 10 years to develop effective antivirals. A commensurate effort into the development of IBTs may offer equally important hopes that the immune system can be restored and the virus can be contained.

The Boston AIDS Writers Group consists of Robert Folan and Lou Pesce of ACT UP Boston; David Scondras, Robert Krebs, Derek Libby and Larry Bresslour from Search For A Cure.

Vaccine Therapy Trial

If you are interested in participating in the Remune study, you live in the Portland area and your T cell count is between 300 and 550, you should contact The Research & Education Group at 229-8428 or 1-800-875-8428 and ask for Joyce St. Arnaud, RN, FNP. This is a very user-friendly trial because the vaccine is given only once every three months, and you can simultaneously take any antivirals that you want.

If your T cell count is above or below the range for the trial and you want access to this experimental therapy, call 1-800-684-8624 for more information.

IL-2 Trial

There are many trials of this experimental therapy going on around the country. If you are interested in participating in a study using IL-2 you should call 1-800-TRIALS-A for more information. IL-2 is already licensed by the FDA, so your doctor can prescribe it for you, but you need to make sure that you use it correctly and are prepared for its serious side effects.