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## reason for hope

### On the horizon

by David Scondras  
Special to Q-Notes

[This is the first installment of a three-part series.]

Recently, there has been a big breakthrough in how we can effectively fight HIV. Understanding how HIV gets inside of T-cells has led to the creation of a new class of drugs called entry inhibitors that block the virus from hijacking a cell.

We now know that it takes three steps for the virus to get inside a cell, and scientists have developed drugs that interfere with each of these steps. Some of these drugs are almost ready for drugstore shelves, others are being tested in people, and still others are in test tubes.

Because these drugs do not get into your cells, they will have very different side effects from the ones we use now. This is big news for people who need a change from their cocktails. And because these drugs are so different from the others, they will stop virus that is resistant to all of the drugs we have now. This may be lifesaving news for people who have used up all of their options.

#### The three steps

In the first stage of HIV infection, the virus has to attach to the cell. Scientists have found drugs that stop this in the test tube. They will soon be tested in people.

Secondly, the virus must change its shape in order to insert itself into the T-cell. It does this using two parts of the surface of the T-cell. These parts of the cell are co-receptors called CXCR4 and CCR5. There are drugs that stop the virus from using either of these parts of the cell that have already been tested in some people.

The third and final step the virus must take to get into the cell is called fusion. The virus fuses with the cell wall. This happens very quickly, but new drugs have been found that interfere with this last step, even though it only occurs for a fraction of a second.

In other words we have "attachment inhibitors," "co-receptor inhibitors" and "fusion inhibitors" being tested. These inhibitors look promising in the laboratory when they are used together — like locking all the doors and windows of your house to stop anyone from getting in.

#### To market

The first of the entry inhibitors will soon be ready for the drugstore shelf. T-20 (Trimeris & Roche), a fusion inhibitor, is already in phase III testing. This means it is being tested in enough people to prove that it works and get a license from the FDA. It looks very powerful and effective on people who have used up all their other options. Unfortunately, T-20 needs to be given with a needle, like insulin for diabetes. It seems to have virtually no side effects so far except for irritation at the injection site.

Although T-20 has been successful at helping people who have had many drug failures, it won't be able to rescue people alone and will need to be used with other drugs or possibly with other entry inhibitors as they become available.

And there is already a cousin of T-20 called T-1249 that has been shown in the test tube to work on virus that has grown resistant to T-20. It is at an earlier stage of development than T-20.

Six additional entry inhibitors also look very promising: for inhibiting attachment there is PRO 542; for co-receptor inhibition there is AMD3100 (that inhibits at CXCR4) and PRO 140, TAK 779 and SCH.c and SCH-d (which target CCR5). All of these drugs are in various stages of development.

Over the next two years, we will see the creation of even more drugs that stop HIV from getting into cells, pushing this exciting therapy even further. ▼

[David Scondras is the founder of Search For A Cure, a not-for-profit organization providing education and advocacy for people living with AIDS. Contact Search For A Cure at 34 Edgerly Road #1, Boston, MA 02115; call 617-536-2474; fax 617-266-0051; email hope@sfac.org; online www.searchforcure.org. This article was reviewed by Dr. Alfred De Maria, Assistant Commissioner of Communicable Disease, Massachusetts Department of Public Health.]