



TROPISM TESTS

WHAT IS VIRAL TROPISM?

When HIV attaches to a CD4 cell it is going to infect, it uses molecules on the cell surface. These are called receptors or chemokine co-receptors. The first receptor HIV uses is the CD4 molecule. The virus then uses a "co-receptor." This is either a CCR5 molecule or a CXCR4 molecule.

The virus usually uses one type of co-receptor or the other. HIV that uses the CCR5 co-receptor is called "CCR5 tropic" or "R5 tropic." However, viral tropism can be CCR5, CXCR4, or "dual/mixed" (or D/M) if some of the sample of virus uses each co-receptor. When people are first infected, their virus is usually CCR5 tropic. As HIV infection progresses, tropism usually changes to include more CXCR4 tropism.

Researchers thought that the co-receptors would be a good target for anti-HIV drugs. There is now an approved antiviral medication active against CCR5-tropic HIV. This attachment inhibitor is maraviroc (fact sheet 462.) Maraviroc only works against R5-tropic HIV.

There are many other attachment inhibitors in development (fact sheet 460.) Most block the CCR5 receptor. Some target the CXCR4 receptor.

SOME PEOPLE "NATURALLY" BLOCK THE CCR5 RECEPTOR

While scientists were researching CCR5 blockers, they discovered that some people do not have the CCR5 receptor on their T-cells. They have a genetic mutation called a "delta 32 mutation." These people seem to be at least partially resistant to HIV infection. Because these people live a healthy life without a CCR5 receptor, researchers believe that using a CCR5 blocker may not have dangerous long term side effects.

HOW IS THE TEST USED?

The tropism test is helpful in deciding whether a CCR5 blocker will be useful in controlling a patient's HIV. Currently, a tropism test is required before maraviroc is prescribed.

This situation may change in the future. For example, if a new drug is developed that is active against X4 virus, the tropism test could help choose which type of drug would be most effective.

HOW IS VIRAL TROPISM MEASURED?

Viral tropism is measure by genetic testing of a blood sample. The most common test is called "Trofile." The blood and virus sample is grown (amplified.) Then it is tested against cells that are known to express the CCR5 molecule or the CXCR4 molecule. If the sample is active only in the CCR5 cells, then the virus is R5 tropic. If it is active only in the CXCR4 cells, the virus is X4 tropic. Finally, the sample can be active in both the R5 and X4 cells. This would indicate D/M (dual/mixed) tropism. It takes about two weeks to get tropism test results after a sample is sent in.

A genotypic has also been developed. This involves analysis of the HIV genetic code rather than growing the virus. Results are available more quickly than for the Trofile test.

HOW RELIABLE IS THE TEST?

Tropism tests may not work if the viral load is below 1,000. Also, the lower the proportion of X4 virus, the harder it is for the test to detect it. For example, if X4 virus is at least 10% of the sample, the test will detect it every time. However, if the X4 virus is only 5% of the total, the tropism test will detect it 85% of the time.

Newer tests may be more accurate.

WHAT DO THE RESULTS MEAN?

Tropism test results are reported as:

- R5 or CCR5 tropic
- X4 or CXCR4 tropic
- D/M or dual/mixed tropic

The test tells you which type of co-receptor the virus prefers to use.

Early research on HIV found that people with more advanced disease had X4 tropic virus. When drugs were developed to block R5 virus, some people were worried that this would lead to more X4 virus and faster progression of HIV disease. However, results from research studies so far do not show this happening.

Use of an R5 inhibitor suppresses the R5 HIV. If there was some X4 virus present, then it will show up more easily when the R5 virus is suppressed. However, there is no evidence that the virus is "switching" from R5 to X4.

ARE THERE PROBLEMS WITH THE TROPISM TEST?

Trofile tropism tests are very expensive. It can take two weeks to get results.

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