Clinical Indications for Testing and Information for Patients
CfE Research Laboratory Assays

HIV Drug Resistance Testing

The ultimate goal of anti-HIV drug therapy is to reduce the amount of HIV in an individual's blood (viral load) to an 'undetectable' level. Anti-HIV drugs work by stopping the virus from reproducing inside the body. These drugs are used in combination and can be effective for a very long time.

What HIV Drugs are available?

There are multiple classes of anti-HIV (antiretroviral) drugs:

- Nucleoside analogue reverse transcriptase inhibitors (NRTIs) including zidovudine, lamivudine, abacavir, emtricitabine, and tenofovir
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs) including nevirapine, etravirine, efavirenz, rilpivirine and doravirine
- Protease inhibitors including lopinavir, atazanavir and darunavir
- Integrase inhibitors (INSTIs) including raltegravir, elvitegravir, dolutegravir, bictegravir and cabotegravir
- Entry inhibitors include fusion inhibitors such as enfuvirtide, attachment inhibitors such as fostemsavir, and CCR5 inhibitors such as maraviroc
- Capsid inhibitors including lenacapavir

What is drug resistance?

Anti-HIV drugs work by stopping the virus from reproducing inside the body. HIV mutates (changes) as it reproduces, and sometimes the mutations make it possible for the virus to reproduce even in the presence of anti-HIV drugs. When this happens, the virus is said to have drug resistance. It is important to note that these mutations cause resistance to some drugs but not others.

Why test for drug resistance?

Drug resistance testing can identify the mutations that prevent certain drugs from working. By identifying these mutations, doctors can then modify the treatment regimen to include different drugs that are not affected by the mutations. This can then return an individual's viral load to an 'undetectable' level.

In some cases, a person can be infected by a virus that already has drug resistance. If the doctor knows this from the beginning, a tailor-made drug combination therapy can be chosen rather than the standard therapy that works well for most people.

How does drug resistance testing work?

The BC-CfE laboratory extracts genetic material from the HIV in a person's blood and uses sequencing technology (similar to DNA fingerprinting of the virus) to identify drug resistance mutations. Lists of specific mutations associated with drug resistance are available in the scientific literature. The laboratory report shows whether the virus has these mutations and which anti-HIV drugs are likely to be affected by the mutations. Drug resistance to NRTIs, NNRTIs, PIs and INSTIs is included on the clinical report.

If someone has had routine HIV viral load testing done at St. Paul's Hospital, drug resistance testing can be done using left-over, stored blood samples from this test. In this case the client does not need to have blood drawn again. The test usually takes about two weeks.

When should drug resistance testing be performed?

Individuals newly diagnosed with HIV should be tested even if treatment will not be started right away. Testing will identify whether the transmitted virus already contained drug resistance mutations. Drug resistance testing should be repeated before switching to different drugs to ensure that the new drugs will be effective.

Testing for drug resistance is especially important if a person is experiencing poor or no response to anti-HIV drugs as indicated by rising viral loads. Test results will help the doctor choose appropriate new drugs for a successful therapy.

Can the likelihood of drug resistance be decreased?
Yes. HIV cannot mutate if it is not reproducing. When anti-HIV drugs are working HIV reproduction is minimal. HIV drugs only work at their best when taken as directed, with no missed pills. This is one key factor in preventing drug resistance.

HLA-B*57:01 Screening for Abacavir Hypersensitivity

What is abacavir hypersensitivity, and who is at risk?
Abacavir is a drug used to treat HIV infection, similar to zidovudine (AZT) and lamivudine (3TC). Abacavir is available as a single drug (Ziagen) or in single-pill combinations with other antiretrovirals.

Most people can safely take abacavir; however, a small number of individuals experience a severe side effect known as abacavir hypersensitivity. The most common symptoms are skin rash, fever, nausea, vomiting and diarrhea. About 5% of individuals who take abacavir experience abacavir hypersensitivity. This reaction can be very serious and, in some cases cause death.

People who have a specific gene called HLA-B*57:01 are much more likely to experience abacavir hypersensitivity than those who do not. Therefore, individuals with the HLA-B*57:01 gene should not take abacavir. Approximately 5-8% of people with European-, 1-2% with Asian-, and 2% with African ancestry have this gene.

How does HLA-B*57:01 screening for abacavir hypersensitivity work?
A test called HLA-B*57:01 Screening should be ordered before the start of therapy containing abacavir. The test requires drawing a single tube of blood which will be sent to the BC Centre for Excellence in HIV/AIDS laboratory for analysis. The laboratory extracts genetic material from the individual's blood and uses sequencing technology to identify whether the person has the HLA-B*57:01 gene.

In contrast to other HIV laboratory tests such as viral load and CD4 count, and HIV drug resistance tests, the results of which can change over time, a person's HLA-B*57:01 result does not change. This test needs to be done only once.

What do the HLA-B*57:01 abacavir hypersensitivity test results mean?
A positive test result means that the person has the HLA-B*57:01 gene and therefore is at higher risk of the abacavir hypersensitivity reaction. This person should not take abacavir. A negative test result means the person does not have the HLA-B*57:01 gene.

Having a negative test result does not guarantee that abacavir hypersensitivity will not develop. It only means the individual is at low risk. You should let your doctors know immediately if you develop a rash, fever or have any of the above symptoms when taking abacavir.

Information on Specialized Laboratory Tests:

Fusion Inhibitor (gp-41) Resistance Testing

Specialized, Research Use Only Assay

What are fusion inhibitors and how to they work?
Fusion inhibitors (e.g., enfuvirtide, aka Fuzeon or T-20) is a type of drug that doctors may prescribe to people living with HIV, especially when some of the more common anti-HIV drugs are not working.

Fusion inhibitors prevent the virus from fusing (attaching) to human cells.

Fuzeon (enfuvirtide, T20) is no longer available in Canada as of March 31, 2025. Fusion inhibitor (gp41) resistance testing has been discontinued.

CCR5 Inhibitors Including Maraviroc
Specialized, Research Use Only Assay

What is HIV tropism?
Tropism refers to the way HIV enters cells. The virus enters the human cell by attaching to specific host proteins on its surface. Some types of HIV attach to a protein called CCR5 and others attach to a protein called CXCR4. “Tropism” refers to which proteins the specific strain of HIV attaches to: HIV strains that attach to CCR5 are called "CCR5-using" while those that attach to CXCR4 are called "CXCR4-using".

Most HIV infections are caused by CCR5-using virus. However, as HIV reproduces it can sometimes change from a CCR5-using virus to a CXCR4-using virus. As this transition is taking place a person can have both types of virus at the same time (dual tropism). Without testing, there is no way to tell whether a patient has CCR5-using, CXCR4-using, or dual tropic virus.

Why test for HIV tropism?
If HIV is not able to enter the cell, it cannot reproduce. One type of anti-HIV drug works by blocking the CCR5 protein on a person’s cells, preventing CCR5-using strains of HIV from entering the cell. This type of drug is called a “CCR5 antagonist”. Currently, the only drug of this type is maraviroc (Celsentri).

Maraviroc prevents CCR5-using virus from entering the cell, but cannot stop the CXCR4-using virus. This is why it is essential to know which tropism a person's virus has before initiating treatment with maraviroc. Individuals with dual tropic or CXCR4-using HIV are not good candidates for maraviroc because CXCR4-using virus would continue to reproduce. Maraviroc should only be prescribed to individuals who exclusively have CCR5-using HIV.

When should the tropism test be done?
HIV tropism can change as the virus reproduces and mutates over time. If the last tropism test was done too long ago, the test result may not represent the individual’s current virus. Tropism testing should be done just prior to starting maraviroc, and should be repeated if this drug treatment begins to fail.

How does tropism testing work?
The BC-CfE laboratory extracts genetic material from the HIV in an individual’s blood and uses sequencing technology (similar to DNA fingerprinting of the virus) to identify which type of virus the patient has.

There are two different tropism tests. Which test to use depends on the person’s current viral load. If the viral load is ≥500 copies/mL, a regular (plasma HIV RNA) HIV Tropism Test should be ordered. If the client has had HIV viral load testing at St. Paul’s Hospital, this type of tropism testing can be done on a stored sample, and no additional blood needs to be drawn.

If the viral load <500 copies/mL, a Proviral HIV DNA Tropism Test should be ordered. This type of tropism testing requires drawing an additional tube of blood.

Hepatitis C Drug Resistance Testing
Specialized, Research Use Only Assay

What are direct-acting antiviral agents (DDAs) for Hepatitis C (HCV) disease?
New therapies have been developed to specifically target the Hepatitis C virus replacing non-specific therapies used in the past. These antiviral agents act directly on viral targets.

Why test for certain mutations in the Hepatitis C virus?
Resistance-associated mutations have been found after treatment, and occasionally in treatment-naive individuals. DAA treatment regimens may need to be modified for persons living with HCV carrying drug resistance mutations.

What causes Hepatitis C virus drug resistance mutations?
It is thought to result from selective pressure from drugs during treatment or genetic variation inherent in the virus itself.

How does this testing help?
The testing is able to detect mutations and/or variations in the Hepatitis C virus that would prevent a drug from being fully effective. With this information, the physician can choose a therapy that the individual's particular virus will respond to.

Therapeutic Drug Monitoring
Specialized, Research Use Only Assay

What is therapeutic drug monitoring?
When someone takes anti-HIV drugs, the drugs are absorbed into the body's cells and the virus in the cells is then affected by the drugs. The amount of drug must be high enough to be absorbed by the body's cells, but not so high that they cause side effects. Therapeutic drug monitoring (TDM) measures whether an individual has too little or too much drug in their system. Not all drugs can be measured using this test, but many of the most common anti-HIV drugs can be (PIs, NNRTIs, INSTIs).

Why is therapeutic drug monitoring done?
If the drug level is not high enough in the body, or the drug is not absorbed well by the body, HIV will continue to reproduce. On the other hand, if levels are too high, the drug may cause toxicities or unwanted side effects.

Why do drug levels vary?
Various factors can influence drug levels. Genetic makeup, kidney or liver problems, body size, food intake with medication, and pregnancy are examples. Taking other medications or supplements can also increase or decrease anti-HIV drug levels. If pills are not taken according to schedule or are skipped altogether, this will also have an effect on drug levels.

When should patients receive therapeutic drug monitoring?
Most people do not need Therapeutic drug monitoring (TDM). Nevertheless, it can be helpful if drug treatment is not working, and the failure cannot be explained by drug resistance.

What is involved in therapeutic drug monitoring?
There are two types of therapeutic drug monitoring (TDM): timed and untimed.

Timed TDM detects the quantity of drug present in an individual's plasma. Timed TDM is offered at the BC-CfE as part of a Research Study approved by the PHC/UBC Research Ethics Board. It requires consultation with a physician at the BC-CfE, and the participant is required to provide written informed consent to participate. Participants will be asked to follow a specific set of instructions. A blood sample will be drawn immediately before taking medication and at specific times afterwards. This is the best method for seeing precisely how much and how quickly the drug is being absorbed. Results will be discussed with the Principal Investigator or co-investigators (who are physicians at the BC-CfE) of the study along with the responsible physician and/or pharmacist.

Untimed TDM only detects whether the drug is present (or not) in plasma. Untimed TDM is currently a pilot project that can be performed on stored samples from routine viral load testing in British Columbia. As such, untimed TDM does not require any additional blood draws. .

General Information

Confidentiality
CfE Research Laboratory test results, like other laboratory results, are kept strictly confidential.

Turnaround Time
CfE Research Laboratory test results are usually available within 2 weeks (after samples received from other clinical laboratories).

Who can I contact if I have any questions?
If you have any questions, please contact Dr. Chanson Brumme at 1-800-517-1119 during business hours or email lab@bccfe.ca .

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