Evaluating the Patient w Newly Diagnosed HIV Infection

“Interpreting tests, clinical findings and symptomatic complaints”

Steven C. Zell MD / AAHIVMS
Professor of Medicine
University of Nevada School of Medicine
Co-director Nevada AETC
Client Intake to Establish Care

- **Purpose:** 3 key functions
  - prioritize immune status / overall health
  - screen for public health purposes communicable dz
  - treat STDs / administer vaccines

- **Goals:** two-fold
  - advanced disease need be seen more quickly
    - “protocols” to offer CD4 guided OI prophylaxis
      - PCP / toxo / MAC / Herpes / Thrush
    - screen for the company kept w HIV
      - STDs: syphilis / GC / Chlamydia / HSV
      - Hepatitis B and C

- **Personnel:** nurse / medical assistant
Requisite Evaluation-Initial Intake
The Newly diagnosed HIV

- CD4 lymph count
- HIV-1 RNA by PCR quant
- STD screen:
  - Syphilis RPR or VDRL titer and confirm w TPPA
  - GC / Chlamydia: NAA 1st void urine or APTIMA® Unisex Swab
- CxR: TST (PPD)
  - or QuantiFERON-TB Gold test?
    - Only in most advanced cases
- CBC / chem panel / fasting lipids / urinalysis
- Hepatitis panel for A / B / C
  - Total antibody for Hep A /
  - anti-HCV
  - HBsAg / anti-HBs
    - HBV DNA if surface antigen positive
Initial clinician medical evaluation

- **Purpose:** key issues to address
  - Screening and Tx for OIs
  - Response to screening serology for Hepatitis / STDs
  - Screening for significant co-morbid conditions
    - Type 2 DM / DLD / CKD
- **Goals:** multi-fold
  - Reduce short-term illness from OIs
  -Respond to screening tests to treat underlying STDs
  - Vaccinate as dictated by intake serology
- **Personnel:** MD / PA / NP

*Antiretroviral therapy is never an emergency as long as appropriate prophylaxis against OI is provided*
Diagnostic Tests-Initial Clinical Exam

- CD4 ct and VL done to establish “immune pattern”
- HIV-1 genotype for naïve patients or 1st line failure
- Phenosense- GT for class-experienced failures
- Specific labs to guide ARV Testing-drawn if considering abacavir or entry Inhibitior
  - HLA-B5701 to assess Abacavir HSR (Epzicom)
  - Co-receptor tropism assay for use of Selzentry
    - Trofile or Trofile DNA (if VL< limits)
- Specific labs to guide OI screening
  - G6PD screen for Septra DS “allergic”
  - Toxoplasma IgG?
Eosinophilic folliculitis
Subtle Laboratory Findings Seen in Chronic HIV

- **Hematologic parameters of note:**
  - Leukopenia / thrombocytopenia

- **Chemistries**
  - Fasting triglycerides high:
  - Abnormal albumin to globulin ratio (decreased)
    - Polyclonal increase a result of frequent infections?
  - High LDH level-surrogate for NHL / PCP / MAC?

- **The company HIV keeps**
  - Hepatitis C / Hepatitis B / RPR positivity
Physical exam in HIV infection

- **Eyes**
  - CMV retinitis / HIV retinopathy

- **Mouth**
  - Thrush / KS / apthous ulcers / OHL / angular chelitis

- **Skin**
  - Infectious bacterial: syphilis / BA / folliculitis
  - Infectious viral: HZV / HSV / molluscum / KS
  - Miscellaneous: exaggerated response in HIV
  - Psoriasis / eczema / seborrhea / xerosis / eosinophilic folliculitis
Oral thrush
Oral Kaposi’s
Aphthous ulcers
Angular cheilitis
HIV Retinopathy
Primary syphilis
Bacterial folliculitis
HSV infection Type 2
HSV infection
advanced
disease
Herpes Simplex type 1
Herpes Zoster
Molluscum Contagiosum
Seborrheic dermatitis
Eczema
Initial Clinical Exam (continued)

- **Tests to better define “co-morbidity”**
  - Metabolic syndrome: fat / htn / FBS / lipids
    - Insulin Resistance: 75 gm 2 hr OGTT
      - >140 mg c/w impaired glucose
      - +1 proteinuria or > excretion
    - Urine P/C spot ratio or 24 hr collection
      - >150 mg is worrisome

- **Tests in response to specific serology**
  - Anti-HCV + = HCV RNA quant by PCR
    - If detectable-HCV genotyping
  - HBsAg + = HBV DNA quant by PCR
Genotypic Testing: Attributes

- Looks at gene sequence for replication / assembly of HIV virus:
  - RT (reverse transcriptase)
    - Replicates HIV RNA to DNA
  - Pr (protease enzyme)
    - Cleaves transcribed HIV RNA into assembly
- Indirect measure of resistance
  - Not to be confused w culture and sensitivity!
- Requires interpretation utilizing expert algorithm
  - Derived from clinical trials
- Must be updated as knowledge advances
## GenoSure MG

**HIV Drug Resistance Assay**

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**Monogram Biosciences Clinical Development**

345 Oyster Point Blvd.
South San Francisco, CA 94080 USA

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**Client:** 03914  
**Project:** 02526  
**Reference Lab ID/Order #:** 10-132004

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**Patient Name:**

**DOB:**

**Date Collected:** 06/03/2010 10:57  
**Date Received:** 06/03/2010 10:57  
**Date Reported:** 07/09/2010 12:41

**Monogram Accession #:** 10-132004

**Gender:**

**Mode:**

**Report Status:** FINAL

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**Referring Physician:**

**Patient ID/Medical Record #:**

**Comments:**

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### Drug Resistance Table

<table>
<thead>
<tr>
<th>Drug</th>
<th>GenoSure® MG Drug Resistance Associated Mutations Detected</th>
<th>Assessment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dldanosine</td>
<td>M41L, E44D, D67N, V75I/M, M184V, L210W, T215Y</td>
<td>ddi</td>
<td>Resistant</td>
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<tr>
<td>Zidovudine</td>
<td>M41L, E44D, D67N, V75I/M, L210W, T215Y, K219R</td>
<td>ZDV</td>
<td>Resistant</td>
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<td><strong>NNRTI</strong></td>
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<tr>
<td>Delavirdine</td>
<td>K103N, Y188L</td>
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<td>Efavirenz</td>
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<td>EFV</td>
<td>Resistant</td>
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<tr>
<td>Ettravirine</td>
<td>V179T, Y188L</td>
<td>ETR</td>
<td>Resistance Possible</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>K103N, Y188L</td>
<td>NVP</td>
<td>Resistant</td>
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<tr>
<td><strong>PI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atazanavir</td>
<td>L10V, V32I, K43T, M46I, V82T</td>
<td>ATV</td>
<td>Resistant</td>
</tr>
<tr>
<td>Darunavir</td>
<td>V32I, K43T, M46I, I47A</td>
<td>DRV</td>
<td>Resistance Possible</td>
</tr>
<tr>
<td>Fosamprenavir</td>
<td>L10V, V32I, K43T, M46I, I47A</td>
<td>AMP</td>
<td>Resistant</td>
</tr>
<tr>
<td>Indinavir</td>
<td>L10V, V32I, M46I, I47A, A71T, V82T</td>
<td>IDV</td>
<td>Resistant</td>
</tr>
<tr>
<td>Lopinavir</td>
<td>L10V, V32I, E34Q, K43T, M46I, A71T, V82T</td>
<td>LPV</td>
<td>Resistant</td>
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<tr>
<td>Nelfinavir</td>
<td>L10V, V32I, M46I, A71T</td>
<td>NFV</td>
<td>Resistant</td>
</tr>
<tr>
<td>ritonavir</td>
<td>L10V, V32I, K43T, A71T, V82T</td>
<td>RTV</td>
<td>Resistant</td>
</tr>
<tr>
<td>Saquinavir</td>
<td>L10V, K43T, A71T</td>
<td>SQV</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Tipranavir</td>
<td>L10V, K43T, A71T</td>
<td>TPV</td>
<td>Resistant</td>
</tr>
</tbody>
</table>
Phenotypic Testing: *PhenoSense*

- Measures the sensitivity of a patient’s HIV to medications
  - isolated virus vs. varying levels of ARV drug in test tube
    - IC 50 level determined for patient isolate
    - Compared to lab standard (Wild type)
    - Fold change in susceptibility reported
- Quantitative measure of resistance
- Fold changes in susceptibility relate to clinical trial data
  - Used to make final assessment
  - Exception: biologic or assay cut-offs
Phenotypic Testing

Advantages:
- Direct measure of resistance
- Can be used with new drugs
- Quantitative (more than a yes or no answer)
- Report form: easy to read; easier to interpret

Limitations:
- Can be less sensitive to mixtures
- Can’t test for synergy of drug combinations
## PhenoSense HIV Test Report

### Replication Capacity

**Virus Replication Capacity = 97%**

(Range 61%-154%)

Replication capacity (RC) indicates the ability of the virus to replicate in the absence of drug. Range represents 95% confidence interval around RC measurement. 100% = median RC of wild-type viruses.

### Drug Susceptibility

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Cutoffs (Lower - Upper)</th>
<th>Fold Change</th>
<th>Drug Susceptibility</th>
<th>Assessment</th>
</tr>
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<tbody>
<tr>
<td><strong>NNRTI</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Abacavir</td>
<td>Zidovudine</td>
<td>(4.5 - 6.5)</td>
<td>2.90</td>
<td></td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Didanosine</td>
<td>Videx</td>
<td>(1.3 - 2.2)</td>
<td>1.69</td>
<td></td>
<td>Partially Sensitive</td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>Emtriva</td>
<td>(1.0 - 2.5)</td>
<td>1.76</td>
<td></td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Epivir</td>
<td>(1.5 - 3.5)</td>
<td>1.37</td>
<td></td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Stavudine</td>
<td>Zerit</td>
<td>(1.7 - 2.0)</td>
<td>2.00</td>
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<td>Sensitivity</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Viread</td>
<td>(1.4 - 4.0)</td>
<td>1.24</td>
<td></td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Retrovir</td>
<td>(1.0 - 1.9)</td>
<td>8.04</td>
<td></td>
<td>Resistant</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>Virecept</td>
<td>(3.9 - 4.8)</td>
<td>5.13</td>
<td></td>
<td>Resistant</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>Norvir</td>
<td>(2.5 - 4.0)</td>
<td>2.59</td>
<td></td>
<td>Resistant</td>
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<tr>
<td>Saquinavir</td>
<td>Invirase</td>
<td>(1.0 - 1.7)</td>
<td>1.69</td>
<td></td>
<td>Resistant</td>
</tr>
<tr>
<td>Tipranavir</td>
<td>Aptivir / Faizol</td>
<td>(2.3 - 8.0)</td>
<td>1.77</td>
<td></td>
<td>Resistant</td>
</tr>
</tbody>
</table>

**PI**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Cutoffs (Lower - Upper)</th>
<th>Fold Change</th>
<th>Drug Susceptibility</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir</td>
<td>Reyataz</td>
<td>(2.2 - 3.2)</td>
<td>1.44</td>
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<td>Sensitivity</td>
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<td>Darunavir</td>
<td>Prezista / Faizol</td>
<td>(10.0 - 40.0)</td>
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<td>fosamprenavir</td>
<td>Lexiva</td>
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<td>Indinavir</td>
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<td>Kaletra</td>
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<tr>
<td>Nelfinavir</td>
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<td>Norvir</td>
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<tr>
<td>Tipranavir</td>
<td>Aptivir / Faizol</td>
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<td>Sensitivity</td>
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**Other**

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<tr>
<td>ATV</td>
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<td>Sensitivity</td>
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<td>ATVr</td>
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<td>Sensitivity</td>
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<td>NFV</td>
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<td>Sensitivity</td>
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<td>RTV</td>
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<td>TPV</td>
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<td>Sensitivity</td>
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**Limitations**

- Lower Clinical Cutoff (in bold)
- Upper Clinical Cutoff (in bold)
- Biological Cutoff

**Mode**

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**Date Collected**

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**Comments**

- ABC
- ddl
- FTC
- 3TC
- d4T
- TFV
- ZDV
- DLV
- EFV
- NVP
PhenoSENSE GT
Combination HIV Drug Resistance Assay

Valerie McWhorter, MD, Medical Director - 345 Oyster Point Blvd
South San Francisco, CA 94080 - Tel: (800) 777-0177

<table>
<thead>
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<th>Patient Name:</th>
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| Comments | HIV-1 Subtype: | B |

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Cutoffs (Lower - Upper)</th>
<th>Fold Change</th>
<th>Increasing</th>
<th>Drug Susceptibility</th>
<th>Decreasing</th>
<th>PhenoSense Gene Seq</th>
<th>Net Assessment</th>
</tr>
</thead>
</table>

**NRTI**

- **Abacavir**: Zagen (4.5 - 6.5) 1.36
  - Y  N  Resistant 1
- **Didanosine**: Videx (1.3 - 2.2) 1.15
  - Y  N  Sensitive 16
- **Emtricitabine**: Emtriva (3.5) 3.69
  - N  N  Resistant 1
- **Lamivudine**: Epivir (3.5) 3.57
  - N  N  Resistant 1
- **Stavudine**: Zerit (1.7) 1.18
  - Y  Y  Sensitive 3
- **Zidovudine**: Retrovir (1.9) 0.43
  - Y  Y  Sensitive 2.3
- **Tenofovir**: Viread (1.4 - 4) 0.76
  - Y  Y  Sensitive 2.3

**NRTI Mutations**: A62V, V75I, M184I

**NNRTI**

- **Delavirdine**: Rescriptor (6.2) >MAX
  - N  N  Resistant
- **Efavirenz**: Sustiva (3)
  - N  N  Resistant
- **Etravirine**: Intence (2.9 - 10) 5.75
  - P  N  Partially Sensitive
- **Nevirapine**: Viramune (4.5)
  - >MAX

**NNRTI Mutations**: K101Q, K103N, Y181C, P225PH

**PI**

- **Atazanavir**: Reyataz (2.2) 0.96
  - Y  Y  Sensitive
- **Atazanavir / rit**: 0.96
  - Y  Y  Sensitive
- **Darunavir**: Prezista / rit (10 - 90) 0.78
  - Y  Y  Sensitive
- **Fosamprenavir**: Lexiva (2)
  - 1.82
- **Fosamprenavir / rit**: Lexiva / rit (4 - 11)
  - 1.82
- **Indinavir**: Crixivan / rit (10)
  - 1.26
- **Lopinavir**: Kaletra (9 - 65)
  - 1.32
- **Nelfinavir**: Vircap (3.6)
  - 2.07
- **Ritonavir**: Norvir (2.5)
  - 1.09
- **Saquinavir**: Invirase (1.7)
  - 1.11
- **Saquinavir / rit**: Invirase / rit (2.3 - 12)
  - 1.11
- **Tipranavir**: Aptivus / rit (2 - 8)
  - 1.06

**PI Mutations**: L10I/L13F, V60A, I62A/V

<table>
<thead>
<tr>
<th>Lower Cutoff (in bold)</th>
<th>Lower Clinical Cutoff (in bold)</th>
<th>Hyper-susceptibility</th>
<th>Sensitive</th>
<th>Evidence of Drug Sensitivity</th>
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</thead>
<tbody>
<tr>
<td>Cutoff</td>
<td>Biological Cutoff</td>
<td>Partially Sensitive</td>
<td>Y</td>
<td>Evidence of Partial Drug Sensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resistant</td>
<td>Y</td>
<td>Evidence of Drug Resistance</td>
</tr>
</tbody>
</table>

For more information on interpreting this report, please visit www.MonogramHIV.com or call Customer Service at 800-777-0177 between the hours of 6:30am to 5:00pm PST Monday through Friday.
The HIV Life Cycle Provides Many Targets for Therapeutic Intervention

Co-Receptor Binding Is an Essential Step for Viral Entry

Viral gp120 protein binds to CD4 on host cell

gp120-CD4 complex binds to CCR5 or CXCR4 on host cell

Virus fuses with host cell membrane, facilitating viral entry

Why is Trofile® DNA Needed?

- Trofile® is the original assay and gold standard for determining tropism
  - viral loads greater than or equal to 1,000 copies/mL

- The ability to determine tropism has been precluded by the viral load requirement
  - Inability to switch out to R5 antagonist
  - Drug intolerance to other agents in a suppressed regimen

- Trofile® DNA will enable tropism determination in those patients whose virus is undetectable
Cell-associated viral DNA may be from two sources:
- Integrated DNA
- Cytoplasmic DNA
## Comparison of Trofile® and Trofile®DNA

<table>
<thead>
<tr>
<th>Trofile®</th>
<th>Trofile®DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV RNA is isolated from plasma (front end of assay)</td>
<td>Cell-associated HIV DNA is isolated from whole blood (front end of assay)</td>
</tr>
<tr>
<td><strong>gp 160 envelope</strong> sequences are amplified from the extracted RNA and incorporated into the test vector. Remaining steps are identical.</td>
<td><strong>gp 160 envelope</strong> sequences are amplified from the extracted DNA and incorporated into the test vector. Remaining steps are identical.</td>
</tr>
<tr>
<td>Requires &gt; 1,000 copies/mL of virus</td>
<td>Consider when viral load is below the limit of detection</td>
</tr>
</tbody>
</table>

**The RNA viral load level in the plasma does not match the DNA viral load level**
**Tropotype Result**

**TROFILE® DNA - Report**

**TROFILE® - A HIGHLY SENSITIVE TROPSM ASSAY**

Tropfile is a cell-based approach to determine a patient's HIV co-receptor tropism (or "Tropotype"). Tropfile uses the complete gp120 coding region of the HIV-1 envelope protein ensuring that all of the determinants of tropism are tested. CUA® validation experiments demonstrate that Tropfile is 100% sensitive at detecting CCR5/CXCR4-using minor variants.

**TROFILE VIRAL CLASSIFICATION**

Co-receptor tropism is defined as an interaction of a virus with a specific co-receptor on the target cell. To gain entry into CD4+ cells, HIV must bind to the cell surface CD4 receptor and to one of two co-receptors, CCR5 or CXCR4.

**CCR5 Tropic (R5) HIV-1**

Virus uses CCR5 to enter CD4+ cells.

**CXCR4 Tropic (X4) HIV-1**

Virus uses CXCR4 to enter CD4+ cells.

**DUAL/MIXED Tropic (D/M) HIV-1**

Dual-tropic viruses can use either CCR5 or CXCR4 to enter CD4+ cells. Mixed-tropic populations contain viruses with two or more tropisms.

**Non-reportable**

Co-receptor tropism could not be determined by the Tropfile assay. Common causes of a non-reportable result are viral load <1,000 copies/ml, reduced viral fitness, or compromised sample collection/handling.

**Co-RECEPTOR ANTAGONISTS**

This class of drugs binds to and blocks CCR5-mediated HIV entry into host cells. Tropfile is used to determine whether a CCR5 antagonist may be an appropriate drug for a patient. Several clinical trials of CCR5 antagonists have demonstrated the positive and negative predictive value of Tropfile in clinical settings.

**Activity of CCR5 antagonist anticipated?**

- YES
- NO

**ABOUT TROPISM**

**TROFILE® - A NEW TROPSM ASSAY FROM MONOGRAM BIOSCIENCES**

Tropfile DNA meets the US standards for performance characteristics and all other quality control and assurance requirements established by the Clinical Laboratory Improvement Amendments (CLIA). Tropfile is a proprietary, whole-virus, single-application nucleic acid test that uses the complete gp120 coding region of HIV-1 to evaluate tropism. Instead of using HIV-1 RNA isolated from patient plasma, Tropfile DNA uses cell-associated viral DNA taken from virally infected cells infected with HIV-1 envelopes encoded by the viral DNA are tested in a cell-based viral infectivity assay in order to determine which co-receptor the HIV-1 virus population is capable of using: CCR5, CXCR4, or both, known as D/M (full overlap).

**TROFILE DNA VIRAL CLASSIFICATION**

Co-receptor tropism is defined as an interaction of a virus with a specific co-receptor on the target cell. To gain entry into CD4+ cells, HIV must bind to the cell surface CD4 receptor and one of two co-receptors, CCR5 or CXCR4. Tropfile DNA uses the complete gp120 coding region of the HIV-1 envelope protein ensuring that all of the determinants of tropism are tested.

**CCR5 Tropic (R5) HIV-1**

Virus uses CCR5 to enter CD4+ cells.

**CXCR4 Tropic (X4) HIV-1**

Virus uses CXCR4 to enter CD4+ cells.

**DUAL/MIXED Tropic (D/M) HIV-1**

Dual-tropic viruses can use either CXCR4 or CCR5 to enter CD4+ cells. Mixed-tropic populations contain viruses with 2 or more tropisms.

**Non-reportable**

Co-receptor tropism could not be determined. Common causes of nonreportable results are reduced viral fitness or compromised sample handling. Please note that Tropfile DNA sample collection and handling instructions differ from Tropfile and other Monogram assays.
Expected Abnormal Lab results: CBC

- **Leukopenia:** WBC < 4,000 / ul
  - Prevalence up to 45% : frequent in advanced disease / AZT
- **Neutropenia:** PMNs < 1500 /ml and <1200 /ml (blacks)
  - Degrees of neutropenia
    - Mild 1000-1500
    - Moderate 500-1000
    - Severe <500
  - Bacteremia in patients with advanced disease is rare
    - Absolute CD4 count, not ANC = the predictor of morbidity
    - Most OIs a function of poor cell mediated immunity
  - USPHS/IDSA guidelines for OI prophylaxis do not recommend routine use of G-CSF in neutropenic HIV-infected pts
    - Theoretical (in vitro) risk of activating latent CD4s?
Expected Abnormal Lab results: CBC

- **Thrombocytopenia**: platelet ct < 100,000/mm$^3$
  - Spontaneous bleeding rare till <10,000 / mm$^3$
  - Consider treatment 30-50,000 /mm$^3$

- **Mechanism of action:**
  - Almost always immune mediated / reduced survival
    - Complex, not well understood
      - Platelet - Ab, Ag-Ab complexes, Ab-anti-HIV?
  - Normal or increased megakaryocytes in BM
  - Platelet Assoc Ab (IgG): false – positives high
  - Rare: decreased production / infiltrative disease
    - BM aspirate if Platelet IgG negative?
**Expected Abnormal Lab results: CBC**

- **Anemia**: hemoglobin < 12-13 gm / dl
  - Common in HIV / less since AZT decreased
    - 30% prevalence w CD4 counts< 50
  - Macrocytosis is almost expected w HAART Therapy
    - MCV in 100-115 ranges

- **Standard w/u**: Ferritin plus Fe / TIBC % saturation
  - Caution to Ferritin levels
    - Often very high: HIV / chronic liver dz

- **Special concerns**:
  - Pure red cell aplasia: consider parvovirus B19 infection
    - parvovirus B19-DNA detection by PCR
  - Anemia w reticulocytosis: peripheral destruction
    - Coombs test / haptoglobin / LDH / indirect bilirubin (<4)
Expected Laboratory Abnormalities-CMP

- **Albumin / globulin ratio:** often deceased
  - polyclonal increase a result of frequent infections?

- **Abnormal LFTs:** in absence of Hep B or C / HAART Tx
  - Fatty infiltration of liver (NAFL)?
    - May not always see evidence on ultrasound
    - TNF-α has a role in regulating *in vivo* insulin sensitivity.
      - Induction of ↑ free fatty acids via stimulation of lipolysis
    - “Classic workup”: non-infectious increase in LFTs
      - ANA / smooth muscle Ab / mitochondrial Ab / Ferritin
        - Caution: ferritin often ↑ in HIV
          » Fe/TIBC %Sat > 60 specific for Hemochromatosis
Expected lab Abnormalities-Proteinuria

- **Proteinuria:** 30% incidence at baseline evaluation
  - Usually with preserved renal function
- **Trace proteinuria:** less < 1+ dipstick
  - Benign causes include:
    - fever, intense activity or exercise, dehydration
    - Repeated positive: requires urine microablr / cr ratio
      - Elevated ratio may warrant more close f/u
        - CKD / CAD / HIV progression?
- **Significant Proteinuria:** +1 or greater
  - Quantification: 24 hr or Urine P / C ratio (spot)
    - >150 mg = abnormal
    - Nephro Consult:
    - Target groups: black race / CD4<200 / Hep C
Expected lab Abnormalities-Hyperglycemia

- Impaired fasting glucose: 99 < blood sugar < 126
  - Common: baseline HIV pts ↑ incidence
    - HAART worsens “metabolic syndrome”
      - Insulin resistance (IR) antedates Type 2 DM
      - Metformin of value in HIV pts (pre-diabetic)
        » AUC for insulin less post-Tx / less VAT
  - GlycoHbg insensitive indicator for early IR
    - 1st effect: inability to dispose of a high glycemic meal
    - Better physiologic test: 75 gm 2 hr OGGTT
      - Normal: < 140 mg%
      - Impaired: 140-199 mg%
      - Diabetic: > 200 mg%