UMC Utrecht

How do we measure HIV drug resistance

Monique Nijhuis

Measure HIV drug resistance

Genotypic resistance test vs Phenotypic resistance test

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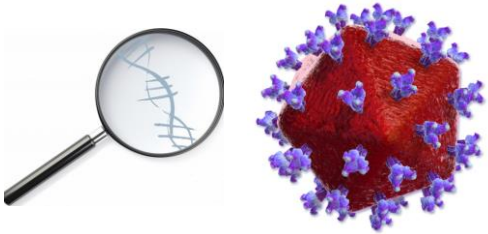
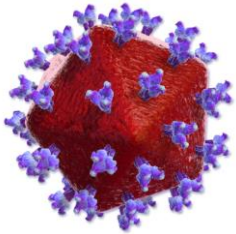
Genotypic resistance test vs Phenotypic resistance test



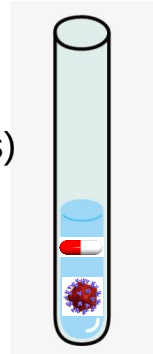
Examen if HIV has changes
(mutations) in the genetic structure

Measure HIV drug resistance

Genotypic resistance test vs Phenotypic resistance test



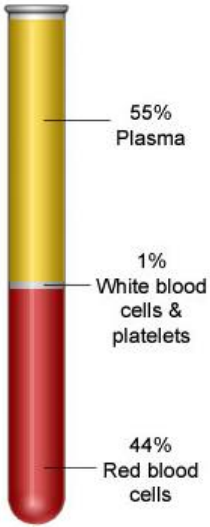
Recombinant phenotypic test
(part of the virus with mutations)



Examen if HIV has changes
(mutations) in the genetic structure

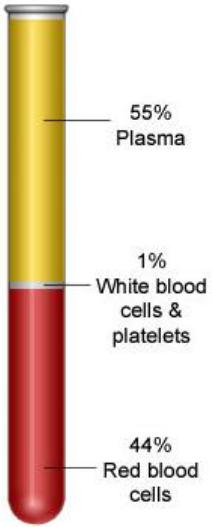
Examen if drugs
can inhibit the replication of HIV

Measure HIV drug resistance: blood sample



Centrifugation of blood sample

Measure HIV drug resistance: blood sample

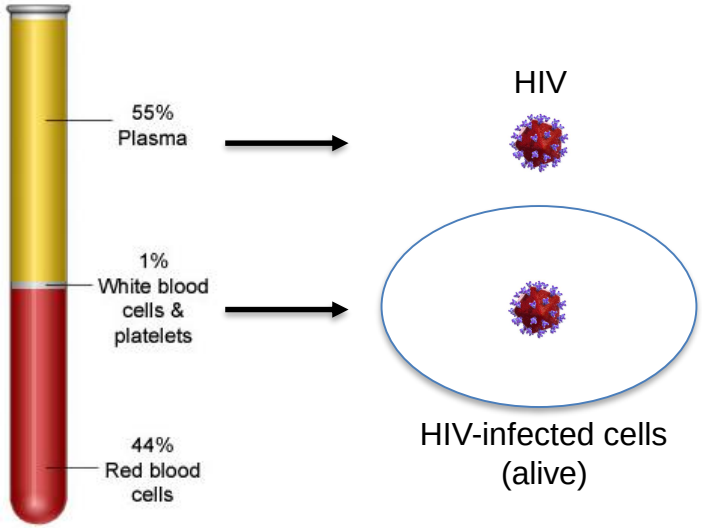


Centrifugation of blood sample

HIV

genotypic resistance test
recombinant phenotypic test

Measure HIV drug resistance: blood sample

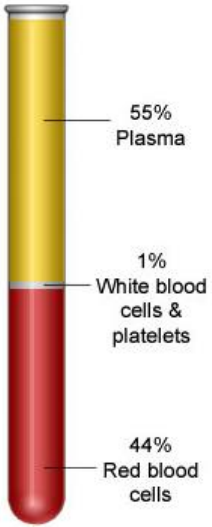


Centrifugation of blood sample

genotypic resistance test
recombinant phenotypic test

genotypic resistance test
phenotypic resistance test

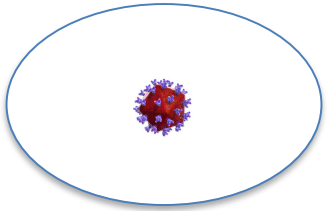
Measure HIV drug resistance: blood sample



Centrifugation of blood sample

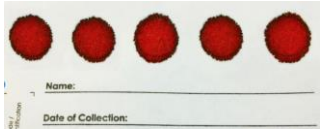
HIV

genotypic resistance test
recombinant phenotypic test

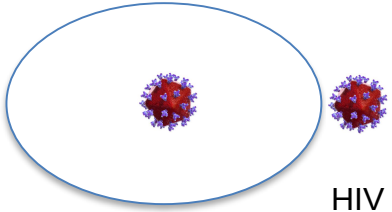


HIV-infected cells
(alive)

genotypic resistance test
phenotypic resistance test



Dried blood spot

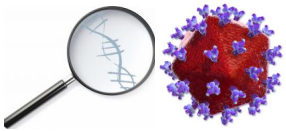


HIV-infected cells (dead)

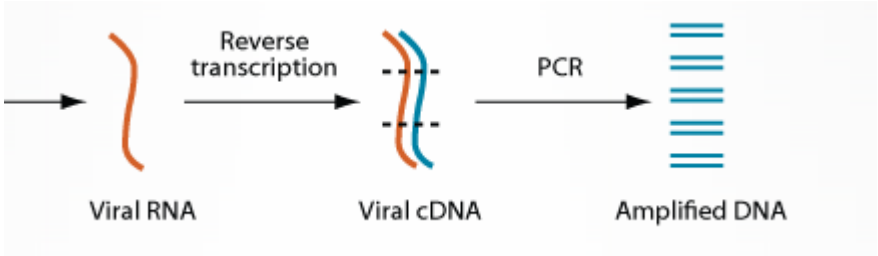
HIV

genotypic resistance test
recombinant phenotypic test

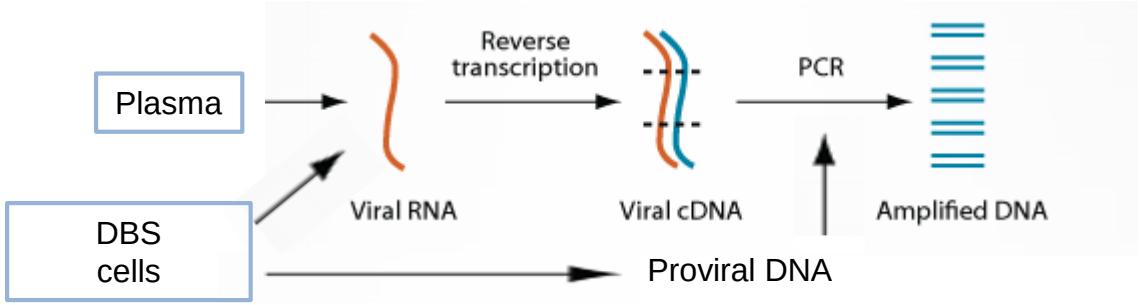
Genotypic drug resistance test



Plasma



Genotypic drug resistance test



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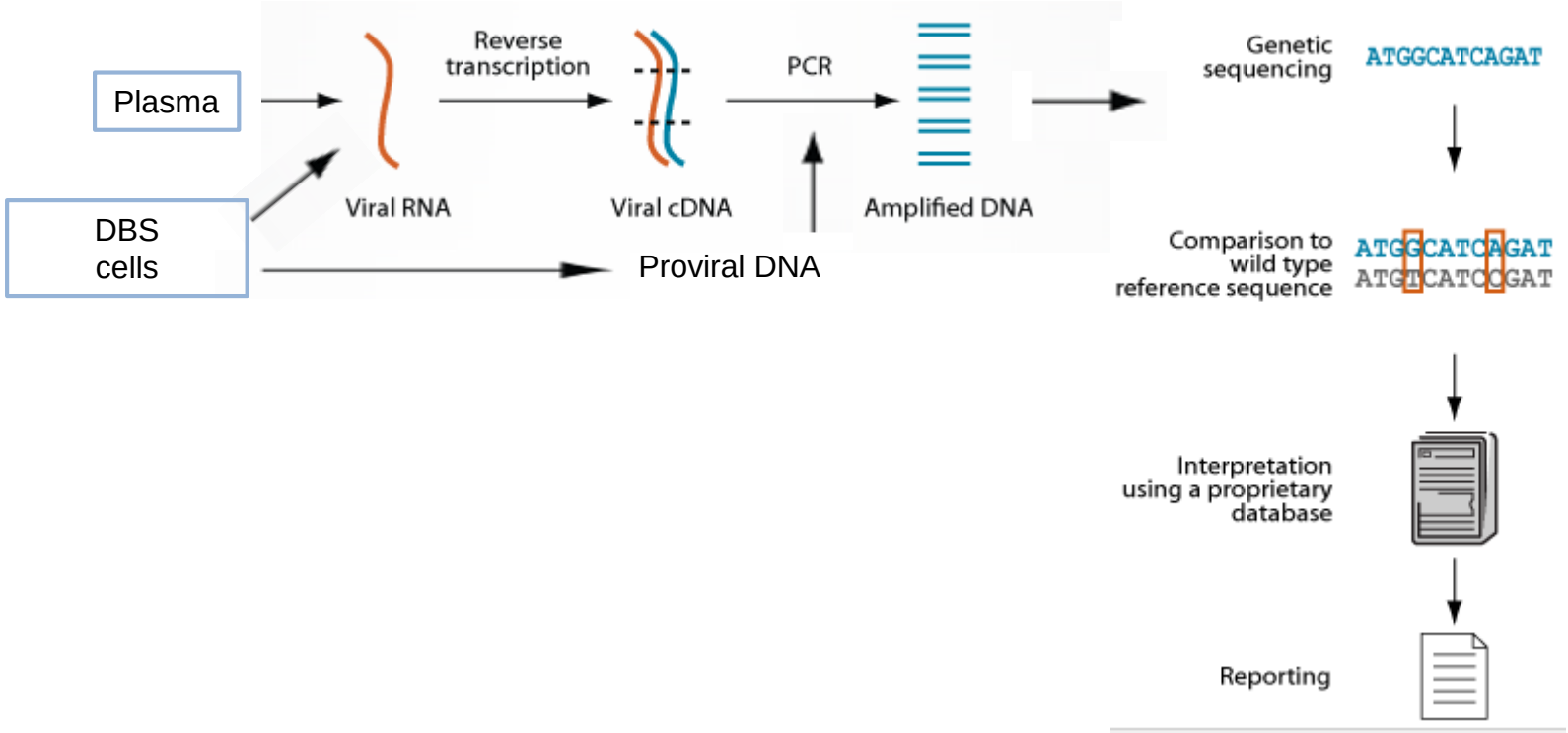
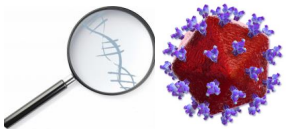
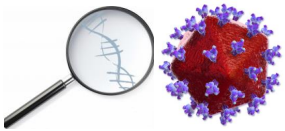


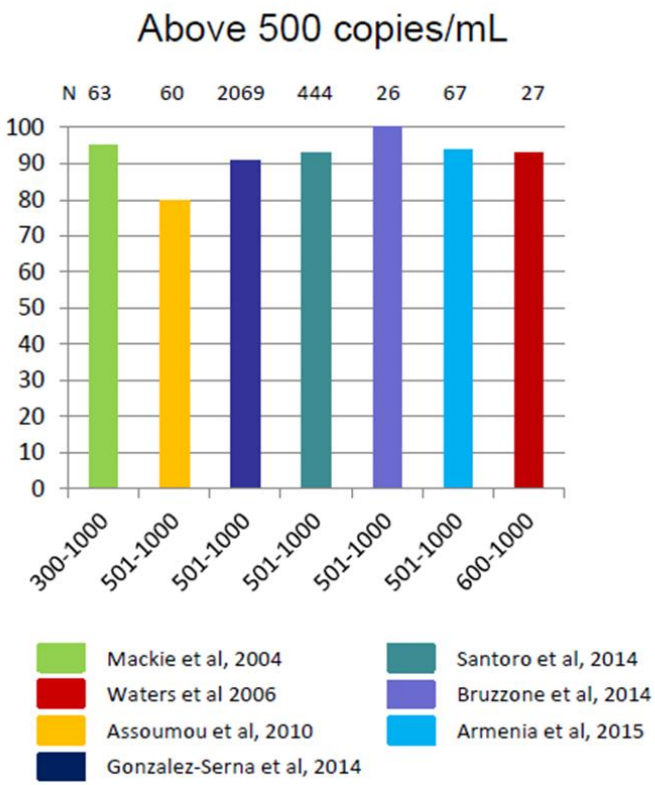
Genotypic drug resistance test pro/cons

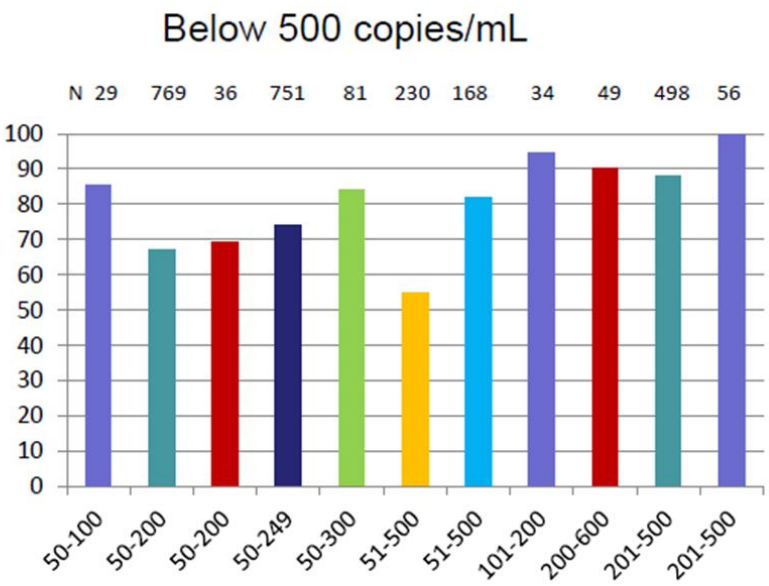


Pro:
-relatively fast and cheap
-relatively successful on low level viremia samples

Genotypic drug resistance test pro/cons

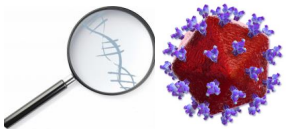






Hofstra, personal communication

Genotypic drug resistance test pro/cons



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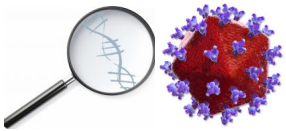
-indirect measurement of drug resistance
-need to have a database with known impact of mutations

Interpretation of genotypic resistance



Identification of relevant drug resistance mutations:

- www.iasusa.org

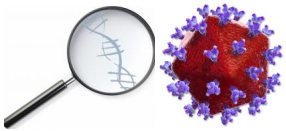
IAS–USA Topics in Antiviral Medicine

Special Contribution

2017 Update of the Drug Resistance Mutations in HIV-1

Annemarie M. Wensing, MD, PhD; Vincent Calvez, MD, PhD; Huldrych F. Günthard, MD; Victoria A. Johnson, MD; Roger Paredes, MD, PhD; Deenan Pillay, MD, PhD; Robert W. Shafer, MD; Douglas D. Richman, MD

Interpretation of genotypic resistance



Interpret impact of (combinations) of resistance mutations: Algorithms

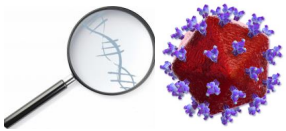
- www.hivdb.stanford.edu
- www.hiv-grade.de

HIV-GRADE

Sequence Analysis | Mutation List Analysis

STANFORD UNIVERSITY
HIV DRUG RESISTANCE DATABASE
A curated public database designed to represent, store, and analyze the divergent forms of data underlying HIV drug resistance.

Genotypic drug resistance test pro/cons



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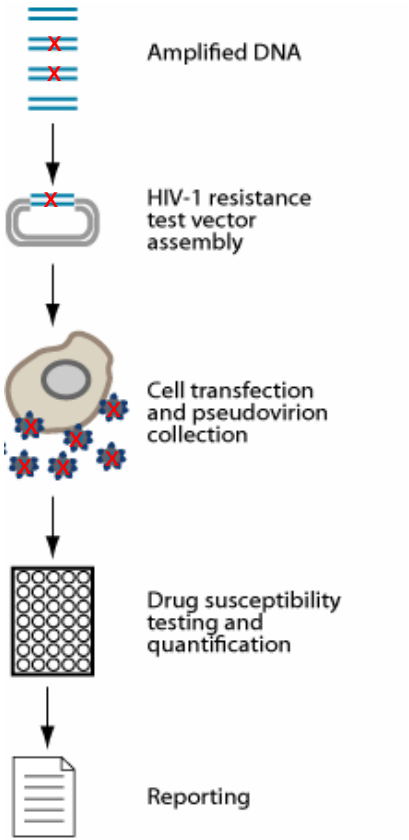
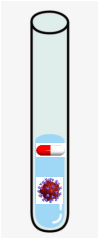
-need to have a database with known impact of mutations
    -resistance may depend on the interaction of mutations
    -virus background, subtype
    -challenging for new drugs and especially new drug classes

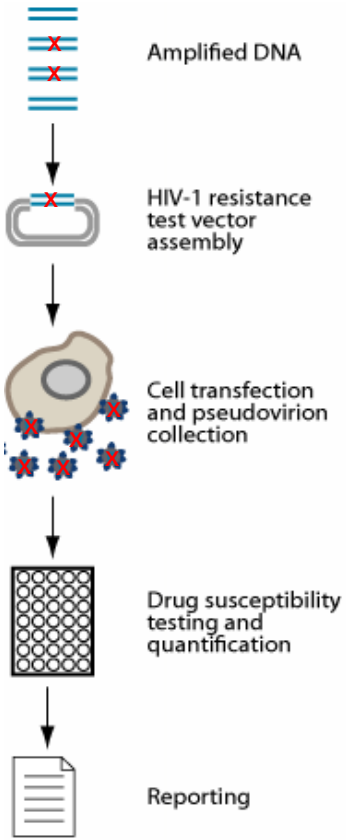
-Phenotypic drug resistance assay (recombinant phenotypic test)

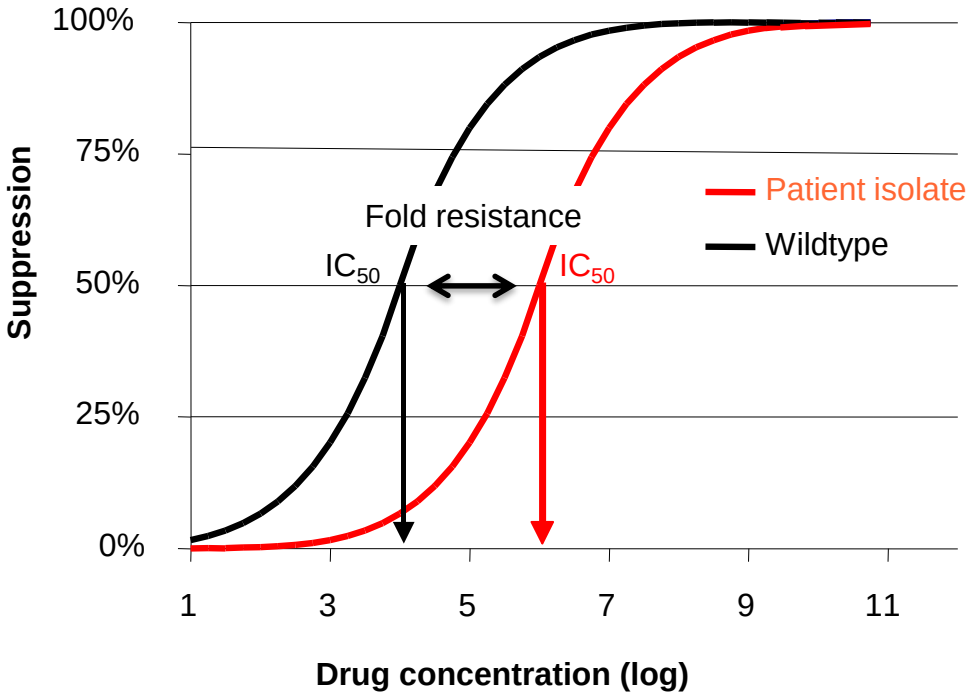
Recombinant phenotypic resistance test





Recombinant phenotypic resistance test





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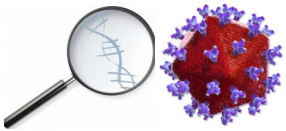

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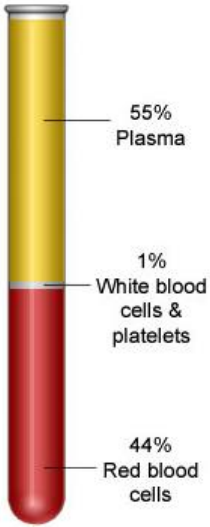
-Phenotypic drug resistance assay

Measure HIV drug resistance: blood sample



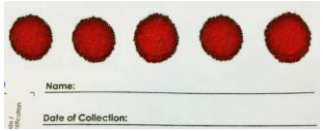
Centrifugation of blood sample

HIV

genotypic resistance test

HIV-infected cells
(alive)

genotypic resistance test
phenotypic resistance test



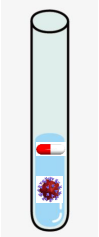
Dried blood spot

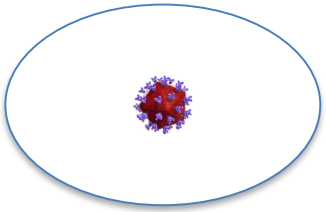
HIV-infected cells (dead)

HIV

genotypic resistance test

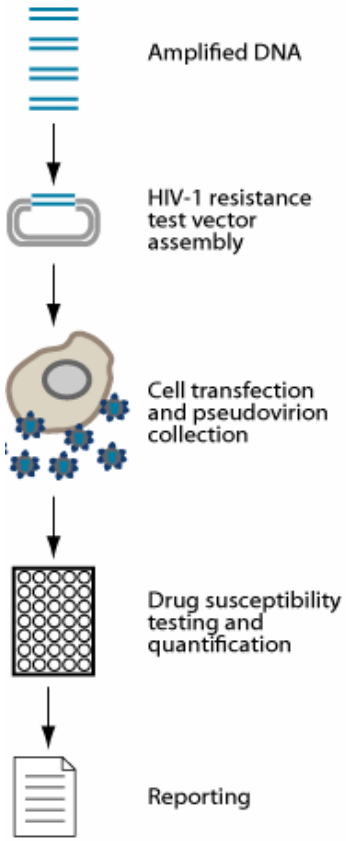
Phenotypic drug resistance test



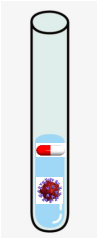


HIV-infected cells
(alive)

Virus culture



Phenotypic drug resistance test



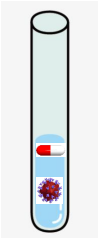
Pro:
-direct measurement of drug resistance
-you do not need to know the location of the mutation

Con:
-relatively time consuming and expensive
-clinically relevant levels of drug resistance are not always available
-require specialized laboratory (BSLIII)

Biosafety level III laboratory

double door entry, inward air flow, biosafety cabinets, on site autoclave

Choose your resistance test wisely…



Genotypic resistance test:

-known antiretroviral drugs with good interpretation algorithms

Phenotypic resistance test:

-virological failure can not be explained based on genotypic resistance profile

-new drugs or new drug classes