



UMC Utrecht

# How do we measure HIV drug resistance

Monique Nijhuis



# Measure HIV drug resistance

Genotypic resistance test

vs

Phenotypic resistance test

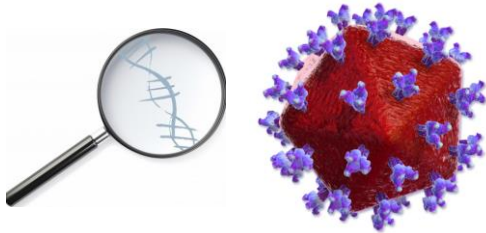


# Measure HIV drug resistance

Genotypic resistance test

vs

Phenotypic resistance test



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

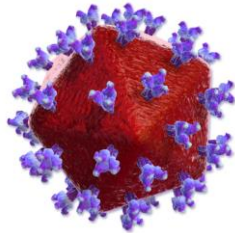


# Measure HIV drug resistance

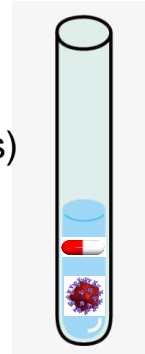
Genotypic resistance test

vs

Phenotypic resistance test



Recombinant phenotypic test  
(part of the virus with mutations)

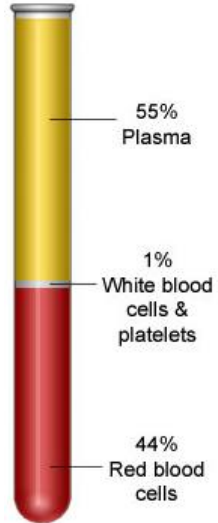


Examen if HIV has changes  
(mutations) in the genetic structure

Examen if drugs  
can inhibit the replication of HIV



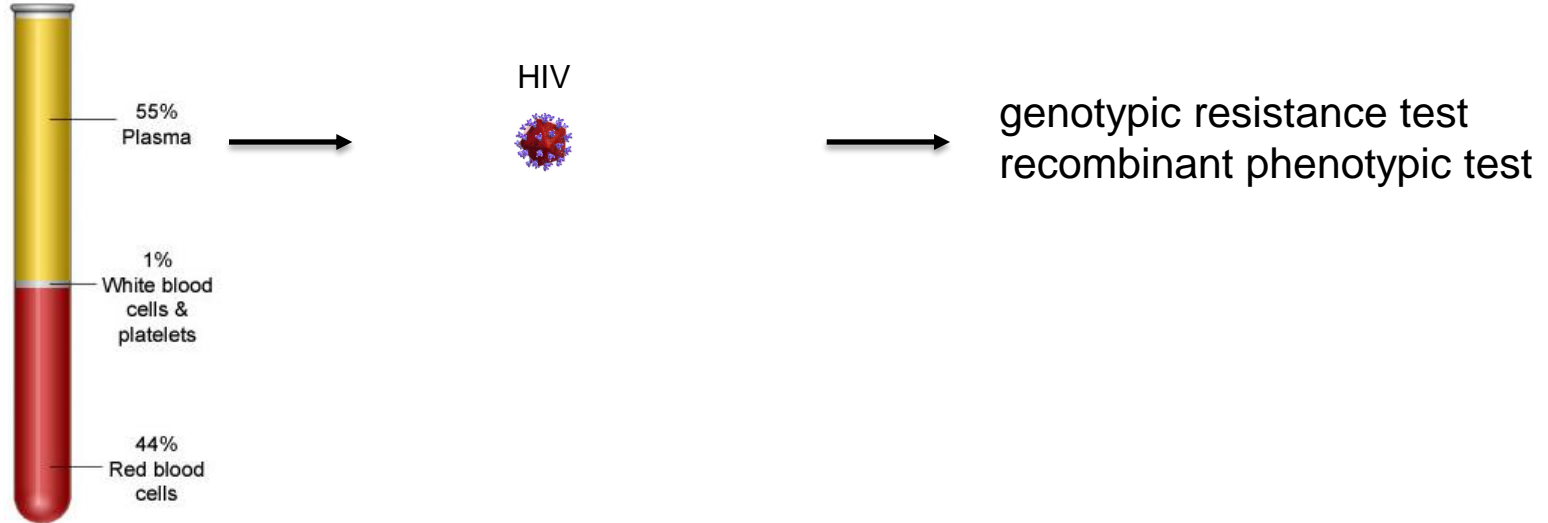
# Measure HIV drug resistance: blood sample



Centrifugation of blood sample



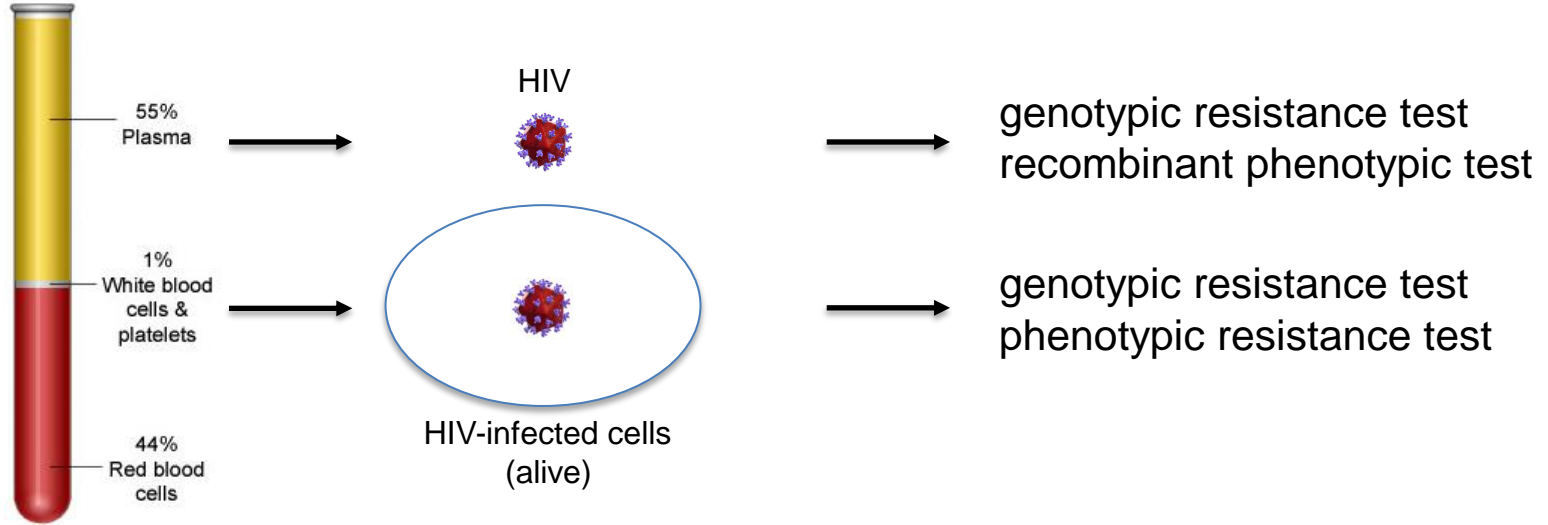
# Measure HIV drug resistance: blood sample



Centrifugation of blood sample



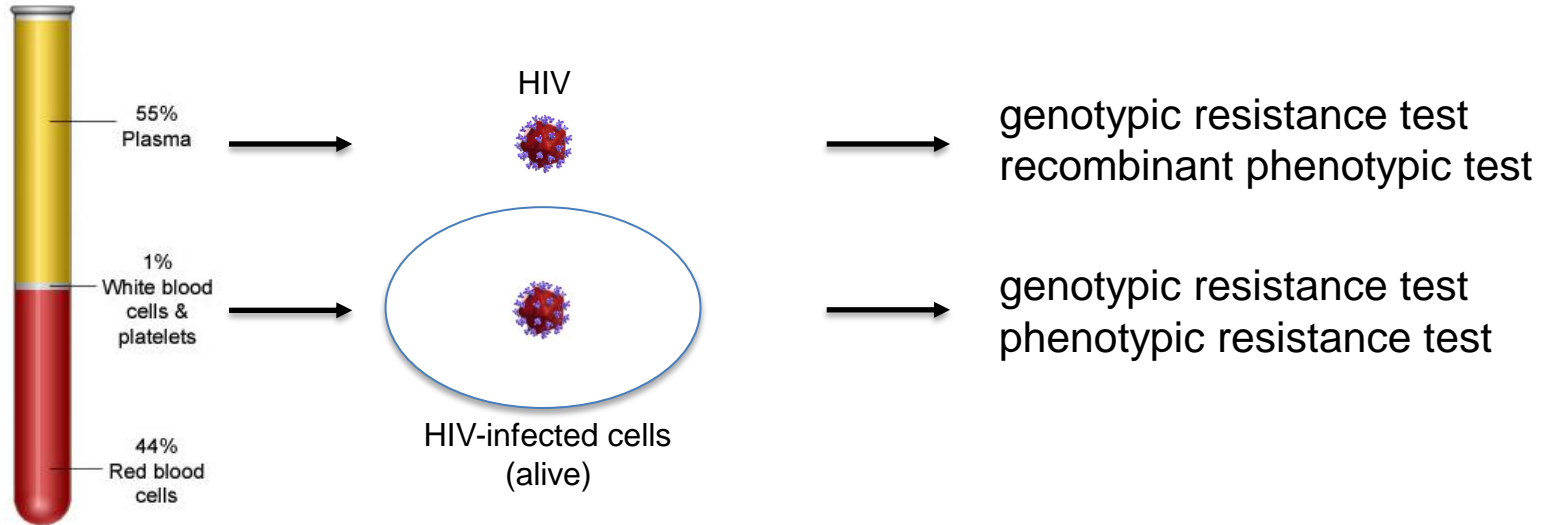
# Measure HIV drug resistance: blood sample



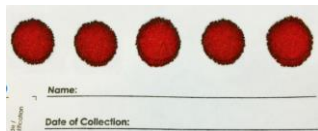
Centrifugation of blood sample



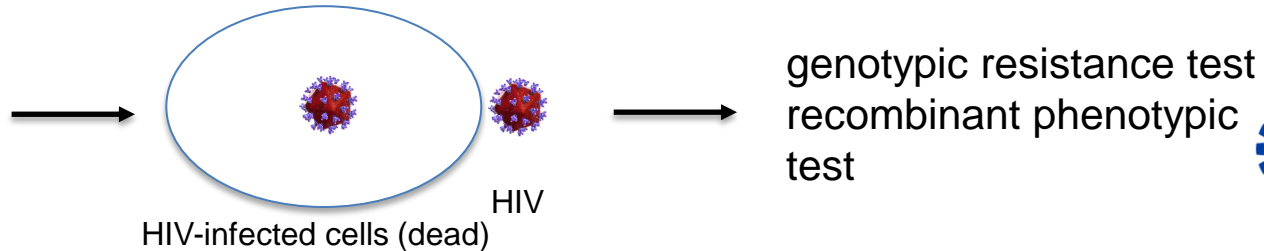
# Measure HIV drug resistance: blood sample



Centrifugation of blood sample

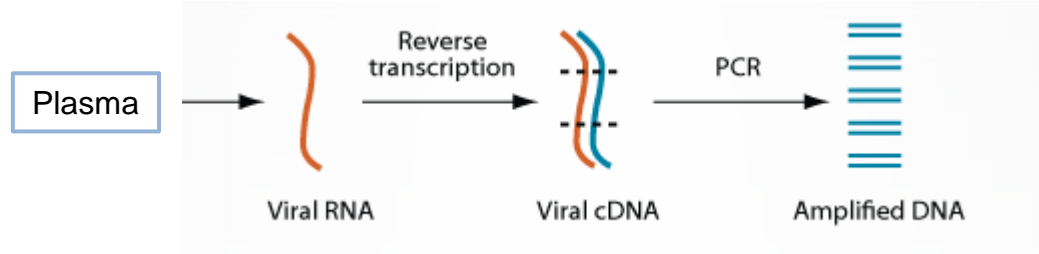
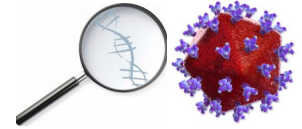


Dried blood spot

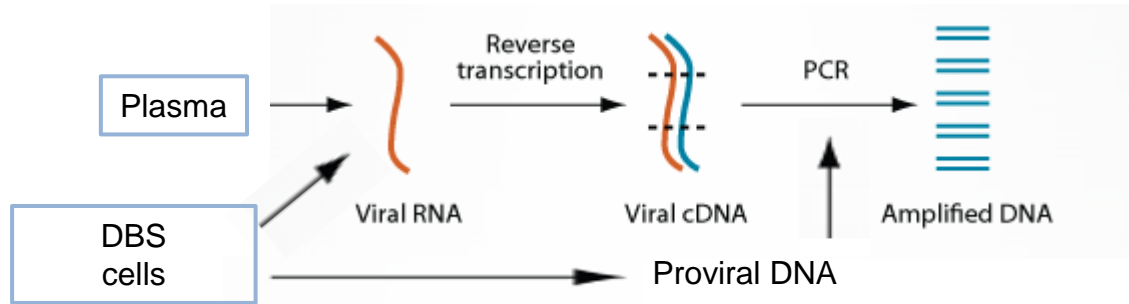
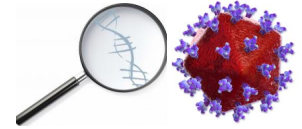




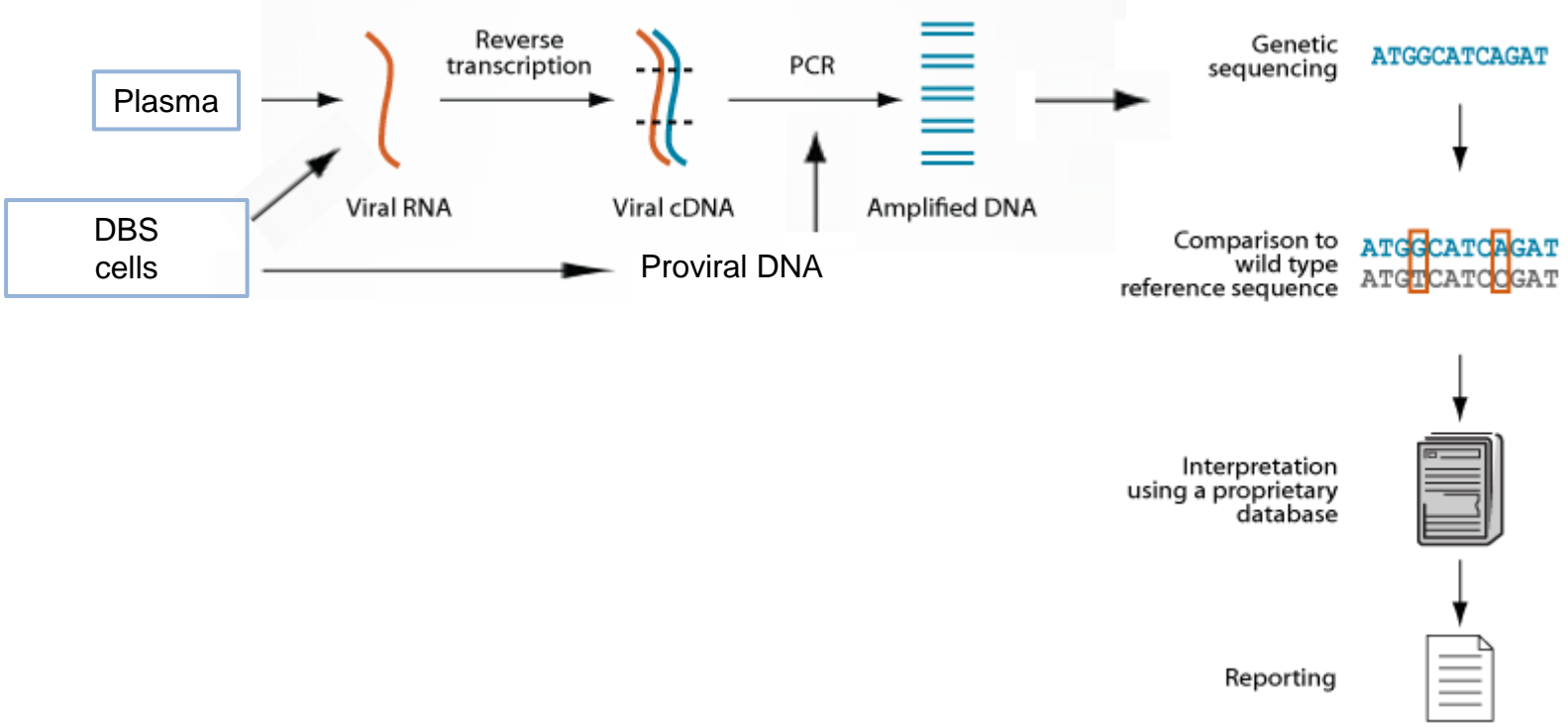
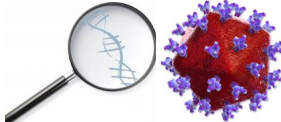
# Genotypic drug resistance test



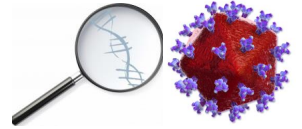
# Genotypic drug resistance test



# Genotypic drug resistance test



# Genotypic drug resistance test pro/cons

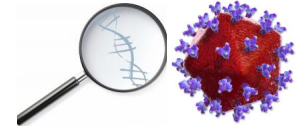


Pro:

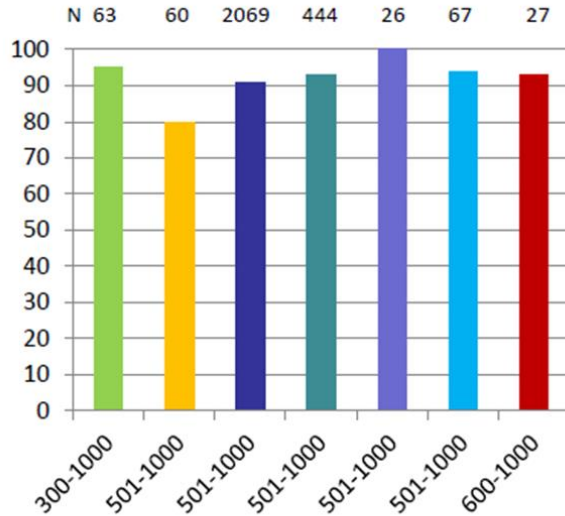
- relatively fast and cheap
- relatively successful on low level viremia samples



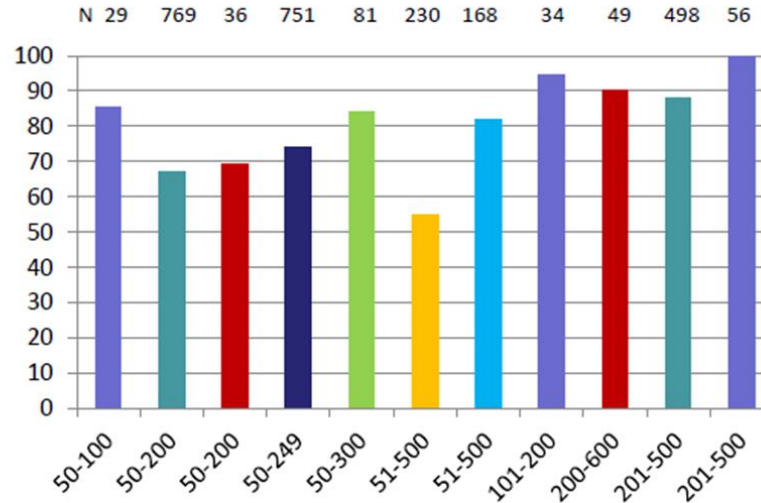
# Genotypic drug resistance test pro/cons



Above 500 copies/mL



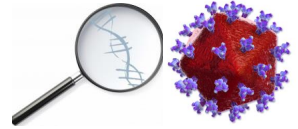
Below 500 copies/mL



- Mackie et al, 2004
- Waters et al 2006
- Assoumou et al, 2010
- Gonzalez-Serna et al, 2014
- Santoro et al, 2014
- Bruzzone et al, 2014
- Armenia et al, 2015



# Genotypic drug resistance test pro/cons



Pro:

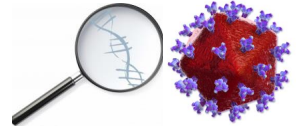
- relatively fast and cheap
- relatively successful on low level viremia samples

Con:

- 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](http://www.iasusa.org)

IAS–USA *Topics in Antiviral Medicine*

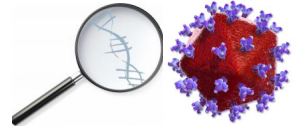
*Special Contribution*

## **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](http://www.hivdb.stanford.edu)
- [www.hiv-grade.de](http://www.hiv-grade.de)

## HIV-GRADE

[Sequence Analysis](#) | [Mutation List Analysis](#)



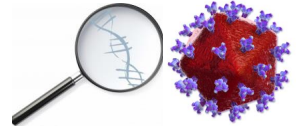
STANFORD UNIVERSITY

### 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



Pro:

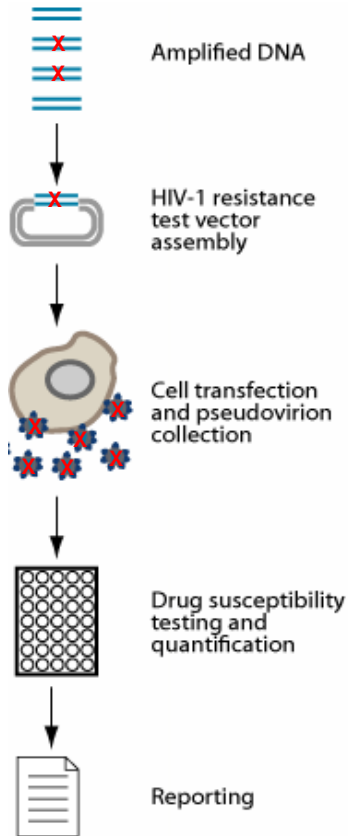
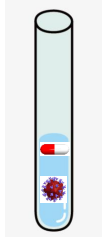
- relatively fast and cheap
- relatively successful on low level viremia samples

Con:

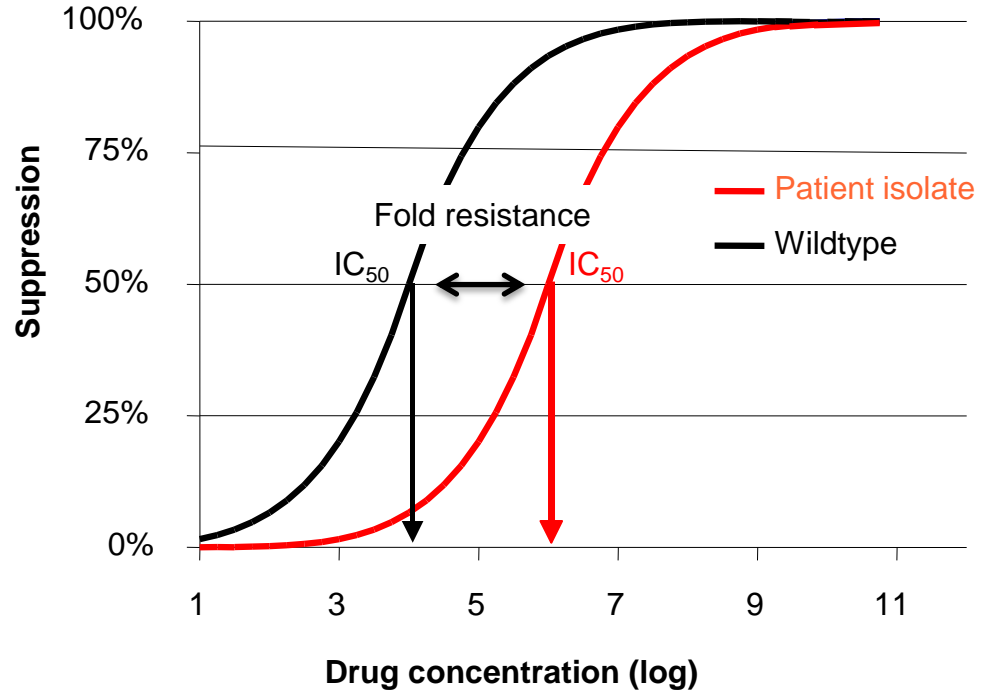
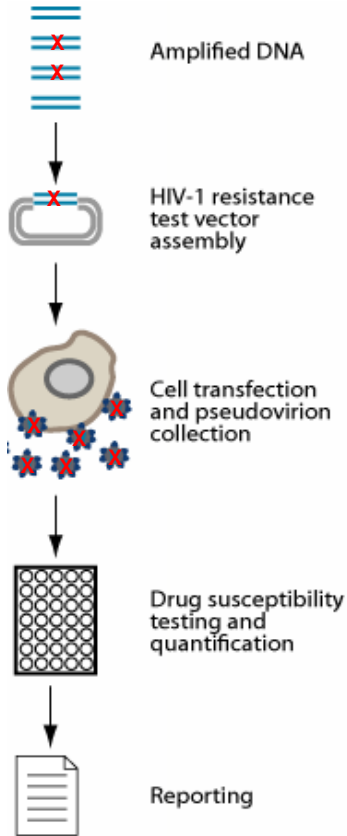
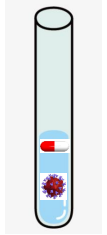
- indirect measurement of drug resistance
- need to have a database with known impact of mutations
  - resistance may depend on the interaction of mutations
  - virus background, subtype
  - challenging for new drugs and especially new drug classes
- Phenotypic drug resistance assay (recombinant phenotypic test)



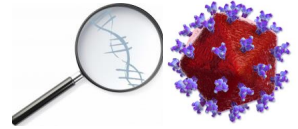
# Recombinant phenotypic resistance test



# Recombinant phenotypic resistance test



# Genotypic drug resistance test pro/cons



Pro:

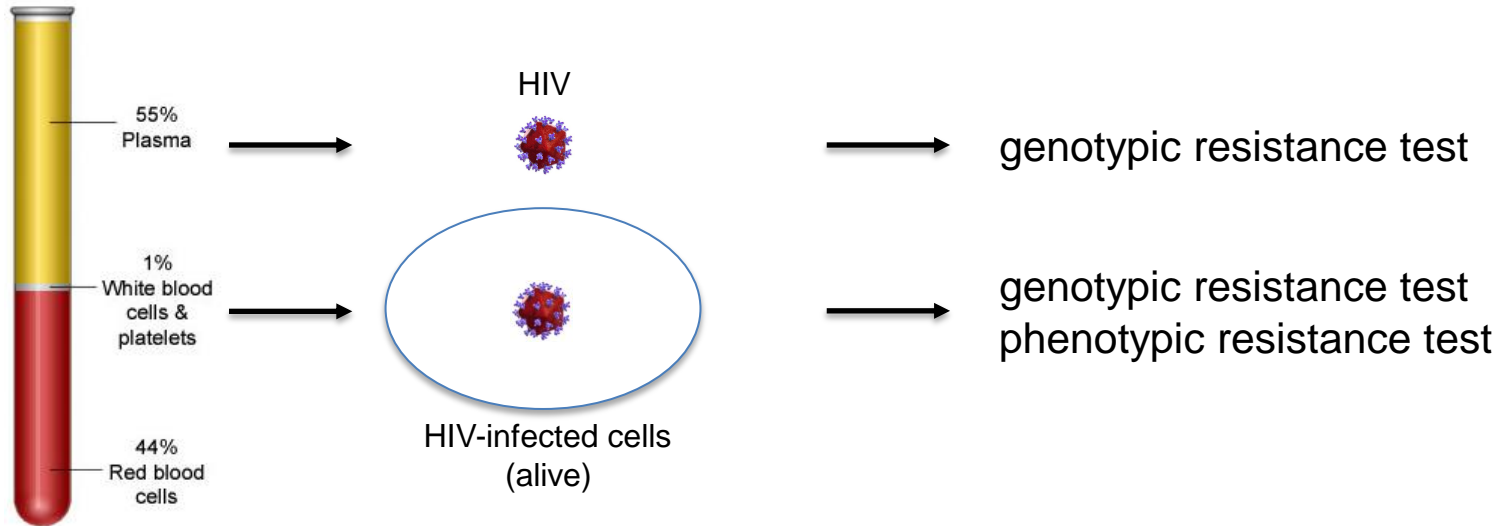
- relatively fast and cheap
- relatively successful on low level viremia samples

Con:

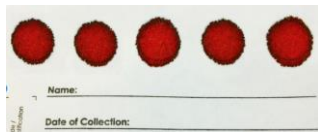
- indirect measurement of drug resistance
- need to have a database with known impact of mutations
  - resistance may depend on the interaction of mutations
  - virus background, subtype
  - challenging for new drugs and especially new drug classes
- Phenotypic drug resistance assay (recombinant phenotypic test)
- Phenotypic drug resistance assay



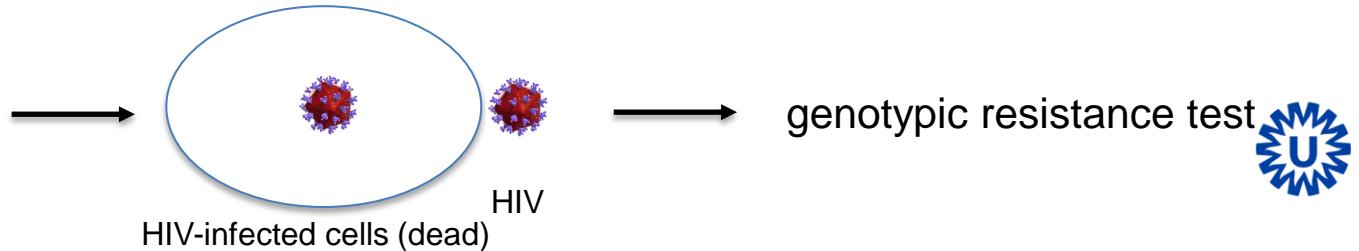
# Measure HIV drug resistance: blood sample



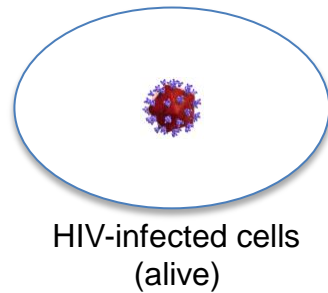
Centrifugation of blood sample



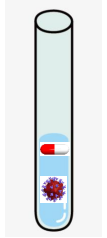
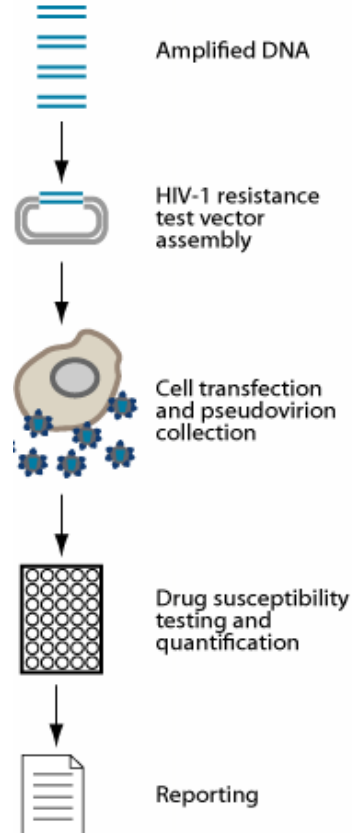
Dried blood spot



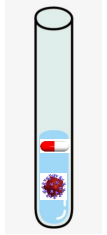
# Phenotypic drug resistance test



Virus culture



# Phenotypic drug resistance test



Pro:

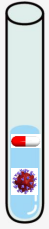
- direct measurement of drug resistance
- you do not need to know the location of the mutation

Con:

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



# Biosafety level III laboratory

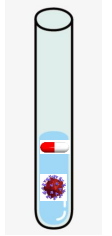


double door entry, inward air flow, biosafety cabinets, on site autoclave





# 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

