

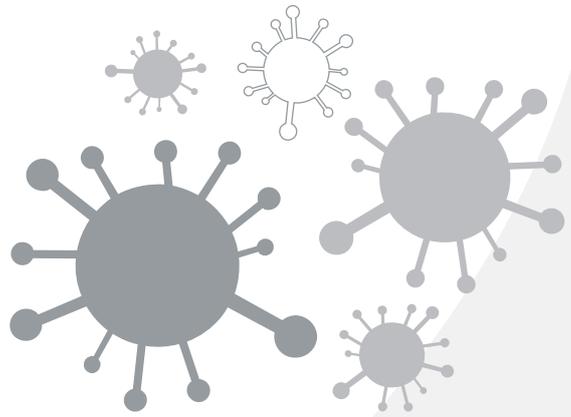
## HIV DRUG RESISTANCE ANALYSIS

### Background information

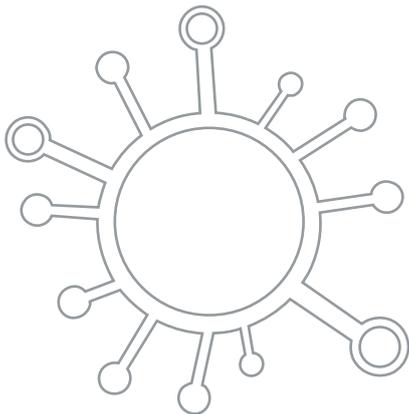
The Human Immunodeficiency Virus (HIV), the causative agent of AIDS, is a highly mutable lentivirus. It is a member of the Retroviridae, with an RNA encoded genome. HIV has the gag/pol/env gene organization typical of retroviruses. Because of the high mutation rate of HIV, acquired drug resistance has to be monitored continuously in patients.

Schemes for automated prediction of drug resistance have been developed, based on mutation rules for the pol gene.

Unfortunately, resistance rules are often trapped in closed systems, hiding which particular rules are applied and by which events they were triggered.



### HIV drug resistance analysis in BioNumerics



The BioNumerics HIV drug resistance analysis application is a plugin-based expert system for automated prediction of antiretroviral drug resistance/susceptibility of HIV strains based on pol gene sequencing. It offers an open expert system that allows researchers to import and compare publicly available rule sets (algorithms) and create, adapt and (re)evaluate their own expert rules.

The system does not just show resistance/susceptibility results, but reports the particular rules that are triggered and the mutations that are responsible for the triggering. The application offers a fully integrated and automated workflow starting from sequence assembly to final resistance reporting and is designed for professional high-throughput diagnostics.

## YOUR ADVANTAGES



WHY USE **BioNumerics**  
FOR YOUR HIV RESISTANCE ANALYSIS?

- ✓ Automated import and assembly
- ✓ Automated processing
- ✓ Detailed reporting
- ✓ Rich database environment

## Automated import and assembly



Batches of forward and reverse chromatogram files of the HIV-1 pol gene sequence are automatically assembled, with detailed error and problem reporting and feedback. The batch assembly reports are stored inside the database and can be viewed at any time.

## Automated processing



The assembled sequences are processed in batch and include alignment to wild-type (consensus) at nucleotide and amino acid level, and the detection of mutations. The AA sequences are used as the input for one or more publicly available or proprietary drug resistance algorithms, offering rules for predicting drug resistances based on specific SNPs in the sequences analyzed.

## Rich database environment



All processing and analysis steps happen fully automatically on batches of any number of sequences and generate detailed reports, making the system extremely suitable for high-throughput screening. BioNumerics provides a powerful multi-user database and multi-experiment platform for the repository and management of information at all levels, ranging from patients to strains and samples.

### NOTE:

The HIV plugin is a free add-on. The minimum configuration for installation of the plugin includes the "Character Data", "Sequence Data" and "Classifiers and Identification" modules. Please contact us for more information.

## Detailed reporting

Up-to-date prediction is based on the latest releases of publicly available algorithm databases (HIVDB, ANRS, REGA and others). Detailed batch reporting of resistance levels is given for all currently known antiviral drugs. Frame shifts on nucleotide sequences (usually due to sequencing problems and/or base-calling errors) are recorded and reported. Double and triple degenerations at nucleotide level as well as unresolved positions (N) are also recorded and reported. In case of degenerated nucleotide base positions, all possible translations are evaluated in the decision network, and the worst case (i.e. inducing highest resistance) is reported. Detailed comparisons can be generated between multiple algorithms and for multiple strains.

DrugClass	Drug	SIR	Level	Mutations
NRTI	abacavir (ABC)	R	5	41L, 74K, 215Y
NRTI	didanosine (DDI)	R	5	41L, 74K, 215Y
NRTI	emtricitabine (FTC)	S	2	41L, 215Y
NRTI	lamivudine (3TC)	S	2	41L, 215Y
NRTI	stavudine (D4T)	R	5	41L, 215Y
NRTI	tenofovir DF (TDF)	I	4	41L, 215Y
NRTI	zidovudine (AZT)	R	5	41L, 215Y

Mutations at algorithm positions: 41L, 74LV, 215Y  
Other mutations: 4PS, 106AV, 123E, 135T, 142T, 177E, 179I, 181CY, 196E, 275Q, 286A, 288G, 293V, 294T, 297X

**HIV Drug Resistance Report**  
Report generated by: JH  
Report date & time: 2016-12-08 16:06:45

Key	NRTI			NRTI			NRTI			NRTI		
	ABC	DDI	FTC	3TC	ABC	DDI	FTC	3TC	ABC	DDI	FTC	3TC
NCT40-1997	1	1	1	1	1	1	1	1	1	1	1	1
NCT78-1997	1	1	1	1	1	1	1	1	1	1	1	1
NCT79-1997	1	1	1	1	1	1	1	1	1	1	1	1
NCT97-1997	1	1	1	1	1	1	1	1	1	1	1	1

SIR code: S = Susceptible, I = Intermediate, R = Resistant  
Algorithm: HIVDB Version 7.0 F  
Levels: 1. Susceptible, 2. Potential low level resistance, 3. Low level resistance, 4. Intermediate resistance, 5. High level resistance

Created using BioNumerics Version 7.0



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