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Determination of the Optimal Cut-offs for Predicting the Phenotype of Nine Different HIV Drug Resistance Algorithms

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OBJECTIVES : The interpretation of HIV drug resistance data is one of the most fascinating and exhausting things to do. Phenotypic resistance data are still lacking clinically relevant cut-offs for most drugs, and the interpretation of genotypic data is dependant on the algorithm or system used. Furthermore, some algorithms are predicting phenotypic resistance, some others clinical response to antiretroviral therapy. This study was performed to standardize the interpretation systems without a gold standard.

METHODS : For the comparison of algorithms, a database was used containing phenotypic and genotypic data obtained by a recombinant virus assay and directly sequencing of the protease gene and the first 690 nucleotides of the RT gene, respectively. The following algorithms were included: Retrogram v1.4, Rega v5.0, ANRS AC11, CHL v3.2, Grupo de Aconselhamento Virologico (GAV), Detroit Medical Center 2000 (DMC), VGI 5.0, Beta Test of Stanford database (SDB-β) and geno2pheno (g2p).

RESULTS : 454 samples were classified by each system. The results were monitored for the percentage of correctly (sensitivity and specificity) and falsely (error rate) classified samples by using a continuum of phenotypic cut-offs (from 1 to 100). As final result the respective cut-off exhibiting the lowest error rate was determined for each algorithm and drug. The optimal cut-offs varied from 1.5-fold to 80-fold, the error rates ranged from 4.7-30.3 %.

CONCLUSIONS : This study offers the opportunity to evaluate the optimal cut-off of each drug and different drug resistance algorithms. The differences between the interpretation systems might help to understand the influence of single mutations which are part of the different rules to predict drug susceptibility or resistance. In addition, drug resistance interpretation systems are now characterized by a certain cut-off for each drug instead of predicting categories of resistance. Furthermore, if clinically relevant cut-offs will be defined in the future, it should be easier to identify the algorithm which fits best.

Abstracts