
To the Editor—In a recently published article, Hirsch et al. [1] reviewed HIV drug resistance assays used in clinical practice and described a “virtual phenotype” that correlates genotypic data on the plasma HIV-1 RNA of a candidate gene with a large database of paired phenotypes and genotypes. Although the authors cite other bioinformatics systems that generate a calculated fold change (FC), our comments are specific to the Virco Type HIV-1.

Hirsch et al. [1] state that virtual phenotype resistance interpretations are limited by a methodology that relies on matches that are based on preselected codons and not on the entire nucleotide sequence and that the “predictive power depends on the number of matched datasets available” [1, p. 274], with high variation for newer drugs with smaller datasets. We would like to note that the matching system used to calculate the FC in their article is no longer the methodology used by the Virco assay. Since July 2006, Virco’s bioinformatics engine has been used to calculate the FC for a given sample by the following method [2].

First, linear regression modeling is performed periodically to analyze the relationship between genotype and phenotype in the Virco correlative database, which, to date, has >53,000 samples with paired genotypic and phenotypic data. Significant mutations and mutation pairs that affect phenotypic susceptibility to each drug are identified, and their negative or positive impact on the FC is quantified by a resistance weight factor.

Second, all of the mutations in a sample genotype are compared on a drug-by-drug basis to the current list of resistance weight factors for the drug. An FC score is then generated by calculating the sum of the values for all resistance weight factors identified in the sample genotype.

This methodology is unlike the first generation of the virtual phenotype, which sought to identify matches to viruses with very similar mutational profiles. With the current linear modeling engine, accurate FC values can be reported regardless of whether there are viruses with similar mutational profiles in the database.

Acknowledgments

Potential conflicts of interest. N.A.B. is the Director of Medical Affairs USA/Canada for Virco Lab. L.B. is the Vice President of Clinical Virology for Virco Lab. J.V. is the Senior Director of Global Medical Affairs for Virco BVBA.

Nobel A. Bellosillo,1 Lee Bachelor,2 and Jorge Villacian3

1Virco Lab, Bridgewater, New Jersey; 2Virco Lab, Durham, North Carolina; and 3Virco BVBA, Mechelen, Belgium

References


Reply to Bellosillo et al.

To the Editor—Bellosillo et al. [1] correctly note that our description of the procedures used to generate a virtual phenotype was incorrectly based on an older approach that is no longer in use. We appreciate their highlighting the linear regression models that form the basis of the current system. We do note that the overall size of the database of paired genotypes and phenotypes is still important, that the number of phenotypes for newer drugs will be fewer than that for older drugs (and, hence, the strength of the linear regression models will be correspondingly weaker), and that the number of samples with a given mutation in the database does have an effect on the precision of the estimated contribution to the drug susceptibility of that particular mutation [2].

Acknowledgments

Potential conflicts of interest. D.R.K. has served as a consultant to and has received honoraria from Abbott Laboratories, Avea, Boehringer Ingelheim Pharmaceuticals, Bristol-Myers Squibb, Gilead, GlaxoSmithKline, Human Genome Sciences, Idenix, Merck, Monogram Biosciences, Pfizer, Roche, Schering-Plough, Siemens, and Trimeris and has received research grant support from GlaxoSmithKline, Human Genome Sciences, Merck, and Schering-Plough. M.S.H. has served on data safety monitoring boards for Merck and TaMed Biologics.

Martin S. Hirsch1 and Daniel R. Kuritzkes,2 for the International AIDS Society–USA Panel on Antiretroviral Drug Resistance Testing

1Virco Lab, Bridgewater, New Jersey; 2Virco Lab, Durham, North Carolina; and 3Virco BVBA, Mechelen, Belgium

References


Reprints or correspondence: Dr. Nobel A. Bellosillo, Virco Lab, 430 US Rte. 22 East, Bridgewater, NJ 08807 (nbellosi00@its.jnj.com).

Clinical Infectious Diseases 2009;48:687
© 2009 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2009/4803-0031$15.00
DOI: 10.1086/597016

Potential of Helical Tomotherapy for Sparing Critical Organs in a Patient with AIDS Who Was Treated for Hodgkin Lymphoma

To the Editor—Acute gastrointestinal toxicity has been frequently suggested to occur in patients with AIDS who undergo external beam radiotherapy. Moreover, HIV infection is significantly associated with an increased risk of late (i.e., >6 months) rectal adverse events [1]. Al-