
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.

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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].

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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-

CORRESPONDENCE • CID 2009:48 (1 March) • 687
circulating HIV-1 RNA level was time that lymphoma was diagnosed. The patient subsequently underwent HT, which consisted of 30 Gy via 6 MV photons, at 2 Gy per daily fraction (total duration, 27 days). Weekly routine blood cell counts were determined during treatment. No acute toxicity was observed, including gastrointestinal toxicity. Two months after completion of HT, the patient presented with a partial radiologic response, with retroperitoneal residual masses (diameter, 0.8 cm) (figure 1c). No additional toxicities occurred. Figure 1b shows a CT after completion of radiotherapy. Currently, the patient is considered to be in complete remission.

Enhanced mucosal reactions have been reported in patients with AIDS who are undergoing radiotherapy [3]. It has been suggested that this increased radiosensitivity would be related to inherent cellular radiosensitivity and glutathione deficiency. Markedly increased morbidity has been observed after receipt of standard radiotherapy if the pretreatment CD4 cell count is <200 cells/mm³ [4]. Other studies have suggested that HIV infection is an adverse prognostic factor. In such patients, particular attention should be paid to decreasing normal tissue toxicity and to strict follow-up. HT combines intensity-modulated fanbeam radiotherapy delivery with megavoltage CT imaging for patient positioning, providing a potential tool for decreasing the risk of gastrointestinal toxicity in patients who are at risk of developing high-grade toxicity [5]. It is reasonable to assume that HT may, in part, have permitted us to spare structures that normally would not have been efficiently spared with more conventional 3D conformal radiotherapy (figure 1b).

In patients with AIDS, special attention should be given to gastrointestinal organs localized in the radiation fields. These could require more-conformational treatment modalities.

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References

Head of a Young Man

To the Editor—With regard to the drawing *Head of a Young Man* by Hans Holbein the Younger, which recently appeared on the cover of volume 47, issue 10, of *Clinical Infectious Diseases*, I wonder whether the facial pustules could correspond to the very famous “bubas,” which was the Spanish popular name for such lesions at the time [1]. During the final years of the 15th century and throughout the 16th century, a great outbreak (probably of a treponematosis known as the French pox) swept all of Europe [1]. In my opinion, this is a reasonable and interesting diagnostic possibility. Although the cover commentary asserts that there is no obvious cause for the pustules, they may well represent a typical case of tertiary syphilis during the Renaissance.

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