HIV-1 Drug Resistance and Molecular Epidemiology in Honduras

Department of Microbiology, Tumor and Cell Biology

AKADEMISK AVHANDLING
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av

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ABSTRACT

The high genetic diversity and rapid evolution of HIV-1 poses a challenge to the worldwide prevention and treatment programs. Effective antiretroviral treatment has significantly improved the quality of life for HIV-infected patients. However, it came with a cost because resistant viruses emerge and sometimes are transmitted, which can reduce the efficacy of first-line antiretroviral therapy. Sequencing of the HIV-1 genome can provide information on both viral diversity and antiretroviral resistance profiles. This thesis work investigated HIV-1 resistance and molecular epidemiology in Honduras.

In paper I the prevalence of antiretroviral drug resistance was investigated in 138 HIV-positive Honduras patients with signs of treatment failure by partial sequencing of the HIV-1 pol gene. The prevalence of antiretroviral resistance was high and resistance mutations were detected in 112 patients (81%). Virologic failure was the strongest predictor of treatment failure and poor access to viral load testing in Honduras was identified as an important problem. Paper II investigated transmitted drug resistance in a representative sample of 200 treatment-naïve, newly diagnosed Honduran HIV-1 patients. The prevalence of transmitted drug resistance was 7%; 5% for NNRTI, 3% for NRTI and 0.5% for PI. Recent infection, as determined by the serological BED assay, was observed in 12% of the patients and was associated with a higher prevalence of transmitted drug resistance.

Little is known about how HIV-1 has entered and spread in Honduras and Central America. In paper III the molecular epidemiology of HIV-1 in Honduras was investigated using pol gene sequences from a representative sample of 257 Honduran patients. The Honduran HIV-1 epidemic was found to be dominated by six subtype B clades that were introduced into Honduras between 1966 and 1984. One HIV-1 clade has been particularly successful and accounts for 64% of the current HIV-1 cases in the country. The analyses suggested that HIV-1 was introduced into Honduras from the United States of America. In paper IV phylogenetic analyses were also used to understand the spread of HIV-1 in Central America using 625 HIV-1 pol gene sequences collected between 2002 and 2010 in Belize, Costa Rica, El Salvador, Honduras, Nicaragua and Panama. Published sequences from neighboring countries (n=57) and the rest of the world (n=740) were included as controls. Maximum-likelihood analyses showed that almost all (98.9%) sequences were of subtype B and that 436 (70%) sequences formed five significantly supported, monophyletic clades, which almost exclusively contained Central American sequences. One clade contained 386 (62%) sequences from all six countries; the other four clades were more country-specific, suggesting a compartmentalized epidemic. Bayesian coalescent-based methods were used to time the HIV-1 introductions and showed that the most recent common ancestor of the main subtype B introductions into Central America dated back to 1960-1970’s.

In conclusion, this thesis highlights the importance of drug resistance surveillance in treated and untreated patients, and points to a need for increased access and use of HIV testing, CD4 counts, viral load and resistance testing in Honduras. Understanding the factors responsible for the HIV-1 epidemic in Honduras and Central America has important implications in terms of intervention and control strategies.

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