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Abstract (publication only)

HIV drug-resistance testing at low viral load may help differentiate between ongoing replication and release from reservoirs

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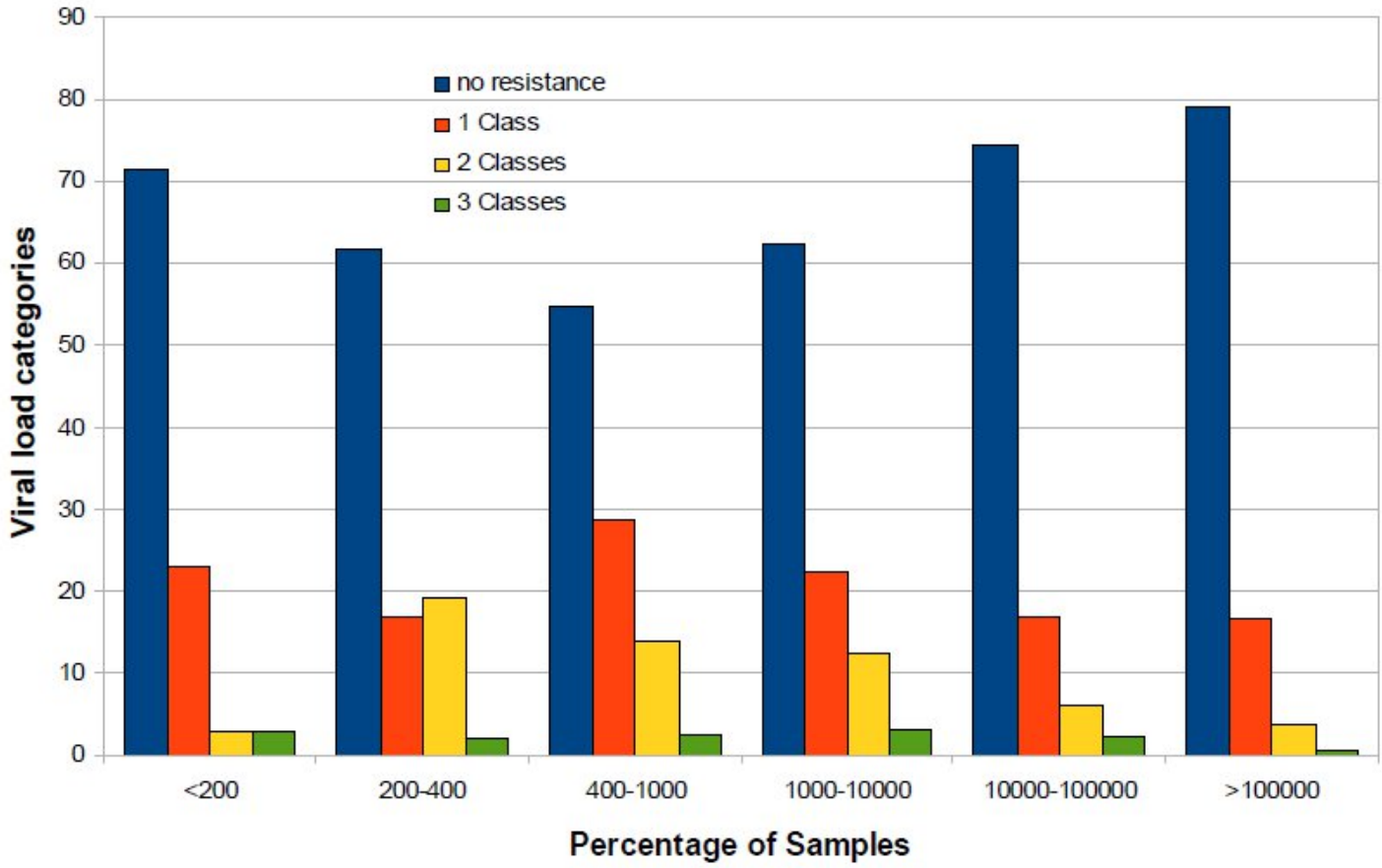
Objectives: Low level viraemia in HIV infected patients treated with anti-retroviral therapy is a phenomen still not fully understood. If the observed viraemia is a result of ongoing replication or if virus is released from cellular reservoirs remains unclear. We analysed our database of viral load and genotypic resistance interpretations to analyse the effect of viral load on frequency of detected drug resistance. Methods: 1939 viral load and Protease and reverse transcriptase sequence pairs from the year 2009 to 2011 were analysed. Drug resistance interpretation was performed the HIV-GRADE resistance interpretation rule set. Pairs were split up into viral load categories of below 200 cop/ml, 200-400, 400-1000, 1000-10000, 10000-100000 and more than 100000 cop/ml. Resistance interpretation was stratified in the following categories: no resistance, resistance against one, two or three drug classes. The collected data was then analysed using chi-squared test. Results: 1390 sequences showed no relevant drug resistance, while 336 sequences showed resistance against one drug class (two classes: 145, three classes 38). In 25 samples viral load was below 200 cop/ml (200-400: 29, 400-1000: 63, 1000-10000:275, 10000-10000: 526, above 100000: 472). In both groups below 400 cop/ml no significant increase of resistant variants was observed compared to the mean distribution, while in the groups with 400-1000 cop/ml viral load and 1000-10000 cop/ml significant more resistant variants were found than expected ($p<0.001$). This reverses above 100000 cop/ml, where significantly ($p<0.001$) more susceptible variants are observed. Conclusion: As in most of the samples with a viral load below 400 cop/ml, no mutations leading to resistance could be found, we conclude that virus in these cases is released from cellular reservoirs. Viral loads between 400 cop/ml and 10.000 cop/ml are a clear sign for ongoing replication, and in this group the highest rate of drug resistance is observed. Viral loads above 100000 cop/ml are a sign of missing selective pressure and thus no drug resistance is observed.


90
80
70
60
50
40
30
20
10
0
no resistance
1 Class
2 Classes
3 Classes
Viral load categories
<200
200-400
400-1000
1000-10000
10000-100000
>100000
Percentage of Samples