The genetics of HIV-1 resistance

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Drug resistance is a major problem when treating infections. This problem is multiplied when the infection, like HIV-1, is chronic. New research published in BioMed Central's open access journal *Retrovirology* has examined the genetic footprint that drug resistance causes in HIV and found compensatory polymorphisms that help the resistant virus to survive.

Currently the strategy used to treat HIV-1 infection is to prevent viral replication, measured by the number of viral particles in the blood, and to repair the immune system, assessed using CD4 count. Over the past 20 years treatment and life expectancy have vastly improved. However, due to drug resistance, complete viral suppression requires an array of drugs.

For the virus drug resistance comes at a cost. In the absence of the drug the virus carrying drug resistance mutations is less 'fit' than the wild-type virus and so should not be able to replicate as efficiently. During interruptions to treatment wild-type viruses quickly predominate. However newly infected people can be drug resistant even before they have received any treatment.

Researchers from the SPREAD project have been monitoring HIV infections across Europe. This multinational team has looked at 1600 people, newly infected with HIV-1 subtype B. Almost 10% of these patients had HIV-1 harbouring transmitted drug resistance (TDR) and worryingly, when they measured virus production and CD4 count, there was no indication that these strains of HIV-1 were weaker.

In recent years there has been much talk about polymorphisms, naturally occurring differences in the genes that are responsible for the differences between animals of the same species, for example blood groups or the ability to digest lactose in milk. They may also increase propensity for certain diseases including cancer and type 2 diabetes. But animals are not the only organisms that harbour polymorphisms – they are present in viruses as well.

By examining polymorphisms in these strains of HIV-1 the researchers discovered that certain polymorphisms in the gene coding for protease (essential for viral replication) known to act as compensatory mechanisms, improve the 'fitness' of resistant strains, even in the absence of the drug. Kristof Theys, one of the researchers involved in the project commented, "Our worry is that over time we will be seeing more people presenting with TDR HIV-1."

Prof Anne-Mieke Vandamme, who led this study, fears "Contrary to what was expected, transmission of TDR virus may also contribute to a 'fitter' and more virulent HIV, which has important clinical implications in how we best treat these people."

More information: Treatment-associated polymorphisms in protease are significantly associated with higher viral load and lower CD4 count in newly diagnosed drug-naive HIV-1 infected patients, Kristof Theys, et al. *Retrovirology*, (in press)

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