Scientists investigate genetics of HIV-1 resistance

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Credit: AI-generated image (disclaimer)

Investigating the genetic footprint that drug resistance causes in HIV, researchers in Europe have discovered that compensatory polymorphisms enable resistant viruses to survive. Presented in the journal *Retrovirology*, the study was supported in part by three EU-funded projects: VIROLAB, EURESIST and CHAIN.

Both the VIROLAB ('A virtual laboratory for decision support in viral diseases treatment') and EURESIST ('Integration of viral genomics with clinical data to predict response to anti-HIV treatment') projects were funded under the 'Information society technologies' (IST) Thematic area of the EU's Sixth Framework Programme (FP6) to the tune of EUR 3.3 million and EUR 2.1 million, respectively. CHAIN ('Collaborative HIV and anti-HIV drug resistance network') has received almost EUR 10 million under the Health Theme of the EU's Seventh Framework Programme (FP7).

Preventing viral replication is the current mode of HIV-1 infection treatment. Researchers measure the number of viral particles in the blood and analyse the cluster of differentiation 4 (CD4) count to repair the immune system. Since the early 1990s, the research world has seen a marked improvement in the treatment and life expectancy of HIV patients. But drug resistance has forced researchers and physicians to come up with an array of drugs to obtain complete viral suppression.

According to the researchers, virus drug resistance comes at a cost. The virus carrying drug resistance mutations is less 'fit' than the wild-type virus when the drug is not present. Because of this, replication should be no simple task. During interruptions to treatment, wild-type viruses quickly predominate. But newly infected people can be drug resistant even before treatment begins for them.

The SPREAD project researchers monitored HIV infections across Europe, assessing 1 600 individuals who were newly infected with HIV-1 subtype B. They found that HIV-1 harboured transmitted drug resistance (TDR) in 10 % of the subjects. The team measured virus production and CD4 count, observing there was no indication that these strains of HIV-1 were weaker.

Recent studies have put the spotlight on polymorphisms, naturally

occurring differences in the genes that lead to differences between animals of the same species, including blood groups. They may also increase propensity for certain diseases like cancer and type 2 diabetes. However, viruses also harbour polymorphisms.

In this study, the team discovered that polymorphisms in these strains of HIV-1, specific polymorphisms in the gene coding for protease, which is needed for viral replication, and known to act as compensatory mechanisms, make resistant strains 'fitter', even in the absence of the drug. 'Our worry is that over time we will be seeing more people presenting with TDR HIV-1,' said lead author Kristof Theys of the University of Leuven in Belgium.

Senior author Professor Anne-Mieke Vandamme, also from the University of Leuven, said: '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.'

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