

Geneticists map human resistance to HIV

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The key to future HIV treatment could be hidden right in our own genes. Everyone who becomes infected deploys defense strategies, and some even manage to hold the virus at bay without any therapy at all. This immune system struggle leaves its mark within the pathogen itself – genetic mutations that indicate how the virus reacted to its host's attacks. Scientists from EPFL and the Vaud university hospital center (UNIL-CHUV) retraced the entire chain of events in these battles, from the genome of the virus to the genome of the victim. They have created the first map of human HIV resistance. The goal of their research, which has been published in the journal *eLife* on the 29th of October, is to find new therapeutic targets and to enable individualized treatment strategies.

The human [immune system](#) is constantly developing strategies to fight HIV. Unfortunately, "the [genome](#) of the virus also changes rapidly, at a rate of millions of mutations a day," explains Jacques Fellay, co-author and EPFL researcher. In the majority of cases, the pathogen finds an effective strategy via this natural selection.

Sometimes the virus is faced with a tougher opponent. It resists, but its ability to replicate is compromised. "The virus survives but replicates more slowly, and thus its capacity for destruction is in some sense neutralized," says the scientist.

By studying strains of HIV that have been living in human hosts, the researchers can identify specific [genetic mutations](#). These are like scars that each bear witness to a very specific attack launched by the immune system. What are the human genes involved in these defense strategies?

And which, among all our genetic variations, predispose us to increased HIV resistance or, on the contrary, increased vulnerability? The scientists developed a method that allowed them to find answers to these questions.

A supercomputer, 1,071 patients and millions of combinations

To draw up the first map of human HIV resistance, the researchers had to analyze an enormous amount of data. They studied various strains of HIV from 1,071 seropositive individuals. They crossed more than 3,000 potential mutations in the viral genome with more than 6 million variations in the patients' genomes. Using supercomputers, they studied all these possible combinations and identified correspondence between patients.

"We had to study the virus before the patient had undergone treatment, which is far from easy," says Fellay. This meant they had to search in data banks established in the 1980s, before effective therapies were made available.

This novel, indirect method made it possible to obtain the most complete global overview to date of [human genes](#) and their implications in terms of HIV resistance. It allows us to not only better understand how we defend ourselves from attack but also how the virus adapts itself to our defense mechanisms. "We now have a true database that tells us which [human genetic variation](#) will induce which kind of mutation in the virus", explains Amalio Telenti, co-author and UNIL-CHUV researcher.

Therapies inspired by our own natural defense

This research has two major implications. New therapies could be

developed based on studying humans' natural defenses, particularly those that result in a reduced replication of the [virus](#). In addition, the scientists hope that by profiling the genome of HIV-infected individuals, it will be possible to develop individually targeted treatments that take into account the patients' genetic strengths and weaknesses.

Provided by Ecole Polytechnique Federale de Lausanne

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