

# How 'hidden mutations' contribute to HIV drug resistance

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One of the major reasons that treatment for HIV/AIDS often doesn't work as well as it should is resistance to the drugs involved. Now, scientists at McGill University have revealed how mutations hidden in previously ignored parts of the HIV genome play an important role in the development of drug resistance in AIDS patients. Their study will be published Aug. 8 in the *Journal of Biological Chemistry*.

"HIV develops resistance very rapidly, and once that happens, drugs don't work as well as they theoretically should, or they stop working altogether," explained Dr. Matthias Götte, an associate professor in McGill's Department of Microbiology and Immunology. "Physicians routinely have the patient's virus tested for resistance in advance of treatment to help make the appropriate clinical decisions."

The study was conducted by a team of researchers led by Dr. Götte at McGill's Faculty of Medicine, with assistance from the B.C. Centre for Excellence in HIV/AIDS at the University of British Columbia (UBC). It was funded by the Canadian Institutes for Health Research (CIHR).

HIV genotype testing is now widely established in HIV drug resistance screening. However, for technical and economic reasons, the entire HIV genome is usually not sequenced.

"The focus has been on specific areas of the HIV genome where we expect these resistance-conferring mutations to occur," Dr. Götte said. "We focus on a particular sequence on an important gene from amino

acid 1 to 300, and as such, we miss roughly a third of this gene. Until recently, most researchers believed that this hidden area was of little clinical significance."

Within the last few years, however, studies started to suggest that the first 300 amino acids alone may not completely describe the drug resistance landscape. Dr. Götte and his colleagues selected a few of these previously uncharacterized mutations and subjected them to a battery of highly sensitive biochemical tests.

"People were skeptical," Dr. Götte said. "The mechanism about how these mutations could be involved in resistance was not clear. However, in our paper, we present data that explains in considerable detail how these mutations work."

Nevertheless, he cautioned, the debate about whether to routinely screen these areas of the HIV genome will still likely continue for some time.

"It's extremely time-consuming and expensive to validate genotype testing," he said. "However, we probably will be testing these areas in a couple of years."

Source: McGill University

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