Gene Mutation Might Affect HIV Drug Levels in Body

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Researchers at Ohio State University announced that they have discovered a gene mutation that can significantly increase blood levels of roughly half of all drugs on the market—including many HIV drugs. This finding could ultimately lead to individualized dosing of medications and potentially reduce the risk of side effects, depending on whether a person has the mutation.

Many medications are broken down by enzymes in the gut and liver. One enzyme in particular, CYP3A4, is responsible for metabolizing between 45 and 60 percent of all drugs on the market today. A number of HIV treatments, including most protease inhibitors (PIs), rely on CYP3A4.

Researchers have long known that some people metabolize drugs affected by CYP3A4 more slowly than others—leading to higher toxicity in some people—but scientists hadn't yet found a genetic mutation, called a single nucleotide polymorphism (SNP), that could explain this difference.

Two Ohio State researchers, Danxin Wang, PhD, and Wolfgang Sadee, identified an SNP on the Intron 6 gene that affects CYP3A4 blood levels. They tested the SNP's influence on a group of 273 HIV-negative Caucasian patients taking statin drugs to lower cholesterol. Wang and Sadee found that roughly 10 percent of the participants carried the SNP they'd discovered and that the SNP's presence was strongly linked to blood levels of the statins.

"Right now, because there are no biomarkers available to predict CYP3A4 activity, trial and error determines whether cholesterol goes down with the prescribed dose," Wang said. "You never know who has what enzyme level, so you never really know what dose to give an individual if you don't have a biomarker."

Though the researchers have not studied the SNP's influence on HIV drugs, it is possible that the gene mutation will one day guide dosing studies of HIV drugs and, eventually, be incorporated into the clinical care of people living with HIV.

A commercial test for the SNP isn't yet available, but Wang hopes technological advances will help make the test available for research studies, and ultimately patients, in the future.

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