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New study raises the possibility that some antiviral drugs could make diseases worse

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As the flu season continues in full-swing, most people can appreciate the need for drugs that stop viruses after they take hold in the body. Despite this serious need for new drugs, a team of researchers from the University of Texas at Austin raise serious concerns about an emerging strategy for stopping viral infections.

According to their research report appearing in the January 2010 issue of the journal *Genetics,* medications that cause viruses to die off by forcing their nucleic acid to mutate rapidly might actually, in some instances, cause them to emerge from the process stronger, perhaps even more virulent than before drug treatment.

"This work questions whether the practice of 'lethal mutagenesis' of viruses works as predicted," said Jim Bull, Ph.D., a researcher involved in the study from the Institute for Cellular and Molecular Biology at the University of Texas at Austin. "It remains to be seen whether an elevated mutation rate that does not cause rapid viral extinction enhances treatment or may instead thwart treatment by enhancing viral evolution." Bull's research collaborators included Rachael Springman, Thomas Keller, and Ian Molineux from the same institution.

Scientists tested the model of viral evolution at high mutation rates by growing a DNA virus in the presence of a mutagenic agent. The current accepted model predicted that the virus would not be able to handle the high mutation rates and would eventually die off. However, this study proved the model false, as the virus actually increased its fitness at

elevated mutation rates. During this study, scientists found molecular evidence that rapid mutations had two effects. The first effect of most mutations, which was expected, was that they killed or weakened the virus. The second effect of some mutations, however, was that they actually helped the virus adapt and thrive. Although the researchers did not question that extremely high mutation will lead to viral extinction on the whole, this discovery raises the specter that forcing viruses to undergo rapid mutations could, if the mutation rate is not high enough, accidentally lead to well-adapted "super viruses."

"This study should raise more than a few eyebrows over this approach to stopping viruses," said Mark Johnston, Editor-in-Chief of the journal *GENETICS,* "because the last thing anyone wants to do is make a bad situation worse. More work must be done to determine the actual likelihood of this approach yielding a super virus, knowing that it is possible is a big help in preventing what could be a very big problem."

More information: R. Springman, T. Keller, I. J. Molineux, and J. J. Bull, Evolution at a High Imposed Mutation Rate: Adaptation Obscures the Load in Phage T7, *Genetics*, Jan 2010; 184: 221 - 232.

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