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# Researchers discover target for treating dengue fever

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Two recent papers by a University of Colorado School of Medicine researcher and colleagues may help scientists develop treatments or vaccines for Dengue fever, West Nile virus, Yellow fever, Japanese encephalitis and other disease-causing flaviviruses.

Jeffrey S. Kieft, PhD, associate professor of biochemistry and molecular genetics at the School of Medicine and an early career scientist with the Howard Hughes Medical Institute, and colleagues recently published articles in the scholarly journals *eLife* and *Science* that explain how flaviviruses produce a unique RNA molecule that leads to disease.

More than 40 percent of people around the world are at risk of being bitten by mosquitoes infected with the virus that causes Dengue fever and more than 100 million people are infected, according to *eLife*. Many develop headaches, pain and fever, but some develop a life-threatening condition where tiny blood vessels in the body begin to leak. Other flaviviruses, such as West Nile virus, are rapidly spreading around the globe. Flaviviruses are considered dangerous emerging pathogens.

The *eLife* paper shows that the virus causing Dengue fever and other closely related viruses like West Nile and Japanese encephalitis use instructions encoded on a single strand of RNA to take over an infected cell and reproduce. The viruses also exploit an enzyme that cells use to destroy RNA to instead produce short stretches of RNA that, among other things, may help the virus avoid the immune system of its host. Ironically, these viruses use a structured RNA molecule to resist an

enzyme that normally "chews up" RNA.

The *Science* paper reveals the discovery that the resistant RNA folds up into an unprecedented "knot-like" structure. The enzyme, normally adept at breaking up RNA structure, encounters this particular structured RNA and cannot "untangle" it; thus the enzyme is thwarted. This is the first time this sort of RNA structure has been observed and it has characteristics that may be amenable to targeting by new drugs. To discover this structure, the researchers used a technique called x-ray crystallography, which allowed them to determine the structures of individual molecules.

This understanding of how an RNA found in many different flaviviruses thwarts a powerful enzyme may help scientists develop treatments or vaccines.

**More information:** "The Structural Basis of Pathogenic Subgenomic Flavivirus RNA (sfRNA) Production," by E.G. Chapman et al. *Science*, 2014.

Provided by University of Colorado Denver