IIT Roorkee develops a potent molecule to treat chikungunya

Pointed: “These two molecules are very specific to chikungunya virus,” says Shailly Tomar.

A team of researchers at the Indian Institute of Technology (IIT) Roorkee has achieved a measure of success by finding a small molecule that has good antiviral activity against chikungunya virus. The antiviral activity was so high that the small molecule was able to achieve almost 99% reduction in the virus when 5 microMolar was used.

Currently, there are no drugs to treat chikungunya or any vaccine to prevent it.

Virus structure

Using structure-based studies of chikungunya virus-specific nsP2 protease, the team led by Prof. Shailly Tomar from the Department of Biotechnology had earlier identified two small molecules — Pep-I and Pep-II — for their inhibitory activity. Protease inhibitors have already been used successfully against HIV and hepatitis C virus.

In the latest study, published in the journal *Biochimie,* the researchers report that one of the two molecules — Pep-I — has superior antiviral activity against chikungunya virus. The small molecule was found to effectively bind to the protein of the virus (nsP2 protease) and prevent the virus from replicating. The researchers hypothesised that any molecule that inhibits nsP2 protease should have antiviral activity. To test the hypothesis they carried out antiviral studies using cell lines. “The studies confirmed that both molecules had significant ability to kill the virus. The Pep-I molecule was very efficient in killing the virus — 99% reduction in virus at 5 microMolar,” says Prof. Tomar. The Pep-II molecule showed reduced antiviral activity of only 50% even at a higher concentration of about 200 microMolar.

“When 10 microMolar of Pep-I was used no viable virus could be detected in the culture. The antiviral activity was tested by adding the molecules directly into the virus culture. The two molecules also reduced the viral RNA thus confirming the antiviral activity,” says Rajat Mudgal from the Department of Biotechnology at IIT Roorkee and one of the first authors of the paper.

“We found even when the concentration of the two molecules was less than 50 microMolar, they were able to effectively inhibit the protease. Generally, when less than 50 microMolar concentration produces good enzyme inhibition it is considered good in terms of potency and effectiveness,” says Harvijay Singh who is the other first author of the paper.

Specific action

The team then tested whether the molecules were specifically inhibiting only the chikungunya virus. They used Sindbis virus, the model virus of the genus alphavirus to which chikungunya belongs, to test the specificity. “These two molecules did not show antiviral activity against Sindbis virus indicating that they are very specific to chikungunya virus,” says Prof. Tomar. The specificity of molecules to inhibit only the chikungunya virus is not surprising as these molecules are structure-based.

“We will try and improve the potency of the inhibitors by making derivatives of the molecules through in silico work,” says Prof. Tomar.

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