Cellular calpain proteases can cleave the enteroviral polyprotein

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Enteroviruses are small, non-enveloped RNA viruses, which belong to the family of picornaviruses. Although most of the diseases that enteroviruses cause are symptomless or mild, enteroviruses are the most

common viruses infecting humans. In addition, enteroviruses can cause more severe diseases such as encephalitis or myocarditis.

Despite their prevalence, there are no antivirals on the market against enteroviruses, and vaccines have been developed only against a couple serotypes. The production of vaccines against all enterovirus serotypes is not feasible, and so antiviral drugs may be the solution for most of the enterovirus infections.

"For antiviral development, it is crucial to obtain detailed information about factors that contribute to efficient infection. In the future, these factors could then be the targets of antiviral development," says Mira Laajala.

The information related to Mira Laajala's research can potentially be used in antiviral development against enterovirus infections. The research showed that in addition to viral proteases, cellular calpain proteases can cleave the enteroviral polyprotein.

"This was shown in an *in vitro* study, but it gives a good starting point to study the phenomenon also in the cells during infection. In addition, a synthetic inhibitor against calpains was shown to prevent enterovirus infection in cells, which highlights the potential of calpain inhibitors as an antiviral against enteroviruses," says Laajala.

New infectious intermediate particle was found in the research

Laajala also found another cellular factor that contributed to enterovirus infection. The study showed that cellular vimentin protein formed a cage-like structure around the replicating viral RNA and viral non-structural proteins during infection. In addition, it was revealed that the formation

of a vimentin cage was needed for efficient production of these viral non-structural proteins.

"This is an interesting finding since the non-structural proteins are the ones that are contributing to the pathogenesis of the virus," says Laajala.

In addition to the cellular factors, Laajala also studied the uncoating of the virus—the step where viral RNA is released from the capsid. The study revealed a new, more open, but still infectious, particle form. "Uncoating intermediate particles has been described for enteroviruses before, but our new particle differed from those particles as it still contained all the capsid proteins and was able to bind on the receptor protein on the cell surface and cause infection," says Laajala.

More information: Mira Laajala. JYU DISSERTATIONS 146, Cellular and Viral Factors Promoting Efficient Enterovirus Uncoating and Replication: jyx.jyu.fi/bitstream/handle/12 … quence=1&isAllowed=y

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