Viral infections decrease muscle health, cause other collateral damage

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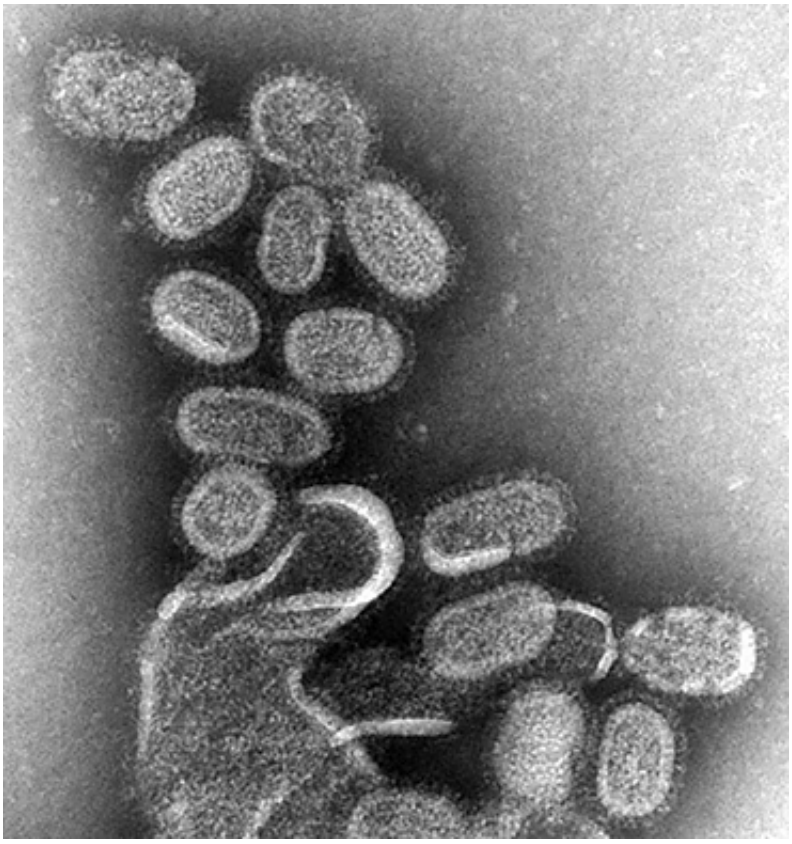

Electron microscopy of influenza virus. Credit: CDC

Researchers at UC Berkeley have found unexpected effects of viral infections, a discovery that may explain why viruses can make people feel so lousy.

The UC Berkeley bioengineers found that viral infections turn down the intensity of a key cell-signaling pathway linked to healing and health of skeletal muscle and bone, mental well-being and prevention of obesity. The signaling pathway, called oxytocin receptor MAPK, or OXTR, has been well studied for its role in trust and bonding and more recently was found to be needed for muscle maintenance and regeneration, which declines with age.

"Our results suggest that viral infections in general may play a role in decreasing muscle health and regeneration, a decline in metabolic health and a lower sense of well-being, as these rely on effective OXTR signaling," said Irina Conboy, an associate professor in the Department of Bioengineering, whose lab performed the study.

The research was recently published online in the journal *Skeletal Muscle*. The study was funded by the National Institutes of Health, Packer Endowment and SENS Foundation.

The research team discovered these not-so-obvious effects of viral infection by studying a standard method for inserting genes inside cells and organisms, one that deploys viruses as tools of molecular biology.

Viral vectors are tools regularly used by researchers to insert pieces of genetic material into cells or animals for further testing. To ensure that any observed effects from this delivery are caused by the genetic material of interest, and not by the viral vector, a key experimental step is to test the effects of the viral vectors alone. This is called an experimental control, and the vectors tested are called control viral vectors, as they are not supposed to change anything in a cell or organism. Yet the study's results show that cells and animals exposed to control viral vectors differ from unexposed organisms in a number of ways.

The Berkeley researchers discovered that control viral vectors actually changed the intensity of OXTR signaling, which diminished the regenerative ability of any direct descendants of these cells or tissues, thus aging them rapidly.

In one experiment, OXTR declined by 70 percent in mouse and human muscle cells that were given the control viral vectors. The researchers saw a similar effect in live mice.

The researchers then tested how a downregulated OXTR pathway affected muscle cells, and found that control viral vectors decreased mouse muscle cell proliferation from 85 to 20 percent; and cells also lose a key marker of muscle stem cell proliferation.

"Our study further implies that viral infections may play a role in decreasing OXTR and thus broadly interfering with regeneration and maintenance of multiple tissues," Conboy said.

The researchers also examined a database of human studies and found that OXTR becomes severely diminished in humans after viral infections compared to healthy individuals.

The study's data suggest that in addition to known pathological manifestations, viral infection may play a less direct role in decreasing the health and regeneration of skeletal muscle, bone, brain-psychological well-being and inducing obesity by skewing key cell-signaling networks that regulate homeostatic tissue maintenance.

"We are now working on a therapeutic mix that should alleviate this collateral damage of viral infections and this work in progress is promising," Conboy said.