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Genetic breakthrough supercharges immunity to flu and other viruses

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Researchers at McGill University have discovered a way to boost an organism's natural anti-virus defences, effectively making its cells immune to influenza and other viruses.

The research was conducted by post-doctoral fellows Dr. Rodney Colina and Dr. Mauro Costa-Mattioli, working in collaboration with Dr. Nahum Sonenberg, a Howard Hughes Medical Institute International Scholar at McGill. They worked with colleagues at l'Institut de Recherches Cliniques de Montréal (IRCM) and the Ottawa Health Research Institute (OHRI). Their results are to be published February 13 in the journal *Nature*.

Their process – which could lead to the development of new anti-viral therapies in humans – involved knocking out two genes in mice that repress production of the protein interferon, the cell's first line of defence against viruses. Without these repressor genes, the mouse cells produced much higher levels of interferon, which effectively blocked viruses from reproducing. The researchers tested the process on influenza virus, encephalomyocarditis virus, vesicular stomatitis virus and Sindbis virus.

"People have been worried for years about potential new viral pandemics, such as avian influenzas," Dr. Sonenberg said. "If we might now have the means to develop a new therapy to fight flu, the potential is huge."

Viruses are sub-microscopic infectious agents which can reproduce only by hijacking a cell's reproductive machinery, a process that usually leads to disease and even the death of the host organism. Interferon, in particular the type 1 interferons (IFN-α and IFN-β) suppress virus propagation. Production of type 1 interferon is controlled by the interferon regulatory protein 7 (Irf7), which researchers believe to be the "master-regulator" of interferon production in the body. The McGill researchers found that protein synthesis of Irf7 is controlled by the repressor genes called 4E-BP1 and 4E-BP2.

"In a sense, it's quite a simple story," Dr. Costa-Mattioli explained. "When you get rid of the repressors, you have more of the key protein Irf7 present, which induces an anti-viral state in the cell. You're basically removing the brakes."

The researchers detected no abnormalities or negative side-effects resulting from enhanced interferon production in the mice, Dr. Costa-Mattioli said. Dr. Sonenberg explained that the process of knocking out genes is not possible in humans, but the researchers are optimistic new pharmaceutical therapies will evolve from their research.

"If we are able to target 4E-BP1 and 4E-BP2 with drugs, we will have a molecule that can protect you from viral infection. That's a very exciting idea." Dr. Costa-Mattiolo said. "We don't have that yet, but it's the obvious next step."

Source: McGill University