Study could help improve gene therapy for heart disease, cancer

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A Loyola University Chicago Stritch School of Medicine study could lead to improved gene therapies for conditions such as heart disease and cancer as well as more effective vaccines for tuberculosis, malaria and other diseases.

Senior author Christopher Wiethoff, PhD, and colleagues report their findings in the October issue of the Journal of Virology. Editors spotlighted the report as one of the "articles of significant interest."

The study involved a virus that causes the common cold, called adenovirus. Scientists have been trying to use a version of this virus as a delivery vehicle for gene therapies and vaccines. (The virus is not able to reproduce and cause disease.) Administering this virus to patients causes an inflammatory reaction, which can be a double-edged sword: The reaction aids in the use of the virus in vaccines but limits its use for gene therapies.

In gene therapy, one or more desired genes are introduced into the adenovirus, which is then administered to the patient. Once in the body, the virus enters targeted cells and delivers the desired genes. In heart disease patients, for example, the virus delivers genes that trigger the growth of new blood vessels in damaged heart muscle. However, when the adenovirus enters a cell to deliver a desired gene, it causes an inflammatory immune response. In extreme cases, this can endanger the patient. In one highly publicized case, a University of Pennsylvania gene therapy patient named Jesse Gelsinger died from a massive immune

response triggered by the use of the adenovirus.

In vaccines, the adenovirus delivers one or more genes. These genes instruct cells to produce a specific protein, which is normally part of the targeted pathogen. This protein, in turn, jump-starts the patient's immune system to attack a specific pathogen, such as the bacterium that causes tuberculosis or the parasite that causes malaria. Here, the inflammatory immune response has the beneficial effect of revving up the immune system to attack germs.

The Loyola study provides new insights into how the adenovirus triggers an immune response. The study involved immune cells from humans and mice. Researchers discovered how cells sense the adenovirus as it enters a cell. This recognition, in turn, triggers the immune response. The finding could help researchers tailor the adenovirus so that it causes less of an immune response in gene therapy applications and an enhanced immune response in vaccines.

"These results will help with future studies of innate immune responses to adenovirus," Wiethoff and colleagues wrote. "Additionally, our understanding of this process could allow us to either enhance or attenuate [weaken] the innate immune response to adenovirus to generate novel vectors for gene therapy and vaccination."

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