Promising Antimicrobial Attacks Virus, Stimulates Immune System

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DENVER — A promising antimicrobial agent already known to kill bacteria can also kill viruses *and* stimulate the innate immune system, according to researchers at National Jewish Health. In a paper appearing online June 4 in the *Journal of Investigative Dermatology*, Michael Howell, PhD, Assistant Professor of Pediatrics, and his colleagues demonstrated that the synthetic compound CSA-13 can kill vaccinia virus in cell cultures and in mice. Additionally, they showed that CSA-13 stimulates cells to produce their own antimicrobial proteins.

"This compound is demonstrating broad effectiveness," said Dr. Howell. "While our experiments were designed to test its ability to attack the vaccinia virus, its immune-stimulating ability was a surprising observation."

CSA-13 is one of a class of compounds known as ceragenins, which were developed by Brigham Young University Professor Paul Savage to mimic antimicrobial proteins that occur naturally in the body. The ceragenins are smaller than antimicrobial proteins, and are not as vulnerable to degradation in the body. They have previously been shown to be effective against a variety of bacterial species.

Dr. Howell and his colleagues wanted to learn if CSA-13 could fight vaccinia virus infections. Vaccinia virus is closely related to the organism that causes smallpox and is used in smallpox vaccines. However, millions of people in the United States who have had eczema are susceptible to a serious and potentially fatal complication of the vaccination, known as eczema vaccinatum, which occurs when the vaccinia virus infects the skin. Dr. Howell is part of a team, led by Professor of Allergy and Clinical Immunology Donald Leung, MD, PhD, that is seeking protection against this complication so that eczema patients could receive the vaccination in case of a bioterrorist attack with smallpox.

CSA-13 demonstrated effectiveness against vaccinia in three different tests. When CSA-13 and vaccinia virus were directly incubated together, the CSA-13 killed more than 96% of the virus at a 25 micromolar concentration. When CSA -13 was added to cells infected with vaccinia, it both reduced vaccinia virus gene expression and allowed more of the infected cells to survive. Finally, the researchers infected immune-compromised mice with vaccinia virus, then applied CSA-13 onto their skin. The CSA-13 reduced the number of skin lesions caused by vaccinia virus.

"These experiments definitively showed for the first time CSA-13 can effectively fight vaccinia virus infections," said senior author Dr. Leung.

Within their experiments, the researchers found that, in addition to directly killing the virus, CSA-13 also stimulated cells to produce their own antimicrobial proteins, LL-37 and HBD-3. Dr. Howell and colleagues have previously shown that these antimicrobial proteins also exhibit antiviral activity against vaccinia virus.

"We knew from our plaque assays, that CSA-13 was directly killing the virus," said Dr. Howell. "But these experiments show that it also stimulates cells to produce their own antimicrobial proteins, which contribute to its disease-fighting capabilities. Our next step is to learn how CSA-13 stimulates cells' own innate immune defenses."

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Our team is available to arrange interviews, discuss events and story ideas.

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