

Making viruses pass for 'safe'

March 8 2011

Viruses can penetrate every part of the body, making them potentially good tools for gene therapy or drug delivery. But with our immune system primed to seek and destroy these foreign invaders, delivering therapies with viruses is currently inefficient and can pose a significant danger to patients.

Now scientists at the University of Pennsylvania have engineered a virus with potential to solve this problem. They describe the new virus today at the 55th Annual Biophysical Society Meeting in Baltimore, MD.

"We would like to find a way to avoid the immune system and maximize the dose delivered to a tumor or diseased tissue," explains professor Dennis Discher of the University of Pennsylvania. He and his colleagues have created a lentiviral vector that expresses CD47, the "marker of self" protein, on its surface. The protein gives cells a free license from macrophages, the immune system's policemen.

"This marker of self protein is found on all of our cells and tames our immune system," says Discher, senior study author. Discher explains that every cell is like a driver. A macrophage 'policeman' pulls each cell over at a traffic stop and checks its drivers license -- the marker protein. "The policeman says go on if it's valid. If not, then the macrophage eats you," he says.

By tagging CD47 with green fluorescent protein, the team confirmed that the engineered virus, which is hundreds of times smaller than human cells, was carrying the marker of self. "Assessing the expression of the



protein on the surface of an individual virus has been a real biophysical challenge, addressed with a combination of single molecule fluorescence methods and atomic force microscopy," says lead author Nisha Sosale, a graduate student at the University of Pennsylvania.

In cell culture experiments in the laboratory, the engineered virus passed inspection and was eaten less frequently by <u>macrophages</u>. "It looks like, by engineering the viral surface, we have made the viruses look like self," says Discher.

More information: The presentation, "Reducing Immune Response Against Lentiviral Vectors: Lentiviral Vector Presentation of CD47, the 'Marker of Self'" by Nisha Sosale, Richard K. Tsai, Irena Ivanovska, and Dennis E. Discher is at 1:45 p.m. on Tuesday, March 8, 2011 in the Baltimore Convention Center, Hall C. ABSTRACT: tinyurl.com/4wc4o2q

Provided by American Institute of Physics

Citation: Making viruses pass for 'safe' (2011, March 8) retrieved 3 May 2024 from https://medicalxpress.com/news/2011-03-viruses-safe.html

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