Microfibers help virus fool the body's immune system

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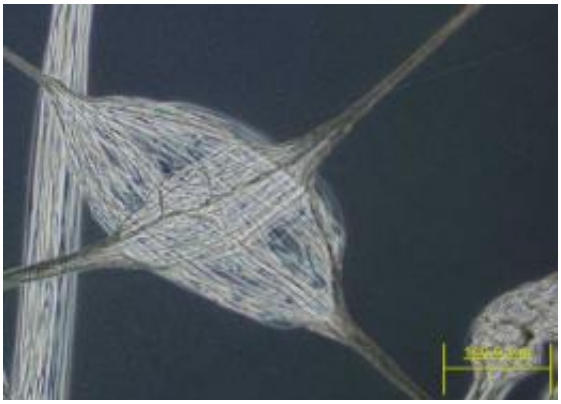

Bio-macromolecule fibers formed by the electrostatic interaction between plasmid DNA and positively charged peptides.

A key challenge in virus-based gene therapy is avoiding detection by the human immune system so that the virus would not be deactivated before it reaches its intended target. Now, researchers at the Institute of Bioengineering and Nanotechnology (IBN) have succeeded in circumventing the body's own defense mechanism by combining two IBN innovations.

In a recent study published in *Advanced Materials*, IBN researchers demonstrated that cancer cells could be more effectively eliminated when therapeutic viruses were encased in microfibers or synthetic tissue fibers.

Using a novel method developed at IBN, the researchers were able to encapsulate an insect virus with fibers produced from peptides and DNA for gene delivery. As the structure of the microfibers closely resembles human tissue fibers, they were able to 'disguise' the virus by reducing the body's ability to recognize the virus and prevent its premature deactivation. Tests conducted on mice with brain tumor show that the microfiber-coated viruses could significantly slow down tumor growth and prolong survival, in comparison to treatment with uncoated viruses.

Gene therapy is a technique for correcting defective genes responsible for disease development. It involves using DNA encoded with a functional gene to replace a mutated gene, and viruses that are stripped of its disease-causing ability are used as a tool to deliver the therapeutic gene into the target cells.

IBN has been investigating the use of engineered insect virus to treat cancer and neurological disorders since 2003, and the first successful gene delivery to human embryonic stem cells using a baculoviral vector was achieved at IBN in 2006. That same year, IBN researchers published a paper in *Cancer Research* demonstrating the delivery of therapeutic genes by baculoviral vectors for cancer treatment in an animal tumor model.

In trying to prevent the body from disabling the virus before it reaches the diseased cells, the research team led by IBN Group Leader Dr. Shu Wang turned to a unique microfiber fabrication technique developed by Dr. Andrew C. A. Wan at IBN. In the human body, tissue fibers are naturally formed by the assembly of two different types of macromolecules, such as proteins and DNA. Currently, synthetic tissue fibers are fabricated with only one type of biomolecular material because fibers composed of more than one type of biomolecule are difficult to produce.

Using a water-based chemical process, IBN scientists were able to construct tissue fibers from two biomolecular materials – peptides and DNA. The researchers flanked two droplets of the oppositely charged peptide and DNA molecules after it has been dissolved in water. Upon contact, the droplets zipped together to form a two-component fiber. Fiber formation presumably occurs from the electrostatic interaction between the positively charged peptide molecule and the negatively charged DNA molecule. Through the same procedure, baculoviral vectors were added to the DNA solution to coat the virus with the fibers.

Dr. Shu Wang shared, "For the very first time, we have shown that two biomolecules, namely peptides and DNA, can interact with each other to form structured fibers in a test tube. Since these biomolecules are readily metabolized in the human body to naturally occurring molecules and have no adverse toxicity, they hold strong biomedical potential for the delivery of therapeutic drugs, genes, proteins and viruses to combat cancer."

"This innovative application of microfibers with viral vectors is an exciting development for gene therapy that was made possible through multidisciplinary collaboration between biologists, chemists and materials scientists at IBN. Our fibrous materials are also of great interest as biocompatible tissue engineering scaffolds for applications in regenerative medicine," said Professor Jackie Y. Ying, IBN Executive Director.

More information: 1. J. Yang, et al. "Microfibers Fabricated by Non-Covalent Assembly of Peptide and DNA for Viral Vector Encapsulation and Cancer Therapy," *Advanced Materials*, (2012) DOI: 10.1002/adma.201201145.

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