Nanotubes transport gene therapy drug into T-cells known to block HIV from entering cells in vitro

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A promising approach to gene therapy involves short DNA fragments (interfering RNA) that bind to specific genes and block their "translation" into the corresponding, disease-related protein. A stumbling block has been the efficient and targeted delivery of RNA into the cells. Researchers led by Hongjie Dai at Stanford University have chosen to use carbon nanotubes as their "means of transport".

This has allowed them to successfully introduce RNA fragments that "switch off" the genes for special HIV-specific receptors and co-receptors on the cells' surface into human T-cells and primary blood cells. This leaves few "entry hatches" for the HIV viruses. The researchers report in the journal Angewandte Chemie that this allows for much better silencing effect to the cells than current transport systems based on liposomes.

T-cells are one of the types of white blood cells important for a good immune defense; they detect and destroy virus-affected cells. However, they themselves are among the targets attacked by HIV. In order to enter into a T-cell, the virus must first dock to a receptor known as CD4. Also involved is the co-receptor CXCR4. The use of short interfering RNA strands allows the CD4 and CXCR4 genes of the T-cell to be shut off. The T-cell then strops producing these receptors and the virus cannot find any points of attack on the surface of the cell. This could significantly slow down an HIV infection, as previous work have shown.

But how to get the RNA fragments into the T-cells? The shells of nonpathogenic viruses can be used to smuggle genetic material into cells, but this is dangerous in therapeutic applications because they can trigger allergies. Liposomes, tiny bubbles of fat, are safe but have proven to be ineffective for use in T-cells. Dai and his co-workers have tested a new transport system: carbon nanotubes are known for their abilities to be absorbed by cells and to smuggle other molecules in at the same time. The researchers attached phospholipids—molecules from which cell membranes are also made—to chains of polyethylene glycol. The phospholipids nestle securely onto the outer wall of the carbon nanotubes while the polyethylene glycol chains protrude into the surrounding solution. The required RNA molecules were fastened to the ends of these chains. Once inside the cell, the RNA could easily be split off by means of a sulfur–sulfur bridge.

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