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TECHNOLOGY UPDATE

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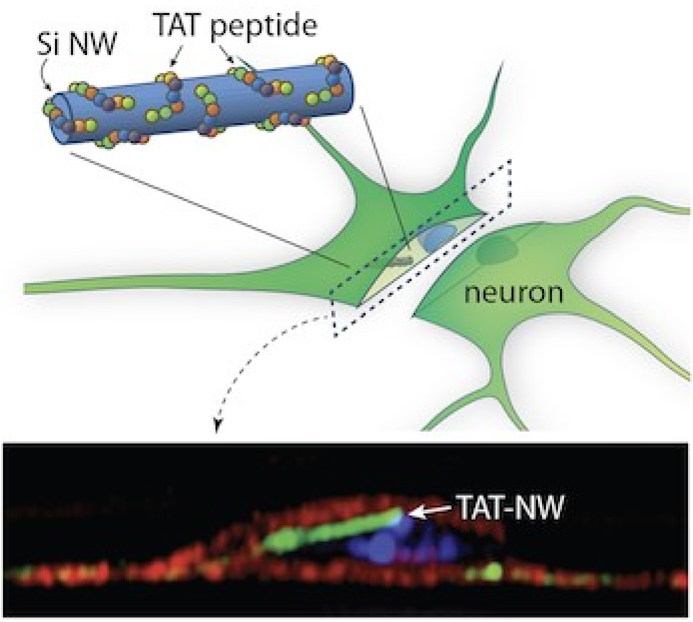
Making nanowires enter neurons more easily

By linking the cell penetrating peptide "TAT" onto the surface of nanowires (NWs), researchers at Harvard University in the US say they can now make these nanostructures penetrate the neuronal membrane more easily. The new technique could allow for high-resolution electrophysiological studies of neuronal cells for a better understanding of how the brain works.

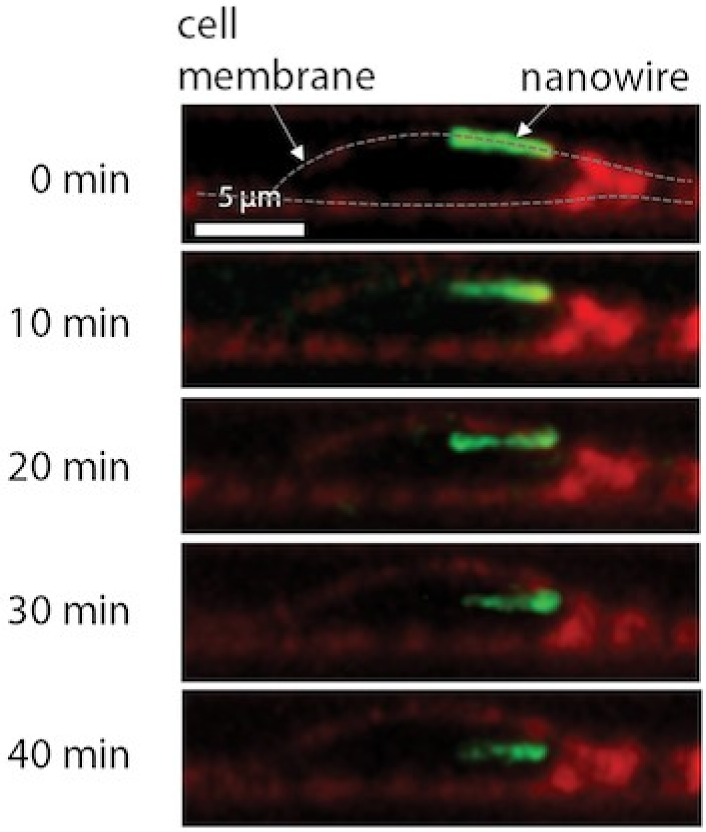


(http://images.iop.org/objects/ntw/news/15/1/16/pic1.jpg)

A TAT-modified Si NW entering a neuron (http://images.iop.org/objects/ntw/news/15/1/16/pic1.jpg)

"NW devices can be used to study the electrical activity of neurons, but until now it has been difficult to place these nanostructures into these cells," explains team leader Charles Lieber (http://cml.harvard.edu/). "And in cases where this was possible, the cell membrane could be damaged, which meant that intracellular recording was highly invasive and only transient. Our new approach overcomes these problems and allows us to internalize nanowires into neurons in a minimally invasive way and allow the nanowires to directly target subcellular structures."

Using confocal microscopy imaging, Lieber and colleagues showed that TAT-conjugated nanowires (TAT-NWs) completely enter mouse hippocampal neurons. TAT is the so-called trans-activating transcriptional activator from the human immunodeficiency virus 1 (HIV-1), which can penetrate cell membranes and even deliver materials of various sizes into cells. What is more, live cell imaging revealed that the TAT-NWs start entering the cells just 10-20 minutes after binding to the cell membrane, and find themselves completely inside the cell within 30-40 minutes. The nanostructures are also able to make their way into other types of neuronal cells, such as primary dorsal root ganglion ones.



(http://images.iop.org/objects/ntw/news/15/1/16/pic2.jpg)

Confocal images of TAT-NWs entering a neuron (http://images.iop.org/objects/ntw/news/15/1/16/pic2.jpg)

Previous methods to penetrate the neuron membrane with nanoscale devices required physical methods, such as mechanical force or electrical pulses that rupture the cell membrane. “Our internalizing process is non-invasive, spontaneous and does not damage cells,” says Lieber. “It does not require any mechanical or electrical assistance and is in fact similar to how viruses transfect cells. It will allow us to monitor intracellular neuronal electrical activity over the long term.”

The researchers, reporting their results in *Nano Letters* DOI: 10.1021/acs.nanolett.6b00020 (http://pubs.acs.org/doi/10.1021/acs.nanolett.6b00020), say that their work has “addressed the most critical step in the development of intracellular recording of primary neurons using nano-bioelectronic devices,” and has “opened up many important and exciting new directions,” that they will now pursue. “For example, we plan to internalize silicon NW devices into cultured neurons to measure their electrical activity,” Lieber tells *nanotechweb.org*. “Our first step is to use TAT to modify the tip of a free-standing kinked-NW probe that we will then be able to insert into neurons for measuring intracellular signals.”

And that is not all. Multiplexed measurements on cell networks may also be possible, he adds. “TAT-NW devices can be scaled up to target wired multiple neurons in culture and be used to investigate neuronal connectivity and signal propagation,” he adds.

About the author

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Further reading

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