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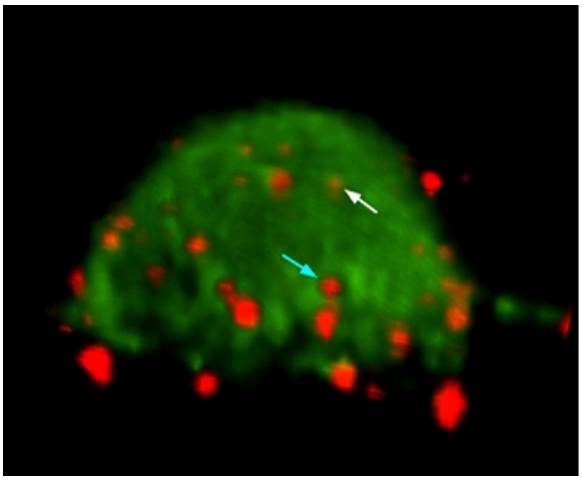
Nanotechnology May Hold the Answer to Treating Depression

Barb Ruppert | TATRC

July 12, 2010

Alleviating the immeasurable impact of depression may come down to a single molecule measured in nanometers, or billionths of a meter. That is what Dr. Tania Vu of Oregon Health and Science University believes.

She and her team, with collaborators Drs. Paul Greengard and Marc Flajolet at the Rockefeller University, are the first to develop a way to "tag" single molecules in live cells to track their movement. They have successfully tracked serotonin receptor molecules through a cell and back to the surface.



Serotonin is a neurotransmitter that regulates mood. A clearer understanding of its mechanisms of action may lead to more effective treatments for clinical depression and PTSD.

The team's work is supported by the U.S. Army Medical Research and Materiel Command's Telemedicine and Advanced Technology Research Center. Vu's project is managed by Dr. Sylvain Cardin.

TATRC chief scientist Dr. Charles Peterson says, "The science here is very exciting, and TATRC is pleased to be supporting what could lead to significant breakthroughs in treating a range of neurochemical disorders."

According to Vu, current drugs to treat major depression and PTSD target serotonin receptors, yet they may take weeks to be effective, have often debilitating side effects, and their mechanisms of action are often unclear. To identify more effective drug targets, her team began work in 2006 to develop technologies to understand neural signaling mechanisms involved in depression, particularly the role of serotonin and BDNF-TrkB pathways.

Vu's team will be applying their technology to help evaluate a new potential target for antidepressants called p11. Greengard's laboratory at Rockefeller University found that p11 causes elevated levels of serotonin receptors on the cell membrane surface. Vu hopes that within a year her team may be able to elucidate the exact mechanism by which p11 regulates serotonin expression at the cell surface—does it attach the receptors to something that slows their movement into the cell, or does it increase the recycling of the receptors back to the surface?

Says Vu, "There is a lot of excitement about its potential, but no one is yet sure of the mechanism. Understanding this would help better assess strategies for developing p11 as well as serotonin receptor targeted antidepressants."

Vu has developed nanotechnology that can tag an individual protein receptor on the surface of a neuron with a quantum dot, which is a nanocrystal semiconductor that glows brightly for a long period of time. The quantum dot is attached to an antibody to create a probe that binds chemically to a specific receptor molecule. Quantum dots fluoresce in blue light, enabling researchers to count individual probes. The team has proven that the QD probes can tag serotonin receptors with high accuracy and that one can watch and count serotonin receptors as they move from the cell's surface through the cell and back again.

Says Vu, "We can identify the pathways that these receptors take in the cells and give a detailed description of the kinetics that has never before been available to researchers. This will help us test the effectiveness of various drugs and see what is going on when signaling is defective."

The team has published their results in several recent journals and textbooks. They have begun similar studies to characterize the pathways of TrkB receptors, which are also implicated in depression.

TATRC Psychological Health Portfolio Manager Dr. Jay Shore notes, “Dr. Vu is bringing membrane transport technology into the clinical world. Her novel approach holds great promise.”

Says Vu, “The technologies we have developed can readily be transferred to any disease involving cell surface receptor dysfunctions, such as Parkinson’s disease, schizophrenia, anxiety, migraines and stress-related disorders.”

TATRC seeks to harness advanced technologies and new knowledge to address the evolving health and medical needs of today’s service members, veterans and their families. It is supporting approximately 800 ongoing research projects.