A nanoelectronics-blood-based diagnostic biomarker for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) PNAS – April 29, 2019

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Dr. Ron Davis introduces the nanoneedle publication in PNAS.

Hello I'm Ron Davis.

I'd like to tell you a little bit of a story about a recent publication involving a new diagnostic device we call the **nanoneedle.** The history of this is that we wanted to develop a very small device for making measurements of either the proteins that were available or nucleic acids. This fabrication was done at Stanford nanofabrication facility. It's a very small device, has a nano-channel and nano-electrodes that can measure electrical properties of molecules that are bound, or in this case of cells that are attached, to the electrodes.

We first thought that maybe we could get a measurement of ME/CFS white blood cells if we stressed them—that they might not be able to handle stress, and the stress we chose was just adding sodium chloride. The very first experiment worked, and then we began to pursue it.

The problem with trying to develop a diagnostic test is that all of the patients you're sampling have to have the disease, and if you don't have a good diagnostic, you have a problem that maybe some of the patients actually don't have the disease. So it's hard to develop a new diagnostic test, because of the inability to maybe diagnose the patients.

So we chose to in fact make sure that the patients met all the criteria for all the different diagnostic tests for ME/CFS, and we also required them to be seen by a specialist in ME/CFS and then to validate that they were convinced that this person did have the disease. That would help us a great deal in actually performing these tests.

It's a very simple procedure: we simply take a blood sample, [we] remove the red cells, and then put a drop of blood on the detector. What was really surprising to us was that every patient shows this signal—which is a change in impedance—but none of the healthy controls showed the same signal.

And so that's what you really like to have in a diagnostic test. It's not uncommon to have a medical approved diagnostic test, to have as much as a 10% false positive and a 10% false negative. In our case we found no false positives and no false negatives.

We will continue this work. What we were trying to do at the very beginning was to distinguish ME/CFS patients from healthy controls. And the reason for that really is to say that if you get a signal, you're not healthy. And we thought that was probably the most important thing we could do first.

Second phase is to try to figure out how to diagnose that it is ME/CFS and not some other related disease. That's gonna take some time because we have to look through a lot of, large number of other diseases, but that is proceeding at the moment.

In the future we will use this device for a number of things. We are already using it for doing other types of diagnostics that don't involve cells, but in fact involve molecules. The other thing we can use this device for is to see if we can block the effects that we see in the nanoneedle assay with a drug. This then is a drug that might have some benefit to the patients. We'd also like to explore, 'Why are we seeing the signal?' We have a lot of ideas, but we haven't really validated any of them to be the real cause of this signal.

In the future, we would like to set up this assay to be much higher throughput. The device you see here behind me can do two samples at the same time. We really need to increase that throughput. That means redesigning it. We possibly can use the same chip, or we'll do a new design of the chip. We manufacture the chips here at Stanford. Rahim (Esfandyarpour, PhD), who is the first author on this publication, has recently moved to the University of California at Irvine where he is now an assistant professor. We will continue to work together on this development.

Thank you to our OMF volunteer for transcribing this video.