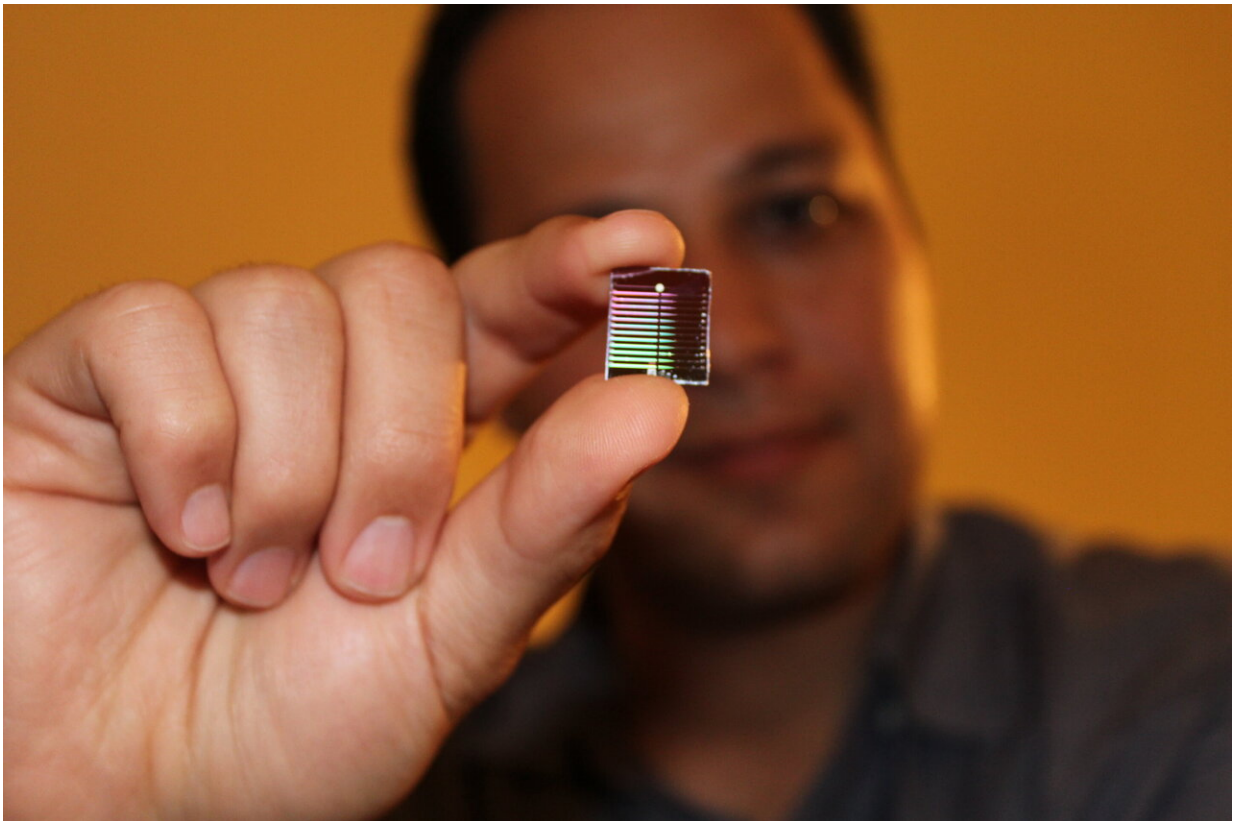


Researchers identify biomarker for chronic fatigue syndrome

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A diagnostic device for ME/CFS. Credit: R. Esfandyarpour

People suffering from a debilitating and often discounted disease known as chronic fatigue syndrome may soon have something they've been seeking for decades: scientific proof of their ailment.

Researchers at the Stanford University School of Medicine have created a [blood test](#) that can flag the disease, which currently lacks a standard, reliable diagnostic test.

"Too often, this disease is categorized as imaginary," said Ron Davis, Ph.D., professor of biochemistry and of genetics. When individuals with chronic [fatigue](#) syndrome seek help from a doctor, they may undergo a series of tests that check liver, kidney and heart function, as well as blood and immune cell counts, Davis said. "All these different tests would normally guide the doctor toward one illness or another, but for chronic fatigue syndrome patients, the results all come back normal," he said.

The problem, he said, is that they're not looking deep enough. Now, Davis; Rahim Esfandypour, Ph.D., a former Stanford research associate; and their colleagues have devised a blood-based test that successfully identified participants in a study with chronic fatigue syndrome. The test, which is still in a pilot phase, is based on how a person's immune cells respond to stress. With blood samples from 40 people—20 with chronic fatigue syndrome and 20 without—the test yielded precise results, accurately flagging all chronic fatigue syndrome patients and none of the healthy individuals.

The diagnostic platform could even help identify possible drugs to treat chronic fatigue syndrome. By exposing the participants' blood samples to drug candidates and rerunning the diagnostic test, the scientists could potentially see whether the drug improved the immune cells' response. Already, the team is using the platform to screen for potential drugs they hope can help people with chronic fatigue syndrome down the line.

A paper describing the research findings will be published online April 29 in the *Proceedings of the National Academy of Sciences*. Davis is the senior author. Esfandypour, who is now on the faculty of the

University of California-Irvine, is the lead author.

Providing the proof

The diagnosis of chronic fatigue syndrome, when it actually is diagnosed, is based on symptoms—exhaustion, sensitivity to light and unexplained pain, among other things—and it comes only after other disease possibilities have been eliminated. It's estimated that 2 million people in the United States have chronic fatigue syndrome, but that's a rough guess, Davis said, and it's likely much higher.

For Davis, the quest to find scientific evidence of the malady is personal. It comes from a desire to help his son, who has suffered from chronic fatigue syndrome for about a decade. In fact, it was a biological clue that Davis first spotted in his son that led him and Esfandypour to develop the new diagnostic tool.

The approach, of which Esfandypour led the development, employs a "nanoelectronic assay," which is a test that measures changes in miniscule amounts of energy as a proxy for the health of immune cells and [blood plasma](#). The diagnostic technology contains thousands of electrodes that create an [electrical current](#), as well as chambers to hold simplified blood samples composed of immune cells and plasma. Inside the chambers, the immune cells and plasma interfere with the current, changing its flow from one end to another. The change in electrical activity is directly correlated with the health of the sample.

The idea is to stress the samples from both healthy and ill patients using salt, and then compare how each sample affects the flow of the electrical current. Changes in the current indicate changes in the cell: the bigger the change in current, the bigger the change on a cellular level. A big change is not a good thing; it's a sign that the cells and plasma are flailing under stress and incapable of processing it properly. All of the blood

samples from chronic fatigue syndrome patients created a clear spike in the test, whereas those from healthy controls returned data that was on a relatively even keel.

"We don't know exactly why the cells and plasma are acting this way, or even what they're doing," Davis said. "But there is scientific evidence that this disease is not a fabrication of a patient's mind. We clearly see a difference in the way healthy and chronic fatigue syndrome immune cells process stress." Now, Esfandyarpour and Davis are expanding their work to confirm the findings in a larger cohort of participants.

Doubling up

In addition to diagnosing chronic fatigue syndrome, the researchers are also harnessing the platform to screen for drug-based treatments, since currently the options are slim. "Using the nanoelectronics assay, we can add controlled doses of many different potentially therapeutic drugs to the patient's [blood](#) samples and run the diagnostic test again," Esfandyarpour said.

If the [blood samples](#) taken from those with chronic fatigue [syndrome](#) still respond poorly to stress and generate a spike in electrical current, then the drug likely didn't work. If, however, a drug seems to mitigate the jump in electrical activity, that could mean it is helping the immune [cells](#) and plasma better process stress. So far, the team has already found a candidate drug that seems to restore healthy function to [immune cells](#) and plasma when tested in the assay. The [drug](#), while successful in the assay, is not currently being used in people with [chronic fatigue syndrome](#), but Davis and Esfandyarpour are hopeful that they can [test](#) their finding in a clinical trial in the future.

All of the drugs being tested are either already approved by the Food and Drug Administration or will soon be broadly accessible to the public,

which is key to fast access and dissemination should any of these compounds pan out.

More information: R. Esfandyarpour et al., "A nanoelectronics-blood-based diagnostic biomarker for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)," *PNAS* (2019).

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Provided by Stanford University Medical Center

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