

BIOMARKERS AND PD

Dave Iverson of KQED spoke to Ken Marek, MD, of the Institute for Neurodegenerative Disorders and Katie Hood, CEO of The Michael J. Fox Foundation on the critical importance of Parkinson's disease biomarkers and the Foundation's new clinical study to speed biomarker development.

A transcript of the interview follows. To listen to a podcast version, visit www.michaeljfox.org/PPMI.

Opening Narration: I'm Dave Iverson with a report on new developments in Parkinson's research. As anyone who has Parkinson's can tell you diagnosing and evaluating the disease is an inexact science. You walk into your doctor's office, you are asked to stretch out your hands or tap your toes, and the neurologist jots down a number. There's no blood test, no precise measurements. In fact tracking the progression of Parkinson's is a bit like keeping track of a football game without either yard makers or a scoreboard — you're never exactly sure what's going on or what's going to happen next.

Neurologist: "Put your hands close to your chest but don't touch your fingers. Look here ...and look here."

Dave Iverson: That's the sound of a neurologist conducting a Parkinson's evaluation. The patient is then given a rating on something called the Unified Parkinson's Disease Rating Scale or UPDRS. But as the Institute for Neurodegenerative Disorders Dr. Ken Marek observes, it's hardly a precise test.

Ken Marek: As most people with Parkinson's disease or family members of (people with) Parkinson's disease know there is a lot of variability in how individuals feel that day. And so if it's a good day their score may be better than if it's a bad day. If they've just taken their medicine, it's going to be better than if they haven't just taken their medicine. And, of course, not only is there variability from the patient's perspective but from the examiners perspective. So while this is objective, it's kind of quasi objective.

Dave Iverson: And that means we can't really measure what's going on with the disease starting right at the beginning, which matters because by the time someone shows up at the neurologist's office the disease is already a ways down the field. It's a problem that sets Parkinson's and other neurological conditions apart from many other diseases.

Ken Marek: We are all familiar, for example, with the use of blood pressure as a tool to help us to know who might be at risk to develop a stroke, or the use of cholesterol as a tool to help to know who might be at risk to have a heart attack and potentially to reduce that risk. In neurology we have not had those types of tools.

Dave Iverson: And beyond the problem of early diagnosis there's the fact that the disease and its progression varies wildly from individual to individual.

Ken Marek: All Parkinson's disease isn't the same, so individuals may have more trouble with tremor or more trouble with walking or more trouble with their memory. And having a kind of a global score has some value but we'd like to be able to hone down on what type of problem people have.

Dave Iverson: So remember that football game analogy? With Parkinson's it's not only like you're playing the game without yard markers and a scoreboard, you also don't know what play to call next. And that's why scientists really want to find what they call a biomarker — a better way to both understand the game and figure out the best play to call next.

Ken Marek: If we could pair the evaluations methods with the therapeutic goals that would be a lot more desirable.

Dave Iverson: In fact, having a better measuring stick would also speed the development of new treatments. Here's why. Because the disease has so many variations it may well be that a new drug might work for some and not others. But in a drug trial, all Parkinson's patients are lumped together, potentially scrambling the results.

Dave Iverson: If there are three people who are participating in a clinical trial and they each have different manifestations of the disease, it is entirely possible that one might do well with whatever the prescribed agent is in this trial, another not improve, another be kind of ambiguous so you would wind up with results that don't tell you much. But in fact that agent might be really useful for person A, it's just not useful for person C, is that right?

Ken Marek: That's exactly right and I think that has been a major problem in how we measure the effect of medications so that if we had in the case you mentioned one person who is doing well while another who may be doing not so well or had no effect, it is easy to wash out that effect of the well person and come up with a general answer that is equivocal or negative.

Dave Iverson: The need to find a better measuring stick is clear but finding that biomarker is no simple task.

Katie Hood: When we first started investing in biomarkers in 2002, I remember being told by some of our advisors, this is a moon shot, a shot in the dark that we are going to be able to develop some of these markers.

Dave Iverson: Katie Hood is the CEO of the Michael J. Fox Foundation which is now launching a major effort to identify a better way to diagnose and measure the disease.

Katie Hood: The exciting news is that we've actually developed some really compelling leads. And so now we're at the stage where we want to keep proving those leads and showing that they may have merit.

Ken Marek: While I think there are a number of exciting tools that are being developed. And I think these include blood tests or tests that come out of the spinal fluid.

Dave Iverson: Dr. Marek is directing the Fox Foundation effort. He thinks that spinal fluid may hold the key because in Parkinson's, there's an abnormal build up of certain proteins in the brain, proteins that can also be found in spinal fluid.

Ken Marek: Spinal fluid is the fluid which bathes the brain, so it surrounds the brain, and therefore is the fluid in the body which is most indicative of what is happening in the brain.

Dave Iverson: And Marek thinks the new research effort might yield results very soon.

Ken Marek: The goal of that project is to identify these biomarkers within the next three to five years. I would be fairly confident that we will have markers within that time frame that will truly change how we monitor and diagnose Parkinson's disease and can assist as we develop these new therapies.

Dave Iverson: New therapies that will make a big difference in making the right call for Parkinson's patients in the years ahead. To learn more about the biomarkers research project, visit michaeljfox.org. I'm Dave Iverson.