Michael J. Fox: This is Michael J. Fox. Thanks for listening to this podcast. Learn more about the Michael J. Fox Foundation's work and how you can help speed a cure at michaeljfox.org.

Dave Iverson: This is Dave Iverson. We've all heard that developing new drugs to treat disease is a long and expensive proposition. In fact, on average, it takes 13 years and
[00:00:30] nearly 2 billion dollars to develop a new drug for neurodegenerative diseases like Parkinson's. That's one of the reasons why so-called drug repurposing, or drug repositioning, is so attractive. You take a drug that's already been approved for one disease and see if it might work in another. Fox Foundation CEO, Dr. Todd Sherer.

Dr. Todd Sherer: The goal of repurposing is to try to take a drug that has one use and see if we can
[00:01:00] find additional uses for that drug. Specifically, in a lot of examples, we're looking at drugs that are already available, already on the market for people to treat one disease, and based on an understanding of the way that drug works, we're now looking to see whether we can apply that drug to treat other diseases or symptoms.

Dave Iverson: It may sound odd that a drug for one disease might be effective in treating a very different condition, but Sherer says the key question is not so much disease similarity but how the drug in question affects the body.

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Dr. Todd Sherer: The most important thing about searching for drugs that you can repurpose into Parkinson's disease treatments is related to the underlying biology and scientific mechanisms through which that drug is affecting the body. It's less important, in a lot of ways, to understand what the current disease is being treated by that drug. It's much more important to really look at what the drug's doing to the body.

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Dave Iverson: Take the example of two very different diseases: hypertension and Parkinson's. It turns out that a blood pressure drug called Isradipine could prove to be useful in preserving the dopamine neurons that are lost in Parkinson's.

Dr. Todd Sherer: So in the case of Isradipine and its role in as a high blood pressure medicine, Isradipine's function is to block the activity of certain channels, certain receptors in the body that have to do with getting calcium in and out of the cells. And that's how the muscle of the heart sorta controls its activity, is by regulating the
[00:02:30] flow of calcium in and out of those cells.

What's important for Parkinson's is that we also know that the survival of brain cells is also dependent on the regulation of the flow of calcium in and out of those cells. So by using a drug like Isradipine that impacts the same mechanism, we have the potential to really examine whether Isradipine can have an impact in Parkinson's disease.

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Dave Iverson: The idea of using an already approved blood pressure drug to treat Parkinson's came about by way of both basic science and epidemiological study. A Northwestern University researcher named Jim Surmeier discovered the role calcium channels play in the survival of dopamine cells, which in turn suggested that a calcium channel blocker like Isradipine might be useful in treating Parkinson's disease. That fundamental research insight was strengthened by epidemiological studies, which showed that people who took Isradipine were less likely to get Parkinson's. Put those findings together and you have a candidate for drug repurposing.

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Dr. Todd Sherer: So you can get data from the laboratory but also data on the potential of some drugs to be repurposed from human studies, observational studies as well. So in the case of Isradipine, it's sort of hitting both of those levels of evidence.

Dave Iverson: Another drug repurposing candidate for Parkinson's comes from drugs currently used to treat diabetes. Again, the diseases would seem to have little in common, yet they share an underlying common denominator that could mean a drug used to treat one might be effective in treating the other.

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Dr. Todd Sherer: I do think this area around repositioning of diabetes drugs for Parkinson's is very interesting and it's getting pretty exciting. And a lot of that has to do with the commonalities of some of the underlying biology. It just seems ... Some of the proteins that are being targeted by the diabetes drugs, and to improve the symptoms and treatment of that disease, those same proteins are also involved in the survival of brain cells. And the same way that you'd want to impact that protein in the diabetes context is the same way that you'd want to impact that protein to promote the survival of those brain cells. So there's a commonality of the underlying science.

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Dave Iverson: But identifying good drug repurposing candidates is only half the battle. For starters, there's the question of safety. Just because a drug has been found safe to treat one disease doesn't mean it will necessarily be safe to use in another.

Dr. Todd Sherer: To give some extreme examples: There could be a drug that is approved for a treatment of a disease that is seen in children. While the drugs on the market, it has really only been given to people who are children. To now reposition that drug to give to a disease that's impacting adults or elderly individuals, there may not actually be a lot of experience with that drug in that new population. So you still need to go and do the thorough safety testing.

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Dave Iverson: That testing process includes examining basic questions like drug dosage. Something that could vary greatly between the disease the drug was initially designed to treat and the disease for which the drug is hopefully being repurposed. And there can be other safety hurdles to clear as well.

[00:06:00] The blood pressure drug Isradipine, for example, is designed to lower blood pressure. But since many people with Parkinson's already have low blood pressure, researchers had to determine whether taking Isradipine would lower blood pressure in Parkinson's too far. So far, Isradipine has passed all the safety tests. Still to be determined is the key question of whether that drug would actually modify dopamine loss. Those results should come in the next two years. Safety in preliminary efficacy results for the diabetes drug, Exenatide, will be known later this year.

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Dr. Todd Sherer: So while there are a lot of shortcuts with repositioning, there's still a lot of work to do to make sure that the benefits would outweigh any risks of these medications.

Dave Iverson: Yet another challenge to bringing a repurposed drug to market is the marketplace itself.

Dr. Todd Sherer: As everyone knows, when a new drug is made, there is a time limit through which there's an exclusivity around the manufacturing and selling of that drug
[00:07:00] based on the patent life of that drug. And the advantage of that exclusivity is what motivates pharmaceutical companies to put significant money into the research, so that they could get the drug on market and then have their period of time where they're selling that drug.

Dave Iverson: But as the patent runs out, drug companies have less motivation to invest in further research. So the cost of researching and testing a drug's repurposing potential has fallen to foundations and the federal government. That's what
[00:07:30] happened in the case of Isradipine, where research costs have been shouldered by the Michael J. Fox Foundation and the National Institutes of Health.

Dr. Todd Sherer: What's exciting is that if we can get enough data around this, these drugs are available, so people could then get access to them relatively quickly.

Dave Iverson: In the end, Sherer says the key to finding a successful drug repurposing candidate comes back to basic science.

Dr. Todd Sherer: The hypothesis and rationale for selecting a particular medication to test in
[00:08:00] Parkinson's has to be grounded in solid scientific understanding of the disease. You really can't just do a scattered shot, like "Let's go to the pharmacy shelves and we'll just go through every one of these drugs." So you still have to have a very good rationale and rigorous process through which this is tested, because the whole goal is to then provide actionable information to both the patient and physician community from these trials.

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Dave Iverson: That's Todd Sherer, CEO of the Michael J. Fox Foundation. He'll join us as part of our next third Thursday webinar on July 20, when we explore the topic of drug

repurposing in Parkinson's disease. To register, visit michaeljfox.org. I'm Dave Iverson.

Michael J. Fox: This is Michael J. Fox. Thanks for listening to this podcast. Learn more about the Michael J. Fox Foundation's work and how you can help speed a cure at michaeljfox.org.