

Seizing Life, episode 117
Epilepsy Researcher Compounds Lab Work with Fundraising
Guest: Dr. Patrice Jackson-Ayotunde
(Transcript)

Kelly Cervantes: Hi, I'm Kelly Cervantes and this is Seizing Life, a biweekly podcast produced by CURE Epilepsy.

Today I'm happy to welcome Dr. Patrice Jackson-Ayotunde to the podcast. Dr. Jackson-Ayotunde is an associate professor of pharmaceutical sciences at the University of Maryland Eastern Shore. She also runs a research lab there, which focuses on early drug discovery and design of potential compounds to treat epilepsy. She has been working in epilepsy research for more than 20 years and is a longtime fundraiser through her involvement with the UMES Strides for Epilepsy 5K. She is here to explain the process of finding and creating new epilepsy drugs in the academic space as well as to discuss her fundraising efforts. Dr. Jackson-Ayotunde, thank you so much for joining us today. It is a pleasure to have you. To start off, I want to get a little bit of your background. Can you tell us how long you have been doing epilepsy research and what drew you to the field?

Dr. Jackson-Ayotunde: Let me first say thank you for having me, inviting me to do this podcast. I have been in the field of drug discovery for potential anti-seizure agents for about 23 years, which tells a little bit how maybe old I am, but I started work doing my master's at Tennessee State University. My master's in organic chemistry, so I was in the lab of Dr. Cosma Socorro, who is still there, and his focus at the time was drug design and discovery of novel potential anti epilepsy agents. That's where we were first introduced to the neurological disorder, and I became very passionate about the field. From Tennessee State University, I then moved on to Howard University in DC, worked under Dr. Kenneth Scott, who had a library of over 200 compounds, all with the focus of finding, discovering a treatment for epilepsy. My passion for the epilepsy field grew and grew from there until joining UMES in 2010 as assistant professor on the tenure year track, having my own laboratory, designing, discovering, developing potential antiepileptic drugs.

Kelly Cervantes: Well, we are incredibly grateful for your years of dedication in epilepsy research, but specifically to this particular focus, I want to dive a little deeper into what it is that you do specifically in your lab because you are not studying epilepsy or the brain or seizures, as we've had lots of other researchers on the podcast talking about. You are specifically studying and researching compounds that hopefully could then go on to become treatments. Is that correct?

Dr. Jackson-Ayotunde: That's correct, Kelly. My laboratory engages in what's considered to be early drug discovery and development of small molecules or small compounds that could be used for treatment. My focus is generalized epilepsy and drug resistant epilepsy.

Kelly Cervantes: All right. I'm going to hit pause on what you do in your lab for a minute so that we can get some definitions of some words so that moving forward, all of our lay listeners who do not have PhDs will be able to follow along with our

conversation. You talked about a molecule and a compound. What is the difference between those two and what is a ... I think generally we understand what a molecule is, but what is a compound?

Dr. Jackson-Ayotunde: Everything starts with chemistry. Chemistry is in everything, especially organic chemistry. That's your molecule or your compound. So in a drug regiment, even if you go to look at the back of your bottle of aspirin or your Tylenol, you would see a term or a acronym for active pharmaceutical ingredient. The active pharmaceutical ingredient is that compound, that molecule, that chemical compound, that chemical molecule that's in the drug with different other, what we call excipients, but other ingredients to make that tablet. But the important active pharmaceutical ingredient is that chemical compound that reduces the fever, reduces the headache. That's what my lab focus on, is to design, develop that active pharmaceutical ingredient. It's a art. We do art of ... I call it art of drug design.

A lot of times in my lab we might start from a blank canvass or we may start from something that's known. Then as a artist, you start to develop and create a new compound in hopes that it will be effective in preclinical studies.

Kelly Cervantes: Okay, thank you for that. That was so super helpful. I also would love to get an understanding, you sort of talk about efficacy and toxicology also I think are two words that are going to come up for us here. Can you define those for us?

Dr. Jackson-Ayotunde: Yes. Because I do early drug discovery, preclinical studies is what my compounds are involved in. So in vitro studies, which are studies in the cell or in a Petri dish or what have you, using a microscope, and with that, how we define or determine that our compounds are efficacious, are effective at stopping or reducing seizures in the animal. I do have a partnership with NIH, the National Institute for Neurological Disorders and Stroke. They have a program called the Epilepsy Screening Therapy Program and in that program they do in vivo in the animal type of studies. In those preclinical studies are compounds are tested for efficacy if they are effective at stopping the seizure.

Toxicology, that is related to side effects, adverse reactions, and so we know that the anti-seizure drugs or anti-epileptic drugs that are currently on the market, one of the issues is the side effect profile. In researching potential therapies is not only for them to be effective or efficacious, but also for the drugs to be safe and have limited side effects. That's the difference between the term efficacious and toxicology.

Kelly Cervantes: That's amazing. Thank you so much for that. I also think it's incredible the partnership with the NINDS through the NIH, that you don't have to have the animal models in your lab, that you can just work on the compounds because I know that sometimes getting the specific animal models that you need, that that can be incredibly difficult, maintaining them and all of that. That's incredible to me that those kind of programs exist.

Brandon: Hi, this is Brandon from CURE Epilepsy. Did you know that 30% of those diagnosed with epilepsy do not respond to current medications? That is why for 25 years CURE Epilepsy has been committed to inspiring hope and delivering impact by funding patient-focused research to find a cure for epilepsy. Learn more about our mission and our research by visiting cureepilepsy.org. Now back to Seizing Life.

Kelly Cervantes: Now that we have a better understanding of all the terminology, I want to dig into what that drug discovery process looks like in your lab. What is it that you're doing on a daily basis?

Dr. Jackson-Ayotunde: My training is medicinal chemistry, so that's what we do in my lab, medicinal chemistry. As you said, Kelly, I do not have any animals in my lab, so we only do the chemistry. We only do designing and synthesizing or just making of the compound.

Kelly Cervantes: You're testing these compounds, you're working on them, but where do you get them from? What is their origin story?

Dr. Jackson-Ayotunde: From working in with Dr. Kenneth Scott at Howard University, some assistant professors will have to start really, really from scratch. I didn't have to necessarily do that. I was able to take what I had started working on in my PhD and carry it on to my new lab at UMES and start to develop and design and create compounds that are potentially to be used in the epilepsy models. So where we start from wasn't a blank canvas per se.

Kelly Cervantes: What are the steps that you take from choosing which compound to ideally sending it off to the NIH to have it tested in animals?

Dr. Jackson-Ayotunde: Everything pretty much starts at researching, looking at various articles that are out there, other labs that are doing similar work, and then looking within our compounds, looking at what has been done, what has been tested. We look within and out to come up with our new chemical compounds in terms of what we design. Everything is done really, first of all, on a computer system. Then once through that computer system, the compound has been designed, we feed it through a software that can basically determine if the compound is druggable in the sense that it should be able to get to the brain.

Kelly Cervantes: That was going to be my next question. I was like, "Okay, druggable", does that mean that it can be distributed in a pill form or a capsule form or that you're actually talking about it making its way through the blood brain barrier?

Dr. Jackson-Ayotunde: Yes, correct, that it has a high affinity probability to get across into the brain. That's very important for us to know because epilepsy is a brain disorder, so we want the drug to get to the brain. That's very significant. If other parameters are checked, if there's any red flags, the software that we use can even tell us if the compound has the potential of being toxic and what those toxicities could look

like. Once we have determined that our compound is druggable through this particular software, then the next step is actually to make it, is actually to come up with a recipe, a recipe to actually make the compound. Once we have made the compound, the next step is to purify the compound. I ask my students, "Do you want to take a drug that that's crude or not purified?" Of course not, so we have to purify our compounds.

We use a lot of technology, a lot of instruments to determine that we have the chemical structure, that the compound is pure. Once we have that data that we have determined that yes, we have made the desired chemical compound, yes, the chemical compound is a purified compound, the next step is to send it off to the NIH, the epilepsy therapy screening program. They ask for a certain amount. We are able to give them that certain amount to test in their battery of mice and wrecked models for seizures.

Kelly Cervantes: Now, I want to take that sort of timeline a step further. Let's say the NIH determines that it is effective and the toxicity is acceptable. What happens to the drug then? Or to the compound, excuse me.

Dr. Jackson-Ayotunde: Once they have determined that it is effective and the side effect profile is looking pretty good, then the request is for more compound for them to do more advanced studies, detailed toxicity studies. For an example, there's studies to say, okay, what is the distribution? Okay, the animal is taking this medicine either orally or through injection. How is it distributed in the body? How much of that compound is actually getting to the brain? There's more advanced studies that will need to be done. If that drug continues to check through and pass through those advanced studies, then the next step would be for things to be produced on a much larger scale, very similar to how it is in the pharmaceutical industry, and to go through those check marks before going first in man.

Kelly Cervantes: Now, I understand that in 2018 you received a patent for a compound that could potentially lead to a new drug for treatment resistant epilepsy. Can you tell us about that compound and what happened to it since 2018?

Dr. Jackson-Ayotunde: Yes. So in 2018, it was a series of compounds. It was a small library of similar compounds, a similar class of chemical compounds that I had made during my dissertation studies that were effective, very efficacious in the drug resistant animal model that NIH had. On those series of compounds, NIH and I, we have moved forward or from those compounds. My lab has developed a new class of compounds that are more effective, that have a safer profile than the ones with the patent in 2018 and so right now we're more focused on a new chemical class of compounds that my lab is working on.

Kelly Cervantes: That is based on the original compounds from 2018 have now been improved-

Dr. Jackson-Ayotunde: Modified and changed, yes.

Kelly Cervantes: Modified and improved to be better, more effective, less side effects. What are the next steps for that compound? So you go back and you do this testing again at some point. When does it end up with a pharmaceutical company?

Dr. Jackson-Ayotunde: Currently, just maybe like a month ago, we submitted a patent, a new patent, on a new class of compounds that are effective for generalized and drug resistant epilepsy according to the NIH. So more detailed preclinical studies that would need to be done to determine the safety of the compounds as well as the effect of the compounds before going into man. That would be years. But I am fortunate enough that there is a small pharmaceutical company that is interested in working with my lab, working with myself and my team to actually develop drugs to go first in man. I'm really excited about that new collaboration.

Kelly Cervantes: It's quite a process, it sounds like, to get a drug into the hands of a pharmaceutical company that can then be developed and tested in humans and ideally into the market. To toot CURE Epilepsy's horn a little, we are so proud that we personally have our catalyst program, which is sort of ... we learn from talking to scientists like yourself that there is this sort of ... there's a gap where a researcher will develop a compound, you will get it approved, there'll be a patent, but there is this gap, this need, getting it from that animal testing model to a human testing model, getting it into the first in man test because so much additional research needs to be done, which is important. We need to keep people safe. We don't want to be haphazardly throwing drugs on out into the world.

However, there's this gap in funding and so this is something that CURE Epilepsy has taken very seriously and listening to researchers to try and meet this demand, this research gap to help push these potential compounds forward so that we can help get them ideally to market faster. All that said, I also know that we're talking about decades for these compounds to be studied before they ever make it into a pharmacy. I think that there was a bit of misconception when the COVID vaccines made it onto the market as quickly as they did, that this was something that was feasible and could happen with other vaccines or drugs or treatments. I'm wondering, with your experience, do you wish to see that sort of FDA approval timeline sped up? Are there ways that it could be sped up? Should it be sped up?

Dr. Jackson-Ayotunde: That's a really good question. That's actually a hot topic right now to shorten that timeline, because to go from 10,000 potential chemical compounds in the lab that will go through cell studies, go through animal testing to the one drug ... from that group of 10,000 for that one drug to make it to the market in the hands of the pharmacist, that length of time could be anywhere from 15 to 20 years. Billions of dollars, millions of dollars spent on research for that to happen and so that's the drug discovery process.

Kelly Cervantes: It's painful to hear that as a mother, for anyone, there's so many people out there who are desperate for these treatments and to hear 15 to 20 years, it's

like a sucker punch. On the lay side here, we're like, "Oh my gosh, speed it up. What are your feelings on that?"

Dr. Jackson-Ayotunde: Well, I really do think that because safety is first, safety outweighs efficacy a lot of times. A lot of drugs don't make it to the market because of their side effect profile. In terms of the efficacy, that's a check mark. But safety, it's just not good and that therefore it doesn't make it. Would I like to see that timeline shorten for it to be less? That will be great. What happened with COVID is that work was already been done behind the scenes and so when it came to making the vaccines for COVID, it was easy because research was already ongoing in the background. What several labs are doing now is going back to say, "Hey, let's look at what has been made, produced. Can we take that and modify those drugs to either increase the efficacy or decrease the side effects of that drug so it can be more efficacious and safe."

So that's what some researchers are doing. But when you start at a blank canvas, as you will, and you go through that art of drug discovery and you're making new compounds, it's going to be that length of time. I think that to go through the safety channels, the efficacy testing that the compound must do at the preclinical level as well as the clinical level, I think is important.

Kelly Cervantes: I agree with you. I would love for you to share you had mentioned in an earlier conversation with us about the history or the story behind Keppra and how that came to market. I would love for you to share that story because I think it's fascinating.

Dr. Jackson-Ayotunde: I love to talk about how Keppra was discovered. It always gives me hope because I call it the drug that make it to the marketing class. I call it, when I'm teaching, the golden egg, and I as a medicinal chemist, I'm always like, "Well, you never know where the golden egg is." Keppra is that compound that is widely used in the field of epilepsy to treat epileptic patients. Keppra was that chemical compound that was tested in preclinical models and compared to Phenytoin, it did not test well. It was a group of scientists that said, "Well, let's resurrect this other model that is used for drug resistant epilepsy and let's test Keppra in that model." Now, when Phenytoin, which is the godfather of all of the epilepsy drugs, when Phenytoin was actually tested in this resurrected model, it was not effective, but Keppra was.

Just the point that that determination, that persistence I like about what the researchers did because Keppra could have been in the back of a storage space or in a drawer and would've never known about the efficacy and safety of that drug.

Kelly Cervantes: Which sort of goes to show, I suppose, that if you rush science, you could be missing the golden eggs that you speak of.

Dr. Jackson-Ayotunde: Yes.

Kelly Cervantes: Now, you are not just an epilepsy researcher, you are also a fundraiser. You and your students are longtime fundraisers. In fact, one of our longest running Cure Champions events, UMES Strides for Epilepsy 5K, you just completed your 10th year, which is amazing. Tell us about the event and how it got started.

Dr. Jackson-Ayotunde: Yeah, really excited about it. When I got the email from CURE Epilepsy letting me know that our race or our event was one of the longest running events. I mean, my smile was so huge and I couldn't wait to tell the students. We just celebrated our 10th annual 5K Strides for Epilepsy at the University of Maryland Eastern Shore School of Pharmacy. I am the faculty advisor of the Pharmacy Student Government Association, PSGA for short. Back in ... I want to say it was around 2011, 2012, where the president and the executive board of PSGA, they were interested in doing something really big to involve the community and to bring awareness to a particular disorder, bring awareness to the School of Pharmacy, because at that time we were really new and so the students wanted to do something big, and they surprised me by telling me that "We want to do a 5K race for epilepsy and to raise funds for your research."

I was really surprised and I was like, "Wow, that's great. That's a great idea. Because of the university, you cannot do that for my research, but thank you for supporting." But then I told the students, I thought about it and I said, "Well, for the community and on the national front, we can donate the proceeds from the ... proceeds from the race can go to CURE Epilepsy now and a local organization." Now the race, 10 years, student led, they organize the race and promote it and advertise. We get help from CURE, we get swag from CURE and that's 5K Strides for Epilepsy at UMES.

Kelly Cervantes: I love it so much, and we are so incredibly grateful to you and your students for putting that event together, and we're honored to be one of the beneficiaries of that event. It's incredible. You are in such a unique position being a researcher in the epilepsy space, being a fundraiser, and really putting yourself into this community in that way. I wonder where have we made progress during your 20 plus years in the epilepsy field, and conversely, where do we still have a lot of work to do?

Dr. Jackson-Ayotunde: Wow, that's a really good question. I think that we have made some strides, we keep striving forward, but I think we have made some home runs for sure in the field of epilepsy. But we have things that we can continue to do, I think, to bring awareness to epilepsy in the community, to the folks on the hill, legislators and things of that nature that could help bring more money to the research. Epilepsy is one of the fourth leading neurological disorders that we have. As I tell my students, it's not the hottest topic, unfortunately, but it's one that if we could scream it from the rooftops, we need to continue to do that to help the individuals that suffer from this really harsh disorder.

Kelly Cervantes: Research is the key. That is for sure. Dr. Patrice Jackson-Ayotunde we are so grateful for your time, for your efforts, your expertise. It has been an absolute

pleasure to speak with you and to learn from you today. Just know that as a community, we are incredibly grateful for the work that you do.

Dr. Jackson-Ayotunde: Thank you so much, Kelly. I have had a really good time chatting with you, and I thank you guys again for this opportunity.

Kelly Cervantes: Thank you, Dr. Jackson-Ayotunde, for your continued work in epilepsy research, and thank you to both you and your students for 10 years of supporting CURE Epilepsy's research with the 5K Strides for Epilepsy event. We're looking forward to 10 more years. If you would like to support CURE Epilepsy's mission to end epilepsy by becoming a CURE Epilepsy champion like Patrice and her students, please contact events@cureepilepsy.org, CURE Epilepsy, inspiring hope, and delivering impact. Thank you.

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