

Kanchi: Hi everyone. Welcome to Carry the One Radio, the Science Podcast. I'm Kanchi Mehta and I'm here with another episode for our Young Scientist Spotlight series! In this series we interview grad students, post-docs, and other young scientists to learn about their research and their journeys in science. For this episode I had the joy of speaking with Rebekah Rashford a Ph.D candidate at Princeton University. Let's get started!

\*Carry the One Radio Tag\*

Kanchi: Okay, so first, can you introduce yourself to our listeners?

Rebekah Rashford: Yeah, sure. So my name is Rebekah Rashford. I am a third year PhD candidate at the Princeton Neuroscience Institute. I work in the lab of Catherine Peña. And my project is studying the effects that early life stress can have on epigenetic processes in the brain, so not affecting the genetic sequence, but the regulation mechanisms of the genetic sequence in the reward pathway of the brain. So that's me.

Kanchi: That's very cool. And what drew you to this program at Princeton?

Rebekah Rashford: Oh, that's a really good question. The thing that drew me initially when I was on the interview circuit for Princeton is just how much, I guess, the vibe or the environment of the place just valued progressive thinking in science. A lot of the other places I went were focused on finding a specific mechanism for a disease or something. But when I got to Princeton, the drive of the department, in my eyes, was just discovery. People were so excited about just learning the truth about the brain, like how does it work, what is it doing, how can we model these things, and all that stuff. So just being around these people that were so excited just to learn, I think that's what really drew me to this program.

Kanchi: To backtrack a little bit, what drew you to science in general? Like what motivated you to pursue this path?

Rebekah Rashford: Yeah, yeah, totally. So what initially drew me to science is, in undergrad, I started in a program at the University of Maryland, Baltimore County, UMBC, called the Meyerhoff Program. And that program really sparked my interest for science. It's a program that's designed to diversify academia and all these things that you were talking about before, in that training undergrads to be successful graduate students, be successful med school students. And so I joined this program kind of being like, "Okay, I'm interested in bio. I think it's really cool how our bodies are just these amazing machines that can do so many different things."

And so being in that program helped me get into a lab early in my undergrad career, and that was just an amazing experience. I think that I learned that research is just asking questions and then being able to use techniques to answer those questions. And those are questions that no one's asked before and you're figuring things out that no one knows yet. And I think that that's

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just so incredibly exciting. And so in terms of just science in general, it's just, I think the fascination with the unknown and that I'm actually able to figure out things about the unknown, that's really cool.

Kanchi: That's really exciting. Yeah. It's one of those things like no one's ever answered these questions before, it's very cool to be the one answering that. And the fact that you can try... There are techniques that exist to let you answer, it blows my mind.

Rebekah Rashford: Yeah, exactly. And it's like you just put all the different techniques together in a new way. Yeah.

Kanchi: Did you have mentors to help guide you along this journey?

Rebekah Rashford: So in undergrad, I think my main mentor was... Well, I guess I had a couple. So in lab, my advisor, Dr. Lindahl, who is now retired. He just was always so encouraging. And he made sure that we also had a relationship also outside of science so that when it came to talking about the science, he would challenge me to really think critically about the things that I was doing and why it mattered and helping me curate my undergrad experience just to make me a better scientist and prepare me well for graduate school. So just Dr. Lindahl is amazing.

And I think in terms of development as a student, one of the staff members of Meyerhoff and the MARC program, which is Maximizing Access to Research Careers, if I remember that correctly, Dr. Jacqueline King, she was just such a cheerleader. Like, I could go into her office being like, "I don't know what I'm doing. This is super hard." And she'd be like, "Okay, well, you're working hard. You know what to do. Here are things that you can do to do better." And just having her in my corner, I think was amazing, as well as everyone on the staff at Meyerhoff, and my friends too. But yes, I guess if I had to choose two, Dr. Lindahl and Dr. King.

Kanchi: That's awesome. Are you still connected with them?

Rebekah Rashford: Yeah. Every once in a while, I'll email Dr. Lindahl, or he'll email me. And I talked on the phone with Dr. King recently and I got to see a bunch of Meyerhoff people when I went to a conference.

And I was still like... My roommate was in my program and we're still like very strong bonds and everything, so it's great.

Kanchi: Is this program unique to just your undergrad? Or...

Rebekah Rashford: So this program was started at UMBC at my undergrad institution, but they're replicating this program in a similar way at a couple of other schools. So it's definitely something that's gaining traction. So I don't know what it's called at other places, but very similar.

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Kanchi: Oh wow, that's really great to hear that they're expanding the program! Hopefully it inspires many more people down the same path you took!

\*Musical Interlude\*

Kanchi: Let's dive into your research now!

Rebekah Rashford: Awesome.

Kanchi: So what drew you specifically to neuro development and epigenetic regulation?

Rebekah Rashford: So when I got to Princeton, I got here and I was like, "Okay, awesome. People love to think. This is amazing. I'm here for it." And then I realized that a lot of it was like computer programming. And I was like, "Oh, I'm a bio major and I don't really know how to do this stuff." But I learned. That was like the biggest thing I learned. And now I can program. I can follow a long code if you tell me what it's doing.

Kanchi: How did you learn it, by the way?

Rebekah Rashford: So we had boot camp in our classes. It was just like a requirement that we knew, so got my computer, downloaded Python. And what I say, "I jumped off the deep end. I was like from the lifeguard chair, like we were really in the water there." So it was something. But yeah, there was a bootcamp before classes even started. And we just learned from the very basics, which was good.

Okay, after I learned all those different things, I was really interested in modeling and systems and all that stuff. But then I was like, I miss bio mechanisms. I miss learning about how the cellular affects the macro things. How are these things happening, and how are all the little cellular mechanisms influencing behavior and stuff? So a new faculty member, Katherine Pena, joined the department in my first year, actually. So it worked out perfectly. And she was looking for grad students and I was looking to get back into bio mechanisms. So it's just a match made in heaven, I guess. So I got back into bio and all the molecular mechanisms and looking at how ... Well, the question that I think I alluded to earlier, is just how does early life stress, which affects behavior in adulthood, how did all the different processes affected by early life stress give rise to the risk of the altered behaviors?

That was just super interesting to me, because I think it's a question that is so relevant to now, because one of our undergrads actually looked at how crossing the border down in Texas, interviewing families with children who had to cross the border and how stressful that was for them. So I think that having something that's so translationally relevant is really like keeping up my motivation. But yeah, that's how I got back into the specific question that I'm looking at now.

Kanchi: So early life stresses as in moving in these crazy circumstances on their own, or even things like access to food. I read somewhere that even things like access to food, education, those kinds of stressors as well, actually influences people's genetic makeup.

Rebekah Rashford: Wow. So the stressors that we're really looking at and modeling ... It's interesting that you bring that up, because in our lab meeting the other day, we were talking about how as our lab, we're not able to model those specific chronic stressors, but that are definitely still chronic stressors, like discrimination that minorities might face, right? That is a stressor. That's an everyday chronic stressor, but we're not able to model that, because we're using mice, which are all very similar and we don't know how they discriminate against each other. So we can't really measure that. But the stressors that we're really looking at are models of maternal separation. So that's when children are left alone without a caregiver for a while. Also included in our stress definition are forms of abuse, parental neglect, the loss of a caregiver, like the death of someone that was caring for them, parental incarceration, also being separated from someone that's giving care to you, surviving natural disaster. So all those different things that are very stressful for-

Kanchi: How do you mimic that in the lab?

Rebekah Rashford: Yeah, that's a great question. We use a stress paradigm called maternal separation, where between when the little mouse pups are 10 days old, we separate them from their mother every day for three to four hours for a week. And that has been shown to give an increase in altered behaviors, if we were to test those pups on behavioral tests later in life, if they go through another stressor. Because what happens is, if they go through early life stress, then they grow up and then they go through another stress in adulthood like you and I, we go through normal stressors. We have to move, things go bad at work or whatever. But when you have a history of being stressed out when you were younger, when you're exposed to those stressors now as an adult, you're just way more likely to succumb to those and develop depression, develop anxiety. So that's the relationship that we're looking at there.

Kanchi: The developmental period is so crucial. It's very cool that you're examining that relationship. I feel like it underscores just how important an emotional support system could help too. That reminds me...I remember this psych class I took and they talked about how there's a study with monkeys and "wire moms" where they gave baby monkeys inanimate moms -- one was made of wire and wood, and the second was softer and covered with terry cloth. And I think in one round of the study, the wire mom had a milk bottle, and the cloth mom didn't, and they did a second round where the food was switched between the moms. And I think both times, monkeys spent way more time with the cloth moms. And when placed in stressful situations, they would seek comfort from the inanimate cloth moms.

Rebekah Rashford: Yeah. I remember learning about that study too. It's just so crazy how in the developmental period while we're growing, it's just so important to have these types of connections. And even if it's not your mother per se, but some sort of figure that you can emotionally depend on, grow up with, it's just really important. Yeah.

Kanchi: Do you think there's something related to evolution there for us as humans?

Rebekah Rashford: That's a really good question, and I have not thought about that before. I think if I were to speculate, maybe. But I think I'd have to look at other species, because it's been done in monkeys because monkeys are very similar to humans, but the species that are the ... I forget what it's called, like the progenitor of both of those species throughout evolutionary history, I wouldn't know. But that's a really good question. Yeah. Because it's conserved in mice, we see altered behaviors. I'm sure in rats too, they get stressed out as well. But yeah, that's a good question. I'm not totally sure.

Kanchi: And what kind of altered behavior do you see in the mice?

Rebekah Rashford: Yeah. So in mice, there are some typical behavioral tests that you do. One that you could do is called an open field test where you just put a mouse in a box, and you measure how much time they spend in the center, versus how much time they spend just around the edges, being really close to the corners and stuff like that. And so, although it is definitely up for debate about what exactly that means, you can compare one mouse that has gone through stressors to a mouse that has not. And usually the mouse that has gone through the stressors, will spend more time around the corners, instead of going into the open field, and I guess is less anxious or less worried about something that could happen to them if they're in the middle. So that's one behavioral test. Another is forced swim. You just drop them a little thing of water and then you measure how long it takes them to stop trying to swim.

Kanchi: Stop trying to swim?

Rebekah Rashford: Yeah. Mice don't like to swim. So if you drop them in a little bit of water, then they'll try to paddle for a little bit, but after a while they'll just float. Yeah, it's very debatable what that actually means. Is it them conserving energy, or are they just trying less because they're more depressed or something, quote unquote? But forced swim isn't something that we use a lot to determine altered behaviors. But I know that's one in the literature that people use.

Kanchi: That's really cool. And what other lab techniques do you use to assess their epigenetic changes specifically?

Rebekah Rashford: I'm going to try to explain this without getting too technical. Yeah, yeah, yeah. So as I alluded to before, there are epigenetic mechanisms in the brain, meaning that there are regulatory mechanisms for the genetic sequences. So not changes that are happening to the DNA, but the things regulating what's happening to the DNA. And so one of the things is chromatin, and chromatin just describes how DNA is packaged. So if DNA is more open and accessible to all this machinery that helps it do whatever the DNA needs to do, that is just more open. And then there's more other confirmations of chromatin that are closed, where you can't actually access the DNA. So my hypothesis is that when mice go through this early life stress experience, that, that loosens the chromatin, which means that it's making the DNA have the

possibility to be accessible. If that makes sense. So that when you stress them out again as adults, then it's just going to be much easier for all the transcription to happen and stuff. So it's like a comparison of how much the chromatin changes. I hope that made sense.

So yeah, just different things in the brain. And I'm looking at the ventral tegmental area, which is a huge player in the reward pathway, because it's one of the very few brain regions that provides dopamine. And dopamine is associated with reward.

Kanchi: What do you love about your work and what are some challenges to it?

Rebekah Rashford: I love that question. One thing I love about my work that I recently began to even fall in love with more, is that I'm learning. There's just so much that I don't know, and there's so much to find out. And I get excited that I'm able to be a part of learning about this mechanism and contributing to the understanding of it. I think that's just something I love. I love being at the bench, thinking through my experiments and being able to just figure things out. That's what I love so much. The challenge, I think ... The challenge that at least I'm going through right now is just making sure that all of the steps I'm doing, are going to help me answer the question I'm ultimately aiming to answer. And so I think the planning and making sure that I'm very meticulous in choosing which mice I'm going to use, getting the right genotypes and just being so detail oriented about how I'm going through each step, is one of the key things. And then also analysis.

So I think that in undergrad, I learned how to gather data, got really good at actual bench work and pipetting and stuff, good times. And then analysis, I would just bring it to Dr. Lindell and be like, "I've got data here, tell me what it means." So I think that one thing that Kate and I are definitely working on, and something that is a goal of mine for graduate school specifically is, I know how to collect data, but I want to learn how to really analyze it and get meaning out of it. So I think that's one of the challenging things about grad school, but it's also very exciting, because when I'm able to interpret my own data, it's going to be like, wow, I'm really excited about it.

Kanchi: Yeah. That's awesome. That's awesome. And that's certainly understandable. We're generating so much data, that sometimes we just don't know what ... Even as the best platform team to use to analyze it.

Rebekah Rashford: Exactly. Exactly. There's so many options.

\*Musical Interlude\*

Kanchi: What are your words of wisdom for anyone in undergrad?

Rebekah Rashford: I think one thing I would say, especially to people in undergrad who are even more than looking to get into science or STEM, just as you pursue your careers, make sure that you're taking time to develop your hobbies. I think in undergrad I was like so, I have to

do school, I'm always doing it. That one day I finally woke up and it was senior year, and I was like, Oh my gosh, I had all this time to do all these random things that I probably couldn't do because I'd be working. So just taking the time to enjoy things, meet new people, do the things you want to do. Don't forget to do things you want to do. And I think that, that's something that I'm learning now, honestly. Thankfully I'm still pretty young, so I can afford to do these random things that I want to do. But yeah, take the time. The earlier you do it the better. There's so much life to live and you can't just always be working.

Kanchi: I know we've talked a lot about science. But scientists have so many more interests too. What are some of your favorite things to do in your spare time?

Rebekah Rashford: Yay. I really love to read, and it kind of dropped off because I was just reading so much in the first couple of years of grad school, but I've gotten back into it. And so I found a lot of cool books, and it feels so good to get back into reading. I also really liked to write. In undergrad, I had a minor in creative writing, specifically fiction writing. So I very, very much enjoy fiction writing. I've tried to get into screenplays, haven't finished one, but we're trying, we're going to see where it goes. So I'm very much into storytelling and stuff. Not great at poetry, took one class and I was like, this is really cool, but I'm bad at it. But yeah, I really like writing. And recently I've gotten really into taking walks, just because I think of quarantine. But it's so much fun. Thankfully there's a lot of places to walk around where I live. So that's been really, really amazing.

Kanchi: What are you reading right now?

Rebekah Rashford: Right now I am reading two books, but I'll tell you about one of them. I'm reading ... Well, I'll just tell you the one that I'm reading, but that I'm not going to go into. It's called Hinds' Feet on High Places. My mom was like, "You should definitely read this book." Because she read it to us when we were little, I think. But honestly, I don't really remember, if I'm being honest. Sorry, mom. And it's like an allegory for the Christian walk of life. But the other book that I'm reading that's very, very good is called The Four Loves by C.S. Lewis. And that's a book that talks about ... Well in the English language, we only have the word love, but in Greek and I feel like a lot of other languages, they have more words for love. And so he goes through four types of loves that are described by four different words in Greek.

So it's like affection, like a familiar love. Like, I don't know, your neighbor that's been living there for years or whatever. Friendship which has been so insightful to learn about. And that type of love that you have for someone who's a friend. And then there's a romantic love, and then there's a charity type of love. So he describes it as a love that like God has for people. It's very interesting, I feel like I'm learning a lot. I'm only halfway through, but that's been really, really cool. So that's what I'm reading right now. Yeah.

Kanchi: Oh that sounds really interesting! I remember reading the lion, the witch, and the wardrobe way back when! I'll have to check out this one too! Thanks for sharing!

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\*Musical Interlude\*

Kanchi: This episode was produced by me, Kanchi Mehta, with help from the rest of the team at Carry the One. I'd like to thank Rebekah for taking the time to speak with me about her story and her infectious enthusiasm for science! This episode would not be possible without our Patreon supporters who deserve a huge round of thanks: Sama Ahmed, Carly Van Orsdel, Jeanine Cuevas, Samantha Ancona-Esselman, and David Cabral for supporting us financially through our Patreon. If you like this episode, please support us on Patreon at [patreon.com/carrytheone](https://www.patreon.com/carrytheone). Please feel free to share your favorite CTOR episodes with your community -- be it your neighbor, your dentist, your physician, parents, or friends or whoever. With your support we can bring you more content and improved audio quality. We also want to hear from you! Please leave a comment or review! You can find us on Twitter, Instagram, or Facebook, or email us at [carrytheoneradio@gmail.com](mailto:carrytheoneradio@gmail.com). Thank you so much listening and as always, stay curious folks!

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