Young Scientist Spotlight 13: Balint Kascoh

[Blue Dot Sessions – Lissa]

Ryan Morrie:
Hi Everyone. 2020 is over! Yeah! Here's hoping all your 2021's will be better. And if you have any New Year's resolutions, I'm sure you'll love our Spotlight guest today – Balint Kacsoh. He's a postdoc in Dr. Shelly Berger's lab and will be telling you all about what he studies -- the molecular basis of social interactions in ants. We'll unpack this a bit more in the interview, but the questions he's interested in are oddly fitting for both the general moment -- in terms of social isolation -- as well as the beginning of a new year – when people have lots of resolutions to change themselves. As you'll hear, ants have really interesting social structures, and while an individual ant's genes remain the same, they can dramatically change their place in this ant society. I hope you find this conversation as fun and interesting as I did. In fact, other CTOR members said they never cared about ants before hearing this -- but now find them fascinating!

[CTOR tag]

Ryan Morrie:
Just to introduce yourself to our listeners, can you tell me what your current position is? Where, where you are and like a really brief overview of what you study?

Dr. Balint Kacsoh:
Yep. So my name is Balint Kacsoh. I'm a postdoc at the University of Pennsylvania in the lab of Dr. Shelly Berger.

Ryan Morrie:
What are you studying?

Dr. Balint Kacsoh:
So I'm really interested in just social learning and interaction on a social level between organisms. So as an, as an undergrad, I looked at the ecology evolution portion in fruit flies and their arms race between parasitoid wasps and their immune response, relative immune responses. And then I became more and more interested on like, well, you know, flies are in nature from they're constantly getting parasitized, right? Presumably there must be some social defense network to alert each other that there's a threat nearby. Um, and so in grad school I'd identified that they were actually talking to each other. So if you expose flies to parasitic wasps, they will communicate to naive flies that, Hey, there was a threat nearby and we should change our physiology accordingly. And then I wanted to kind of continue with this social question, but in a much more social organism. So I picked ants, um, and Shelley's lab allows us to actually look at molecular effects of ants. So like sequencing, you know, we have access to all of these like high end techniques. And so now I'm looking at how does disease state and progression, how are those factors affected in our combination with the social state? So if you're alone, are you more likely to get a disease state or is your physiology change faster versus when you're in a group and we have three different species of ants with increasing social complexity that allows me to ask that question

Ryan Morrie:
That seems really relevant right now in terms of forced social isolation due to Covid.

Dr. Balint Kacsoh:
Yeah, I started about a year ago and you know, at that point, this whole social distancing isolation was not a thing. And serendipitously, I guess now it is. And so, um, we're kind of, we're actually assembling a manuscript now and thinking that it might be very relevant to today's issues.

Ryan Morrie:
So why are ants such a good model system for like social interactions or class systems?

Dr. Balint Kacsoh:
Yeah, so they're called the super organism. So it's almost like a colony acts as an individual. So there's the reproductive, which is the queen. All other individuals in the colony are almost genetically identical because they're all coming from the queen and they're all sisters, which is crazy to me to think about, right? Like how could a colony thousands of thousands of individuals all have the same mother? Yeah. That's already nuts. And then there's epigenetic regulation that determines castes. So each ant has a particular job as it's caste forms. And there's also an age effect that's put on top of it. So young workers of particular castes will do one behavior. And as they age, they'll progress to do a different behavior and it's all by modifying, you know, they're all genetically almost identical. So it's not a DNA sequencing change, but rather a modification of what's on and what's off. And so it essentially lets you do these twin studies where, you know, in humans you can have twin sisters and twin brothers, but one will get cancer and one will get Alzheimer's and you know, it's not due to their genetic code, but rather the environment or epigenetic changes, that's kind of why we really like the ants as an epigenetic model. And then there's a social model again, it's just because they're so complex, they're always interacting, smelling each other touching. And that like creates this sense of like a social hierarchy within the colony.

Ryan Morrie:
Yeah. Can you, uh, define epigenetics or explain how that works?

Dr. Balint Kacsoh:
Yeah, that's a good point. Um, so epigenetic inheritance or modi--- or epigenetics in a developmental context is where the DNA itself, the coding sequence doesn't change. Rather you have the histones, which the DNA is wrapped around modified in order to have a closed state of chromatin so you limit transcription of particular gene sets. Or you have an open state. And so these fact factors that affect chromatin act in concert, so turning on and off certain regions. And so what have is even though these identical sisters of ants like eggs and embryos should be the same. You have two castes that can emerge or more depending on the ant species. And it's all because of what genes are turned on and off within the developing embryo. Furthermore, when they grow up, they eclose and they're adults, you also have the epigenetics acting. So instead of having, you know, when you have the same genes and both individuals, their behaviors are now changed because of what genes are actually expressed.And it all depends on the state of the chromatin, whether it's open or closed at particular sites of interest. And there are certain transcriptional repressors and activators that are recruited to these particular genes to create a nurse, worker, or soldier and their respective behaviors.

Ryan Morrie:
[Blue Dot Sessions – Town Market]

So what Balint is saying here is that just because someone, or something, has a particular gene, there are many factors that determine whether that gene is actually expressed in an organism. The DNA in your cells is not just floating in space, but instead is wrapped around balls of proteins known as histones, kind of like beads on a string. This histone-DNA complex is referred to as chromatin. If the chromatin is “open”, or the DNA is more loosely wrapped around the histones, then those genes in that section of DNA will be expressed a lot. However, if the DNA is wrapped tightly around the histones, or in a “closed” state, then you’ll get very little gene expression from that section of DNA. So in Balint’s situation, even though all the ants have the same genes, ants with different jobs express different sets of those genes because they have different “open” and “closed” chromatin sections on their DNA. The factors that affect chromatin state are collectively referred to as epigenetics. As Balint explains, changing these factors can have dramatic consequences:

Dr. Balint Kacsoh:
And what's really gnarly is you can change behavior. So you can actually have a soldier ant, if you inject HDAC inhibitors. So these would be, um, so deacytylases, so ones that would cause certain changes in chromatin

Ryan Morrie:
[Blue Dot Sessions – Town Market]
The molecules that Balint is injecting into the ants here cause the chromatin to go from “closed” -- or no gene expression -- to “open” -- or lots of gene expression. This changes what genes are expressed.

Dr. Balint Kacsoh:
and you could actually shift their behavior to be more nurse like, or be more foraging like, so they have that genetic information there to be the nurse or forager, but instead they're a soldier and you could artificially shift them in a direction. That’s really cool.

Ryan Morrie:
How do you inject something into an ant?

Dr. Balint Kacsoh:
These are experiments I've started to do in the past month. So you put them to sleep with ice. So insects have this amazing ability to be on ice for hours and not be affected in a negative way, uh, you then poke a tiny hole in their head. You can inject X amount of liquid and then you put them back in their box and wait for them to wake up, and then they're doing new behavior or whatever phenotype you're studying.

Ryan Morrie:
Wow. That's crazy

Dr. Balint Kacsoh:
It's terrifying. Because they're, they're small. Right? They're so small, but that you're trying to inject. They're tiny, tiny little head.

Ryan Morrie:
Yeah. Ant mind control is tough to do.

[Ants Go Marching – CoComeleon Nursery Rhymes]

Ryan Morrie:
So just to back up a little bit. How'd you end up working on ants in Dr. Shelly Berger's lab?

Dr. Balint Kacsoh:
And I decided on the ant side of things, because when I spoke to Shelly, she was like, you ever heard of leaf cutter ants? I was like, yeah, and so she has this picture on her wall, that, uh, when she traveled to Costa Rica and she saw these ants and was like, Oh, this would be a great epigenetic model, but no one in her lab had picked it up. And so she was like, yeah, if you come, we could work on leaf cutters. And I was like, all right, sold, let's go for it. I want to be a PI hopefully one day, and my ideal lab will have these three ant species plus fruit flies. And any students that I get can choose their organism based on the questions that they're interested in. So that kind of would be, you know, I want a big picture question of how epigenetics controls social interaction and sociality and insects and apply that like the disease state question and ask, like, how was it human relevant?

Ryan Morrie:
Yeah, that's really cool. I mean the leaf cutter ants are amazing. I was in Belize last year. Um, yeah. And you'd be hiking and then there'd just be little trails of leaves and ants all along the hiking trail.

Dr. Balint Kacsoh:
So cool. Right. And it's all like, actually there's an olfactory cue trail that they're following. So the first one that comes back, will lay a trail and then the ones that come out, if they like that source they'll lay a stronger trail. And so it constantly feeds back. So you have these like insanely long lines going back and forth. It's so complex. And so cool.

Ryan Morrie:
You mentioned that you have three different ant species that you work with. What are the different types of ants you have? And how big are they?

Dr. Balint Kacsoh:
Yeah. I always thought of ants as like the picnic ants. Like, you know, they're really itty bitty ones, but I would say probably the, like the length of a one ML tube.

Ryan Morrie:
Okay. Oh wow. That's like a little over an inch.

Dr. Balint Kacsoh:
Yeah. And then even for the biggest one for context are the super majors in the leaf cutters, which are probably half the size of your thumb. Okay. Those actually can bite so hard that they, in Costa Rica, they're used as staples. So if you cut open, like you have a laceration, you can take these super soldiers and have them bite and it's, they cut through skin. So they act like a staple.

Ryan Morrie:
Oh man. Wow. That's crazy. Yeah. So I guess how often have you been bit, by the leaf cutter ants?

Dr. Balint Kacsoh:
So those, those have been quite nice to me. I haven't been bitten although our, our lab manager, she was once in the nest and she had pulled her hand up and there was blood running down her hands. Like they, you know, they're defending. So it makes sense. It's more likely that we get stung by the Harpegnathos, or the Indian jumping ants. So those are the, the hunters that's sting, the crickets paralytic venom. And they're very docile when they come on your hands. So that they're very visual. So they see you and they respond to seeing you. But if you upset them, they'll sting you at first. You're just, it feels like a pinch, but it eventually it swells up kinda like a wasps sting. So it's not so much that it hurts. It's just irritating. The Camponotus like our carpenter ant and they bite you, but it's more of like, Oh, that's very cute that you bite me.

Ryan Morrie:
Friendly nibbles.

[Blue Dot Sessions – Town Market]
In case you missed it, Balint is using 3 different types of ants for his studies. There's the leaf cutters, which are native to Costa Rica and have a really complex social structure with many castes. The 2nd ant is the Harpenathos, or Indian Jumping Ant, which hunt with visual cues and can sting. And the 3rd ant is the Camponotus, or carpenter ants, that live in wood. Both of these latter ant species also have multiple castes: for example workers, soldiers, and a queen.

how do you tell different ant uh, like soldiers or nurses from each other?

Dr. Balint Kacsoh:
Depends on the species. So our big, Harpegnathos are Indian jumping ants. So those are the visible hunters are the most ancestral, the ant species we have. And it's very interesting because there it's a very plastic system. So any worker can actually become a queen. And that's what, why we studied because it, when a worker becomes a queen, their lifespan multiplies by six, uh, their brain changes size and rewires, their ovaries activate and they stop hunting and they start laying. So it's a very epigenetic system, right? This is the same genome. And actually you can revert them. So you can take it a queen put her into an established colony and she'll revert back to a worker. And if she's lived longer than when a worker needs like set lifespan, she dies right away after reversion. So there, they all look alike. And so it's very much a behavioral analysis of who's the forager and who's the queen. For our carpenter ants it's a little bit more straightforward. So the soldiers are bigger. They're actually called the caste. They're called majors. They're big. Minors are little and they're the nurses and the foragers and the queen is probably three to four times the size of a soldier. for the leaf cutter is there's eight castes in addition to the queen. And it's very much a, there is a size effect, some of the very little ones do certain jobs, the bigger ones do other jobs. And we're actually quantifying that now, like what's the correlation between like the sizes of the jobs, but if you watch them, it's fairly straightforward of what they do. It's harder to just to like pick out an ant out of the box because it could be like you have a range. It'll either be like a cutter or leaf carrier and not a nurse or a rider or a gardener because they're so much smaller, but you have a little bit of wiggle room there too.

Ryan Morrie:

How do you keep track of individual ants? Like a shifting population ones? Like, uh, if you move a queen around or like move one that becomes a queen?

Dr. Balint Kacsoh:
I was shocked when I started working in the lab and this is the technique and maybe you won't find that shocking, but we paint them. So enamel paint and you put a spot or a series of colored spots in their back to give them their unique identifier. And that's how you know, so it's a bigger thing for the Harpegnathos, this where you can, they shift casts kind of will. So if you're tracking them for who's the queen there, you really need it marked. Um, for some of our aging experiments, if we're aging them in the colony, you know, even with Campanotos you'd want to paint them. So you go into the nest and find the painted ones and you know what age they are. For the leaf cutters, we tried painting them, but they actually cleaned the paint off, which is, it was very unfortunate. So we actually wire tag them. So you tire wire around their abdomen and snip the edges as you look for the wire tag ones.

Ryan Morrie:
Oh, wow. Yeah. That seems pretty tedious.

Dr. Balint Kacsoh:
Uh, but it's, it's fine. Yeah. But like we try, you know, I thought it would be like QR codes. Right. So you could like, but the humidity actually like wipes away the code. So I like in four months, it's just a white square and you're like, well…

Ryan Morrie:
Do the leaf cutter ants have more castes because their like system's kind of just more complicated where they get the leaves and then have to make this like fungal bed. Right. That then they eat the fungus actually.

Dr. Balint Kacsoh:
Yeah. So that's what we think is the most advanced social structure, at least that we've discovered in ants. So that it's almost an assembly line. So you have the leaf cutter that actually goes out and cuts the leaf. And then there was another one that picks up the cut leaf and takes it back to the nest. Usually there's a little one that rides the leaves that's being taken back and it actually fights off parasites that could be trying to infect the carrier. Um, there's more, there's the gardener cast, which takes care of the fungus. There is the nurse cast that takes care of the babies that are within the fungus. Um, there's the trash ant, which I find hilarious. So their job, that's an age effect. So once they're old, they become a trash ant, and their job is to take out the trash cause they have to have a separate, like trash room and they're not allowed back in the colony. And it, it makes logical sense because like, you wouldn't want any potential pathogens to be brought to the fungus that could kill it. Right. But something so logical to be created in nature. I just find like mind blowing. Right.

Ryan Morrie:
Yeah. That's crazy that they created their own little like clean room.

Dr. Balint Kacsoh:
Yeah. It's, it's awesome. And then you have the super soldiers, which are the really big ones that defend the queen and the colony. And so it's just a bevy of various individuals. And again, they're coming from the same queen. So it's all genetically identical. And we don't know, this is

an insane amount of complexity, right? Like the brains are so different. The behaviors are so different. So trying to figure out how that's being regulated is a big question.

Ryan Morrie:
Where do the ants come from and how often do you get them?

Dr. Balint Kacsoh:
Havrbinathis, so it's the Indian jumping ant. So as the name suggests, they're originally from India. Because any one of them can become a queen in that setting, they can mate. Because they're the most ancient of the systems. And we actually got them from a collaborator in Arizona. Interestingly, it is now illegal to go collect them in India. So there's a law now in India preventing the export of these ants because they're considered as scientific property for their country. Our carpenter ants. So they're called Campinodis Floridanus. So they're from Florida and we'd go down to the Keyes around November, end of December, every couple of years. So that's after their mating flight and collect fresh queens that just started their colonies. And actually it's, they they're carpenter ants. So you'd think they'd be in wood, but first they have to establish workers. So, you know, there's crabs in the Marsh that dig holes and the holes that they dig, you know, they'd get dig out and mud and all this dirt. And so the ants actually will bury under that dirt that the crabs have dug out.So we look for crab holes and then you look for the dirt and flip it up and you'll usually find like maybe the one queen and she might have two workers at that point. And then we suck them up into a tube and bring them back So the leaf cutters, we're trying now to get a huge colony into the lab, but due to coronavirus, it's been difficult to have our source who is in the UK, bring over a massive colony. So we actually work with the Liberty science center in Jersey city who have an exhibit of leaf cutters where we can go onsite, we can dissect and actually bring samples back. So we have a cool partnership with them where we're providing them with images and data that they can share to kids who come visit and actually learn about how, why this is such a cool system to study.

Ryan Morrie:
No, that's awesome. So yeah. Are they like in a big ant farm?

Dr. Balint Kacsoh:
Yeah. So good, good, que-. Yes. I thought naively that it would be like the ant farm, you know, with like the sand as a kid and you see the tunnels. So no, not at all. So what they have is a clear plastic box of the various sizes and you pour plaster dental plaster on the bottom of it. And so you let that cool and you could add water to the plaster, so to increase the humidity. And then what we do is we can drill holes in the boxes and connect them with either tubing or smaller boxes to make these like very big arenas. And because there are clear, you can look in and see them. Some of them, we have the chambers as dark. And so you can actually trick ants, into believing that the dark by putting in red film, because they can't see red wavelength of light, they think it's dark and underground. So in our Campinodis nest, we have a divot and the plaster covered by this red like plastic material and they crawl underneath and they think they're underground, but you can look through the red and see, Oh, they're there. So you can very easily manipulate the colony and ask questions to your heart's desire.

Ryan Morrie:
I actually did my PhD in the retina, what color do ants see then?

Dr. Balint Kacsoh:

So not much has been worked out. So like this is a, you're asking really important questions that are, unfortunately, it's still just now an evolving system. Um, it's hypothesized that they see, you know, blues and greens, uh, pretty well, which make - cause like for the leaf cutters, they can differentiate between flowers, colors. And actually, so they there's something about like, you know, their don't see red, but whatever color they see instead of red, they really hate red flowers, at least in our hands for our colony, but they really loved yellow flowers and avoided, um, blue flowers. So there seemed to be like pretty strong delineation, even though it was the same species. So it was all like tulips. They would only cut a particular kind of tulip. And the other is, they were just like, I don't like this.

Ryan Morrie:
What's the best part about taking care of the ants?

Dr. Balint Kacsoh:
one of the most fun things of what I do, and most repetitive things, is just feeding the ants. But what's cool is when you look at them, each colony has its own personality.

Ryan Morrie:
Do the different colonies get like excited differently? Like do some know oh Balint's coming, like food's coming.

Dr. Balint Kacsoh:
So I think the Harpenathis, which are the visual mediated ants, I think they recognize people. So our lab manager she's convinced that they would recognize her when she opened up the lid. Cause they look at you and they start wiggling their butts?, Like almost like a dancing behavior. Um, and then some of the Campinodis, which if you open it up, they start running around like crazy. But some, it seemed like we're aware that when they have that gust of air come in, when you open up the lid, that food is coming. And the leaf cutters, I was, there was ones where they have a arena where they have their fungus and the brood and they hang out. And then we have a second chamber where we put their leaves and I would open up that chamber and put in a leaf and there were always, this one super major would run as fast as she could to that area. And I could tell her, cause she had a black spot on the back of her head and none of the others did and she would always run. And then she jumped up on the leaf and look at me and like, you know, first two times maybe it's coincidence. But like every time she would be ready to look at me, I'm just like, Oh, Hi Antonio. So I, and then same with like the, some of the cutters too were always the same ones. Like we wired tag them and they would be the first to show up versus like some would be much slower. And so you could see like this difference in personality, even though they are epigenetically even now pretty similar. Cause they're supposed to do the same job, but I don't know. It's just really cool.

Ryan Morrie:
I never knew ants had so much personality. Sounds like a lot of fun

Dr. Balint Kacsoh:
And it's just, I still, like, I've been here for over a year and I still get mesmerized, like looking at them, like, like I always pull out my phone and take a picture or like daily there's pictures of ants. Like they got more pictures of ants, now than of my wife.

[Ants Marching – Dave Mathews Band]

Ryan Morrie:
What are some applications of your work? I mean, we kind of talked about that at the beginning. Like studying social structure and how we've had a disrupted social structure right now, but uh, yeah, just in general, like, um, what are the broader implications?

Dr. Balint Kacsoh:
The main project I have is looking at, you know, social state and disease progression. So right now we're in phase one of testing, you know, what's the effect of being alone on an ant and it looks like they die faster. Um, it's on a caste specific level. So depending on the caste, you can die faster than like so like the nurse caste, which is highly social dies, much faster than the soldier caste when it's alone. But they still die rapid compared to a group house state. It's a rapid death and we've done sequencing to identify certain genetic factors. They're actually differentially expressed in human meta analyses when individuals are alone. And so there's a very nice conservation between it. So the big experiment, I just did this past week was trying to knock down that these genes that are very up-regulated in isolated ants, but not in our group housed ants and see, you know, the necessary and sufficient for this genetic information. Um, what gets cool is we can also rescue the effects of the isolation. So I really, really like technology. That's the one thing we've been doing is three D printing ants at ant scale. So a 3D printed ant doesn't rescue the effect, but if you coat it in odorants, um, it actually, they live as much as long as if they had been in a group. So you can actually rescue the effect. Then it's not just the odorants. So if you'd given them a glass bead, that's coated with the odor and they live much longer, but not at all to the effect of having the three D printed model with them. So there is some primary olfactory cue and then visual or tactile come into play. And so we did sequencing on those too and those, those gene levels that we thought were good targets actually go back down to a wild type state. So if we could, especially in this era where we, if we can trick ourselves into thinking we're not alone, or we're not overcrowded that could have huge implications. And the next step is going to be, um, mutate genes to induce a disease state and ask similar questions. Okay. Like there's two genes in insects. If you mutate, you can create a cancer, especially colon cancer. And so now, okay, does it go faster when you're alone or when you're in a group and how can we reverse and fix that?

Ryan Morrie:
What’s your method for genetic manipulations in ants?

Dr. Balint Kacsoh:
So, unfortunately, right. So it's not a model system as easy as fly. So injection of double stranded RNA, like the head injections is one thing that we're doing. Of course it's not a permanent knockdown. So we're trying to get CRISPR I and these other metrics to work in the ants system.

Ryan Morrie:
To learn more about CRISPR and how its revolutionizing biological research and medicine, including making Balint’s experiments possible, be sure to check out our episode: CRISPR: The Unauthorized Biography that came out last June.

Dr. Balint Kacsoh:
In ants it turns out you can't breed them in the lab for Campinodis that I'm working with, you have to catch them in the wild and bring them back. So you can never have a line generated in

that system. At least not in occurrence. I'm sure there's going to be an awesome student is going to figure out how to do this. it's harder to work with them for that reason. But I think, you know, depending on what question you're asking they're the ideal system to work with.

Ryan Morrie:
So you're interested in like disease modeling, uh, what diseases can you give to, to the ant?

Dr. Balint Kacsoh:
Yeah. So actually I wrote a fellowship, I got it recently from Damon Runyon. So it's a cancer agency. We have funding for four years to look at this question. And in particular I'll be giving the ants colon cancer. So you can mutate two genes, and that's analogous to colon cancer in human. And the reason I picked this model is because in humans, there's a lot of meta analysis showing if you live in isolation, you're more likely to get a more aggressive form of colon cancer and type two diabetes than those living, like not in an overpopulated city because there's been an analysis to show the opposite direction as well, but in the more of a, what they determined as an optimal setting. So I was really interested in this idea of isolation and overcrowding affecting disease progression. And so the baseline we've established, we're starting -- we've finished establishing now. Yes, there's an effect of being alone and being overcrowded on just essential physiology. And now it will be introducing that those series of mutations into the ant and seeing if we can have a differential effect on social state with respect to disease. And like, because we can rescue lifespan with an odorant. It'd be interesting if we can reverse, you know, tumorigenesis by having, you know, these fake individuals put in or identifying the actual odor and molecule and question and trying to reverse the tumorigenic state. I obviously have this pipe dream of doing, uh, a drug screen to also slow down tumor progression because you could just feed it to them at that point and see if that has an effect or not. I mean, obviously that's a way downstream, but I get really excited about the project and its prospects.

Ryan Morrie:
So for the situation where like you have, uh, a queen that reverts and then like dies or, uh, a worker, I guess that'd becomes a queen, what keeps them alive longer?

Dr. Balint Kacsoh:
So that's a very good question. Um, we're actually in the midst of trying to figure that out now with sequencing various age points of these aged Queens and performing comparisons. And I can't tell you yet, well, what is actually the answer? Cause I don't know. Um, one of the other postdocs in the lab that's his primary project is figuring out, um, what is it that it's being activated? Obviously we need to do experiments to figuring out like how that site is being changed and modified to like not be activated in a worker. And then our end goal is obviously to activate this site in a worker and see if we can get an extended lifespan, to show that's the actual site of interest, I'm telling you the answer as soon as we know, but yeah, but there is again like the, the selling point of like, Oh, we'll figure this out. We can make grandma live forever maybe.

Ryan Morrie:
When you're doing your experiments, how can you look at the chromatin state? Are there different chromatin marks you can see?

Dr. Balint Kacsoh:

Yeah. So it's, it's very difficult to say like what the mark is, that's causing it. So for example, um, we have a collaborator down the hall from us who is a mass spectrometrist and they can actually mass spec all histone modifications that are known So we're trying an unbiased approach and putting brains that we dissect from the ants and putting them into the mass spec and seeing just globally, how the marks are changing. so once we ID like, hey, this mark is really, really high in super soldier, but not in nurse. You know, let's pull out that mark and see what genes are being regulated. So we're trying to go from like a really, really big global picture down to the mark that makes a caste unique.

Ryan Morrie:
[Town Market – Blue Dot Sessions]
The mass spec that Balint is referring to is a machine that actually allows him to know the types of histones that the DNA is wrapped around in the ant brains. Some of these histones will have markers on them that indicate the chromatin is in an open state, for lots of gene expression, while other histones have marks that designate a closed state, for no gene expression. Balint's using the mass spec machine to find which histone markers are specific to nurse ants or soldiers ants.

[Over the Fence – Blue Dot Sessions]

Ryan Morrie:
Can you tell us a little bit about like your career trajectory? How did you get into science? Um, like how'd you end up at Penn, um, and how how'd you end up studying like ants and social genetics?

Dr. Balint Kacsoh:
So as my name suggests, I am foreign, um, Balint Kascoh is not an American name by any stretch of the imagination. So both my parents are from Hungary, and in Hungary, you don't go to college. You go straight from high school to university as in, so you get, your PhD, or your MD right away. And so when I was growing up, I grew up in Georgia, the state, not the country. Um, my parents really didn't know about American college. And so it was, my mom was an MD and my dad was an MD PhD. So I was surrounded by either science or medicine. And my dad worked at a small or works at a small medical school in Macon, and he really didn't like the bureaucracy. So he was not, he ended up not being happy with the university chose, but my mom was the breadwinner. So we stayed. Right. So he was like, for college, you have to go to a college that we've heard of, right. Because foreign parents who were like, if it's not Harvard or Yale or something with a name, it doesn't matter. Right. Which is not at all true. You should go to the school that best fits your career ambition. But at that point, they were like, well, you should become a doctor because that's very good in America. Um, so I went to Emory and luckily to apply to medical school, you need to work in a lab. And so freshman year I started working in a research lab that I worked in all of undergrad, I still did the volunteering at hospitals and I applied to medical school and at the MCAT I even got in. Um, but at the end, decided to go to graduate school. My parents were not the happiest about it, but, you know, I think it's worked out so far. Um, I ended up going to Dartmouth for graduate school and that was more dictated by my now wife, who was, we worked in the same lab when I was an undergrad. She was a master's student in public health. And so she was like, well, we should go to graduate school. I'm going to Dartmouth. So like, Oh, I guess I'm going to Dartmouth too. And we worked in the same lab during our graduate student time up and, uh, Gio[vanni] Bosco's lab at Dartmouth. And then we both want to be academics. So we both needed good postdocs that

we were interested in. And again, this is like the two body problem that people were running into is, we picked universities where both of us could ID at least two people we were interested in, like two potential labs. And so at Penn, uh, both of us kind of fell in love with the labs that we interviewed with. And so it seemed like the perfect fit.

Ryan Morrie:
Yeah. So you mentioned your parents are both your moms, uh, medic and your dad's MD-PhD. So you talk about science, with your family.

Dr. Balint Kacsoh:
Um, yeah. So you would think it would be easy because they're both trained in science, right. Um, but my mom is a pediatrician, so she's not at all in the aware of fruit flies or basic research. And my dad had a lab for a long time and it worked on breast cancer models and cell lines, but had lost funding. And now his lab is inactive for the past 10 years. So while they came to my thesis defense, it was very much a we are coming to support you. And not because we actually understand what's going on. I find it analogous to conversations with like my wife's mom. Who's also not, who's not a scientist at all. She's a learning education specialist and it's much more, you know, fundamental basics of like, you know, we're studying this phenomena of like how they interact so that we can introduce human mutations. Like, you know, if you could introduce the autism gene into an ant, which is highly social, then we can figure out like maybe a druggable target. So it's much more downstream elements that when you talk, I find it's easier to talk to people about, rather than the basic science side of things. So you kind of have to make it more broadly accessible, I think, to non-science audiences, which is kind of our job anyway, right. To justify our research to the taxpayer, so it's important to learn those techniques.

Ryan Morrie:
Yeah, and then you mentioned, like you want to have your, your own lab. You have any thoughts about like the state of science or PhD/postdoc training and like any ideas about how you're going to go about that.

Dr. Balint Kacsoh:
it's probably not the most controversial thing to say. It's like not very in a good state right now. I find that the, the funding situation is quite dire. Um, so having to justify everything with the human element, I think is very shortsighted. Um, because there presumably are going to be biological phenomenon that we cannot yet predict that exist in a very basic organism or a non-model system that only upon after discovery of the mechanism can we make translational values to it. So for that reason, I think it's, we're kind of falling behind on what we can research and the importance of it. And I really like to create an environment where I don't have to tell my students, no, because it doesn't fit into a human disease context. Um, that's like a terrible way to have to think about it, right. I would love to tell you that, you know, I want, you know, you come into the lab and you're interested in like how antennae develop in the ant. Let's just go for it. Um, but unfortunately it's not like that. And it seems like a lot of PhD labs and postdoc labs are very much now stuck in this mindset of this is my factory. A student comes in, they're going to do this one technique over and over for four years or five years, and they'll get their PhD and they can move on and I can renew my grant. And I really don't want it to be that way. Like I want like the naive look in your eye when you discover something new to be there when you leave. Because otherwise, if it's, if you're not having fun and you're not loving what you do and loving the discovery, then it's not worth it. And as I say this, like, I really hope I don't become what I'm preaching against, but I really think the environment is super important. Like I've been part of

those churn and burn labs as well. And it's not like you fizzle out at the end if you're, and if you lose that twinkle in your eye, it's not worth it. So I try to be really aware about these things. And luckily I get to mentor graduate students in the lab because we're such a big lab where postdocs are assigned graduate students to help them and progress them. And one of my students now I love talking to him because he's always smiling and like always coming up with ideas of like, what if this, how, how would we do this? It's just, it's so refreshing to see after coming from locations where it was just like, you just saw dead eyes of like, Oh, I have to run this next assay rather than the excitement of I get to run this next assay and like ask the next step question. It's probably super naive. I know, please don't judge me on that. But.

Ryan Morrie:
No, I think that's great. I mean, I think like having the excitement and everyone enjoying what they're doing makes such a big difference. Like you said, it just makes like science more fun. But also I think it makes it better.

Dr. Balint Kacsoh:
Yeah. I mean, I feel like if you're in a workplace where you're not happy to go in your, the quality of your work won't be as good. And that's when we were picking postdoc labs. The most important question that I asked students in the lab was, are you happy? Right? If there were usually three responses, there was the instant. Yes. Which was great. There was the pause. Yes. Which is like, all right, you may be okay, but there's something up. And there was like the instant, no. Joy is important. No matter how interesting the question is.

[Over the Fence – Blue Dot Sessions]

Ryan Morrie:
I actually saw on your website, this Antonia thing. Is that still happening? It looks really cool.

Dr. Balint Kacsoh:
Yeah. So that is, so Antonia is my pet project. Um, I she's gonna make her debut soon. So essentially for the listeners it's a cartoon ant that I've made that I've tried to think is really cute. Um, and the goal of it is, is to show kids at a younger audience, like elementary and middle schoolers, that ants and insects are not gross, right. They can be relatable to, and we can use them to study very interesting questions. And I always think that it's something it's like, there's those websites of like ugly animals, right. That people don't really gravitate towards, or they're grossed out by if we can make them cuter and accessible, then all of a sudden people will be more accepting of it. So I'm trying to three D print Antonia now. And so she could be like a teaching tool and you know, by naming her Antonia, you kind of get rid of the idea that most ants are male. So like Bug's Life and the movie Antz right, is led by a male ant, which it actually is wrong. Uh, most of them are female. The males live two weeks and are pretty useless. Like you're getting that context. Um, leaf cutters are most are endemic to Costa Rica. So you, with Antonia you get the Latin [element] - so like bringing in all these different factors, and I'm trying, I'm learning graphic design now and having Antonia where she's playing soccer or where she's, I'm trying to hockey outfit now. So like each time there's something like relevant. You could, I can advertise and say, Oh, check this out. Or like I did one with a face mask. And obviously the learning thing there, there will be, yes. Wear your masks during Corona, but also ants don't breathe through their mouth. They actually breathe through the sphericals on their exterior. So you can use it as a teaching tool as well. I mean, maybe this is naive of me to think that this will work, but I just get so excited about the possibility that like, I'll just go for it.

Ryan Morrie:
It seems really awesome. So I like that idea too. It's like learning about the ant through the anthropomorphizing and seeing what's different and what's the same, I think that's really cool.

Dr. Balint Kacsoh:
I appreciate it. Yeah. It's, you know, maybe it's goofy, but I don't know. I have a lot of fun with it. And so far, like I'm going slow to make sure I just get it right before putting it out there.

Ryan Morrie:
Has any of your work been picked up in the media?

Dr. Balint Kacsoh:
Yeah. So my biggest claim to fame was when I was an undergrad. I had a paper in Science that I was lead on and The Onion picked it up. So that was, that's probably the apex of my career, unfortunately. So we were looking at, um, if fruit flies are given a choice to lay on alcohol laden food or regular food, if there's a parasitic wasp around they lay their eggs on alcoholic food because it actually protects the eggs from infection. Cause these wasps were not adapted to ethanol. Beyond that, you know, like some news sources picked up a recent paper where we had where we found flies communicate to each other about the wasp. And that was about the talking flies. Um, and for the most part, it has been quite representative of what we actually found. You know, like The Onion one obviously like went like totally loosey goosey, but the rest was quite, well picked up and not over sensationalized, which is always the danger of some of these like coming out to the mainstream media of like, Oh, we're going to cure cancer with this. Like, Oh, it's like five steps away, but okay.

Ryan Morrie:
Yeah. So you kind of mentioned, you take a lot of pictures of your ants and yeah. I was looking at your Twitter and there was some really cool pictures on there. Is that like one of your main hobbies, even outside of the lab is photography or you just like the ant pictures?

Dr. Balint Kacsoh:
Yeah. So I, I know it's quite silly, but I really like, while I'm feeding, I'll have our camera, like it's just a Nikon hooked up and then I'll see an ant doing something cool. And I'm like, Oh, I should take a picture. And so I know I do some photography outside of the lab, like at home, but it's mostly, I really like the ants and the aesthetics of them. And then I also think that by having these pretty pictures, they makes them more accessible to other people. Like, again, that mentality of like, Oh, this is actually quite cool. You see like an ant carrying a leaf. Like that's really pretty. Um, so I try to promote the system in that way as well. And it's really fun. Like I like editing the pictures. It's like sitting on the couch at home, like playing on the iPad, changing the colors and settings. And I find it actually really relaxing, which again is weird. It's like, do I really have a work life balance? I don't know. I don't know. My wife would argue I don't, but it's fun. Like I just like to really look at them that you see new features of them, like what they're doing. And it's just really interesting.

Ryan Morrie:
Do you have anything else that you want to talk about?

Dr. Balint Kacsoh:

I guess like just echoing back to what we talked about, the importance of having fun, like for any like PhD students thinking about going to a postdoc or incoming students thinking about joining the lab. Remember you're not only gonna study, you're not there just to study a cool question. Like you really want a strong atmosphere that's supportive and a right kind of mentoring style for you. It's not just any mentoring style work cause you're just here to work. And then being finding something you're really passionate about being, making a three D model of a cartoon ant sounds crazy. Um, but it's, I think it's because I'm passionate about the project and I think people finding those kinds of scientific questions kinda will help promote, you know, STEM retention, uh, having a greater diversity of scientists rather than the, you know, the old white male that we have, we can recruit more diverse backgrounds and actually opening up the tent to everyone, you know, rather than just a select few, I think making it more accessible and fun to everyone is almost a mandate that we have as scientists like that we're in the field. And so, you know, if anyone was listening, it has that like drive to do something, you know, pursue it. It's kind of in our, our job descriptions to make this fun for everyone, bring in more people into the tent as best we can like imagine today's world, if people understood science better, what do we really be arguing masks. Probably not.

Ryan Morrie:
No, I think the three D printed ants is actually really cool.

Dr. Balint Kacsoh:
It's great to be able to incorporate it to experiments. But the other thing we've been really enjoying is printing them really large scale. And so we have this great program in our epigenetics institute where we bring in middle schoolers and high schoolers to learn, like we showed them the lab and we're trying to get it more like experiment based that kids can actually do experiments, but showing them the large models of the ants and pointing out morphological features and then showing them the real ants has been a really, really good way to teach. I can't, it's so gratifying to be like that excitement in their eyes afterwards. Like the modeling actually serves two purposes really well. For experiments too, like so asking, can the Campinodis differentiate between features of their species versus a Weaver ant species, but also like from the scientific outreach perspective, that's just like, Whoa, that's really cool stuff.

Ryan Morrie:
Yeah. I think that's super helpful. Cause I've, I've taught little kids and tried to make them look at stuff under the microscope. And they're like, I just see my eyelashes.

Dr. Balint Kacsoh:
or they just don't see it right away. And then it's for you because without, you know, the teaching scopes where you can hook up like an iPhone or an iPad and point at it, I mean, that's rare. Right? So like being able to show, like we also made a three D render of an ant brain and I showed the kids, this is what the ant brain looks like. They're like "what this is crazy." And so like, you know, it's just a really fun thing. If you could make it more accessible, these little kids, one of them will be the next big scientist. And it's like, if you've had any help in making a difference, then like, is there a better feeling I'm probably not like maybe that feeling of discovery, but also a feeling of inspiration.

[Yarrow and Root – Blue Dot Sessions]

Ryan Morrie:

This episode was written and produced by me, Ryan Morrie, with a lot of help from the rest of the team at Carry the One Radio.

Thank you so much to our guest, Dr. Balint Kascoh for sharing his time and telling us so many cool ant facts.

Music in this episode included “Ants Marching” by Dave Mathews Band, as well as recordings from Blue Dot Sessions.

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Otherwise, share this episode and tell your friends about us! Leave us a review! You can find us on Twitter, Facebook, Instagram! As always, thanks for listening, and stay curious!

[Ants Marching – Dave Mathews Band]