Transcript

Speaker 1: You are tuned in to 90.7 FM, k a l x Berkeley. My name is Tesla Munson and this is the graduates they interview talk show where I speak with UC Berkeley graduate students about their work here on campus and around the world. Today I'm joined by evolutionary biologists, Katia Mack from the Department of integrative biology here at Berkeley. Welcome Katja. Hello. Thanks. Yeah, not not, not a problem. My pleasure. It's great to have you here. So evolutionary biologists, that could encompass any number of things, but [00:00:30] what is your specialty? So I work on how species diverge. So how you get one lineage turning into two and what underlying molecular mechanisms are at play there. And specifically I'm interested in the role of gene regulation, which is how genes get turned on and off or modulated over evolutionary time. Okay, that sounds really complex. So why does it, why is it important? I mean, is it important that lineage is turned into more than one? Is that something we should care about?

Speaker 2: Yeah. So [00:01:00] the process of speciation, these lineage is turning from one to two is the basis of all the amazing biodiversity we have on earth today. So it's interesting from a basic science perspective and Darwin actually called this the mystery of mysteries because how's two species could become diverged is actually a really interesting question in terms of like why are, is selection favoring a situation where two species can no longer interbreed. And so that it's been very upgraded interest scientists for a really long time for that reason as well. Do you [00:01:30] know if Darwin had any ideas? You know, um, I think he had certain ideas about how it worked, but not, it's actually only in the last, you know, hundred years that we've made a lot of progress on this issue.

Speaker 1: So I, yeah, I was going to say Darwin was, you know, a pretty long time ago actually. So it's interesting that we can reference questions that he had is still being really relevant to science today.

Speaker 2: Yeah, I mean, we still have like really basic questions about how speciation proceeds, like what are the main, like [00:02:00] I mentioned before selection. So, but that's a big question about whether speciation is happening due to selection or random processes like drift. Okay. Can you tell us a little bit about what drift is for people who might not have had a selection that's like scope, stochastic processes. So like things that are happening at like randomly where you know, you have a species moving onto a separate island and just getting separated. And so over time they're accumulating differences from, you know, a mainland species, but that's not because they're necessarily on your [00:02:30] selection for things. Um, but maybe just because they have a small population and so weird things are popping up. Okay. So I'm going to ask you a really tough question. Are you ready right at the beginning?

Speaker 1: Did you say to people who would argue that things are too complex to be random? So of course the example, everyone gives us the human eye, right? Like how could we, how could random processes result in such a complex organ that allows us to see so many cool things? Yeah. So I think like the big thing here

Speaker 2: [00:03:00] is that there are many intermediates that are happening between having a fully functional vertebrate eye like we do and just not having an eye at all. And all of those intermediate steps can be beneficial. So you have like a situation where maybe you have the beginnings of an eye and it can just see shades, like whether something is light or dark and that may be beneficial, but you know, as time goes on you build on that framework. And so that's kind of how evolution proceeds. The [00:03:30] metaphor a lot of people use is like a blind watchmaker where if by making tiny changes over time, you can kind of get to very complex, um, phenotypes so he doesn't have to have the watch, you know, designed before he gets going. Right. Okay. Yeah. Sorry, that was tough. I knew it was going to be tough. Um, but I guess another question I would have is why are you focused on molecular questions about speciation?

Speaker 2: Is there way to figure this out without DNA or was this question never broached [00:04:00] before we understood molecular biology? Well. So I think, um, there's kind of a distinction between, so speciation proceeds for men, like one reason that speciation happens is because vcs will become isolated and once you're isolated, then you can have genetic differences accruing between species. But why those species when they meet again can't interbreed that's something you fundamentally need to understand on the molecular level. And so that's why I'm interested in that [00:04:30] question. And also I think it's kind of fundamentally interesting why you could have the situation where like some things go so horribly wrong that you can't produce offspring. So can you take us back to like intro biology and give us a sense of some of the reasons that two species might not be able to interbreed. What causes that to not work?

Speaker 2: Is it just a mechanical failure? So there's two different, um, well there's a couple of different types, but I'll say that there's posts zygotic isolation and there's prediabetic isolation. [00:05:00] So pre psychotic isolation is when you have species that can't breed because, um, they don't mate basically. And a good example would be like if you had two plants that were next to each other and like literally the pollen just doesn't fit or something like that, that would be a priest I gotta isolation. So that could be a mechanical failure. That's fairly common as well. Now posts, I got it guys. Relation is when they do breed and they do produce offspring, but those offspring die or are less fit. And so [00:05:30] they're isolated in that way. And a big part of that is like they've formed these hybrids that either die very early or themselves sterile.

Speaker 2: Okay. So you said you're focused on the sterility aspect of it? Yeah. Okay. So how do you go, I mean, do you just like go out and watch animals and like, like they're doing it but they're not gonna have success or how did, how does that work? So that's a great

question. Um, so actually we, so the that I work on is house mice. And these are a great system [00:06:00] because a these two species, a Mus Musculus and must domesticus which are actually the common house mouse that you would find in your house, like just hanging out in Europe. They actually formed this thing called a hybrid zone and that's where these two species meet and they've met after being isolated for very many years. In the last 4,000 years they've met back up and formed this hybrid zone where there are all these infertile mice running around. That is like one way that this has been studied pretty extensively is like looking at the that [00:06:30] area where these species are in contact in the hybrids they're producing. I mostly work in the lab with these mice and I study actually by create like doing crosses, so we have mo Musculus and domestic is in the lab and we can cross them and then we can look at their offspring and see what's going on there, see what's gone wrong.

Speaker 1: Doesn't it seem like there must be something inherently wrong with like a hybrid zone where all the offspring are sterile? I mean, wouldn't, why would a mouse be drawn to form offspring that are sterile? I [00:07:00] mean, why would they even want to do that?

Speaker 2: So that's a really good question. And there is some evidence in this hybrid zone that they'll preferentially choose their own species, but there's not really good evidence for that at this point. It's kind of, um, something that's still very, uh, hotly debated about whether they're making choices based on, you know, the sense of they're con specifics or Hetero specifics. But the reason is really they can't necessarily distinguish, they're pretty closely related. They've only diverged in the last 500,000 years, and that's pretty recent in evolutionary [00:07:30] time. So they just don't basically don't know any better.

Speaker 1: So you're actually watching the process of evolution and speciation take place then? Yes. So this is like a very [inaudible]

Speaker 2: early on the speciation continuum, you could say. So they're not completely reproductively isolated. And in the hybrid zone, these hybrid offspring are varying levels of sterility. So some of them can produce offspring, just not as well as, you know, a pure mouse.

Speaker 1: Does it always require geographic isolation to get speciation? [00:08:00] No, no, not necessarily. I mean, actually that's

Speaker 2: something that's also pretty, pretty much debated because a lot of people would argue that you do need that geographic isolation and if you don't have geographic isolation, you need to at least have like genetic isolation. But there are some examples of cases where there's been some Patrick speciation and that's when the ranges of two species are actually overlapping and you can yet, um, isolation in that way. But those are kind of contested in terms of what does it really mean to be an overlapping species. [00:08:30] If you have something that's living on an apple and something that's living on a pear exclusively, and those apple and pear trees are in the same range. Is that really an

example of some Patrick speciation if they're living on these host plants? Or is that like an instance of them being geographically isolated?

Speaker 1: What about, I've heard that there's some debate about what a species is, can address that.

Speaker 2: Absolutely. There's a huge debate on what species [00:09:00] is. Um, because it's hard, uh, for us as humans we're, we're kind of, it's a little bit arbitrary what a species is. Um, so one of the big concepts that we use is called the biological species concept where basically if species are unable to breed with each other, if they're reproductively isolated, then we call them a species. However, that's really hard to apply it to the fossil record, for example, where you can't [00:09:30] like grab two fossils and get them to mate and figure out whether they could have offspring. It's really hard when you're applying it to something that's like clonal, like bacteria. So bacteria are just replicating themselves, like what do you call it, bacterial species and what does it really mean to be reproductively isolated? Do you have to be completely reproductively isolated? We now know a lot about the movement of genes from different species into one another.

Speaker 2: Like the, uh, a recent example in the news of course is the neanderthals where there's been movement. [00:10:00] There was in the past movement from neanderthals into humans. Does that make them the same species as us or are they still a separate species? This is all stuff that's really difficult to disentangle. Yeah. And you could also, my, one of my favorite examples is the great Dane and Chihuahua example. Like can they actually reproduce physically? We know they're both dogs, right? Yeah. Tough one. Although there's been some human influence in that for sure. There's definitely been a lot of artificial selection there, which kind of muddies the waters [00:10:30] further. So if you're just tuning in, you're listening to the graduates here on calyx. My name is Tesla. Today I'm joined by evolutionary biologists, Katya Mack from the Department of integrative biology. Okay. So you mentioned neanderthals. So I have to ask a, you have a background actually in physical anthropology, don't you?

Speaker 2: Yes, I do. Yeah. Um, I got my undergraduate degree in physical anthropology and one of the reasons I switched to molecular biology was because of the neanderthal genome paper, which came out when I was in college [00:11:00] and it was just fascinating to me. Yeah. What, what about it was fascinating? Well, it was very exciting, like as someone who is up until that point, like I spent most of my undergrad sexing pelvises and it was very excited. It was exciting to me that you could actually get all of this information from DNA about a species that lived so long ago. And the person that I worked for was really interested in the question of whether neanderthals and humans had bred. And that was just like this ongoing debate that he was intensely involved in and there was never [00:11:30] going to be evidence from the fossil record that could definitively say whether or not there was a likelihood of that. But with the new DNA evidence that was something that they could actually speak to and now it appears there in all likelihood that did happen. So. Okay. So at playing devil's advocate here, as someone who is more

on the paleontology side of things, I mean, do you think that we still need fossils? Oh, okay, good. [inaudible]

Speaker 2: I mean there's many reasons we do need fossils and I'll just give one example is that [00:12:00] like, we don't really understand how quickly mutations arise between species. And we don't know how divergent humans are from chimpanzees. And so understanding the Luminary Church actory of humans and chimpanzees from molecular data alone, it's like five to 12 million years ago. And if we had good fossils for that period, we could really calibrate that. And I think that's true for, for every species pair just as one example. I know. Okay. So you got interested in molecular biology and uh, [00:12:30] you had sort of an interesting path that brought you to Berkeley, didn't you? Yeah. Um, I started my degree at the University of Arizona and then the Pi I worked for moved to Berkeley to um, become a director of the museum of fingerprints, ecology. So do you you sit in the Museum of vertebrate zoology?

Speaker 2: I do. Do you utilize those collections? Um, unfortunately I have not been able to utilize those questions as much as other people have because I work with these mice that I am crossing in the lab [00:13:00] and using more experimental approaches. Um, but I think it's a, a, museums are obviously a really great resource and they're now like with our ability to sequence DNA from specimens that are in museums, it's actually like a new way forward in terms of looking at those kinds of patterns. Yeah. So you mentioned that a lot of your research takes place in the lab. Can you paint a picture of what that means? What does the lab you, what does your lab look like? Yeah, so I do, I do both molecular work and I also do a lot [00:13:30] of computational work. And actually I do more computational work now than I do molecular.

Speaker 2: So it's a lot of looking at DNA sequences and comparing them and trying to find patterns that are, that exist in the data. So. And how do you get those DNA sequences? So we sequence tissue from individuals. So like I said, I've crossed mice in the lab and then I'll take tissues from them and we'll sequence them. Um, and then we can use that data to make comparisons. Is there a specific tissue that is more useful for [00:14:00] your work than others? Yeah. So like I said, I work on re hybrid sterility. So the testes are the tissue that I've centrally been using. And one of the reasons is that the reason for hybrid sterility, in this case, it's actually male hybrid sterility. It's not female hybrid sterility. And so the males have like reduced testes weight, they have low sperm count, theirs doesn't move the way regular sperm does.

Speaker 2: They have all these problems that are happening in the testes. And so that's one reason that I'm, I actually look at expression [00:14:30] of genes in the testes between um, fertile and sterile individuals to see if there are differences there. So how do you look at gene expression? That seems like a tough topic. What you can do is you can sequence a RNA, which is the intermediate product between DNA and protein. And so that is basically a proxy for how a gene is being expressed. So if you produce more RNA from m RNA from a gene than it's being expressed at a higher level. And so basically you can

sequence [00:15:00] that and look at the level. Basically you get these stretches of letters and you can use the number of those stretches to figure out how much something is being expressed.

Speaker 1: Okay. So it sounds very complicated, but let me backtrack a little bit. So do these mice that are fertile and infertile, do they have the same genes in general?

Speaker 2: Yes, they do. Have they have all the same jeans I think, yeah, something that makes me maybe this a little bit easier to understand is that basically [00:15:30] almost all cells in your body have the same genetic material, but obviously your skin looks very different than your, like a skin cell looks very different than a liver cell. And the reason for that is because of how your genes are being turned on and off in those different cell types. And so that's called gene expression. And so if genes in a hybrid that is sterile are being turned down or turned off in a way that's causing that, like all those problems I mentioned, like the, the lowered sperm count [00:16:00] and the messed up sperm and et Cetera, et Cetera, like that's something that we can look at.

Speaker 1: So we might be able to imagine, maybe like a football game, for example, where there are people in all of the seats, but then they ask them to hold up signs at different times. And if there's a certain, you know, people in certain seats lift up their signs, you get one message, and if they are people in other seats lift up other signs, you get a different message. So they're all there, but you can get different message based on who's participating. Yeah, that's a great metaphor. That's very much like what [00:16:30] it's like. Okay. And so you're trying to figure out which genes are participating in making these males infertile. Yes. Yes. So do you have any, uh, do you have any like, cool results you can share with us?

Speaker 2: Yeah, so we'd, like I said, we compare these, um, sterile males with half, um, fertile males. And we found actually a whole list of genes that, um, had interesting expression patterns. And I think one of the most interesting things is that expression is not necessarily the thing that could be messed up when you look at, um, uh, [00:17:00] hybrids. It could be, uh, a coding change, right in the DNA that changes the structure of a protein. So like maybe you're just creating the wrong protein component versus I'm turning on the gene and turning off a gene, which would be gene expression. And that's been an ongoing debate in between scientists about whether one of these can be more important to these kinds of processes. Is it going to be changes in like structural proteins or is it going to be changes in how these proteins are just being expressed, how they're being modulated. And so it was just interesting [00:17:30] to us that we saw these changes in expression that were associated with sterility, that were really unique to sterile hybrids. And a lot of these were associated with specific expression patterns where there were multiple changes. And that's um, telling to us because there's a hypothesis that to have hybrid sterility, you need to have at least two interacting to cause hybrid sterility.

Speaker 1: So do you need to changes or not or, yeah, that's a hypothesis. You're still testing.

Speaker 2: Um, so that's a, that's a, [00:18:00] what I'm talking about is this is a model called the de Jensky Bateson Mueller model. And, um, it's basically the idea that like, you wouldn't expect if you had two species diverging, you wouldn't expect them to go through intermediate states of like being sterile themselves to become reproductively isolated from the other species. So you wouldn't expect one species to become sterile so that and then become unsterile. And then that [00:18:30] was the reason for why there's sterility popping up, you know, between them. And that's kind of the basis, and I'm trying to simplify this as much as possible, but that's kind of the basis for how we think speciation proceeds is that it's changes in interacting illegals that cause problems in the hybrid. But these changes have never been seen in the lineages alone.

Speaker 1: Okay. I think I'm balling you. Okay. But another question. So I mean, with the globalization that we see in the world today, it's unlikely that [00:19:00] humans are going to become different species, right? I mean, we're all interbreeding with each other. So does your work have any direct applications to humans? Could you look at sterility in humans for example? Or are you just trying to understand basic science, how evolution works? What, what is your ambition?

Speaker 2: Yeah, so I think, um, this, I think this is a clickable on many levels. I think it has, this is a big basic science question of like just how does the life on Earth we see today? How has that arisen? That's a big basic science question. I think [00:19:30] that chiefly is my interest. However, what we're learning about, um, hybrid male sterility is very relevant for human sterility and there's a reason we study house mice and it's not just because they're a good model for looking at sterility because of this hybrid zone that they form in Europe. It's also because they're a premier biomedical model system. They are something that has been used for a long time as a proxy for looking at things in humans. And so a lot of the resources we have developed from mice are so that we can relate that [00:20:00] information to humans.

Speaker 1: So, I mean, I know that mice are more closely related to humans and a lot of other mammals, but it still seems like they're pretty different. So how can you take things that you learn in mice and apply them to humans? Why does that work?

Speaker 2: Absolutely. That's a good question. And so I'll just back up and say that one of the reasons we use mice rather than something that's more closely related to humans is for uh, you know, a chimpanzee is more closely related to humans, but there are obviously ethical reasons with using chimpanzees. There's also the fact [00:20:30] that mice can, you can get many generations, at least three or four generations of mice in a single year. You can't get that for a chimpanzee and you can't get that for primates. And so this is like kind of, it's, it's a good proxy because it's a convenient proxy and you can make a lot more proud of progress, a shorter amount of time using something like a mouse versus a

primate, even though a primary, it would be more closely related. That being said, there are broad scale patterns that you see in mice and humans.

Speaker 2: Like, and I'll give you an example from gene expression [00:21:00] is that the expression of my liver is closer to the expression of a mouse liver than the expression of my heart is to my liver. So there are conserved patterns there that can be informative and obviously there are really big and important differences. But by making strides in mice, we're also making strides and understanding human biology. And do ma do mice testes work in pretty much the same way as human testes? Yeah, there are some differences, but they're very similar. Yes. So pretty much, you know, the birds and the bees thing [00:21:30] we can think about as applying to mice as well. Yes. Interesting. Cool. So, uh, it sounds like you're doing a lot of interesting work. And do you work with any undergraduates here? I do. Um, I've worked with a bunch of undergraduates here at Berkeley, which is a great thing about being at Berkeley is there's a lot of excited undergraduates who want to participate in this kind of research.

Speaker 2: So do you have advice for undergraduates who are interested in getting involved in research? Molecular research specifically? Yeah, I mean, so if you're at Berkeley, we have some wonderful [00:22:00] programs like your app that you can get involved with to like find a lab. Alternatively, if you're an undergraduate at any university, talking to your professors and talking to um, tas or GSI is definitely a way you can get like your foot in the door and developing a relationship with those people. Uh, the first research position I had, I got from being in an evolution class and I asked the professor of the evolution class if she had anything available and she was nice enough to be like, yeah. Like, let me see if any of my graduate [00:22:30] students need help with anything. And so I think just being bold and trying to get your foot in the door is the way to do it.

Speaker 2: But when I hear words like, you know, DNA extraction and gene expression and m RNA, those sound scary to me. How, how is it that undergraduates, I mean, should they be afraid that they are not technologically skilled enough to perform these seemingly really tough science experiments? Absolutely not. And I'm like you mentioned, my background [00:23:00] is not, was not initially in DNA. And actually further back, I started college as an art student and I made that transition from being an art student for the first year of college into the sciences. And so I really do think that anyone can do it if they would like to. It's just about like being willing to jump in and experience all of it. What about the general public for people who are listening and they're like, man, you know, I'm just so interested in DNA and molecular regulation, but you know, I just don't know where to [00:23:30] learn more about this. Do you have any suggestions? I mean, there's a lot of, uh, well first of all, there's a lot of great literature out there now. Um, a lot of great popular science books which touch on this. Um, but we also have, uh, at Berkeley, a lot of public lectures that people can attend. And I'm sure this is true for other universities that people can attend to learn more about this. And we have outreach like the science cafe, which people can attend to learn more about this.

Speaker 1: Great. Well I'm always at the end of the show. I offer [00:24:00] like sort of what I call the soapbox segment where uh, I allow the guests to get up and say anything they really want about science. Is there anything that you wish the general public like, you know, knew a little bit more about in terms of science? I mean, it could be anything, anything from go outside and take a hike to like, you know, appreciate basic science or fun Fonda so you know, it really anything so, Huh?

Speaker 2: Yeah. No, I think I'm, I'm very lucky in that [00:24:30] I work on house mice and so there, when people ask me like you just did, like how does this apply to humans? I have an answer, but there are a lot of people who I work with who don't and they work on basic science questions and I think basic science, we need to do basic science. Not just because one day we can apply it to humans, but because we as humans should be interested in how the world around us works and those basic science questions will frequently lead to innovations in technology and innovations in human health, but we should also be doing them and supporting [00:25:00] them just from the basis of getting basic science done.

Speaker 1: I should also ask you, do you feel like your background in art is completely gone or do you still see elements of that in your day to day?

Speaker 2: I, I definitely see elements in that in my day to day. I think being a scientist requires being creative and so I think that's something that's broadly applicable. And I definitely, I, I've met people before who were like, well, I'm just not a science type. I'm a creative person. And I don't think there's actually that dichotomy that really exists.

Speaker 1: I've seen a lot of people in the [inaudible] are pretty good illustrators. Yeah. Comes in [00:25:30] Handy, Huh? Yes. Okay. And just as a last question, anything about your dissertation or your research that we didn't, any last words on that or did we cover it all? I think we're good. Yeah, you still, you still got a little more work to do here at Berkeley, but it sounds like, uh, you're feeling pretty comfortable with your project and your research path. Yeah. Awesome. Well, thank you for being here today, Katya. You've been tuned into the graduates here on KALX Berkeley. My name is Tesla Munson, and today I've been speaking with evolutionary biologist, Katia Mack [00:26:00] from the Department of integrative biology. She's been telling us about her work, understanding DNA and gene regulation in house mice, and in particular, how we get these hybrids and you know, how you get infertility and what does that mean in terms of the evolution of new species here on planet earth. That pretty much sums it up. Right. Awesome. Okay, well thank you again Katia, and we'll be back in two weeks with another episode. Until then, stay tuned. You're listening to k a l x Berkeley.