Andrew Saintsing: Hi, you're tuned into 90.7 FM KALX Berkeley. I am Andrew Saintsing. And this is The Graduates, the interview talk show where we speak to UC Berkeley graduate students about their work here on campus and around the world. Today, I'm joined by Elisa Visher from the Department of Integrative Biology. Welcome to the show Elisa. It's great to have you here. So Elisa, you study viruses, is that correct?

Elisa Visher: Yes, I do. And I kind of always backed back from that statement because while I study viruses, I think a lot of times what people hear when I say that I study viruses is that I study kind of the really important human pathogens that you hear about in the news today. So things like Ebola or the flu or HIV, and I did actually study flu for a while, but right now, what I'm really focusing on is kind of generalizable theories about how infectious diseases and viruses evolve, and also how they shape broader ecological and evolutionary patterns that we see across the globe today.

Saintsing: Okay, interesting. So how do viruses actually shape ecological and environmental patterns that we see?

Visher: So there's a couple of key kind of important observations that viruses and infectious diseases more broadly are implicated in. So a lot of the things that infectious diseases seem to explain, actually have to do with diversity. And so some things that we think that infectious diseases affect are how much genetic diversity is maintained within populations. Um, so there's one theory called the red queen hypothesis. That explains why plants and animals were selected to have sexual reproduction and then infectious diseases and parasites and pests more generally have also been implicated in species diversity patterns. So one of the big patterns that we see across the globe is that tropical regions are a lot, have a lot more species than temperate regions. And there's a lot of possible drivers for that pattern. But one of the possible hypotheses is that these infectious diseases or more generally biotic interactions. So that's just any sort of interaction between living things may be causing there to be more species in the tropics.

Saintsing: Okay. So you mentioned the Red Queen hypothesis. What is, what is that, why is it called that?

Visher: So the Red Queen hypothesis actually comes from Lewis Carroll's Alison Wonderland, and there's this one quote that's in all of the red queen hypothesis papers. And it says it takes all of the running. You can do just to stay in the same place. So that name was the Red Queen hypothesis. That name was actually originally used to describe some patterns in macro evolution. So macro evolution is the study of evolution over millions and millions of years. So pass the dinosaurs through the fish through when things were just single celled organisms, kind of macro evolution is concerned with those patterns, right? And so the Red Queen hypothesis, that name was originally used to try to explain why species went extinct. But later on in the 1980s, the name was kind of co-opted by people studying infectious diseases and parasites to explain why organisms or species more generally have evolved sexual reproduction rather than just clonal reproduction

Saintsing: And clonal reproduction is asexual.

Visher: Yeah. So clonal reproduction is just that you make an exact copy of yourself. And so all your offspring are just exactly you. So when we think about natural selection, kind of one of the key tenants is that the point of natural selection kind of what it works on is your reproductive fitness. So your ability to get your genes into the next generation.

Saintsing: And so ideally you would just want exactly your genes.

Visher: Exactly. So if you're clinical, you're getting a hundred percent of your genes into the next generation, but if you're a sec, if you're sexually reproducing, then only 50% of your genes are getting into each offspring that you make. So that shouldn't be a good thing. No, it shouldn't. Um, so there was a bunch of kind of funny paper titles. Um, one of them I remember is called "Why have sex?" And it's trying, they tried to explain why you would ever want to do that. And so one of the key reasons that you might want to have sexual reproduction is to be able to get your genes into the next generation in different combinations. So rather than having me with brown hair and hazel eyes, maybe for some reason next generation, it would be really bad for my offspring to have hazel eyes, but they still want to have brown hair. And so through sexual reproduction, I could possibly make some offspring with brown eyes and Brown hair.

Saintsing: So sexual reproduction is like taking whatever you have right now, throwing it all against the wall and seeing what sticks.

Visher: Yeah. Well, throwing it in with your mate's genes and see what sticks. Exactly. Yeah. Yeah. So you're just mixing it up, kind of try and get different couple of different combinations and hopefully some of those combinations will be better at the future environment than the exact clone of would be. And so one of the big questions there was what sorts of environments make it so that you really want to mix up your genes that way, because a lot of kind of climate change or seasonal change that happens fairly slowly,

Saintsing: Well, except now, right? With climate change.

Visher: So, I mean, nowadays it actually would probably be really good to be able to switch up your genes very quickly, as fast as you can to keep up with climate change. But historically that hasn't yet. But historically that hasn't always been the case and climate change still is often happening over multiple generations of an organism or not of an organism, multiple generations of a species. And also it tends to be more directional. So that means it's, Oh, it's getting hotter for a long time or it's getting colder for a long time. And sexual selection can only really be selected for an a population if kind of the direction of the selection is changing every single generation. So if one generation it's good for me to have Brown eyes, that must mean that the next generation it's good for me to have hazel eyes and then brown eyes again, and then hazel eyes again. And there's not a lot of things in kind of abiotic. So your temperature, your precipitation, there's not a lot of things in those sorts of selection, selective pressures that change the direction of their selection, every single generation. And so the main thing that people realized might be changing the direction of its selection, every generation where

infectious diseases or pests or parasites more generally, where if you have a virus that's specifically of involved to infect a certain genotype, then being able to change your genotype, every generation will allow for you to escape from that virus because that virus will be trying to evolve, to match whatever genotype is most common in the population. And so if you're clonal, it's really easy for a virus to keep up with the clonal population because viruses and bacteria have much shorter generation times than humans or plants. So a virus will have hundreds and thousands of generations to try to adapt in just one human generation, right? So one way that plants and animals host species can keep up with viral evolution is to be able to sexually recombine their genes to make new combinations. And so that means that whenever the host reproducing, it has a whole new set of genes for the virus to try to catch up to again.

Saintsing: Okay. So viruses are very important for maintaining genetic diversity that we see across the world. And then going back, you also said that viruses play a role in shaping genetic diversity across the world. Differences in species diversity actually is what you said. Across the world. And can you tell us a little bit more about that too?

Visher: Yeah. So one of the patterns that we've seen in nature for a really long time now is that there are way more species in tropical regions than temperate regions. So tropical regions are everything around the equator and temperate regions are the things closer to your North and South poles. And so there's way more species there in the tropics. And there's been a ton of hypotheses for why this might be the reason. So one hypothesis is just that climate has been a lot more stable there. Another hypothesis is that they're just warmer and maybe get more sunlight. And so there's just more energy and resources in the tropics, but another really promising hypothesis is that biotic interactions. So again, interactions between living things are what actually drives this higher diversity in the tropics. So we think that if biotic interactions are stronger or more specialized in the tropics, then that means that there's a advantage to being rare. So one of the big kind of areas that this hypothesis is used is to explain tree diversity. So why do tropical rainforests have so many different species of trees? I mean, this is called the Jansen Connell hypothesis, but one of the reasons that we think that they have so many species of trees is that if biotic interactions are really strong in the tropics, then if a seed lands really close to a seed of a tree in its species, then it will have a lot of negative fitness consequences. So whatever insect herbivores are on that tree might come and eat it. If there's any fungus on the tree of it, same species that it might come and eat it again. And so trees really don't want to be near trees of their same species, which means that kind of rarer trees. So trees where there's just fewer of their same species around have an advantage. And so whole forest ecosystems are much more diverse.

Saintsing: So species maintain rarity. So you're saying viruses drive that, but is that just kind of like a consequence of what you were saying about trying to have this genetic diversity to respond to viruses that as viruses become more intense, there becomes more intense pressure from these viruses that ultimately you're just, speciated, you're actually becoming distinct species in terms of how genetically diverse you're becoming.

Visher: So I think there's a difference in, well, sometimes there's a difference in our hypothesis between what driving speciation. So making diversity and what's maintaining diversity that already exists. So I think a fair number of the hypotheses that are trying to explain tropical species diversity have more to do with the maintenance of that diversity than the generation of that diversity. And so for things like the Jansen Connell hypothesis, so that's again just saying why trees that are rare can have an advantage in a forest because they can escape from pests and parasites that specialize on them. So it's taking those species pairs as already existing and trying to just explain why some of them are more competitive than others rather than necessarily explaining why they are speaciating or creating diversity in the first place.

Saintsing: I see. So it's explaining why we would continue to have diversity in the tropics, but not necessarily how we got the diversity in the first place.

Visher: There's other hypotheses for that.

Saintsing: Right. So you're not arguing that viruses or potentially viruses played a role, but when you talk about viruses and diversity in the tropics, you're more talking about the maintenance of diversity. Yes, I see. Okay. Well, cool. So viruses are really important to evolution. Yeah, they are. This is just a reminder that I'm speaking with Elisa, Visher from the department of integrative biology. How do you actually study these viruses?

Visher: So I personally use a method called experimental evolution. And so that's actually one of the reasons that I really like viruses as a study system is because they evolve so quickly. So what I do in experimental evolution is I take populations into the lab. So my particular model system is a moth and baculovirus model system. So it's just a moth, it's the Indian meal moths. So if you've ever had moths that have invaded your pantry before, eat all your flour, it's that one. So what we do in our lab is we have pots of those moths in our lab and we have vials of viruses and we kind of play at, we play at being God, actually an experiment evolution. We basically set up populations with some sort of, if we want to ask some sort of question, we set up populations of mods and viruses under some different environmental condition. And then we see how they evolve to meet that condition.

Saintsing: I see. Wow. Does it make you feel really powerful?

Visher: Yeah, I really like it. I really like it as a method because you get to have the reality of actually using a living biological thing. So a lot of people in my lab actually are just math petitions. So they do all of their work on their computers and on paper using numbers or really at their level, a lot of letters, but they don't, they can talk about why things might evolve, but they can't prove it in a biological system. I guess.

Saintsing: There's math, but there's no driving process?

Visher: Yeah. Yes. And then you need, yeah, there's math and it could explain what you might expect to evolve and then you have to kind of prove it.

Saintsing: Right.

Visher: In an actual living thing. And so I like to say that I do math with malls because I can basically take those predictions that the mathematicians make about whether an environmental condition. So say whether your population is genetically diverse or not. So I can take that math. And then I can ask what a virus that's evolving in a genetically homogenous system. So there's only one genotype everything's clonal evolve differently than a virus that's evolving in a genetically diverse host population. And so I take that math. I find my moths, I make one population that's genetically diverse. I make another population. That's just all one genotype. And then I can put my virus into those two different populations and see how it evolves in response. So what I do kind of sits between the math and then also more kind of the more realistic field work. So experimental evolution still has a level of non-reality to it because we're kind of making up these environmental conditions and we're putting things in a lab and we're just trying to make everything except our exact question that we're asking as consistent as possible. And so that's where it has a bit more power sometimes than field work because in field work, you might have a question about how host genetic diversity affects how a virus evolves, but any sort of system that you find in the field. So if you could just go out into nature or to a farm, there's going to be a ton more variables involved between non genetically diverse populations and genetically diverse populations. So there might be differences in temperature. There might be a differences in precipitation. You might have to look at entirely different species to be able to compare, but with experimental evolution in the lab, I can basically isolate my one variable of interest and test only that one.

Saintsing: Okay. So now you do experimental evolution work on moths. Was that just kind of a project you came to here? Or, I mean, how did you end up working on this virus and this moth?

Visher: Yeah, so I've done experimental evolution for a bit. I did a little bit in my undergraduate, but where I actually started was in biological anthropology. So I like many...

Saintsing: So you did use to study humans?

Visher: I did use to study humans and I've studied human and I don't hate humans in theory. I will always keep some sort of human bent to my work. I'm just right now, I'm studying very things, very far removed, very basic science, right. And so I like many college freshmen originally wanted to be a doctor. I think it's, it's, it's obviously it's something that has a lot of career stability. It's something that kind of allows you to do a bit of science, but a little bit through my freshman year, I started actually shadowing doctors and I realized that it didn't allow that being in medicine as a MD probably wouldn't allow me to kind of explore questions the way that I wanted to. So I had a, I guess, crisis and I was looking to see what else I might want to do. And so I don't remember exactly when I just remember being in my bed in my freshmen dorm and being like, what do I want to do? And remembering this time in high school, where I was going to the California Academy of Sciences with my family, and I had recently seen on the news that, Ardi was

a skeleton that was found actually by a professor here at Berkeley, and already was at that point, the earliest hominid fossil that had ever been discovered. And I was really excited by this. I was reading all the news and I kept on having all these questions about why humans evolved. And I think that experience was actually the first time that I was really exposed to real science because as I was trying to figure out, well, why did Ardi evolve? Like I was trying to look at it like I was doing my high school science classes, clearly the answer should be in a textbook. Right. Um, and I found that there was no answer. That's what the scientists were doing was actually trying to find these answers. And for some reason, as I was looking back on this, my freshman year, this idea that I could be involved in trying to find the answers in being involved in like a very creative process, honestly, that seemed really exciting to me. So I joined a biological anthropology lab that summer. In that lab, I wasn't working on human evolution. I was working on primate evolution. What, what projects was I doing? I was, my first project was looking at chimpanzee poop and trying to kind of use it to track chimpanzees around this natural national forest. I never, no, I never saw chimpanzee. I just got vials of it's poop. And then I played with it in the lab.

Saintsing: Wait, were you in Africa?

Visher: No.

Saintsing: Oh.

Visher: No, just vials of poop in the freezer pulled them out.

Saintsing: Well, you got to start somewhere.

Visher: Yeah. Tried to get the DNA out of it and that entire project failed, but I stuck with it even though I didn't get any data from that project. I really liked the process, I guess. So I continued in biological anthropology for a couple years. And in my classes I started also learning about more recent human genetic evolution and how more recent human genetic evolution was also implicated in kind of genetic diseases of humans and kind of differences in how different populations dealt with infectious diseases. And that seemed really interesting to me. So at that point I started taking more classes in evolutionary medicine and at one point I was like, so I've been learning all of this from the human side. I can either do a lot of genetics in the lab, or I can, I guess, try to like dig up human fossils in the, in the field, or I'm also really interested in how evolution impacts infectious diseases. So I decided to join a lab that would allow me to look at how evolution impacts infectious diseases from the viruses side, rather than just the human immune system side. So I joined another lab my junior year and in that lab was actually where I got started with experimental evolution. So that lab was working with viruses and bacteria. So they were working with bacteria phage, which is a type of virus that infects and kills bacteria. And that lab, I started doing experimental evolution on these very kind of like basic science, theoretical principles. And I really loved it. I really loved the methods of experimental evolution. I really liked how it seems like I could be very creative with what questions I came up with and also kind of designing experiments to try to test them. And

so I decided that I wanted to stay on the infectious disease side of things. Um, and then once I graduated college, I didn't want to go straight to graduate school. I kind of had decided I'd made my final decision that I wanted to do infectious diseases kind of towards the end of things a little bit past when I would have wanted to start applying to graduate school. Right. And I also just wanted a little bit more experience and emotional maturity, I guess, before going into graduate school. So I applied to be a research technician and I joined a lab at University of Michigan that was studying flu evolution because I also wanted to explore what more applied infectious disease evolution looked like since I had done very basic science, infectious disease evolution. And so I worked with flu for two years, and then I started applying to graduate school and came here to Berkeley.

Saintsing: How'd you pick Berkeley?

Visher: Oh dear, should I say this? So I made some interesting decisions, I'll say applying to graduate school. Um, so I started emailing a lot of professors and getting in contact with them. And I think at this point I had decided that I wanted to go back into more basic science, infectious disease evolution. So I realized that I really liked being the one to come up with these more theoretical questions rather than trying to explain actual applied infectious disease systems. And so, as I was looking around at different graduate schools, my current PI Mike Boots had actually just been hired at Berkeley. So I had been checking Berkeley's website a couple of times because I'm from California, it's a very good department. I was like, well, this would be a great school. If it has someone there for me, when the first couple of times it didn't have anyone here for me, but then kind of all at once, both Mike and Brit, Brit Koskella, were hired and suddenly Berkeley seemed like a really great option. And so when I was reading about Mike Boots's work, I really liked kind of the type of question he was asking the fact that the lab looked at these very theoretical infectious disease questions. And I ended up Skyping with him. I really liked the model system. I like the moths. There are, they're a pretty good system. You don't feel as bad about killing them as you do with mice. You can see them a little bit better than you can see bacteria and bacteria phage. So by the time applications came around, I actually only applied to Mike Boots, his lab, which was the choice. I'm not sure I would recommend it broadly,

Saintsing: But being in touch with them, you felt confident.

Visher: Yeah. I'd been in touch with him for quite a bit at this point. And I personally know that I'm very stubborn and my mother has told me that I'm very stubborn. And at that point I just really wanted to come to the Boot's lab. And I figured if it didn't work out the first year, I would make more sensible decisions. The second year I had applied to more labs and luckily I got in and I came here.

Saintsing: That sounds like a good way to get here. And now you're here and you're investigating experimental evolution. And you’re in your third year,

Visher: I'm in my third year. Yes.

Saintsing: And, do you have plans for life after graduate school?

Visher: What happens afterwards. Um, I will say I have a lot of plans just cause I'm in, I am at the type of person who will plan out three 10 year plans and then make rapid decisions between them. But yeah, so I think I personally really want to stay in academia. I want to stay as a research professor. Um, of course that's a very tough career path to get into. So, you know, I might have to make some other choices, but right now I'm definitely, you know, trying to get my PhD in the next two to three years go on to do a postdoc, maybe two, maybe more, I don't know,

Saintsing: Just because that's the way it works in the job market?

Visher: Yeah. It's, I mean, it's the way it works. And then I also, I think there is a lot of value in exposing yourself to different lab systems, to different lab cultures, to like different both intellectual cultures. And also I guess more like, you know, mentorship and those sorts of cultures that you can, I guess, create an individual identity for yourself as a researcher and be able to kind of combine the intellectual perspectives of a number of different groups to make your own research program. So I'm personally actually pretty excited about doing postdocs and kind of doing random things, learning new things, doing cool science.

Saintsing: Yeah. Yeah, that sounds cool. And then after that you want to get an academic job, a tenure track professorship?

Visher: Ideally. Yeah. We'll see how that goes.

Saintsing: Well, I wish you the best of luck in that pursuit. Uh we're about out of time, usually, uh, at the end of the program, we offer the guest time to make any points about, um, their science or social issues or anything you'd like to talk about. So are there any statements you'd like to leave the audience with?

Visher: Let's see. Oh, I gues I know the statement I'll leave the audience with. So I think coming from an anthropology background, I did a lot of social sciences and I also kind of studied a fair bit in medical anthropology. And I think we often think that our biology, that biology, that we study is really apolitical and divorced from kind of social issues. But I would like to say that infectious diseases are inherently political. And a lot of the pressures that you see from infectious diseases across the world are really unevenly, distributed along axes of power. You see things like huge infectious disease burdens in parts of Africa and parts of Southeast Asia. You see that infectious diseases are worse with political instability, with emerging infectious diseases like HIV. You found, you see that we had an epidemic that reached across the globe and infected millions of people before political entities did anything about it because it was infecting people who were already marginalized by society. So I think in my personal work, even though I am very much on the theoretical end of these things, scientists need to pay attention to society, to humans, to marginalized people, and actually integrate them into what we do and kind of integrate the learnings of social sciences into our biological science.

Saintsing: Okay. So we can't avoid politics and science.

Visher: We cannot avoid politics in science or medicine.

Saintsing: Right, yeah. That's an excellent point. Thank you so much for being here, Elisa. I am Andrew Saintsing and I've been speaking with Elisa Visher. She's told us about her work and experimental evolution to understand how viruses can, uh, lead to genetic diversity in populations and maintain species diversity in the world. Tune in, in two weeks for the next episode of The Graduates.