Episode 117: Bastian Minkenberg

# KL: Katie Linder

# BM: Bastian Minkenberg

# KL: You’re listening to “Research in Action”: episode one hundred and seventeen.

# [intro music]

# Segment 1:

# KL: Welcome to “Research in Action,” a weekly podcast where you can hear about topics and issues related to research in higher education from experts across a range of disciplines. I’m your host, Dr. Katie Linder, director of research at Oregon State University Ecampus. Along with every episode, we post show notes with links to resources mentioned in the episode, full transcript, and an instructor guide for incorporating the episode into your courses. Visit the show’s website at ecampus.oregonstate.edu/podcast to find all of these resources.

On this episode, I am joined by Dr. Bastian Minkenberg, a postdoctoral scholar in the Innovative Genomics Institute’s agricultural genomics branch. He started working on genome-editing in the food staple rice during his time as a Beachell-Borlaug International Scholar at Penn State. He now continues his efforts to improve disease resistance and yield of crops at UC Berkeley. Bastian is originally from Germany and obtained his bachelor and master degrees at RWTH Aachen University. His goal during his time at the Innovative Genomics Institute is to develop tools for precise genome-editing and accelerated plant breeding using advanced plant tissue culture and CRISPR methods. Another interest is to develop bioinformatic tools to avoid off-target editing in plants and to increase on-target activity. As ultimate goal, Bastian tries to develop an efficient gene repair system to easily change genetic information in crops to make them healthier and sturdier.

Thanks for joining me on the show today, Bastian.

**BM:** Thank you very much for having me.

**KL:** So I am really interested to dive into genome editing, which I have to admit I know very little about – so let’s start at the begging. First, what’s a genome?

**BM:** So a genome is essentially the summary of all genes for an organism, but what I always want to point out is that there’s nothing like the genome. Every person can have a slightly different genome. There are mutations happening all of the time. So every individual or every organism has its own genome. And what we usually call a genome is a representation of one of these individuals.

**KL:** Okay. And when we start to talk about genome editing, what exactly is going on there?

**BM:** Yeah. So essentially in the genome are the genes –and in 2012 there was a new technology invented called CRISPR cas9. And CRISPR cas9 worked like molecular scissors, so you can actually cut DNA in specific places. And after you make the cut, the cell will recognize that there wasn’t DNA damage, and then it will try to repair that DNA. And we as genome editing scientists or researchers try to use—to hijack this DNA repair mechanism to make changes to the genes that we want to do.

**KL:**  Let’s talk a little bit – I’d like to dive a little deeper into what are some of the reasons you might do this genome editing? You know, what are some of the outcomes you’re hoping for?

**BM:** So one of the reason that people are so excited about genome editing is that a lot of diseases in humans are based on some mistakes or errors that we call mutations in their genes and their DNA, and with genome editing we are now able to repair these DNA segments that are, that have errors in specific individuals and heal diseases that are genetically inherited.

**KL:** So is this something that is only worked on when we’re thinking about human genomes and human DNA, or is this something that has further application than that?

**BM:** So the applications are really widespread. For example, I myself work in agriculture, and I work on rice. Rice is one of the most important crops in the world and it feeds almost half of the world’s population, and there of course are a lot of diseases that plants like rice can get. And we can use the same techniques to repair genes in plants that make them more susceptible to disease, and if we repair them then they will be more resistant, and therefore will have higher yields, and also the product – the grain will be healthier because they need to use less pesticides and also less pathogens that can cause disease on plants.

**KL:** Okay so, I know that part of your work is also with gene insertion, and is this – what is kind of the relationship between that and genome editing? I mean, is it kind of like cutting and pasting where you’re cutting something out and inserting something else? Or is it something completely different?

**BM:** So essentially there – there are two ways that we do genome editing. One way is where we just cut the DNA, and the cell will make some errors and we’ll try to repair it, and we’ll just remove a few pieces or we’ll insert some bit of the pieces, and then this gene is removed and we have a so called “knockout”. And then we can look for the plant, what removing the gene will actually cause to the plant. But what we sometimes want to do is we want to take a gene that we know has many benefits—for example, gives resistance to a plant—and we want to insert it at a specific place inside of the plant genome where we know if we insert it there will have a good effect, and also where we know it will be easy [*indiscernible*] Depending on where you place this insert in the genome, they sometimes have trouble to get inherited into the next generations. But if you put into a place that is easy to recombine, then it will inherited in a higher frequency.

**KL:** Okay so I could imagine that there might be parts of this gene editing work that are a little bit controversial or that maybe not everyone agrees with. Is that, are there tensions kind of within that field in terms of what people think in making these sorts of changes to genomes?

**BM:** Hm yeah. So there are two main concerns. I would say one concern is on the technology side. So when you actually have this genome editing device and you try to make a cut, you cannot also avoid that it will cut at other places. Usually at a very low frequency, but if it cuts at places that you don’t want it to cut you could have some side effects that you also don’t want. And the other part is that a lot of people already start to discuss the possibility of, for example, designer babies, and to edit the human genome in a way where you edit the embryo and make a change prominent. And right now they are actually discussing in the science field about how we should proceed, what kind of safety measurements we need, and what is the best way to proceed so that we can get the benefits, but also do it in a safe way.

**KL:** Okay so, when you’re focusing on this kind of genome editing with rice. What are some of the research questions you’re kind of trying to address or maybe problems that you’re trying to solve through this work?

**BM:** So one of the problems I worked on during my Ph.D. thesis was actually that there were genes known in rice that were involved in signaling for stress response. And we wanted to know if we removed these genes, what ability [*indiscernible*] or to detect stress, and then we know this gene is important for say broad stress, or this gene is important for disease resistance. And many times, those genes are so similar that if you remove only one, you’re going to end up with not a very clear picture of what is going on because the other gene that is so similar could just take over its function. So for example, what we then did during my Ph.D. thesis was to then remove four of these genes simultaneously. Before you couldn’t really do that, but now with his new genome technology we can now even not just go to one place in the genome and change it, we can go to several places. So for example, there was very useful so we could remove all four genes, or combinations of them – or as two combinations, and we had a more powerful way to actually see what is the effect of removing these genes from the plant. Another research question we are looking into right now at the Innovative Genomics Institute is very applied. We mainly try to improve the way people breed plants – right now it’s a very slow and cumbersome process, so we want to use this technique to speed that up. And also we want to a take a so called of elite [*indiscernible*]. It’s a [*indiscernible*] that comes from the farmer schooling, and we want to try to make these sturdier to increase the tolerance to draw, to increase resistance to disease, and we want to try to do this directly in [*indiscernible*], so they can then go right directly to the farmers and they can benefit from it.

**KL:** Okay, so you mentioned CRISPR methods as one way that you’re working with this, and that seems to be a relatively newer technology. I think you said it came out in about 2012. What are the other kinds of tools that you’re using to do this work? What’s kind of involved in it?

**BM:** So we here use CRISPR cas9, because it’s the easiest tool to use. But from a history standpoint there are at least three other tools that you could use. They all have acronyms or names that are derived from signs. For example, ones are called zinc finger nuclease, other ones are called transcription activator-like nucleases and others are called mega nucleases. What they all have in common is that they can all cut DNA at a very specific point. And these older technologies – they actually require us to engineer protein in a way to recognize DNA, and that can be sometimes tricky and it’s not as easy to predict, but with this new technology, we actually don’t use a protein with DNA interaction. We use this cas9 protein that’s actually guided by a piece of RNA, which chemically is very, very similar to DNA, and it’s very easy to predict how the RNA will bind to the DNA. And this makes this new technology very easy to use, very easy to reprogram for a new sight of interest. And this program also allows us to, like the case we discussed before, to target four genes instead of only one.

**KL:** Well Bastian, this is way outside of my wheel house, but it is super fascinating. We’re going to take a brief break, when we come back we’ll talk a little bit more about the practical applications of science in this work. Back in a moment.

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# Segment 2:

**KL:** Bastian, I’m excited to talk with you about some of the practical applications with the work that you’re doing, and I know that at least one of the stakeholder groups is plant breeders. I’m wondering if you could talk about how this work is kind of practically applied with plant breeders or with other stakeholders find it to be really useful.

**BM:** Yes, so one of the problems that we actually have right now is that plant breeding takes a long time. At the moment, we achieve new traits in our crops by finding, for example, white relatives of these plants and then we will try to force them to cross-breed with our crop [*indiscernible*]. And then we will go through a process where we will cross these plants many times themselves, and we screen for the specific effect we are looking for that will be, for example, a new gene to control disease that gives the plant disease resistance, and then after you found this gene and you cross it into the crop species, that’s just the beginning. You found the gene, and now you have a new breeding program with again a lot of crosses just to move it into these elite [*indiscernible*]. And if you think about the whole timeline from let’s say, the idea to find this gene, for example, for submergence in rice – there are some areas where rice will be completely flooded with water, and there actually was a gene identified that makes the plants sturdier and they will not die so easily when they are submerged with water. So this took from the 60’s or even the 50’s until I think it was the 80’s or the 90’s. So we’re talking here decades that we use or that we need right now to find these genes and to make these improvements and to actually bring them to the farmer. And what we can offer right now is that we have technologies where you can skip a lot of these steps, especially these crossing steps where you need to cross plants, wait until they set seeds, then go to the next generation and cross them again. And what we do right now is, we take directly the material that the farmer uses and then use molecular scissor—the genome editing device, like CRISPR cas9, to bring this new resistant gene from our white relative directly into our crop plant without the need for all of the crossing. Essentially you want to experiment, instead of talking decades we’re talking maybe one or two years.

**KL:** Okay so that’s a huge impact on just the timeline, so I’m thinking it could be really useful for you to have a sense of what plant breeders or maybe other stakeholders really need – what are the kinds of problems that they are trying to solve. To what degree are those needs of plant breeders or others influencing what you’re doing in the lab? Or are these just well-established problems that you’re trying to work through?

**BM:** So we try to keep in conversation with a lot of people. For example, just three weeks ago Gurdev Khush came to visit us, and we let him – and he is the recipient of the World Food Prize and also the World Prize for Agriculture. And he got this actually for rice breeding for forty years in the International Rice Research Institute in the Philippines. And we want people like him to tell us actually the history of how breeding was done in the early years, what were the big technologies that improved the breeding for them? And also we asked them, what kind of new technologies do you think would be useful for you? And so gene insertion is something that people of course always, always warned, and um in addition to inviting people for seminars, we also try to actually visit people. I myself was at a nursery recently. The nursery approached me and asked about the genome technology and I drove down to visit them and we talked and I was asking about what actually, what they actually need, and what is important for them. And they, for example, were looking at improving their so-called tissue culture, livability in plants, where is a technique to sometimes propagate pants and also to remove viruses in plants where plants will be cultured on a [*indiscernible*] and then are generated into big full grown plants. And they were interested in using technology to improve the system and to make some plants easier to go into the central purchase system.

**KL:** Okay so you have kind of this front end information that you’re getting from these different stakeholder groups about maybe what their needs are and what you need to be working on, but then you also have this back end of once you’ve actually discovered something, or made a change, or created something that could be impactful that they need to know about it. So how are you ensuring that the right stakeholders end up knowing about the results of the work of what you’re doing?

**BM:** One way we ensure this is we actually work together with a lot of international institutes. There is for example, CIAT – that’s the Center for Tropical Agriculture. Then there’s CIMMYT, that’s the institute for wheat and maize breeding, that is Mexico. For example, lathia was talking to genlo, who was in charge of the sweet potato program in Africa. So we actually make sure that a lot of our projects are within collaboration of these international institutes, and they then will help us to disseminate the seeds let’s say the end product to all of the people and farmers in this country that actually need them.

**KL:** And I’m wondering, to what degree is there translation needed between the kind of science that you’re doing and the results? I mean is it – is the output coming to them in a way that they can understand, or are you needing to kind of further explain what needs to happen based on what you’ve learned?

**BM:** So what we do mainly here is doing the research, and improving the methods and the technology, and we also try to create new plant material that is more resistant and more tolerant. But then we actually go ahead and send the seeds of this new material to our collaborators, let’s say in Mexico, and they will grow these seeds and do field evaluations, because they are the expert for how plants should behave in the field. Many times we may get a good result in the greenhouse and it may not translate into the field where there’s a lot more stress and the soil is different. And they actually make sure that the plants perform how they would like them before they then go out to the farmers and introduce these new seeds.

**KL:** So I’m curious Bastian, if you could describe what it was that got you interested in plant sciences. Because you probably could have gone into the direction of medicine or working with human genomes, but you chose this other direction. What lead you that way?

**BM:** Yes. Actually, when I was young I was more interested in human biology. And I can remember my parents gave me a book about electro microscopy, when there was just a lot of immune cells inside, or I actually got my first own microscope at a very young age and I just looked at – yeah –the smaller microbes that you can see in a microscope, and I didn’t really think about plants. And when I started to take biology, it was actually mandatory for us to also learn about plants and plant biology, and that was the moment when I realized in these lectures that plants are actually alive. It may sound stupid now, but a lot of people I think they just walk around and they look at plants, and they don’t realize how much they actually do. And they have these completely different strategies to solve problems. For example, the water problem or how they make food—they actually take CO2 from the air and sunlight, and water and they make their own food. And I wasn’t really aware of that, and after learning this I discovered that there are so many awesome ways that a plant deals with stress, and it’s much more interesting to learn about plants than it is to learn about me, because I’m already living the human experience.

**KL:** That is super interesting. We’re going to take another brief break, when we come back we’ll hear a little bit more from Bastian about mentoring. Back in a moment.

# Segment 3:

**KL:** Bastian, I know that you’re really interested in the concept of mentoring. What has lead you to find this to be so important?

**BM:** Yeah. During my time at Penn State as a Ph.D. student, I found out that actually a lot of skills that you need to succeed in science are not really conveyed in classes, and it becomes really important to find somebody to teach you that. We’re somewhat expected to absorb this out of thin air, and all of these leadership skills or how to deal when something goes wrong or how to deal with frustration. But actually I think we can start to have the conversation now a days, and start to develop more workshops for students who learn these skills as some sort of formal way in their education, and make sure that they know everything that they need to succeed later.

**KL:** Well I know that – and I mean, we really set up the graduate school structure as having an advisor or having a committee that are supposed to be helping you through this, but maybe an advisor can’t give you absolutely everything you need. I know that, you know, when you were in grad school you tried to assemble a team of people to try to help you do this. How did you go about assembling that team? How did you choose the people who were going to be the best mentors for you?

**BM:** One thing that I try to do, is I try to do networking with people and a lot of different uh – a lot of different situations. Like I started to talk to people in industry. I was lucky that during my masters I got a sponsorship from Bayer, and when I came to the U.S.A I wrote and email to them and I said, “I will move to the U.S.A., I am a Bayer scholar, can you please give me contact information of someone that is working in Bayer in U.S.A?” And I didn’t really expect it, but this actually lead a really nice experience for me. Um I met [*indiscernible*] Hwang, who was really awesome, and he invited me to Bayer to actually give a seminar there. I was just a two year grad student at that time and I gave a seminar in front of a company. And he took me to three different companies in that area, and he introduced me to all of his friends, and I really learned a lot. Another example is when I tried to get a speaker to Penn State to tell us more about her work in Africa, there wasn’t really much money there. And I did know a dean from our college, because we actually did go together on a conference about genome editing, and I knew he knows the system and how everything works. So I approached him, I told him about my idea, and he was really helpful in teaching me how to actually find money to invite somebody, how to find the people that help you to advertise. And for example, my own professor, he would never be able to tell me about industry, or he maybe would have been able to help me with eh invitation, but this was a case where we really didn’t know where to take the money from, and the dean was able to help us with that. And I think it’s just really important to have one person, because we encounter so many problems in our work and in our life, and we encounter so many different situations, that it’s just not enough to have one person that can help you out and give you advice – you need to have several people in different situations.

**KL:** So you had mentioned earlier doing workshops for graduate students to kind of help them understand. What are some of the skills that you think graduate students and researchers need to have to help them develop these effective mentoring relationships? What would help them to create these networks for themselves?

**BM:** So one thing that I have found really useful for myself is actually, I was in two workshops. One work shop was given by Carolee Bull, she’s right now the Department Head of Plant Pathology and Environmental Microbiology at Penn State. And a few things Carolee Bull was teaching us were especially how you can mentor yourself, and it was a lot, and well, for example, 41 – 42 questions that were designed to help you think about what is important to you and what you really care about, and then at the end, we use these guided questions to have a mission statement, and you could use this mission statement to mentor yourself and look at decisions you make, and then to fit them into my mission or not. Her emphasis was very much on making sure that you are satisfied and that you feel that you are in the right spot for your work, because she felt like you can be the most productive when you’re doing something you’re actually passionate about. And I think that’s very true, because sadly now a days, we spend most of our time not with our family members, we spend it at work. And if you don’t like your work, that’s a really bad place to be.

**KL:** Hm. Now I know that you have also been engaged in an international scholars program. I’m wondering what role mentoring has played in that as you have been traveling internationally and doing international work as a researcher and as a scholar.

**BM:** So this program I use essentially for both: to get myself more mentoring and also to give mentoring. And one of the things that I learned from this scholarship was, for example, how to give presentations and how to behave professionally. We actually got invited to Iowa to a company that trains [*indiscernible*] persons and trains companies, and they gave us a workshop over two weekends of how to speak, and how to take questions, how to take good hostile questions especially, and also how to network effectively. And then, in addition to receiving more of these methods, I actually went to China for some of my research, and while I was there I was asked to talk about mentorship and I was asked to talk about the workshop the Carolee Bull is giving. And I set up a mini workshop that was instead of going half day, only going two hours, and I tried to convey some of these skills that Dr. Bull to me to these Chinese students, and they were very thankful. We had a lot of discussions afterward – for them, what is the best way to move forward in their own career, because they have some special um – some special obstacles that we maybe don’t have here.

**KL:** So given all of this professional development that you’ve had for yourself around mentoring, what have you learned about what it takes to be an effective mentor yourself?

**BM:** So one of the things that I always try to make sure is when I work with undergrads, is that they’re not scared to make mistakes. Um I know sometimes, at least I myself, when I was young, and I was doing something, and something wrong happened I felt terrible, I felt ashamed, I didn’t really know how to talk to my advisor at the time point. And this can cause a lot of trouble, because you might end up with let’s say, not going in a specific direction, because it went wrong, or you were too scared to talk about it, and actually this direction might lead to something very useful. So I always try to tell my students, they can mess up whatever they want as long as they tell me, and then we can go on trouble shoot, and we can go ahead and try to find a way to reach the goal, and they don’t need to give up just because they encounter a difficulty.

**KL:** Well this has been so valuable to talk about. I want to thank you so much, Bastian, for coming on the show and for sharing your work with genome editing, and also how you’re practically applying that work to a range of stakeholder groups. Thanks so much for coming on the show!

**BM:** Thank you very much for having me!

**KL:** Thanks also to our listeners for joining us on this week’s episode of “Research in Action.” I’m Katie Linder, and we’ll be back next week with a new episode

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