

## Transcript: Plant Breeding Stories Podcast S1E2 - Phytoform Labs



[Podcast theme tune plays]

Hannah Senior:

Welcome to this episode of The Plant Breeding Stories Podcast, where I talk to leading lights in plant breeding, asking what they do, what makes them tick, and what fascinates them about the world of plants. I'm your host, Hannah Senior of PBS International, world leaders in pollination control. We design and produce specialist pollination bags and tents used by plant breeders and seed producers all around the world and through this, I've been privileged to get a unique perspective on how plant breeding globally affects our diets, farming systems, and the environment. I'm excited to share a little of this with you as we meet some of the amazing people who make plant breeding their life's work.

Hannah Senior:

This week, I'm talking to Will Pelton and Nick Kral of Phytoform Labs Limited. In this episode, Will and Nick discuss their journey in starting a venture capital-backed company, bringing artificial intelligence to facilitate genome editing. They discuss finding a way to exploit the new avenues that advances in plant breeding technology are opening up, the way that they put their values at the heart of the business, and developing new varieties to help improve the sustainability of agriculture and combat climate change. I hope you enjoy it.

[Podcast theme tune fades out]

Hannah Senior:

Nick, Will, why don't you start by just telling me a little bit about your background. Were you interested in plants from early on?

Nick Kral:

I'm Nick, and I grew up actually in Slovakia and then moved to Belgium before eventually ending up in London, UK, for my undergraduate and graduate studies. I wouldn't really say I was actually interested in plants from early on, to be honest. I studied microbiology and sort of genetic engineering too, and sort of as I was progressing in my university studies, I ended up bumping into plants and realizing how sort of awesome they were. So yeah, that's me.

Will Pelton:

Hi. I'm Will. I grew up in the UK, and I've been pretty plant-obsessed from quite a young age. My grandfather was a farmer. His was actually dairy and arable. So I was spending summers on the farm, and then I think most of my family are pretty into gardening. It's a very sort of British hobby, having an allotment, that sort of thing. And I've always been kind of interested in the sort of self-reliance of plants and the fact that with just a seed, you can basically feed yourself, which is a pretty incredible thing, I think. So that sort of drove me to pursue plants as a potential career, which I didn't initially realize was an option.

Hannah Senior :

So the two did your undergraduate degrees at separate institutions but it was a Masters in Molecular Biology at Imperial College that brought you together. Is that right?

Will Pelton:

Yeah, yeah. It was a heavily subscribed course, with six of us, I think? [Will & Nick laugh]

Hannah Senior :

When did the idea of starting a business together develop? Take me through that journey a little bit, because it's one thing to be studying together and to be friends. It's another thing to then decide, A, on an idea and, B, act on that idea.

Will Pelton:

[To Nick] I think you came up with originally...

Nick Kral:

Yeah. Well, so the thing that was going on with our PhD programs was that every PhD student sponsored by them has to take three months off to basically get a professional internship in a completely different setting to their research. At the time, I wasn't very keen on a sort of getting a corporate internship. So I sort of turned to Will. I said, "Why don't we create an internship for ourselves?" That's sort of where the initial idea of should we explore the agricultural market for a sort of possibility to exploit the skills and the tools that we are working with during our PhDs.

Nick Kral:

So we took three months off, and the good thing was that Imperial College has a lot of structure to sort of support budding entrepreneurs. They really sort of force you to get out of the building and create, I guess, business hypotheses each week that you try and challenge by basically interviews with industry stakeholders. This was a huge shock for both Will and me, because we were PhDs. We basically hardly ever spoke to anyone before, and suddenly, we were made to talk to complete strangers week on week. In the three months we learned really a lot.

Hannah :

Did Phytoform spring fully formed from that experience? Or has it been a journey from there to now?

Will Pelton:

Yeah, I think that's an understatement. It's definitely been a journey and an evolution. CRISPR-Cas9 genome editing had recently arrived on scene. It was out before then, but it was still only recently being used in the plant sciences as we tend to sort of get these tools a little bit later. And we'd started using it as part of our PhDs and it's an incredible tool. Initially, we went in thinking we were going to work on, I think saffron?

Nick Kral:

Yeah.

Will Pelton:

Saffron was our initial idea. We were going to increase the number of the actual... What is it? Is it the stigma? Stamen. Stamens that are used for saffron and obviously by increasing that increase the production and since saffron is worth its weight in gold, we assumed that would be a great idea. [Will and Nick are chuckling] As it turns out, it's not a great idea. It's not the biggest market in the world. And it's also an incredibly difficult problem to work on and not to mention 90% of production of saffron is in Iran, which has some challenges in itself. So we ended up exploring so many different options, different business models, initially we were looking at, like, a service type model and also different crops and our technology has evolved enormously as well.

Hannah Senior :

Most people, I think listening will know a little bit about genome editing, but just to make sure we've covered the bases, give me a little overview of what genome editing is and how that's different to other techniques that can be used in crop improvement. And also how you are using that within Phytoform, so what's making Phytoform unique?

Will Pelton:

So yeah, genome editing exists in many different forms but the most recent form is based on the first discovered molecule CRISPR-Cas9. And what was revolutionary about this is it's a very simple system that can make targeted changes in DNA. So previously in plants there's a few options to improve your plants genetically. You can

just go the conventional route, but obviously that's based on chance. Other more recent options include genetic modification and that's a really interesting technology. It's become very contentious but it is very efficient, you can transfer a gene that confers disease resistance very easily into another species. Whereas genome editing the amazing thing about it is there is no need to use any foreign DNA at all, but you can still make very specific changes. And relatively easily, which is like a complete revolution as compared to, you know, randomly crossing two plants together and then just randomly inserting foreign DNA.

Nick Kral:

Yeah about our technology, I guess where Phytoform Labs is unique, is what will said one of the findings we have really discovered is that the GMO technology was really contentious and if we are going to introduce a new biotechnological tool it has to be clear why there is benefit for it. And also why... Like what's the minimum amount of change that we can do with it? And so this is where Phytoform Labs is building its sort of proprietary platform, I guess. So we are really targeting crop traits that can really benefit both the farmers and the consumers. So things like environmental sustainability, like climate change, or disease resistance - all these things that will benefit both the farmers and the consumer as well as nutritional qualities of crops. And we feel that with genome editing we can improve the sustainability of the supply chain. And the secondary thing, as we already mentioned, is that there are many flavours in which genome editing comes - and we are very much focussed on using footprint free genome editing. So we are introducing the minimum amount of changes to the genome and we never actually transform foreign DNA into the plant at any of it's stages. So some people can use genome editing by temporarily transforming the CRISPR molecules and then essentially breeding them out from the gene pool. But we sort of feel like this is quite clunky. Essentially, it's relying on the old GMO infrastructure and that's what we are avoiding.

Hannah Senior:

I know that one of the things that has been a big factor in what you want to achieve with Phytoform is the environmental impact. So tell me a bit about sort of your values underlying it, or why you chose to use a company to go about improving the sustainability of agriculture.

Will Pelton:

Well, so as I mentioned during my PhD, I worked on potatoes because I was looking to have more of an impact. And so that whole project was basically around reducing waste and storage. And we are part of a large consortium and I think the science was amazing, but in terms of what can actually be provided as practical knowledge to a grower or a processor, it was quite limited. And for a variety of reasons, that was the case. And I think at that point I realized perhaps academia wasn't necessarily for me because, as well as being weirdly plant obsessed, I've also been really, really interested in the environmental side of it.

Will Pelton:

So to actually make an impact, I kind of came to the conclusion that the, you know, moving out of academia and trying to push that technology myself as part of a company would be the most effective means. And our kind of aims, when we set out, were to improve the sustainability of agriculture, I'm sure many listeners understand already that it's enormously bad for the environment. One of the dirtiest industries. Which is kind of mad because we see plant life all around us growing quite happily without human intervention, so why on earth has it become this huge energy intensive, input intensive industry. And so that drove us to one to improve sustainability.

Will Pelton:

And the secondary thing is also improving the nutrition of crops. We wanted to make sure that the consumers see the benefit of this technology. And one of the key lessons we've learned from the green revolution is that they made enormous gains in yields, but perhaps they've sacrificed a little bit, the nutritional qualities of those plants. So, we've

got massive calories, but what about all those micro and macro nutrients that you need? You know, the vitamins, the minerals. We've seen them decline slowly over time. So that was kind of the driver. We want to make that change in terms of sustainability and nutrition. And actually for me, a company seems like the best thing, at the time certainly, to facilitate that change.

Hannah Senior:

Now, the big problem that Phytoform faces being based in the UK is that genome editing is, or genome edited plants cannot be freely grown in the UK or indeed in Europe. So just give me a little bit of context around how the regulatory framework has influenced your plans in your thinking and what your take on the regulatory barriers is.

Will Pelton:

Just to put it into context across the world, genetically modified plants have been regulated in numerous different ways. And so genetically modified, we mean plants that have foreign DNA inserted into them. So there's the famous plants like "Roundup Ready Soybean" and plants like that. And in Europe they have been enormously unpopular and been quite heavily regulated. But even in the U.S. there's still a fair amount of regulation around them.

Will Pelton:

So genome editing, as we mentioned, is essentially a different technology and a fairly transformative one without many of those negative problems that conventional genetic modifications have. And so it's been looked at and it has a different technology. It's been judged as a different technology. In Europe just before we actually... Or just after we registered the company and we were very optimistic and we thought, you know, Europe's going to make a decision on how they're going to regulate genome editing. And we're very positive about it because obviously a lot of plant scientists had been very positive about how it can be used and the results. And unfortunately, the European Court of Justice decided that it should be regulated in the same way as genetically

modified plants, which was disappointing, especially as, well, at least at that point, we were in Europe based in the UK.

Will Pelton:

As it turns out the rest of the world has had a slightly different view on this. So in the U.S., South America, Japan they've, I mean, they haven't deregulated it as such, but they put very limited regulations on it. And it's... As long as you make very minor changes and you don't add any DNA, then it's basically treated as any sort of conventionally bred plant. So obviously being a European based company that has forced us to explore overseas markets, and obviously the US is a big one and one that we focused on up till now. But I think we're quietly hopeful that when the UK leaves Europe, that they will review the regulation around genome editing. There's certainly been a lot of positive signals from the government that they would be interested to review that. So who knows for the moment we're focusing on foreign markets, but maybe in the future, the UK would be another place that we can explore.

[Podcast theme tune plays]

Hannah Senior:

You're listening to plant breeding stories brought to you by PBS International, world leaders in pollination control. We're exploring the personal stories behind people who've dedicated their careers to plant breeding, helping us to more productive plants, greater food security and most sustainable agriculture. Now, back to the podcast.

[Podcast theme tune fades]

Hannah Senior: You mentioned in Europe, there has been this quite strong pushback against gene editing and going way back to the original genetic modification days, have you had to handle objections from friends and family around this being the core, gene editing being the core of your business?

Will Pelton:



Not a huge one. I mean, we have done some public events and being in plants and doing genome editing, it was seen as something of... Something quite interesting. And so we did have quite a lot of questions. I think in general, once we got past the sort of initial fear, and once we told people what the technology is and what we have to achieve, most people were overwhelmingly positive. But I mean we did have a few pretty crazy questions from the public but-

Nick Kral:

We don't need to convince anyone. At the end of the day, you know, it is a technology that will benefit the supply chain and if its benefits are explained clearly then I don't think there should be...

Will Pelton:

No, I think education is kind of the key point to that... And I think, you know, as well as... With genome editing, it's such an accessible technology as well. It's very much not just being used by the big agritech giants, which again, tends to create a suspicion when these big juggernauts are the only ones using our technology, but it's definitely being used by, you know, companies like ourselves small startups as well. And there are plenty of others around the world. So, I think that has helped to sort of get rid of some of that suspicion as well.

Hannah Senior:

So it sounds like you are quite optimistic that consumer acceptance is within reach once the benefits and the tools have been explained more fully.

Will Pelton:

Yeah, I hope so. I mean, you know, it's tough to say it isn't within reach, but we we've got some work to do, and we've got to make sure we deliver some products that actually produce some benefit to the consumer. But one of the most interesting things when we speak to people is when we show them before and after images of conventional commercial agricultural crops. So when I say before and after, I mean, what the original

crop looks like. So if you look at an original banana before humans started to change it, it's literally a small fruit that's just full of black, hard berries, sorry seeds, that looked like sort of little buckshots and it obviously took us thousands of years to then produce what we have today, which is this big fruit with seeds that are almost impossible to see. So I think when people see that and they're like, oh, that's not GM. That's actually just how humans have naturally changed plants; they realize that it's not as simple as maybe they think.

Hannah Senior:

One of the things that makes Phytoform different is that you are planning to use AI in the way that you decide on which genes to focus on or how to make those changes. So tell me a little bit more about that.

Nick Kral:

During our sort of process of learning what the market wants and what we would be able to do as well technologically, we realized that there is a lot of both old and new problems in agriculture. Like, you know, long-term storage, shelf life of crops, post-harvest losses, as well as the new challenges, like new diseases and also climate change overall. That there's a lot of problems to which actually there aren't simple answers in biology. And we sort of realized that genome editing is great. It's basically a molecular tool that we can use to improve genetics, but you can only improve it to what you already know. I mean, it's only as good as the targets and the understanding that you have. And so we sort of thought quite carefully about this and sort of realized that even though plant science has made tremendous progress over the last 50 years, we don't actually know a lot about underlying mechanisms in plants or how to base... How to maybe improve crops, to be more stress tolerant, or maybe more disease resistant.

Nick Kral:

And partially because of this is how painful it is to sort of collect data on new traits, how to actually characterize a new trait and then also how to confer it to more commercial varieties. So the understanding about the traits is the key. And we realized that over the

last 10 years, there was a huge explosion in both genomic and also other types of data that it was just sort of been created by plant groups and also all sorts of scientists. But I don't think we have really come up with a sort of very clear and smart way of how to use these massive amounts of data. And for that, we are basically building an engine that is very different to how a usual plant scientist would go about discovering a new trait.

Nick Kral:

Instead of relying on slow hypothesis driven research with a few eureka moments in the lifespan of your career, where you would basically dedicate a whole lifetime to understand one gene or one network, we now rely on these massive amounts of data to use AI and basically try and get an understanding for, of the traits that way. And these sort of learnings and our predictions and suggestions, we can then feed into the genome editing process to come up with traits that basically have never really been seen before.

Hannah Senior :

On what species are you working on first?

Will Pelton:

As a company we are working on tomato and potatoes. Yeah, I didn't think I'd revisit potatoes again, but we are back. So the tomato we are working with a U.S. tomato breeder in Florida, and basically actually for that one, we're introducing a known trait. So this is a trait that was discovered, I guess, using conventional breeding originally. But the issue that our breeder has is that it was discovered in tomato varieties used for canning. So like, you know, processed tomatoes for cooking. And getting that from those types of tomatoes into our breeders fresh market varieties is a huge challenge for him.

Will Pelton:

And for various reasons, like I was explaining earlier, every time he crosses those two different types of tomato, he gets this huge shakeup genetically, and inevitably he ends up with the sort of worst of both worlds type of tomato. That's useless. So with our technology, we can make a very specific change to introduce this trait without any other changes to the rest of the genome, which kind of showcases how powerful this technology is.

Will Pelton:

And then in potato, again, it's a waste reduction, but this time during harvest and processing and also in storage, and that's actually going to be using our AI technology, which Nick just described. And so we're basically going to make two types of traits. The first is to stop bruising in potatoes. So if you find, say, a potato in a bag, if it's been knocked around it browns a little bit. There's actually nothing wrong with that. It doesn't affect like the... How healthy that you raise or, or the quality, but it obviously looks pretty bad and that leads to huge amounts of waste. And then our other potato project again, reducing waste and storage by reducing the amount sugars that accumulate in potatoes when they're stored in the cold. And yeah, so they're both our initial projects on that using our AI and genome editing platform.

Hannah Senior:

You've been in business now for a few years, you've built up the team or the startings of your team, and you've got some early pre-seed investment and your technology is coming along. But tell me which bits have you found the hardest so far?

Will Pelton:

That is a great question. Finding the team has been really tricky. You know, we're looking for individuals who sort of buy into the vision of making agriculture more sustainable and more nutritious and are passionate about it. And at the same time, obviously they need the relevant skill sets, you know, in biology and also the relevant drive. So yeah, it's been really hard to find the right people and not because they aren't

out there, but it's a case of actually connecting with them and finding them, which has been really tricky. So that's been a learning curve in itself.

Nick Kral:

I'm very proud of the team we've assembled though. And we definitely took our time, but I feel like now we have a sort of a little Phytoform Labs machine that's sort of chugging away and working on these very large technological problems because you know, what we can say is all nice and dandy but actually implementing it in real life is a lot more difficult than I guess some people would like you to believe. We've heard a lot over our journey that, you know, anyone can genome edit, you can do it in your garage. I can definitely tell you it's a lot harder, at least for plants than people let on. [Nick and Will Laugh]

Will Pelton:

Another hard thing was definitely in fundraising. That was really far removed from our experience.

Hannah Senior :

Tell me a bit about that. Tell me about your experience and what works and has it affected the way you think about running the business?

Will Pelton:

So we were really lucky to been provided with some support from various competitions that we took part in and also from ground bodies, like Innovate UK. It's fantastic to be able to have that sort of resource. And that got us to the point where we could actually start to look for tech, look for investment because we'd established the basic technology.

Will Pelton:

The majority of it was just us making mistakes and learning. So speaking to the wrong people or speaking to the right people, but not presenting it in the right way or just not delivering the right message to be honest. And so it was a huge learning experience. And then really after a lot of fails, and luckily we were able to learn on those failings, I think it was like the last, like 10, 20% of the fundraising time that we actually managed to work out what we need to achieve and how we present it. And that was thanks to one of our friends from Imperial. And I think it's so important to have those sort of connections with people who've been through that process. Who've been through the fundraising process and who have built a company and who can advise you on it because it's definitely nothing like anything we've ever done before in academia.

Hannah Senior :

So you've had some tough times raising investment and getting close to hitting the wall, being one of them. What motivates you when the going gets tough?

Will Pelton:

For me that's pretty easy. I mean, every day you look at the news and the climate is not getting better. So it's every time it gets tough. I mean, it's far worse for other people on the planet. It's fairly easy to sort of continue that drive. What about you Nick?

Nick Kral:

It's the fear of failure [everyone laughs]. To be honest, I completely agree with Will that climate change is a huge challenge and it really feels like if it's not going to be us who is going to do this work, and we're really happy with those sort of community that we have assembled around us with our employees, with our investors, with our partners, that we're trying to prove the technology with.

Hannah Senior :

So what's next? What's next for Phytoform and for you guys?

Will Pelton:

Well, I mean, hopefully COVID will finish soon and we can get back out, back out into the world a little bit more, but I think, for the near future, we're very much focused on gaining the technology established fully. So that means getting our first crop out, so the tomato project I mentioned, we were hoping to get at certainly in the fields in the U.S. by next year, but to start next year. And then we also need to build out this AI technology fully, initially testing it in a model plant, but we also then want to develop these potatoes and develop those traits. I feel fairly positive. COVID's definitely been a massive challenge. I don't think many startups want that in their first year, but-

Nick Kral:

People will always need food. The question is, if we can sort of demonstrate the benefit of using this new technology to help sort of feed people and feed the world. You know, maybe if it brings it, there might even be opportunities for us.

Nick Kral:

So we're quite positive. We're not too scared. The COVID was a bit of a... We did not expect that, but we, I think in a way it actually made us better managers because we could not be on-site. And we had to do things remotely and we had to trust the team and we had to set up basically online systems in place that we are able to sort of document then record and report everything that goes on without having to actually physically be there every day.

Will Pelton:

And of course COVID did highlight weaknesses in supply chains around the world. So yeah, it's definitely continued to drive us with our vision.

Hannah Senior :

Where can people find you?

Will Pelton:

We are based at Rothamsted. If you ever passed by Rothamsted and you want to meet us face to face, although obviously not for the near future. Otherwise, you can find us obviously online, our website is a [phytoformlabs.com](http://phytoformlabs.com). Our Twitter handle is @phytoformlabs and obviously you can Google me and Nick, you can find some LinkedIn, if you want to contact us.

Nick Kral:

We do also have a satellite office in Boston, which currently because of COVID is sadly unmanned but we do expect to be there more often as COVID recedes.

Hannah Senior :

Will Pelton, Nick Kral from Phytoform labs. Thank you very much for joining me and for sharing your plant breeding story.

Will Pelton:

Thank you very much, Hannah. It's been a pleasure to speak with you.

[Podcast theme tune plays]

Hannah Senior :

You've been listening to Plant Breeding Stories by PBS international, and I'm your host Hannah Senior. Plant breeding is a pretty specialist podcast topic, which can make it difficult for people who share our interest in this kind of thing to find it. So if you enjoyed the podcast, recommend it to your friends and colleagues, and please help others in the plant science community find it by rating this episode and subscribing to the series. If you want to suggest people you'd like us to interview contact me on Twitter @PBSInt or on Instagram @PBS\_Int. Until next time, stay well.

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