How has a groundbreaking genomic discovery impacted thousands worldwide?

Behind the Genes Transcript

Naimah Callachand, Lindsay Pearse, Sarah Wynn and Emma Baple

**Naimah:** Welcome to Behind the Genes.

**Lindsay:** So, this feeling that like we’ve been on this deserted island for eight years and now all of a sudden, you’re sort of looking around through the branches of the trees. It’s like, wait a minute, there are other people on this island and in this case actually there's a lot more people on this island. Yeah, it’s very exciting, it’s validating. It gives us a lot of hope and, you know, it has been quite emotional too and also a bit of an identity shift. Being undiagnosed had become quite a big part of our identity, and so now that’s kind of shifting a little bit that we have this new diagnosis and are part of a new community.

**Naimah:** My name is Naimah Callachand and I’m Head of Product Engagement and Growth at Genomics England. On today’s episode, I’m joined by Lindsay Pearse whose son Lars recently received a genetic diagnosis, made possible by research using data from the National Genomic Research Library, Sarah Wynn CEO of Unique, and Emma Baple, a clinical genetics doctor. Today we’ll be discussing the impact of recent research findings which have found a genetic change in the non-coding RNU4-2 gene, to be linked to neurodevelopmental conditions. If you enjoy today’s episode, we’d love your support. Please like, share and rate us on wherever you listen to your podcasts.

**Naimah:** And first of all, I would like everyone to introduce themselves. So, Lindsay, maybe if we could come to you first.

**Lindsay:** Great, thank you. So, thank you for having me. I’m Lindsay Pearse, I live outside of Washington DC and I’m a mum to 3 boys. My oldest son Lars who is 8, he was recently diagnosed with the de novo variant in the RNU4-2 gene.

**Naimah:** Thank you. And Emma?

**Emma:** My name is Emma Baple. I’m a Clinical Genetics Doctor which means I look after children and adults with genetic conditions. I’m also a Professor of Genomic Medicine in the University of Exeter and the Medical Director of the Southwest NHS Genomic Laboratory Hub.

**Naimah:** And Sarah?

**Sarah:** Hi, thank you for having me. I’m Sarah Wynn, I’m the CEO of a patient organisation called Unique, and we provide support and information to all those affected by rare genetic conditions.

**Naimah:** Great, thank you. It’s so great to have you all here today. So, first of all Lindsay, I wonder if we could come to you. So, you mentioned in your introduction your son Lars has recently been diagnosed with the de novo variant. I wondered if you could tell us a bit about your story, and what it’s been like up until the diagnosis.

**Lindsay:** Sure, yeah. So, Lars is, he’s a wonderful 8 year-old boy. With his condition, his main symptoms he experiences global developmental delays, he’s non-verbal. He’s had hypertonia pretty much since birth and wears AFO’s to support his walking. He has a feeding disorder and is fed by a G-Tube. Cortical vision impairments, a history of seizures and slow growth, amongst other things.

So, that's just a bit of a picture of what he deals with day to day. But he’s my oldest child, so first baby. When I was pregnant, we were given an IUGR diagnosis. He was breech, he had a hernia soon after birth, wouldn’t breastfeed. But all of these things aren’t terribly uncommon, you know. But once he was about 3 or 4 months old, we noticed that he wasn’t really able to push up like he should, and we were put in touch with early intervention services for an assessment. So, we went ahead and did that when he was about 4 or 5 months old. And as parents, we could just kind of tell that something was off from the assessors. And, you know, they were very gentle with us, but we could just get that sense that okay, something is off, and they’re worried here.

So, that kind of kickstarted me into making appointments left, right and centre with specialists. The first specialist that we saw was a neurologist. And yeah, again, that's another appointment that I’ll never forget. She referred us to genetics and to get an MRI and some lab work but at the end of the appointment, she said to us, ‘Just remember to love your child.’ And, you know, that was quite shocking to us at the time because it wasn’t something that had ever crossed our mind that we wouldn't do or felt like we needed to be told to do this. But on the other hand, it certainly set off a lot of worry and anxiety of okay, well, what exactly are we dealing with here?

So, fast forward, we saw genetics and that was about when Lars was about 8 months old. We went through a variety of genetic testing, a chromosomal micro-array, a single gene testing, then the whole exome testing. Everything came back negative, but it was explained to us that what was going on was likely an overarching genetic diagnosis that would explain his like, multi-system symptoms.

And so meanwhile as he was getting older his global delays were becoming more pronounced and we were also in and out of the hospital a lot at this time. At first, he was in day care and, you know, any sort of cold virus would always turn into like a pneumonia for him. So, we were just in and out of hospital seeing a myriad of specialists, trying to put together this puzzle of what's going on and it was really hard to accept that nobody could figure it out. That was just, you know, sort of mind-blowing to us I guess. So, we applied for and were accepted into the Undiagnosed Diseases Programme at the National Institute of Health over here. The NIH as it’s commonly referred to. So, we first went there when Lars was 2. He was one of their youngest patients at the time. But that was a really great experience for us because we felt like they were looking at him holistically and across a bunch of all of his systems, and not just seeing a specialist for sort of each system. So, we really appreciated that.

We also did the whole genome sequencing through this research study. Although that also came back negative and so at that point, we were told to kind of keep following up symptomatically. Keep seeing the specialists and eventually maybe one day we’ll find an overarching diagnosis, but that science just hadn’t quite caught up to Lars. It was hard for me again to believe that and to sort of wrap my head around that. But certainly, it was an education from all of the doctors and geneticists and everyone we saw at NIH, to realise like how far there still was to go in terms of genetic research. How it wasn’t also that uncommon to be undiagnosed in the rare disease community. I would say that being undiagnosed sort of became part of our identity. And it’s, you know, it was something that, you know, you had to explain to like insurance companies and to his school, and it became part of our advocacy around him. Because without being able to say oh, it’s this specific thing and if it was someone who hadn’t met Lars before, trying to explain to them that, you know, yeah, within the range of this community you can be undiagnosed, and they just haven’t found it yet, but I promise you there is something going on here.

And I’d say the other thing too without a diagnosis you have no prognosis, right? And so, trying to figure out what the future would look like. Also, family planning. We waited 5 and a half years before we had another child and, you know, it was certainly an anxiety ridden decision. Ultimately after seeing as many specialists as we possibly could, we still were left with the same answer of well, we just don’t really know if it will happen again. So, that was a big decision to make. But again, it just kind of became part of our identity and something that you did eventually accept. But I would say in my experience I feel like the acceptance part also of Lars’ disabilities perhaps took me a little bit longer. Because again, I didn’t have a prognosis, so I didn’t exactly know what we were dealing with. Only as he has become older and, you know, you’re sort of getting a better sense of what his abilities might be than being able to understand, okay, this is what I’m dealing with. I need to accept that and do what I can to care for him and our family in the best way that we can.

**Naimah:** Thanks so much for sharing that, Lindsay. I feel like you’ve touched on a lot of really, you know, a lot of complications and difficulties for your family. Especially, you know, with regards to keeping hopeful and things about the prognosis as well, I’m sure it was really difficult. You’ve mentioned that Lars was able to be diagnosed recently due to recent research efforts. So, Sarah, I wonder if you can tell us a bit more about these and what the findings have meant for patients with neurodevelopmental conditions.

**Sarah:** Yes. So, I think we know that there are lots of families that are in Lindsay and Lars’ position where they know that there is almost certainly an underlying genetic condition, and it just hasn’t been found yet. And so, I think we know that lots of researchers are working really hard to try and find those causes. I think over time we know that as time goes on and research goes on, we’ll find more of these new genetic causes for neurodevelopmental conditions. I think particularly as we start to look at regions of the genome that we haven’t looked at so much so far. But I think one of the things that's really extraordinary about this one is that actually it turns out to be much more common than we might have expected, for one of these new conditions that we haven’t found before. But I think it’s about one in 200 of those undiagnosed children with neurodevelopmental conditions, have this diagnosis so that's not a small number. That's not a rare finding at all actually, that's much more common than we could ever have anticipated.

But I think one of the things that we do know is that as we look further and deeper into that genomic sequence, so, we’ve started off looking at the bits of the sequence that are genes that code for proteins. This changes in a gene that actually doesn’t code for protein, so it’s less obvious that it would be important but clearly it is important in development because we know when it has a spelling mistake in it, it causes this neurodevelopmental condition. But there will be as researchers look more and more at these kinds of genes, and also the other part of the genome that is not genes at all, we’ll find out more and more the underlying genetic causes of these neurodevelopmental conditions.

I think it’s also really important to stress why this is so important to find these genetic changes and it’s because families really need a diagnosis. Lindsay talked quite eloquently and a lot about that knowing something was off and really wanting to know the reason why. Getting these diagnoses might change care management or treatment, but actually really importantly it just gives an answer to families who have often been looking for an answer for a really long time.

**Naimah:** I just wanted to go back to the point that Sarah made that actually this genetic change is relatively common. Emma, I wondered if you could tell us a bit more about maybe why it took us so long to discover it?

**Emma:** That's an interesting question actually. I suppose the sort of slightly simplified answer to that question is we haven’t been able to sequence the whole of a person’s genetic information for that long. And so, children like Lars would have had, as Lindsay described lots and lots of genetic tests up until they had a whole genome sequencing which is what Sarah was talking about. The types of tests that we had up until the whole genome sequencing wouldn't have allowed us to look at that bit of the genetic code where this RNU4-2 gene can be found. So, we can only really find that using whole genome sequencing. So, before that existed, we wouldn't have been able to find this cause of developmental condition.

**Naimah:** Okay, thanks Emma.

**Naimah:** Now we’re going to hear from one of the two research groups who are responsible for these research findings. First of all, let’s hear from Nicky Whiffin.

(Clip - **Nicky Whiffin)**

How were the findings possible using the Genomics England dataset?

So, most previous studies have only looked at genetic variants that, in genes that make proteins, but only a subset of our genes actually do makes proteins. The Genomics England dataset we have sequencing information on the entire genome, not just on these protein coding genes and that means we can also look at variants in other genes. So, those that make molecules other than proteins. And RNU4-2 for example, makes an RNA molecule.

These findings translated to direct patient benefit for patients like Lars who were able to receive support from Unique. How does this demonstrate the value of the dataset?

Yes. So, it was incredible that we could find so many patients with RNU4-2 variants so quickly. This was enabled by access to Genomics England data but also to other large sequencing datasets around the world. So, we worked with people in the US, in Australia and also in mainland Europe. These large datasets enabled us to spot consistent patterns in the data and by looking across multiple datasets we can also make sure that our findings are robust. When we realised how significant this was and how many families would be impacted, we very quickly contacted Sarah at Unique to see if we could direct patients to them for support.

(End of clip)

(Music)

**Emma:** There's one thing I wanted to raise. It’s important to recognise the way that was discovered was through the National Genomic Research Library that Genomics England hosts. To highlight the value of that, and the value of having this centralised resource where families have been kind enough really to allow their data to be shared with some limited clinical information that allowed these researchers to be able to pull this out. And I think it highlights the power of the National Health Service in that we were able to create such a resource. It’s really quite astounding that we’ve found such a common cause of a rare genetic condition, and it wouldn't have happened in the same timescale or in this way without that resource. And then to just say that as Sarah talked about the fact that we’ve been able to get that information out there, also the researchers were able to get out there and contact the NIH and all of these other programmes worldwide. In Australia, America, everywhere in the world and quickly identify new patients who had this condition and get those diagnoses out really rapidly to people.

But all that came from that power of sharing data and being able to have that all in one place and making it accessible to very clever people who could do this work and find these answers. It’s so important for families like Lindsay’s, and all the families in England and around the world that have got these answers. So, I guess it’s a big plug for the value of data sharing and having a secure place where people feel that it’s trusted and safe, that enables these diagnoses to be made.

**Lindsay:** If I could just echo that, we’re so grateful that that exists in the UK. Just acknowledging like the privilege here that we have had to be able to, I mean for our family in the US, that we’ve been able to, you know, get ourselves into the NIH study and into the study at Children’s National. That takes a lot of work. I feel like not everybody has that opportunity to be able to spend the time to do these applications and to go to all the appointments and get the testing done and have the insurance to cover it. So, very grateful that the system exists in a way in the UK that made this sort of research possible. I just hope that that can be replicated in other places, and also to what Emma was saying earlier, come up with a lower cost test as well for this to further the growth of the community and of course then the corresponding research.

**Sarah:** I think firstly we have to sort of thank all of those families that took part and do share their data, because I think it’s not always clear why you might want to do that as a family. I think this is really a powerful example of the benefit of that. I also think the data sharing goes one stage further. So, it’s partly about getting the diagnosis, but the data sharing going forward about how this condition impacts families, both clinically and sort of day to day lived experience, is how we’ll be able to learn more about these conditions. And so, when families get this diagnosis next week or next year, not only will they get a diagnosis, but they’ll get a really good idea about what the condition is and how it might impact their child.

**Naimah:** And Lindsay, coming back to you. So, we’ve talked about, you know, what it meant for your family before the diagnosis, but what has it meant to have a diagnosis and how did you feel? And what happened whenever you received the diagnosis?

**Lindsay:** Sure. Lars was again part of the NIH Undiagnosed Diseases Research study. So, once you attend this programme and if you are not diagnosed like at the end of your stay, they keep your details on file and you’re part of this database at the NIH Undiagnosed Diseases Programme. So, if you’re undiagnosed after your sort of week-long work up, your samples stay within the research programme. We were also part of a research programme at Children's National Medical Centre, the Rare Disease Institute. So, our samples were sort of on file there in their database as well.

And so, at the end of March I was really quite shocked to receive a call from our long time and trusted geneticist at Children’s National that they had found a diagnosis. It was quite emotional. I really kind of didn’t believe it. I just kept asking, you know, ‘Are you sure? Is this it?’ you know, ‘How confident are we?’ Because I think in my head, I sort of always thought that we would eventually find a diagnosis, but I thought that Lars would be, you know, a 30- or 40-year-old adult. I thought it would be decades from now. Like I felt like for whatever reason we had to wait decades for the science to sort of catch up to him.

So, we were very, very grateful. It felt very validating, I guess. I had always kind of had this intuition feeling that we were sort of missing something and it’s more that the science just hadn’t quite caught up yet. But, you know, it was validating to know that okay, Lars is not the only person in the entire world with this, it is something that is relatively common in fact within the rare disease community. That is also very exciting to me personally because I’m hopeful that that will lead more researchers to be interesting in this, given how, quote on quote, common it is. I’ve sort of been describing it as like a mass diagnosis event but also more so this feeling that like we’ve been on this deserted island for eight years and now all of a sudden, you’re sort of like looking around through the branches of the trees. It’s like, wait a minute, there are other people on this island ad in this case, there's actually a lot more people on this island.

Yeah, it’s very exciting, it’s validating. It gives us a lot of hope. And, you know, it has been quite emotional too and also a bit of an identity shift. Because I spoke earlier about how like being undiagnosed had become quite a big part of our identity. So, now that's kind of shifting a little bit that we have this new diagnosis and are part of a new community. But yeah, we’re just very grateful that the research had continued. And, you know, I think sometimes you sort of have this feeling of okay, our files are up on a shelf somewhere, you know, collecting dust and are people really looking at them? And actually, it turns out that the research was ongoing and yeah, we’re just very grateful for that.

**Naimah:** Thanks so much for sharing, Lindsay. It sounds like it’s been a real rollercoaster of emotions for your family and I’m glad to hear that, you know, you’ve got some hope now that you’ve got a diagnosis as well. So, moving onto the next question. Emma, I wanted to ask you then, how will these findings improve clinical diagnostic services for those for neurodevelopmental conditions?

**Emma:** So, you asked me earlier about why it had taken so long to find this particular cause of neurodevelopmental condition, and I gave you a relatively simple answer. The reality is one of the other reasons is that almost eight out of ten children and adults who have RNU4-2 related neurodevelopmental condition have exactly the same single letter spelling change in that gene. So, actually that in itself means that when researchers are looking at that information, they might think that it’s actually a mistake. Because we know that when we sequence genetic information, we can see mistakes in that sequencing information that are just because the machine has, and the way that we process that data, it’s not perfect. So, sometimes we find these little mistakes and they’re not actually the cause of a person’s problems, they’re just what we call an artefact or an issue with the way that that happens.

So, that is part of the reason for why it was tricky for us to know whether this was, or rather the researchers to know whether this was or was not the cause of this particular condition. But that in itself is quite helpful when we think about how we might identify more people who have this going forwards. Because unlike in Lars’ case where we didn’t know what the cause was and so we were still searching, and we didn’t know where to look in the billions of letters that make up the genetic code to find that answer, we now know that this is really very common. It’s unbelievably common. I think we didn’t think we would be finding a cause of a rare genetic condition that was this commonly occurring at this stage. But the fact that it’s just a single, it’s commonly this one single change in the gene means that we can set up pretty cheap diagnostic testing. Which means that if you were somewhere where you wouldn't necessarily have access to whole genome sequencing, or a more comprehensive testing in that way, we could still be able to pick up this condition. And it’s common enough that even if you didn’t necessarily recognise that a person had it, you could still have this as part of your diagnostic tool kit for patients who have a neurodevelopmental condition. It’s common enough that just doing a very simple test that could be done in any diagnostic lab anywhere in the world, you would be able to identify the majority of people who have this.

**Naimah:** Now let’s hear from the other research group who are responsible for these findings. Here is Dr Andrew Mumford.

(Clip - **Dr Andrew Mumford**)

Why are these research findings significant?

It offers genetic diagnosis not just for a handful of families but potentially for many hundreds of families, who we all know have been searching often for many, many years for a genetic diagnosis. But actually, there are other gains from understanding how this gene causes neurodevelopmental disorder. We know that there's GRNU4-2 in codes, not a protein actually, but a small nuclear RNA which is unusual for rare, inherited disorders. It’s a component of a very complicated molecule called the spliceosome which in turn regulates how thousands of other genes are regulated, how they’re made into proteins. So, fundamentally this discovery tells us a lot about the biology of how the spliceosome works. We already know that some other components of the spliceosome can go wrong, and result in diseases like neurodevelopmental disorders. This gives us an extra insight and actually opens the door to, I hope, a whole load of more discoveries of genetic diagnosis possible from other components of this complicated molecule.

Your research group used a mathematical modelling approach. Can you tell me a bit about this, and what this means for other rare conditions, Andrew?

So, identifying relationships between changes in individual genes and different kinds of rare, inherited disease is notoriously difficult because of the volume of data that's involved and the need to be absolutely certain that observed genetic changes are actually the cause of different rare, inherited disease. So, applying statistics to that kind of problem isn’t new. But what my collaboration group have achieved here, is to develop, actually developed some years ago a completely new approach to applying statistics to genetic data. We call that BeviMed and we’ve been working for many years on the genes in code that make individual proteins. Most rare disorders are caused by genetic changes in genes that make proteins.

What this discovery comes from is actually we’ve applied the BeviMed statistical technique to genes that don’t make proteins, they’re non-coding genes. For example, genes that make small nuclear RNA, it’s just like RNU4-2. What's unusual about the BeviMed approach is that it’s very sensitive to detecting links between genetic changes and rare diseases, and it can detect statistical associations really driven by very, very small numbers of families.

So, we apply it to datasets like the 100,00 Genomes dataset and identify associations using statistics that have got a very high probability of association. Other members of the team then seek to corroborate that finding by looking at if we can see the association in other datasets, and we certainly achieve that with RNU4-2. But also, assessing biological plausibility by investigating what we understand already about in this case, a small nuclear RNA, and how it can possibly result in a disease. And we normally try and employ other independent evidence such as experimental investigation. Or going back to our families and asking for additional data to help really test this sort of theory that changes in this particular gene have resulted in a problem with neurodevelopment.

(End of clip)

**Naimah:** Emma, are there any other ways that we can identify these conditions based on their clinical presentation?

**Emma:** So, Lindsay and I were talking with you just yesterday, wasn’t it? And I asked Lindsay about what sorts of things Lars had in common with other children and adults who have been diagnosed with this condition? I actually think Lindsay probably gives a better summary than I would, so I might ask you to maybe repeat what you said to me yesterday. But the bit of it that really stood out to me was when you said to us that a lot of parents have said, ‘I'm not sure how we weren’t all put together in the first place because you notice so many things that were in common.’ So, maybe if you can give that summary and then I can translate that back into medical terms, if that’s okay Lindsay.

**Lindsay:** Sure, of course. Yeah, it been again, kind of mind blowing, some of the similarities. Especially as we’ve exchanged pictures and such, and baby pictures especially where some of the children like look like siblings. So, definitely some similarities in facial features, you know, everyone seems to experience some of the slow growth, so a short stature or quite skinny. There's feeding issues also that seem to be quite common. Also, you know, things like the global developmental delays, that's certainly across the board and histories of seizures, that's also quite common. Some people have experienced also some, like, bone density issues, that's not something that we’ve experienced so far, but that also seems to be quite common.

But then also, behaviourally, there's a lot of similarities which has been, I think, quite exciting to a lot of us because you’ve always thought okay, so this is just my child. And of course, some of that is true but it’s also interesting to find out some of these other things that are, you know, are quite similar. So, a lot of people have mentioned their child having, like, an interesting sense of humour. Kind of like a very slapstick sense of humour which is quite interesting. Or everyone seems to love water, everybody loves swimming pools and bathtime, and all of that. Lars loves a windy day. Something about the wind, he just loves it and plane noises and things like that have also come up with other people. So, yeah, it’s been really interesting and cool to see.

**Emma:** So, I guess Lindsay’s sort of very beautifully summed up what is written in the research publication. So, there's only two research publications so far on this condition, it’s all really new. And I am definitely not claim to be a clinical expert on this condition, and I don't think there are any yet. It will take people time to see lots of children and adults who have this particular condition. But ultimately what Lindsay summarised was the common clinical features that have been described by parents. In my job as a clinical genetics doctor, part of what we look at is a person’s appearance. So, Lindsay described the photographs of children particularly when they were little, looked very similar. In the photographs that I’ve seen, I would agree with that. And so obviously those children look like their mum and dad, but they have other features that are in common. They have a characteristic appearance and that helps doctors like me to have an idea as to whether a child or an adult might have a particular condition.

Then put together with the sorts of information that Lindsay gave us around the low tone, so being a little bit floppier particularly when they’re little. The slow growth and growth problems, problems with eating, also with seizures. Those are all common things that were pulled out of both of the two research publications on this condition and putting that all together into one picture helps doctors to have an idea whether somebody may have a particular condition. That would help us in this case to potentially request that simple test I was talking about, if maybe we were practicing in a part of the world where we wouldn't have the resources that we thankfully do have in the United Kingdom, and in the USA.

**Naimah:** So, Sarah, just coming to you next. How does this research spread awareness and help other patients with these conditions?

**Sarah:** So, I think one of the things that's been really great about research now is that we are able to, you know, social media and things like that mean that we can spread this information really quickly across the world basically. I think what that does is that as well as helping bring people together that they’ve got this diagnosis, what it does is I think it provides hope for all of those people that Lindsay was talking about at the beginning who don't have a diagnosis. So, that piece around people are still looking, the researchers are working hard and that even if you don't have a diagnosis today you might get one in the future. Lindsay talked about your sample being dusty and not being looked at. I think it gives lots of families, not just those that get this diagnosis but all of those that haven’t got a diagnosis, hope, that hopefully in the future they will get a diagnosis.

I think one of the things we really hope will come out of diagnoses like this is that we will then be able to build up more of that picture about how families are affected. So, that we can give families more information about not only how their child is affected but how they might be affected in the future. That prognosis information that Linsday said is really missing when you don't have a diagnosis. And I think the other thing that hopefully is the next stage in this journey with this discovery is that those two science publications that Emma talked about, what we will want to do here at Unique working with the researchers and those families that have got a diagnosis, is to produce a patient family friendly information leaflet about this condition.

One of the things we know is really important about those patient leaflets is including the photos. Because as both Emma and Lindsay have said that idea that they have facial features in common. And so, if you look at a leaflet and you can recognise your child in it, and you can see others that look like it, that can be a really sort of quite heartwarming experience in what often is a lonely experience with a rare condition.

**Naimah:** And I think kind of on that point about it being a lonely experience, I wondered Lindsay if you could talk a bit more if this research has allowed you to connect with other parents and families who have received a diagnosis, and what impact that's had on your family?

**Lindsay:** Yeah. I mean, and I think everything that Sarah has said was spot on. It’s wonderful to have resources like Unique to connect families and have those diagnoses on the platform, so other clinicians can look for it and sort of grow this group. I think that has definitely been the highlight of getting this diagnosis at this stage, right. Because there's not much more you can do with it, with someone so brand new so being able to connect with the other families has been wonderful. One amazing mum who with this diagnosis set up a Facebook group, RNU4-2 Family Connect. And, you know, it’s just been amazing to see people from all over the world joining this as they receive this diagnosis, you know, sharing their stories. We’ve spent countless hours on the weekends over the past couple of months on Zoom calls with total strangers, but just you find that you can just talk for hours and hours because you have so much in common.

It’s great to see what has worked well for other families and, you know, what has not worked. Sharing resources, just kind of all learning together. Also seeing the spectrum of this diagnosis, I think most genetic disorders have a spectrum and this seems to be the same here. So, that's been very interesting. And of course, our son is 8, Lars is 8. There's now a 33-year-old and a 29-year-old in the Facebook group. Speaking for me personally it’s just amazing to see them and like it’s very cool to see where they’re at. That sort of helps you answer some of those questions about that before were quite unknown when you were thinking about the future. Obviously, everybody’s development whether you have a genetic disorder or not, it is going to be what it’s going to be, and everybody is going to do their own thing. But being able to see what a path might look like is just so helpful. And, you know, we all want community and connection, and so this has been really, really great to have that now.

**Sarah:** I don't think there's much more that I can add because Lindsay articulated so well. But it’s really heartwarming for us to hear the benefits of those connections because that's really why Unique and other support groups exist. Is to provide, partly to provide information, but I think predominantly to put families in touch with other families so that they can find a new home and connect and share experiences. And, you know, stop feeling as alone as they might have done before.

**Naimah:** Okay, we’ll wrap up there. Thank you to our guests, Lindsay Pearce, Sarah Wynn and Emma Baple for joining me today as we discussed the research findings which found a genetic change in the RNU4-2 gene which has been linked to neurodevelopmental conditions. If you’d like to hear more like this, please subscribe to Behind the Genes on your favourite podcast app. Thank you for listening. I’ve been your host and producer, Naimah Callachand, and this podcast was edited by Bill Griffin of Ventoux Digital.