Reaching the full potential of genomic research

The G Word transcript

**Dave:** Welcome to The G Word. My name is Dave McCormick and I'm a member of the Participant Panel at Genomics England. This year, Genomics England is celebrating its 10-year anniversary. So, with that, we are going to reflect on the last decade of genomic research at Genomics England, as well as future research plans.

For today's discussion, I'm delighted to be joined by Professor Matt Brown, Chief Scientific Officer at Genomics England, and associate professor Jenny Taylor, Programme Director for the genomic medicine theme at the University of Oxford, and a member of the Genomics England research committee. Jenny, Matt, welcome both.

**Jenny:** Good afternoon, Dave.

**Matt:** Good afternoon, Dave.

**Dave:** What we have today is a number of questions, which the Participant Panel have kindly forwarded through to me, and what I'm going to do is go through each of these questions and then come to each of you for your answer, and I trust you've had sight of these questions, so I'm not going to throw anything too scary or unpleasant.

So let's make a start if that's okay. So to begin with, first question I have is: Looking back on the evolution of the National Research Library – the NGRL – over the past 10 years, what were you hoping to achieve and is the NGRL meeting its full potential? And I suppose a second question within that: if not, what more needs to be done to achieve what you were hoping for?

So Jenny, if I may, can I come to you first please?

**Jenny:** Sure. The NGRL and the National Genomic Research Library is a tremendously rich resource, and what we were hoping to achieve by using it is to identify novel disease genes and an understanding of biological mechanisms underpinning disease.

And because it's this tremendously rich research resource, which is unparalleled probably in, in the world of 100,000 Genomes and all the clinical, what we call phenotypic data, the clinical data, but also the opportunities through clinicians to recontact some of the patients.

It really is an amazing research resource for being able to do some of this rare disease gene discovery, which is the particular area that I'm working in, but obviously the same, there are lots of opportunities in the cancer arm as well.

So that's what we would've been hoping to achieve. I think what we have achieved, we have definitely identified some novel disease genes. We've definitely identified some genetic diagnoses for some of the patients. I guess if, what more needs to be done to achieve what we're hoping for, I mean, we would obviously love to see that every patient who'd been referred to Genomics England had a genetic diagnosis or that we'd been able to find some novel genes in that.

And we haven't identified as many as we would've expected. And that's in part because we're finding stuff in known genes that maybe the pipelines have missed and could be upgraded. So, I guess what we would be hoping for is to say, let's improve the diagnosis, the pipelines that allow patients to have diagnoses so that we can really get on and focus on more the novel biology and the novel disease mechanisms.

**Dave:** Thank you Jenny. That's very, very clear and I appreciate there were a number of components to that question. So thank you for covering all points. Matt, may I come to you? Is there anything that you would like to add?

**Matt:** Yeah, so as Jenny says it’s, it's a bit of jack of all trades type research environment in that it is supposed to cover both diagnostic discovery, so trying to assist in achieving diagnoses for patients with rare diseases in particular. Of course, 20% of it also currently is also cancer. But let's focus on the rare disease for the moment.

And amongst the rare disease probands, it's really only around 25% that we've actually achieved a diagnosis. So I guess you could say if something more needs to be done, we need to be better at achieving diagnoses.

So though, whether that's actually a fault of the National Genomics Research Library, or whether it's actually just that this is challenging for other reasons is something we could discuss further.

I personally think it's probably not to do with the research library. It's more to do with the challenge of the diseases and the challenges of the microscope that we're using effectively, whole genome sequencing, whether that's capable of doing what we need it to.

The other thing that it's there for though is for more basic research, be it into disease mechanisms, identifying therapeutic targets and that sort of research. And it has had a substantial impact. I mean, there have been hundreds of papers that have come out of it and a lot of basic research that's been achieved, but I think that there's a lot more that it could do in that area.

So that's something that perhaps we can discuss further as, uh, this podcast goes on.

**Dave:** Indeed. Thank you. So when we're looking at how that could develop and, I suppose, the second question is really looking at what more could be done by the different stakeholders involved, and that includes central government, NHS England, the Genomic Medicine Service Alliances, the 7 alliances across England, as well as patient communities to ensure that the NGRL meets its full potential.

So, what more could be done, do we think? Matt, what do you think?

**Matt:** To achieve its potential, one thing is that there's a phenomenal amount of genomics data that's being produced by the NHS, which actually doesn't get captured by either any database or any database which has got an associated research environment with it.

So we’d really love to see a far higher proportion of the total amount of genomics that’s going through the NHS Genomic Laboratory Hubs coming into the National Genomics Research Library. For example, probably over 95% of cancer sequencing currently does not go into the National Genomics Research Library.

Similarly, a very high proportion of sequencing to diagnose rare diseases also is done by panels and does not come into the National Genomics Research Library, and most of that data actually is lost to research as a consequence of that. So we'd really love to see more of it come into the NGRL.

We'd also like to increase the amount of clinical detail that's in the NGRL.

One of the challenges with making diagnoses, and I'm sure Jenny will be able to expand on this, is that we don't have a huge amount of detail about the clinical manifestations of the clinical presentations of the patient that are being seen in it. And that makes it hard to diagnose them and it reduces the value of the NGRL for research.

We don't have, uh, GP record data, and that's something we'd really love in it, because I think that would be of huge value for a wide variety of research.

And then finally, as we move towards cloud computing in particular, this whole process is becoming quite expensive. The more users we have for the National Genomics Research Library and the more use of complex compute-intensive analytic approaches, then the compute costs start becoming quite large. And to ensure that the data gets used as much as possible, some central funding for compute costs is going to be essential.

**Dave:** Thank you. Picking up on a couple of those points there, Jenny, is there anything that you would like to add, please?

**Jenny:** Matt's highlighted some of those issues really clearly, so I will add to some of those.

I mean, he's absolutely right that you, Genomics England did a fantastic job of really trying to get a core amount of clinical detail across all patients, but obviously as soon as you start to get into specific patient groups, you need more different detail in specific areas.

And so, for example, we have a musculoskeletal group and you're not going to have taken radiological images for all the patients across the board, they're particularly relevant to those who’ve had fractures. There are examples of where we need to augment that clinical data and have much deeper phenotyping data.

And I guess that leads on to a second point then, is that we then need to be able to get back to the patients, and we do that through the clinicians. And Genomics England has set up this framework with allowing us, as researchers, to contact, through Genomics England, the clinicians and then going back to the patients to maybe get some of this.

But it certainly is something that’s difficult to do and can be slow because clinicians are very busy, sometimes they've moved on, you know, several years have lapsed now since Genomics England started. The clinicians may have moved on, they've been locums, people have retired, et cetera.

And that's still a very, very slow process for us and requires a huge amount of chivvying on our part, which we really don't like to do, is to sort of follow up clinicians saying, you know, “can you provide us with these details or can you get in touch with the patients?”

So, the clinician contact is important. And actually anything we can do to facilitate that pathway and getting in touch with the patients is really important for us.

And I guess in terms of what more can be done with stakeholders, I mean, if this is a growing resource, it will be even more beneficial than it is at the moment.

So we've got a 100,000 Genomes, but these are now being done in the NHS, and if the NHS genomes are being added seamlessly to the 100,000 Genomes Project, that will be tremendous if we can say to other academics around the world and to other partners that this is expanding. And it becomes more important for patients with rare diseases, we're more likely to find other patients like them, but that needs to be done in a seamless way.

So this is only useful if the data sets are combined together in a seamless way; they've all been sequenced in the same way; they're all analysed in the same way; and we can get to the data and we can access the data in the de-identified way that we can actually find the data that the clinicians want us to look at.

And if there is any sort of barrier between the 100,000 Genomes Project and the NHS genomes dataset, then it's going to lose its remarkable research value. So, I think that's something that NHS England can certainly look at doing is to make sure that the fantastic platform that the 100,000 Genomes Project started is actually maintained.

**Matt:** Also that we would love, at Genomics England, to have an easier way of going backwards and forwards with participants who are in the NGRL directly, so that we could both support with diagnostic discovery and also so that we can better enable particularly rare disease therapy research, but rare disease research where researchers want to be able to reach out to patients. Because I'm convinced that that's actually what our participants want is not just a diagnosis, but they also want therapies.

And the current setup, as you say, is inflexible. It takes a phenomenal amount of effort in Genomics England, with our clinical researcher interface team, to try and support a relatively small number of requests, which hardly meets the demand that's out there and the potential benefit that we could bring if we could directly contact patients.

Yeah, I agree. I think that would be fantastic. And I think perhaps one of the ways of doing this, and this is something again looking forward, is that when the patients are being, (these are all patients that are consented for research), but I think maybe one of the ways forward is actually, for the future recruits, to be asking that question at the point of recruitment about whether they were happy to be recontacted and have that built into the ethics because they will want, as Matt says, to have the therapeutic options.

And they will probably want them quite fast. I mean, some of these are very sort of, you know, these can be life-threatening conditions, so we need to be able to move rapidly.

**Matt:** With our Newborns Programme, which will actually be contacting patients back, there will be a mechanism for us being able to contact patients, but we need to see that spread across also the current NHS Genomic Medicine Service patients, and preferably back into the 100,000 Genomes patients as well.

Over to you, Dave.

**Dave:** Thank you, Matt. And just to pick up on that last point, it is interesting and I myself am a contributor, a participant to the 100,000 Genomes Project. I joined, that was some six years ago. And when you compare the learning and the lessons that we've all learned from how the 100,000 Genomes Project has evolved as opposed to the more recent Newborns initiative, perhaps there's something there in terms of how we implement that, uh, consent/reconsent process.

And of course the whole de-identification issue, which has caused, can cause, problems when going back and forth within the NGRL environment between Genomics England, GMS Alliance communities and the patient community. It is an issue. I agree with you.

That leads me nicely onto our next question, which is: Where would you like to see the NGRL in the next 5 to 10 years, and how can it achieve this? So, Matt, can I come to you first please?

**Matt:** One thing I'm really keen to see is that it grows and continues to be bringing in details on new patients who are experiencing treatments and diagnostic processes in the current day.

This is particularly important for our cancer cohorts where cancer therapies, diagnosis and therapies is changing very fast. Sadly faster than for, or probably good for the cancer patients, but if changing faster than rare disease therapies is. And so if we sit on just using our 100,000 genomes cancer patients as being our cancer dataset, it will become out of date.

So it needs to grow. I think also it will benefit researchers if it gets larger. And we're expecting that over the next three years it will grow to over half a million in size by the end of 2026. We also would like to see an increase in diversity, and I mean that not just in terms of clinical diversity, but also ancestral diversity.

Although the dataset is actually currently representative of the UK population in terms of its ancestry, that still means that there are some ancestral groups that have fairly small numbers in the library, and therefore we'd like to specifically oversample from those groups in order to be able to properly inform genomic medicine for application in those ancestral groups.

And then lastly, the National Genomics Research Library. One thing we didn't mention in the beginning was that it was one of the first, if not the first trusted research environment where instead of us lending data out to researchers, researchers actually had to come in within our research environment to analyse it.

And that took quite a bit of development to do, and I think we'd have to acknowledge that certainly for the first while it was being built, it wasn't the easiest to use and it still could improve a lot. So, we would like to see our research environment improve a lot so that it is much more intuitive over the next 5 to 10 years in use.

There's lots of other things we could talk about future research directions, but perhaps if we go to Jenny.

**Dave:** Indeed.

**Jenny:** Yeah, I mean, I would concur with several of those things. The short list is in the next 5 to 10 years, can we have a diagnosis for everyone that's already in the 100,000 Genomes?

Can we make sure that we're expanding and including the GMS genomes, so those done under the new NHS Genome Medicine Service? That's a growing resource. And can we then have a mechanism for providing therapeutic options for as many of the patients as possible? As I say that, some sort of brokering with patients, bringing in algorithms that help us to convert “what is a diagnosis” into “what are the therapeutic options for that particular patient given a genetic variant”.

So it's a short list of 3 for me, but they're quite big tasks.

**Dave:** They're very large tasks. Absolutely. So, but thank you. Thank you both. Very clear. And I know. Moving on to our next question. We've already touched on some of the limitations and barriers already.

So without necessarily repeating what's already been touched on the previous answers to the questions: What do you think are the biggest limitations and barriers which are impacting upon current research, which Genomics England is driving, and what could be done to help overcome these limitations and remove these barriers? And Jenny, could I come to you first, please?

**Jenny:** Well, as you say we've touched on the clinician contacting ability to contact patients, so we won't go over that again.

I guess something that concerns me is that in the new NHS Genomic Medicine Service, the clinicians need to know who their patients are and what their ID is (the de-identified id) but there's a numerical ID in the research environment. So, in the current system with the 100,000 Genomes Project, the clinician gets a Genomics England ID for their patient, and they can access the details in it.

And we really need to make sure that researchers and clinicians under the same sort of trusted framework can actually access this data and it not to be sort of scrambled. And Genomics England has focused several times on the importance of researchers in helping to find the diagnosis.

This cannot all happen in the Genomic Laboratory Hubs, where they can focus very much on the known genes, but the normal genes are very difficult for the clinical laboratories. So researchers can help to make these diagnoses and identify these disease genes, but they can only do that if there's a clear path through the IDs to understanding which patient is which, as I say, in a de-identified way. I don't know if that's clear, but it needs to be on the same basis that Genomics England set up that works fine at some level.

**Dave:** Thank you, Jenny. Matt, how do you think that you would like to add to that, please?

**Matt:** Yeah, so one of the things that I think is a bit disappointing is that over 90% of the users of our data in the National Genomics Research Library are UK users.

It's not that that's bad that we have a lot of UK users, but what I think is disappointing is that we don't have very many international users and the amount of research that comes out of the National Genomics Research Library is likely to be proportional to the number of users that we've got actually accessing and working on the data.

And so I think for me, the biggest limitation has been that for various reasons we've not been successful in attracting international users to using the NGRL and therefore not getting as much out of the data as we could. There are other things that we could have thought of when we set up the programme that would be helpful now, in retrospect.

In the cancer side, for example, one of the things I think we've always regretted is that we didn't collect any of the cancer primary tissue. It's a bit too late now, and uh, we're trying to address this by other collaborations in future cohort sections.

But really for me, the biggest one is just, although we have a couple of thousand active users of the NGRL, we really could benefit and could get a phenomenally larger number by going international more.

**Jenny:** I think that one of the reasons for that is that it still does take quite a bit of training to understand the research environment and to be able to work within it.

And it's one of the things that I think the GECIPs have found, so these research partnerships in Genomics England, is that it's hard for each one of these to have a bioinformatician. We don't really have enough bioinformatics resource, and you do need to have bioinformatician expertise or bioinformatics expertise to access this and to use this data and move around effectively.

So that can be quite challenging and that's been part and parcel of having this in a trusted research environment is that Matt described the way you have to go into this environment to use this data and you can’t take it out.

But it is then difficult for, and it puts people off accessing it. And in the environment in the UK where we've probably tried to teach the different groups through the GECIPs, that will not be happening with overseas. And I know several overseas academic collaborators that we have, have balked at the idea that they can't take out their genes and analyse them in the same way that they’re used to in very systematic, high throughput ways.

So it's probably an element of training and it's maybe something that if we had more resource, that we would be applying that to bioformatics expertise and genetics expertise across our collaborators.

**Matt:** So if I could just return Dave to just mention some of the things that we're doing to address this, and Jenny, absolutely I agree with you that it, that it is a significant challenge.

Of course, the solution can't be that Genomics England provides more bioinformatic support directly to researchers. That can't happen because there's no way that we could scale that to the demand that's out there. So instead, what we've been doing is looking at a whole, lots of, uh, different support and I guess preventative approaches.

So one is to just to make the NGRL much easier. So for that reason, we're developing different research interfaces, some of which are point and click. For people who are non-programmers and also just trying to make it a much easier interface, even for experienced programmers.

We have worked extensively on our onboarding experience to make it much easier for people to onboard, so we don't lose as many researchers in the onboarding process

And we are also trying to provide better training videos, better manuals about how to operate around the NGRL, provide lists of frequently asked questions and, sort of, user chat rooms so that people can talk about experiences and ask for support from others who are users of the research environment to try and solve it.

The problem that people experience with our research environment is now pretty much the same problem as people have experienced with other major research environments like the UK Biobank research environment and the All of Us research environment, where again, you have to do the analysis within the research environment.

So I think we're all experiencing exactly the same pain, and hopefully by that combination of making things easier and providing better support and better instruction, that we will overcome that to a large extent.

**Jenny:** And I absolutely agree that your training materials have vastly improved.

There's much more of them now and videos and everything than there beginning when it was, uh, was quite a different setup. So I think that's very much appreciated by the users.

**Dave:** Thank you, Matt. Thank you, Jenny. Really, really interesting, detailed answers there. And that's great to be able to see the, both the, the challenge and the possible solutions and way forward.

So thank you both for that. That was, great. Coming on to the next question, and you kind of touched on some of this already, so again, without repeating, uh, yourselves and apologies for that... There's a question about the future research directions for Genomics England to go into and how can it most effectively move in the directions that you would like it to go in?

Matt, can I come to you first, please?

**Matt:** Right. We have more ideas about future research directions that we'd like to go to than we could possibly. So if I give you a long shopping list and you come back to me and say, this is too many things, well you're absolutely right. Um, we are going to have to filter these down.

Genomics is going through a phase of rapid technology development. There are all sorts of new ways of characterising the genome and in assessing patients that are coming up, that we need to then select and choose which ones we want to then see whether they're actually having a use in clinical setting and whether they can benefit patients with cancer or rare disease.

So assessing technology is one area.

Then related to that, we're really interested in using different mixed approaches. So combinations of DNA sequencing with RNA sequencing, transcriptomics; protein profiling, proteomics; metabolite profiling, metabolomics; and so on, together with imaging data like Jenny mentioned, so multimodal datasets using histopathology and imaging, and combining these to see if we can improve the diagnostic rate for our rare disease patients and improve our prediction of outcomes and therapy responses for cancer patients.

Pharmacogenomics is a big area that we are keen on getting into. We think that this has a lot of potential in avoiding adverse drug reactions and improving patient outcomes by ensuring that patients get the right dose of medications.

AI. That's, you know, Chat GPT has brought this to the forefront of everybody's discussion. Clearly it has a phenomenal amount of potential within the genomic space.

And lastly, hoping that we get to discuss more about rare disease therapeutics, which is absolutely booming at the moment in terms of new approaches that could be applied to the thousands of different rare diseases that there are out there.

And I think Genomics England is in a really good place to support those developments.

**Dave:** Thank you, Matt. And we hopefully will be able to come on to, uh, rare disease therapeutics a bit later on in the discussion, but thank you for now for that. Jenny, can I come to you? Is there anything you'd like to add to that, please?

**Jenny:** Well, not surprisingly my list is very similar.

**Matt:** That’s a relief.

**Dave:** Indeed!

**Jenny:** The concise version is: How do we analyse these genomes faster? How do we get the turnaround time really down? And that is going to be through the analysis algorithms, the bioinformatics, but very much I agree to machine learning. How do we get machine learning in and working so that it's not reliant on hoards of bioinformaticians, but we actually have the computer doing some of this?

And that then comes back to our point about making sure it's a growing resource. Because the more data we've got that we can train the algorithms on, the better they'll be.

So very much in terms of how do we better analyse the data using whatever AI and other resources we have. And the second thing is how do we just, as I say, move to that seamlessly throughput therapeutics?

**Dave:** We have one more before we come back round to you getting your chance to ask me some questions. So moving on to question six, what will Genomics England do to help research participants, for example, those with very rare conditions, make connections with the researchers who are interested in their gene condition in the interest of co-producing research for their mutual benefit?

Jenny, any thoughts on this one please?

**Jenny:** Yeah, I think it goes probably back to what we were talking about earlier about directly connecting the research participants with Genomics England. Actually, it would be fantastic if we had the opportunity to consent them upfront for contacting them so that we can both let them know if we think there's a result, either we've got a diagnosis or get through to the therapeutic, or they can follow up and see what are the options for them.

So it's a two-way thing. So they can identify the different groups maybe who are doing this kind of research, particularly if they are encouraging patient-led direct inquiries, which is certainly something we're thinking about in Oxford.

So I think that direct connectivity and making sure that there are mechanisms so both parties understand, you know, what they've signed up to and they can withdraw at any time, but they could be directly contacted about therapeutic options. That would be fantastic.

**Dave:** Thank you, Jenny. Matt, how do you think to add to, uh, what Jenny said here?

**Matt:** Genomics England does support both patients getting in touch with researchers, and researchers getting in touch with patients.

So we employ people within a clinical research interface team to help with that. Typically, that's involved mainly clinicians reaching out, trying to get in touch with patients, or researchers reaching out trying to get in touch with patients.

But we have also supported people going the opposite direction. It is more difficult for us to do patient contact back to researchers just simply because the number of different researchers is quite large, and it's not really clear always what each researcher is actually working on. But we do support people to try and do that.

I think it comes back to the discussion we had earlier about us being able to have better direct communication with patients. That would make life a lot easier if we're able to have that.

**Dave:** Thank you. And yeah, I think that's a really important point, how do we improve that connectivity between researcher and patient, whilst being mindful of the issues around security, de-identification, et cetera, that is a real set of, uh, of issues, I think you're absolutely right.

So, thank you very much for answering my questions so thoroughly. In the interest of balance, it's now your turn to, uh, throw a few questions at me. I believe you had one or two questions for me, please.

**Matt:** We're really always keen to hear from our patient participants what things they'd like Genomics England to be prioritising in rare diseases, noting that of course, If we prioritise something, then that means likely that we have to deprioritise something else.

So Dave, you're in the hot seat.

**Dave:** Indeed.

**Matt:** What would you prioritise and what would you then deprioritise?

**Dave:** I think firstly, we feel like we should be diagnosing more people. I'm thinking about the best way of delineating phenotypes associated with specific gene variants. So it's really focusing on that greater depth and scope and understanding around being able to diagnose more people and getting a better grasp on the different types of phenotypes associated with genotypes.

We think that's really important.

I'd say secondly, once the patient has been diagnosed, helping people with rare diseases make connections with the researchers who are specialists in their particular conditional conditions, where such researchers are already using the NGRL or planning to use it. Because we're mindful that, you know, there may be researchers out there who are not familiar with the research library and the arrangements, but they're doing research into this area. So it's introducing them to that research community and growing it wherever possible.

And ultimately, with the view to collaboration between researchers and people, not necessarily with much Genomics England involvement. It may be that it's between the researcher or researchers, plural, and the individual participant.

Once the connection has been made, for example, and making sure that rare disease support groups are aware that there will be subgroups of interests within the new GECIP structure and helping them to navigate their way to connecting with relevant subgroups of researchers.

And just to add to that point before I comment on my last point for this question, what we're mindful of is the patient community is a very complex, varied beast. No two patients are the same. No two groups the same. So supporting researchers to understand that we feel really important, we want to support you with that, as we can.

And lastly, telling the world about all the new discoveries in the NGRL so that rare patients and families or rare condition patients and their families, their children, and other researchers elsewhere can find these discoveries easily and carry them forward into new work where applicable. Hope that covers everything, but any points you would like me to clarify there, or does that help?

**Matt:** No, I mean, that helps. And you know, clearly one of the goals of the redesign of GECIP partnerships is to improve the ability of patients to interact with them. The current setup with 38 different domains, half of them roughly, are inactive. More than half of them don't actually have active participant involvement.

So the current structure clearly doesn't work. And so that's the key goal of the restructure is to come up with a more functional system, including that we get much better patient participant engagement with them.

So I'm confident that it's going to do that, but you know, prioritising things also means, uh, deprioritising things.

Are there things that you'd like us not to be doing so much of?

**Dave:** Right. Yeah. Again, very good point. So I'd say that whilst new things are of course the most exciting to Genomics England staff, we must not forget the people whose lives have already been touched by genomics after they volunteered to share their genome with Genomics England.

So a diagnosis is not the end of the story, it's the start of a new one. And, and Genomics England should make sure it leaves enough in the tank to support those patients who've already been contacted and involved so far, no matter what else they want to push forward next.

And really just to, to answer that point, really, there is a danger that somebody, for example, like myself, who's been through the 100,000 Genomes Project and in my end situation, we're still looking. We haven't got any clarity on genetic diagnoses yet. It's not forgetting that community of people who are still waiting. There's a lot of them whilst moving the focus more broadly and more in depth with all the amazing development, technological and otherwise that are going on. It's not forgetting the community such as myself, who are still waiting.

So I think it's not to do too much of the new stuff whilst forgetting the patients who are still waiting to hear. I think that's an important consideration.

**Matt:** Yep. Cool. So we definitely get that. And I guess the fact that we've returned over 2000 new diagnoses to the Genomic Medicine Service over the past 18 months, you know, indicates basically the priority and high level of activity that we still put into trying to maximise the number of diagnoses that we can make in our patients from the 100,000 Genomes Project.

**Dave:** Jenny, anything that you'd like to ask me or in relation to those questions?

**Jenny:** Well, I'd really like to emphasize that point that you just made, Dave, which is very important. The core activity and the day job of Genomics England, I guess, is the original 100,000, and also keeping up with GMS genomes.

I would be quite interested to understand more about how the research is viewed by the participants and the scale of that, because I wonder if there's enough understanding of a lot of the researchers are in doing diagnostics discovery and really trying to identify the diagnosis for patients and particularly, obviously in the rare disease side of things, I would be interested if you think that that's well understood by the patients and the patient groups and the Panel?

**Dave:** In short, it varies. You know, that's, I think you probably agree. It very much depends on the individual patient participants, patients who contributed to the discussion thus far.

You can have people like me who's a bit long in the tooth, who's been involved in supporting the Genomics England and the Participant Panel for a number of years. You'll have other people who have newly arrived into the national participant panel, or who are new members of the GMS alliances, whether they're on the patient public views panel or a member of that community in that geographic area.

So you'll have different people with different levels of experience and awareness and understanding of the genomics landscape and what that means to them in terms of the findings that come back for them and general discussion around new developments such as pharmacogenomics or the use of artificial intelligence.

So, it does depend, but I think in general there could always be more work done to raise the general level of genomics literacy, dare I use the term, to ensure that the widest possible group of patient participants and members of the public understand what we mean when we use terms like gene, genome, but also applications such as pharmacogenomics or understanding what that could mean for the future in terms of artificial intelligence going forward.

So more education, clarity on messaging, and being able to have that dialogue with an understanding of some of the concerns that patients have -- we've already touched on it already, around the need to secure and maintain security and de-identification of patient data, whereever possible.

**Matt:** I think we've had a great discussion. Thank you very much, Dave.

**Jenny:** Yeah.

**Dave:** Thank you, Matt. Thank you, Jenny, I think we've covered all of the bases, so can I thank you so much for your time and the detailed discussion that we've had around a number of really interesting topics.

We'll wrap up the conversation there. I just want to thank you both, Matt and Jenny, for joining me today. It's been a real pleasure and a very insightful conversation.

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