**Goodbye 2022, Hello 2023!**

**The G Word transcript**

**Chris:** Hi, I'm Chris Wigley, Chief Executive at Genomics England, and you're listening to the G word. Through the conversations we have on this podcast, we hope to bring the benefits of genomic medicine to everyone. Since launching the G word in January 2021 as part of our national conversation on genomics, we've recorded over 100 episodes. We've been downloaded in over 150 countries and have grown as an organisation from around 200 to over 500 employees. We've had some brilliantly inspiring and powerful discussions with patients, with research participants, with professors, researchers, award-winning genomic specialists, and many more. We want to look back on this journey with you and celebrate so many of the voices we've brought to you so far. Thank you to all of our listeners for tuning in each week, and for all your great ideas and support. Just as a reminder, if you have not already, please do give us a five-star rating on your podcast platform of choice. It really helps others to discover the pod. Welcome to the final episode of 2022.

In December 2012, the 100,000 Genomes Project was announced by then Prime Minister David Cameron with the goal of harnessing whole genome sequencing technology to uncover new diagnoses and improve treatments for patients with rare inherited diseases and cancer. Professor Mark Caulfield led the scientific discovery and delivery of the 100,000 Genomes Project. He was integral to the project's success and was consequently awarded a knighthood in 2019. This year, 10 years on from that first announcement, we heard from him and the brilliant Jillian Hastings Ward, Chair of the Participant Panel at Genomics England, who reflected on what we've achieved since the very beginning of the 100,000 Genomes Project and what Genomics England's future holds.

**Jillian**: I hope that lots of other families in the future are able to benefit faster from genetic diagnoses, and whole genome sequencing does hold the potential for really getting to the heart of what's causing different people's troubles earlier. That means that families will have less time in that diagnostic odyssey that we've heard so much about and hopefully be able to access treatments and that community together faster than we did. That would be the first hope, really, and I know that we're making great strides in that direction already. But there is still more to do there.

**Chris:** I hope you join me in celebrating the accomplishments, hard work, diligence, and commitment that Jillian, Rebecca and the Participant Panel have shown in shaping the past, present and future of Genomics England. Participants are, after all, the heart of everything we do. Now, from facilitating research for COVID vaccines to implementing our ground-breaking new initiatives, Genomics England has been and continues to be at the forefront of genomic medicine. Our diverse data initiative aims to reduce health inequalities and improve patient outcomes in genomic medicine for everyone, including and especially for communities who have historically been underrepresented in medical research. This year, we heard from the leader of this programme, Maxine Mackintosh, who spoke with Alisha Davies from the Alan Turing Institute and Brieuc Lehmann from UCL about the role of data and data science in promoting and improving health quality.

**Brieuc:** The lack of diversity in datasets can also be sort of seen as a form of structured missingness, where ideally, you'd have a representative sample of all the people in the population or across the country. For a variety of reasons, biomedical datasets are biased towards Western, white, rich men typically, which means that historically underserved groups are less likely to be represented in the data.

**Chris:** We also heard from our fantastic interns who joined us through the Black Internship Programme, Samuel and Madison, who discussed the need for black talents in genomics and how the Black Internship Programme is breaking barriers to enable the diversification process.

**Samuel:** I think when it comes to health, especially in a Black community, there can be a bit of distrust with giving over such sensitive information. I think that's why it's so important to have companies that represent these people because if you see people like you who look like you, you're going to feel like they have your best intentions, just a bit of human nature.

**Chris:** Alongside that programme this year, we also launched our Ambassador scheme to open a two-way dialogue with communities where we know that health inequalities exist, and which have historically been less engaged with genomic research. One of our ambassadors, Aman Ali, spoke of the Muslim Census Report with Mai Shehab and Zaynah Asad on the G word.

**Mai:** We've seen that Muslims are more likely to participate in research if they see it benefiting others and their local community. So, if we put out these personal stories and make them available, Muslims are more likely to see exactly where this research is going. And like we mentioned, trust and transparency – so the more transparent, the more likely you are to get involvement.

**Chris:** This year we explored the world of health and data science and imbalanced datasets in our episode with Bilal Mateen, Clinical Technology Lead at the Wellcome Trust and Evan Tachovsky, Director and Lead Data Scientist at the Rockefeller Foundation.

**Bilal:** There's a lack of diverse data, we know that. There have been loads of great pieces that have established that it’s not even that we just tend to collect datasets in high-income countries, but even within those high-income countries we tend to focus on people from privileged backgrounds. It is all of the enabling environment around that. It's not just what we collect, but also who's working with it and the questions they're asking and whether that benefit is equitably distributed.

The really simple way that I like to think about it is: we're basically looking into a dark room through a very tiny keyhole. You're only ever going to see a small part of what's possible, if you do that. We need to basically open the door, walk inside and bring the whole community with us to figure out what's possible.

**Chris:** For Prostate Cancer Awareness Month, we were joined by Errol Thompson, Errol McKellar, and Errol Campbell, who have developed their own organisations to raise awareness of prostate cancer. They talked through health inequalities and how and where they've made an impact in underrepresented communities.

**Errol:** What are we doing about this, then, if it's curable? Should we not be having a conversation? We do not want to be sending people to the doctors and the doctors are not seeing them. You can’t tell us on one hand that this is a big problem and then, on the other hand, you're not doing anything about it. Something needs to be done and it needs to be done now, because the numbers are, what we know, over 47,000 men a year are diagnosed. Over 11,000 men will die. So that currently means we lose one man every 45 minutes. By the end of this day, it's 129 men. These are numbers that were given to us, we did not make these numbers, up. It is currently one in twelve Asian men, it is currently one in eight White men, and it's currently one in four African Caribbean men. The risk is even more frightening if it's in your family, but that's if there's a conversation**.**

**Chris:** Angela Saini, a science journalist and broadcaster also spoke with the inequalities with us, as well as the history of race science, the use of language and its implications on genomics.

**Angela:** Given that we are one human species, we know that now, that we're so homogeneous as a species – that isn't so the difference doesn't exist, but you know that the vast majority of what we think of as human differences – cultural and linguistic – the act of categorisation in science itself, I've come to see as fundamentally fraught and political.

**Chris:** One of the highlights of 2022 was hosting our first Research Summit since 2019. This was a roaring success with over 5,000 attendees from across the world, both in person and online. Sixty-seven speakers over four different tracks, including cancer genomics, emerging technologies, rare disease, and policies and initiatives, with top researchers showcasing their latest scientific findings based on the work they've been doing on our datasets. Let's look back at some of the highlights. Our Chief Partnerships Officer, Parker Moss, spoke with world-renowned Daphne Koller on the use of AI and machine learning in drug discovery and discussed the value of multimodal analysis.

**Daphne Koller:** We're now in a world where there is this abundance of data, which is only, I think, the beginning to what we're likely to be able to see in the coming years. At the same time, of course, on the other side, we have this incredible set of machine learning methods that are able to make sense and extract insights from increasingly large amounts of data and many other areas of human endeavour. This seems to be a moment in time when those two tidal waves are about to come together in a way that I think offers us the opportunity to unlock some of the underlying secrets, the complexities that underlie human health and human disease.

**Chris:** We also heard from Jillian Hastings Ward, and our Chair, Baroness Nicola Blackwood, about the importance and value of patients being at the heart of research and through their lived experience.

**Jillian:** Trying to make sure that everybody who's around the table has an equal voice when it comes to co-producing a research project is really important. The researchers obviously bring their scientific expertise, clinicians come with the scientific and the medical knowledge, but I think patients and their families can also bring a lot of lived experience. You naturally become an expert in the condition that affects your family because you want to find out more answers. I think the energy that comes with having a rare condition and wanting to do something to make it better for yourself and for people like you is a really powerful driving force in moving forward.

**Chris:** At the summit we also heard from Dr. Jack Bartram, who's a Paediatric Oncologist from Great Ormond Street Hospital, about how he's using whole genome sequencing to transform the treatment of our youngest and most vulnerable cancer patients.

**Jack:** Patients are the most important in all of this, and I think if patients start asking for whole genome sequencing, or not just whole genome, advanced genomic testing that's available now through the test directory, that's going to be the way to do it. I think the big barrier, as I said, is this tumour germline match sample because I think, you know, acute leukaemia, it all happens very quickly at the beginning, and once you're hanging around waiting for a remission sample, people have kind of forgotten about whole genome sequencing, and you're well into the treatments. I think if you get everything right at the beginning, that's the key.

**Chris:** Our last clip from the Research Summit, Kate Grafton, one of our wonderful Panel members shared her journey with breast cancer and discussed the importance of engaging with the patient community with Vivienne Parry.

**Kate:** So, my challenge to you guys is: how can you make your patients understand your research? How can you get that out to them more effectively? Because we are interested. When we get offered the choice of treatments and our oncologists say, 'We've got this and we've got that, what do you want to do?’, that has to be an informed decision, and that's really hard if you don't understand the research behind that decision. Oncologists help us with that, but we do talk about the research, and we want to know more. We don't just want to be your sample. We want to work with you to look at how we can make kinder treatments, and how we can have longevity. I don’t just want quantity of life. I want quality of life.

**Chris:** The patient voice has been heard more and more, and our aim is to make it stronger and louder. We were joined by various participants from our Participant Panel throughout 2002. Rebecca Middleton, the Vice Chair of the Participant Panel took us through her clinical and genetic journey, the difficulty of having a rare disease, and how the lack of information can cause great loneliness and uncertainty, which explains why Rebecca opened HPA (Hereditary Brain Aneurysm Support) in response.

**Rebecca:** I know the power of a word, I know the power of a story, I know the power of a phrase. Language really is so meaningful and so valuable. It really does stick. I think everyone around the Participant Panel has an example, perhaps a bad example, of how they have been spoken to by a clinician. Some words really hit home and really hurt. They still talk about six years ago, our consultation with Dr. X, on this date and he said X. It sticks with people; it means a lot. It can really affect their mental health and how they think about themselves and how they think about their condition, or the condition of their children.

**Chris:** Dave McCormick, another brilliant member of the Panel was a guest on our podcast for Genetic Counsellor Awareness Day. Let's hear from Dave.

**Dave:** A number of patients haven't had the clarity of information, and so it's one message or one lesson that we can learn from this. And I'm determined, given my work with the Northwest Genomics Medicine Service, as their Interim Chair of the Patient and Public Voice Panel, is that whatever information you are communicating, you do exactly what it says on the tin: clarity of messaging, what can you provide, how can it be provided, what does this mean for you, the patient? I think it's so important. And I think, partly, one of the key roles of the Genetic Counsellor is to support with that clear messaging.

**Chris:** Dave discussed the importance of using lay language to help patients and families understand complex information relating to genomics. In line with this, the Panel developed a very important piece for the patient community this year, the Language Guide. This guide recommends how to talk about the people whose data is curated by Genomics England, and is actively being used to educate internally and externally.

**Jillian:** One of the things I'm most proud of recently has been the Language Guide, that's been written entirely by the Participant Panel and colleagues at Genomics England who've been able to advise on the kind of terminology in the language around how the researchers might be able to explain to Participants what they're up to, and also help researchers understand how people with rare conditions and other reasons for being in the project like to be talked about, because I think there's still the medical viewpoint coming in, it can sometimes feel quite harsh to a human being living with some of these conditions.

**Chris:** We also had some incredibly powerful discussions this year with guests who have sadly lost loved ones despite the best efforts of their doctors, including Zoe Conway and Julia Vitarello. A sarcoma campaign was led by the patient voice with Zoe Conway, whose husband Chris Martin died of a rare form of sarcoma in 2015. She recounts Chris's journey with sarcoma and how difficult it is to diagnose both sarcoma and its specific subtypes.

**Zoe:** Mentally, he needed to just keep on working. I think he sort of felt like if he had too much time to think, it would have a very sort of negative impact on him mentally. So he had to keep going, but also he absolutely loved his job, absolutely loved his job. I can't say he was at the pinnacle of his career because everyone was predicting he would just keep going, that he would just become more and more senior within the civil service, but it was a sort of dream come true for him, that job.

**Chris:** We also had the powerful story of finding answers for Mila, who was diagnosed with Batten Disease, and was the first patient to receive a medicine developed just for her in response to the molecular signature associated with her condition. Her mother, Julia, who I was lucky enough to meet recently, talked about her mission to help many more families access treatments for their children. As she puts it, from Mila, to millions.

**Julia**: I have been particularly excited as, over the last few months, I've learned more about specifically what Genomics England is doing and just the UK itself and how well poised it is, especially because of the whole genome sequencing effort at birth. But for other reasons as well, including the fact that David Cameron lost a son to a rare genetic disease and really stood up and kind of brought that to the UK and really showed that this is a problem that's not as rare as it looks, you know, and really stoop up for that. I'm excited to see what role the UK will play in trying to pioneer not only whole genome sequencing at birth but also what that could lead to in terms of individualised medicines.

**Chris:** Parker and I had the privilege of interviewing many inspirational leaders and scientists this year, including Bettina Lundgren, the CEO of the Danish National Genome Centre, with whom we discussed genome sequencing to benefit patients and help find better treatments and cures. Lucy Mackay also joined me on the G word and delved into her personal relationship to rare disease through her brother, and how a conversation at the dinner table with her parents opened the door to many opportunities. My fascinating conversation with Serena Nik-Zainal covered personalised treatments for cancer patients and the impact of the 100,000 Genomes Project.

**Serena:** What I would like to be able to see, and I hope it will happen in our lifetime, is that we will start to learn how to use the totality of information that’s available on tumours. I don’t just mean genomics, I mean any form of omics, including all the bits around the tumour, the microenvironment, the immune system, you know, very, very effectively. I just think in the last 10 years alone, cancer research has grown phenomenally. It's been extraordinary to be involved in all of it. It is one to watch, and it's been a real privilege to be in this space.

**Chris:** Right at the start of 2002, I spoke with Ben Goldacre, the Director of the Data Lab at Oxford University, on the use and safety of data, his book Bad Pharma, and the OpenSAFELY project.

**Ben Goldacre:** I think people have got so caught up in chasing metrics of performance that they've, in some cases, forgotten what the overarching objective is, which to my mind is doing everything you can with the skills and resources available to you – in my case particularly, data and people who know how to work with data – to reduce suffering and death. If you want to reduce suffering and death, you don't do that by depositing a PDF in a journal archive that gets read by eight people. You have got to go out there and have penetrance in the real world, you have got to change activity and behaviour.

**Chris:** Parker also had a brilliant conversation with the Nobel Laureate Harold Varmus about the future of cancer research and the major questions that studying diverse ethnicities will uncover through genomics.

**Harold:** As I look at what has happened in the last 50 years or so, I feel we've made a lot of progress, it's right to be hopeful about the future. But I think we have to be realistic and recognise that cancer is a phenomenon that represents an extension of things that happen normally. Mutations are essential to the generation of diversity in life, and mutations are what drive cancers. There are many other factors that influence cell behaviours. Trying to understand all those through the lens of cancer has been beneficial to all phases of biology and medicine.

**Chris:** Following Harold, cancer legend Robert Weinberg and Parker talked through why cancer occurs, why it spreads, the challenges and hopes for early detection, and how research is contributing to improving survival for patients around the world.

**Robert:** There's enormous potential in these recently developed immunotherapies to empower them to eliminate a whole series of different kinds of cancers. We’re not there yet. But I predict with great confidence that, 10 years from now, a whole variety of commonly occurring human cancers will be treatable successfully, and maybe even curable, by future immunotherapies that are developed over the coming decade.

**Chris:** Parker was also joined by the Pulitzer Prize winning author Siddhartha Mukherjee, who released his new book, *The Song of the Cell*.

**Siddhartha:** All of these things – prevention, early detection, the use of immune therapy, the birth of novel drugs, potentially, the birth of combination targeted drugs – should make patients hopeful. We are trying, I think our best, to understand but also now to use that understanding to treat cancer. We have gone from genomics to cell biology to organismal biology of cancer. I think that is yielding new drugs that we hadn't seen before. So I'm super excited about it, and I'm eager to learn what the next steps are.

**Chris:** Professional Drug Developer, Nadeem Sarwar, also joined us to explore the phenomenon of making medicine, how quickly we can change the realm of medicine, and the possibilities of the future. The evolution and future uses of genomics beyond healthcare was the subject of my discussion with Sir Patrick Vallance, the government's Chief Scientific Adviser, who also touched on the impact of the pandemic and how genomic sequencing is crucial to understanding the spread of 2019.

**Sir Patrick:** The whole area is going to be crucial for everything from monitoring waste – you can start to track which ship has discharged things that shouldn't discharge in a port – to monitoring biodiversity, such a key area for the future. You can think about the impact on the environment on the changes in species across the world over time. You know, this is going to be a ubiquitous area of societal discussion.

**Chris:** At Genomics England, we're dedicated to amplifying and strengthening women's voices in STEM (science, technology, engineering, manufacturing). This year, we've had various conversations with some fantastic women in STEM. First up, young Scientist Georgia Whitton took us through some unconventional ways of getting into science and talked about her dedication to inspiring young people to pursue a career in STEM, not least via her own YouTube channel.

**Georgia:** I just really want people to understand that there are other routes into genomic data science that don't involve getting postgraduate qualifications. They involve learning to code. And if we tell undergraduates that earlier, then they will have more opportunities when it comes to finishing their degree.

**Chris:** For the International Day of Women and Girls in Science, we had a special episode with three brilliant women at Genomics England to promote full and equal access in science for women and girls. Dr. Ellen Thomas, a Clinical Director; Arzoo Ahmed, our former Head of Ethics for newborn sequencing who's now with our friends at Our Future Health; and Dr. Cassandra Smith, one of our Senior Bioinformaticians who works in diagnostic discovery, all discussed their careers, the challenges they faced along the way, and how being a woman has impacted their careers.

**Arzoo:** Life is so precious; we really shouldn't be spending any time doing things we don't enjoy and being in places where we don't really want to be. So, I'd say, figure out what values are important to yourself, what brings you that sense of contentment and fulfilment, what it is that life is calling you to in every moment, and respond to that. It will eventually make sense and the dots will join up, and you'll find a coherency that you perhaps didn't sense as you were going through that period.

**Chris:** Stepping back, 2022 brought some fantastic conversations with a range of incredible guests from whom we've learned so much. Huge thanks to all of them. We are really looking forward to what is yet to come for Genomics England and the science world and beyond. Thank you so much for listening to this week's special, the G Word, and for joining us on this journey to highlight and debate the implications of genomics as it comes into the mainstream of healthcare and society. If you have any views on these topics or have a person in mind that you'd like us to interview, do write to us at podcast@genomicsengland.co.uk and remember to subscribe to the G Word on Apple Podcasts, Spotify, or wherever you listen. If you enjoyed listening, give us a great review – that really helps other people find out about the series. See you again on the G Word in the New Year.