MND Matters: Episode 35:

Transforming MND research with AI: Longitude Prize on ALS

Helen
Welcome to MND Matters, brought to you by the MND Association and sponsored by Toyota GB and Toyota Financial Services. Hi, I'm Helen, and I'm part of the fundraising team at the MND Association.

Today on the podcast, we're delving into the Longitude Prize on ALS, an incredible £7.5 million pounds worth challenge prize, which is hoping to transform drug discovery for people living with ALS, the most common form of motor neurone disease, the prize will see some of the best minds across the globe compete to use AI or artificial intelligence to accelerate our progress towards effective treatments. It sounds exciting, but genuinely what does it all mean, and how might it benefit people with MND now and in the future?

Helping me answer those questions today is Tris Dyson, who is the founder and Managing Director of Challenge Works, who has designed and delivered the prize, and the MND Association's, Dr Mike Rogers and Dr Brian Dickie.

Tris, I'll start with you, if that's okay. Some people might be aware of a Longitude Prize, but I imagine there'll be many people out there that aren't familiar at all. So can you start by giving us an insight into Challenge Works and a Longitude Prize?

Tris Dyson
Yeah. Well, good, good to good to be here. Um, Challenge Works is an organisation that designs and delivers challenge prizes. And what we do is we look in all sorts of different sectors, ranging from space to agritech to health, at problems that haven't yet been solved, and we set up prizes that stimulate innovation to solve those problems. And our flagship prize, our most audacious prize, is called the Longitude Prize. And the reason for this is the original challenge prize was actually going all the way back to the 18th century, where there was a big problem, which is, how do you circumnavigate the world effectively when you can't, couldn't, then measure longitude effectively at sea, you could, you could measure latitude, but not longitude. And so the UK government launched a huge prize for anyone

who could solve longitude. And eventually that resulted in the chronometer, which is on display at the Maritime Museum, and that changed the world. And so the Longitude Prize, our Longitude Prize, is a modern reinvention of that prize. Last year, we had a Longitude Prize which focused on antibiotic resistance, and this look for a diagnostic that would tell you, imagine, if you go into a clinic and you've got an infection, it would tell you whether you whether you had a bacterial or a viral infection, and would tell you very, very quickly, if it was bacterial, exactly which antibiotic you needed to take. That's what the challenge prize asked for. And that was won last year, and that's on display at the at the science museum, and we'll be coming to clinics near you soon. So it's really going to transform primary care. So that's what a Longitude Prize is. And then, as you said, we're launching this new Longitude Prize. The Longitude prize this time focused on ALS.

Helen
Amazing. That sounds exciting. And the word that really jumped out at me then was audacious, and solution focused. So if people didn't understand maybe some of that, I hope they heard audacious and solution focused, because we all know that's what the MND community deserve. So Tris, can you tell us a bit more on, on why this prize is now focused on, on ALS specifically.

Tris
Well, I mean, firstly I myself a patient. I was diagnosed about two years ago, and like other patients, I was shocked by the bleak prognosis and the lack of treatments. And so it was that reason, really, that I wanted to develop a prize. And one of the first things we did was talk to to Brian and to the MND Association and lots of other people about what a prize might look like. There's a few things that we discovered in that kind of in talking to people. The first thing is, in recent years, in the last 10/15 years. Is the understanding of the disease has gone from being very, very little to a significant improvement. So there's a good sort of foundational knowledge now of the disease. And so you can see that manifesting itself in new drugs, specifically tofersen, although that only is focused on a small subset of patients, it shows what's possible and it shows how that level of understanding is leading to potential treatments. So there's been that big change, and a lot of that has been through research that the MND Association and others have supported. And a lot of it has been funded by patients. And so the kind of foundations are much better than they were. So I think that's the first thing to say.

The second thing to say, though, is that the reason we don't have treatments is that the disease is extremely complex, and it's highly varied according to different patients have very different types of subset of the disease with very different outcomes, and because of that complexity, it's been very difficult for researchers to really get to grips with it and come up with effective treatments. Now what we think is that AI offers great potential in being able to handle that complexity and really start to uncover patterns in biology that you could fire drugs at, basically. And so that's what this challenge is aiming to do, which is to find targets that would have high potential for drugs to be developed. And then we obviously hope that pharma and biotech will pick them up.

Helen
That sounds exciting and amazing, that that technology of AI is around now, when we've got that foundation of understanding and we will come back to talk a little bit more about AI and what AI is. But I'm going to first bring in Brian, Dr Brian Dickie, who's our Chief Scientist here at the MND Association,

just to ask you to explain a little bit more about the MND Association's involvement in this Longitude prize so far.

Brian Dickie

Thanks, Helen, great to be here. Yeah. First of all, I thought I'd just say a little bit about terminology, because not everybody will be familiar with ALS. Motor neurone disease is a bit of an umbrella term. It covers more than one condition which affects the motor neurons, but amyotrophic lateral sclerosis, or ALS, is by far the most common form. It accounts for over 90% of newly diagnosed cases. The term MND was actually coined by a British neurologist, rather appropriately called Lord Brain. And so MND is most more commonly used here in the UK, but the terms ALS and MND tend to be used interchangeably by the research community. So basically, ALS is the most common form of MND.

And you know, I've been working in the ALS field for almost 30 years now, and as Tris said, you know, when I started, it was very much a Cinderella disease. And I think over the past decade in particular, we've seen this disease move from a relative scientific backwater to the forefront of neurodegenerative disease research, and hopefully in the not too distant future treatment as well. So when Tris first approached, I must admit, I was probably a little skeptical at first, but I could see the innovation and innovation is generally a good idea. We just needed to work out how it could best be applied to the current MND research environment to fill a gap that currently exists in MND research, which could be addressed by collaboration and also pulling in new knowledge and expertise from outside of the traditional neuroscience and neurology fields. As Tris has said, there's been an absolute explosion of MND research in recent years, a lot of new knowledge, and a lot of it has actually been driven by better data collection and sample collection through biobanks, and this is all giving us a huge amount of information into genetic factors that are linked to the disease, the different biological changes that are occurring from cells through to the changes in the whole body, and also a lot more information about what we call the phenotype. In other words, how the first symptoms of the disease appear, how it progresses, how this varies between one person and the next, and it's almost like this data explosion is like throwing 1000s of pieces of a jigsaw onto the table and there's not enough work being done in actually taking a step back and trying to work out how the bits of the jigsaw fit together. And that's really what we need if we're going to build up a clear picture of this disease. You know, to put a face on this disease, we need to work out how these many different pathological events like jigsaw pieces are coming together to cause the motor neurone to die.

And I think that's where artificial intelligence comes in. You know, it doesn't just provide the chance to analyse data much more quickly, but it can also look for patterns that are way, way more complex than humans alone can identify. So hopefully it can come up with completely new ideas and potential solutions as well. So I think it's a very exciting time. I do sometimes say it's a little bit like the wild west with AI at the moment, there's lots of innovation going on. There's lots of AI companies being set up around the world, and this prize approach, it's a little bit like a funnel. It allows you, hopefully, to capture a lot of these new ideas and these organisations and then kind of feed/ award a number of initial prizes to get the ball rolling, and then the most successful of the applicants can then move forward to a smaller number of larger prizes to push these ideas forward, hopefully into new treatment targets,

Helen

Brilliant. I mean, there's probably a lot of listeners that will have heard of AI, Artificial Intelligence, and again, might share that being sceptical or unsure of what it is. They're hearing it in the news. We're hearing it being talked around at a government level. But what I'm hearing today is this is definitely AI for good, and it's harnessing a completely innovative option to try and better understand the disease. So Tris, I'll come I'll come back to you and just sort of ask you again, why? Why AI and why now?

Tris
Oh, I think it is true that we are on the cusp of a new revolution in AI in in the drug discovery process. And Brian's right, it's a wild west. You know, some of it's some of it will be effective, and some of it won't, as with any new technology revolution. And you hear a lot about the potential of AI, and it's normally used in a shorthand, I think when the Prime Minister visited Donald Trump, they talked about AI curing cancer, you know, as though cancer is one single thing. But what's happening at the moment is a lot of these, a lot of the emerging AI powered biotech is is being aimed at the larger diseases. So it's been aimed at cardiovascular disease, cancer, and there has been some, there was quite a lot aimed at COVID successfully as well. So it's starting, perhaps, quite obviously, I guess at those larger disease areas, but those larger disease areas, I think there's already a high level of understanding of those diseases, and there's often quite a lot of treatment options, whereas I think ALS, as we were saying, doesn't have any treatment options. And it's because it's so complex that we think that AI could potentially make a big difference. So what we want to do is attract some of that energy towards focusing on this disease, where we think the potential impact is, is huge.

But what's really important is, is that AI won't do it on its own. An AI company that's got no disease knowledge, that just runs at these like large data sets, could come up with all sorts of things that are not relevant. So it has to be done in conjunction with people who have disease knowledge and disease understanding. So it's a partnership between AI and researchers who are able to guide the AI effectively that we think is going to be successful. I think the other thing I'd just to say about this, which is the what's making this Prize possible, really, is the data. So there's a huge amount of data that we've pulled together. A lot of it has been funded by patients, including through the MND Association, but it's a global set of data. It's it's very rich data, some of it's from the Europe, some of it's from the US and elsewhere that the innovators will be able to access to run their AI models against, and it's that huge data set that's going to make these potential breakthroughs possible I think.

Helen
Brilliant. So I feel like this is a great time to bring in Mike, our Director of Research and Innovation at the MND Association. So the MND Association is the principle funder of the Longitude Prize on ALS. Mike, what will this prize mean for MND research, and how does it fit with our ambition for research innovation?

Mike
Thanks Helen. It's really nice to be here. So we are the biggest charity funder of MND research in the UK, and we obviously want to accelerate progress towards effective treatments for everyone living with MND. Now, there are many different approaches to drug discovery and development, and it's important, I think, that we're working on a number of fronts to maximise our chances of finding transformative treatments, as Tris has said, so as Tris and Brian have covered, AI is a rapidly developing field in drug

discovery. We've seen it in other diseases have some real success, and it's got huge potential in neurodegenerative conditions. I think the three exciting things for me, all of which are going to positively impact MND research. Firstly, it's the international scope of the prize. So this is going to be leveraging expertise and interest from all over the world, which should really maximise the chances of success. Secondly, it will bring new organisations into MND research, and will generate new collaborations, and the more talented people we have working on MND, the better. I think this is really exciting. And bringing in the private sector and their expertise as well, I think is a really kind of unique selling point for this. And thirdly, as Tris has drawn on the consolidation and utilisation of data, there's a lot of data from a range of different sources all across the world, which are going to be brought together here, mostly for the first time, which will really maximize the potential of the data and increase the chances of us finding something transformative. I think the benefits of the prize will go beyond the immediate funding competition. We're going to see new collaborations. I'm confident that we're going to see new insights into MND. As a result of this, we'll see new ways of working between traditional researchers and new entrants, and also raised awareness of the disease across the world. And finally, I think this really exemplifies the power of collaboration in finding new treatments. Drug discovery and drug developments are expensive and they're really, really difficult. We can't do this on our own. This prize offers a unique opportunity to collaborate with a range of funders from across the world, being led by a group of experts at challenge works. So this is really exciting from the from the perspective of bringing on MND research.

Helen
This is exciting again, that hearing collaboration and bringing new people into this sphere of research to find the answers we all deserve is brilliant. It's exciting. I feel like it is going to grow much more hope. Tris, the prize is open now. Can you talk us through what the other milestones are going forward and how this prize will work with its timeframes?

Tris
Yes so the prize is open now and applications close in December, the details on how to apply are on the website. So that gives us 5 months and the reason for that is that we want people to form teams. So if there are companies with AI expertise but don’t have disease expertise, we want them to find people who do have disease expertise and we’re very happy and able to connect people. And the other way round, if people have disease expertise but potentially don’t have the AI capabilities we would like to help connect them with people who do. That doesn't mean that you have to, you have to apply as a joint team right from the start, because it's a long process, and we can sort of support people as they go along. There's lots of international partners in universities and on the private sector who are here to help. So for example, the Packard fellows, which are an international group of research fellows, are part of the partners. We have a number of companies with AI and computational power that are here to support university teams. So we have that five months, which is really to help as much as possible get those really strong teams together. We'll also be allowing access to some of the data over that period, so that teams will be able to come in and play around with the data, run their models and see what they think they might be able to do, and then applications close, and we select, we will select 20 teams internationally, and that they will then have nine months, so from April to December of next year to identify targets in these data sets that and to produce evidence for these targets as to how, how much

potential they might have. So targets means elements of the biology that if you could do something, if you could alter it, you could alter the course of the disease, basically.

We will then down select those 20 teams into 10. We might take in another couple at that point, potentially, we're leaving that, leaving that as a possibility. And those 10 teams will then build their evidence base and prioritise those targets, and they will continue to do that in the data, but they will also be able to test things in the lab at that point as well. So you'll have that feedback loop.

We then close again, and then from August 2028 we will go down to four teams, and those four teams will run in the lab. So probably the AI part of it included that point, although there might well be role for for AI, but this is where you move into the lab over a two year period. And that's really about identifying or validating those targets for their potential drug ability, and then we will reward. We award a prize to the one that's got the highest potential. So we're not going to it's not going to create a drug at the end of it, but it's going to create lots of, hopefully, targets that could become drugs. And what we want at that end is for the private sector, for investors, pharma, maybe biotech to come in and pick them up and run with them. It is also possible that repurposed drugs could maybe an option here as well, depending on what the technology and what the teams discover, and obviously, we hope that a repurposed drug would be viable in some of these cases, because that would be much quicker in terms of potentially turning that around into a treatment for patients. So that end to end takes five years, and that's, that's, that's, that's quicker, much quicker than a traditional time frame.

Helen
And I suppose, given that you you start with many teams, and you're whittling it down, excuse, my ignorance. But if, if other teams don't get the prize going forward, there might be other avenues for their research to continue, if there's hope or there's insight in those in what they're finding out?

Tris
Yeah that’s quite common with teams that come through they may not fulfill the criteria to go on to the next stage, but nonetheless, they've got so far, and they might well progress, and we want as many of them to go forward as possible, and we want as many of them to get investment as possible, or funding as possible, to go forwards. And that's very commonly what happens. It's also worth saying something about. So Brian describes ALS as a term versus MND. So ALS is, yeah, over 90% of MND. And we're using the ALS because it's the international language. It's an international prize, but there may be spin offs for other diseases, so these data sets overlap with dementia, for example, frontotemporal dementia, so that there may be avenues that that that are unlocked to this, that have benefits, potentially for some other neurodegenerative diseases as well, even though, of course, our focus is ALS.

Brian
Yeah, if I can just add a little bit to that, I do think there are some really exciting potential spin off benefits here, for example, one thing that might come out of this is the identification of new biomarkers, so those could be used to help diagnose the disease more rapidly. And common sense dictates, the sooner that a diagnosis is made, the sooner a treatment is given, the more effective that treatment is likely to be. Biomarkers can also help predict how the disease is likely to progress within an individual,

and, very importantly, give a readout of whether a drug in a trial is having effect or not, more immediately than it might be apparent by changes in progression of the disease, for example. So I could envisage that some of the work coming out of this might actually head down that field. Now, it won't necessarily be directly relevant to the prize, but hopefully it will attract its own investment to take that forward. You know, ultimately, what we're trying to do through this prize is home in on what are the key pivotal biochemical pathways that determine life or death for a motor neuron you know, it probably won't be a simple, one size fits all approach to treatment here. I think cancer was mentioned earlier. Well, ALS like, cancer isn't one disease, it's many variations, and we need to understand this heterogeneity if we're going to treat it successfully. So I think the prize will also move us quite rapidly into an era of stratified medicine, working out which of these pathways are dominant in particular subtypes or at particular stages of the disease, and when it comes to trials, that would mean we'd be able to select the patient groups most likely to respond to a particular treatment.

Helen
Amazing, and this is all starting with that artificial intelligence. I'm going to ask you all, um, so whoever comes in first, what? What can our community expect to hear about this prize as we go forward.

Tris
Well, I mean, that will, they'll hear quite a lot as we go through the process. Clearly, a lot of it is, I mean, it's a science prize. So it's we're we're quite a few years away from being able to say this has that effect. So that's obviously where we're aiming for. But it'll be a while until we get there. However, I think one of the things that I'm keen that we engage the patient community around is around this is around the power of the data. So this prize is obviously powered by this data, but whether it's this prize, or whether it's or something else, the only way we're going to come up with solutions is by all likelihood, is by getting into grips with this data inside the prize or outside of the prize. And we've got some fantastic data partners from Europe and North America, but we need to build on that and make that make these data sets much more available globally to anyone, regardless of whether you're in the prize or not, and that, I think that's going to be critical to coming up with a solution. And I think that's something particularly a lot of, I mean, a lot of this data, obviously it's patient data, it is our data, but it's also a lot of it has been funded by patients the collation of this data. So it's really important that we work out well how we are going to make this data much more globally available. There was an initiative in the US, or there is an initiative in the US to pull these data sets together, but and hopefully that will carry on. But we all know what the US funding environment looks like at the moment. So I think that's, that's the sort of thing that we would like to engage the patient community on whilst we're waiting for the results essentially from these teams.

Mike
Yeah, I think one of the really interesting things about this, this approach is, is the different stages. So you notice you're giving somebody a load of money, waiting five years to see what happens. There's almost opportunities for check ins with the community at the different stages as we go through and I think that'll be really interesting in terms of the way that we can describe what's going on, what's being found at each stage, and really keeping a fire let under this. So I think that, I think that'll be really exciting for the community to see how this this prize, develops, and how things are taken forward, and actually watching that happen in real time. That's quite an unusual opportunity with drug discovery and

development. And I think that'll also enable us to talk about that area in a bit more detail with our community. So I'm really looking forward to that.

Brian
I think I'd just like to return to the data bit briefly and say that Tris and Challenge Works have done a fantastic job in bringing the community together, because these data sets were quite disparate. They weren't harmonised, and it's really great to see how the community is internationally, is getting behind this. And of course, you know the there's a saying, garbage in, garbage out. If the data isn't robust and easy to access, then there's a high risk of not coming up with the answers. But so this is a piece of work that was really required, and I think is actually one of the key outputs of the prize before it's even formally got into second gear. So, you know, I think, if you remember, actually the Ice Bucket Challenge, which is what, over a decade ago now, the association used a yard, a large chunk of that funding to build up biobanks to carry out gene sequencing, to stimulate international collaborations. And I think what we'll be seeing and able to report on is the development of that and hopefully the fruits of all that labour that goes back over a decade now.

Helen
Amazing. Thank you all so much for sharing your insight and the enthusiasm behind this prize. I hope what our listeners have enjoyed hearing are those that words audacious and innovation and effectively we can hope for more hope with this prize. So I'm going to end by thanking all of the MND Association supporters, because, as I mentioned, the MND Association is the biggest funder of this prize, and that is only possible because of all the people that tirelessly fundraise. Thank you to all of our amazing MND community for helping to contribute to this prize and for helping unlock the future with every donation. So as you know, the prize has now launched. It's open for entries, and the Challenge Works team are excited to talk to anyone who is keen to apply. We'll put the Challenge Works details in the show notes, so lastly, just a huge thank you to Mike, Brian and Tris for coming on and giving us an insight into AI Artificial Intelligence for good, and the MND Association and Challenge Works' commitment to innovation. Together we will drive forward that drug discovery using artificial intelligence.