



MIGRAINE WORLD SUMMIT

INTERVIEWS WITH WORLD LEADING EXPERTS

TRANSCRIPT



MIGRAINE GENETICS, MTHFR AND CONCUSSION

LYN GRIFFITHS, PhD



Introduction (00:00): So glutamate is a neurotransmitter ... so it's a chemical that's expressed in the brain. And it's been shown that glutamate levels are actually normal in people who suffer from migraine; it tends to be increased in people who suffer from migraine, particularly when they're having a migraine attack. It's also implicated in animal studies: it's been shown that there's some abnormalities in glutamate levels. We also know that glutamate can affect a number of other neurotransmitters in the brain, as well.

Carl Cincinnato (00:35): Is migraine due to your genes or your environment? If migraine is genetic, can we really modify the frequency and intensity of our attacks and how our genes respond to the environment, or are we just stuck with bad DNA? Researchers have been digging into these questions with an unprecedented genetic study of almost 60,000 people with migraine. What they've learned may change the way you manage migraine disease. To help us uncover the genetics of migraine, concussion, and MTHFR, is Professor Lyn Griffiths. She's a molecular geneticist with over 24 years experience studying complex gene disorders with expertise in human gene mapping and gene expression. Professor Griffiths, welcome back to the Migraine World Summit.

Professor Griffiths (01:17): Thank you very much, Carl.

Carl Cincinnato (01:18): Can you share with us some of the major work that's been happening within the field of genetics and migraine?

Professor Griffiths (01:24): Probably some of the most exciting things at the moment in terms of genetics of migraine is that a lot of people around the world are now starting to collaborate by merging all their data sets and looking at genes across all the different chromosomes to try and work out how many genes are playing a role in migraine. By merging different data sets, we've now been able to look at over 60,000 people and compare their DNA to normal people's DNA; and that's given us a lot more power to identify the genes that play a role in the different types of migraine.

Carl Cincinnato (01:57): And how many people are we talking about? Is it a couple of thousand people that have had the genomes mapped with migraine or is it higher than that?

Professor Griffiths (02:04): No, I think the current consorting levels are over 60,000 people are involved in this and this has led to the identification of a greater number of over 40 different genetic loci involved in migraine now. And these are the common types of migraine.

Carl Cincinnato (02:19): What is a genetic loci?

Professor Griffiths (02:22): Genetic loci just means a gene ... a loci is where the gene actually lives in terms of on the chromosome.

Carl Cincinnato (02:28): Does migraine have a genetic basis?

Professor Griffiths (02:31): Yes. Migraine shows strong familial aggregation. This means that migraine is inherited in families. Most of the time, 90% of the time, a first or a second degree relative are affected by migraine; so, most of the time it is genetic. Most of the time, about 50% of the time, it's either one of your parents or first degree relative. But what we found is that it's not always clear cut inheritance patterns. It's just that genetics plays a bigger role in migraine. It's unsure exactly how much, but probably about ... between 45 and



60% of the overall component of migraine is probably genetic. And then the other part would be the environmental factors: things like lifestyle, foods, triggers, things that play a role and interact with the background of genetic susceptibility.

Carl Cincinnato (03:24): What is a causal gene versus a gene association or genetic association?

Professor Griffiths (03:30): Because in the common types of migraine, there's no really clear cut forms of inheritance ... so it means that there's a genetic basis, but it's not absolutely clear cut from one generation to the next. So looking at the common types of migraine, we know there's a significant number of genes that are involved, and we know that there's susceptibility genes that are involved, and this is what's termed an "association" — meaning if you have a particular gene variation, then you're more likely to suffer from the disorder. That's quite different to a causal mutation. A causal mutation is where you actually have a particular variation in a gene and every time you have that variation you will have the disease, definitely.

Professor Griffiths (04:11): And in fact, there are three known causally related genes for migraine. And these are the very severe forms of migraine and, in particular, they're called familial hemiplegic migraine. So they are a subtype of migraine with aura. They result in very severe symptoms; quite often young age of onset, as well. They can result in symptoms such as paralysis down one side of the body, sometimes coma, sometimes extended coma, severe aura symptoms. And as I mentioned, it's inherited through families; quite often young age of onset. And what you'll find is that it is inherited in a dominant fashion, meaning if you have it, then all of your children have a 50% chance of having it. This is what's termed "monogenic" forms of migraine. So people who have mutations in one of three known ion channel genes, actually result in people getting this disorder. And it's inherited every generation. So these are causative mutations — so variations that occur in either a calcium channel, an ATPase, or a sodium channel gene. And people who have these "causative mutations" definitely have the disorder and they pass it on to the next generation.

Carl Cincinnato (05:27): So it sounds like you can have a causal gene and you definitely have migraine, but there's also a broader population of people that have migraine that have a series of genes that are associated, but none that necessarily are guaranteed to cause it.

Professor Griffiths (05:41): Exactly right. So a causative mutation — so a mutation in one of these three known causative genes — results in definitely having the disease and it runs through the family. And if you have that mutation, you have it and your children will have it. Whereas an association is where you may have a large number — it may not just be one particular variant; it could be more than one — that makes people more susceptible to developing migraine.

Carl Cincinnato (06:06): So people could have a number of different genes that are associated with migraine but still not have migraine.

Professor Griffiths (06:12): Correct. It could be that they may have it at different times. It could be that there's an environmental interplay or perhaps a trigger that comes into it. So there may be other roles, potentially even interacting genes, that will result in whether they actually develop the migraine.



Carl Cincinnato (06:27): Why do people have gene mutations? It sounds like quite a scary term. Can you explain how that affects our genes?

Professor Griffiths (06:35): OK. I think everybody thinks that mutations are bad and, "Oh! If I have a mutation, I'm going to have a disease." But in actual fact, mutations cause all the differences between all of us: so the fact that some people are taller, some people are shorter, some people have one disease and the other people don't have that disease. Some people have different intelligence levels, some people have different colored skin. All of these variations are due to mutations. Some of those are mutations that you acquire as you age, such as things like mutations that result in cancer. And some of them are mutations that are passed from one generation to the next and just result in completely normal differences between us. So not all mutations are bad. They're actually the cause of the differences between us, and we want to have differences in our population. But it's the mutations that result in disorders that's important for trying to identify and diagnose particular diseases like migraine.

Carl Cincinnato (07:32): So does our DNA stay the same? Do these mutations change our DNA?

Professor Griffiths (07:37): So the sorts of mutations that are inherited from one generation to the next in families are the ones that are in your, what's called your germline. So you're actually born with those and you pass those on to the next generation. But you can actually acquire mutations. And these are called somatic mutations and they're particularly important for disorders that ... result in things like aging and things like cancer. So cancer is primarily not inherited. Most people think that cancer is inherited, but probably about 5 to 10% of cancers are inherited ... 90% of them, at least, are acquired. So they can occur as you age because we do have mutations all the time. Every cell that gives rise to another cell has to duplicate its DNA. And it's very hard to — it's a lot of DNA there — and it's very hard for every cell to perfectly do that.

Professor Griffiths (08:34): So sometimes there are mutations there, and we have enzymes in our body that correct the incorrect mutations. They go, "Oh, that's a bad one," chop it out, and replace it. And so normally our enzymes control the level of mutation as we age and as our cells constantly divide. But as we get older, the level of those enzymes that we have drop down. They don't work as well; we don't produce as many. We can't keep up with the normal, quite low level of mutations that are there, and we can't correct them. We also, as we age, tend to do things that promote mutations, like smoke cigarettes or go out in the sun and get exposed to high levels of ultraviolet radiation; perhaps eat bad foods that might be mutagenic as well. So there are certain things that can increase mutation rates and as you age, your enzymes can't correct them. So yes, you tend to develop things like aging disorders and things like cancer as you age.

Carl Cincinnato (09:37): So you mentioned there that food can actually cause genetic mutations?

Professor Griffiths (09:43): Well there are certain types of foods — not commonly eaten ones that we have around. And there are things like pesticides or even certain hair dyes, many of which have been banned now. There are certain preservatives that are added to things — again, many of which we don't actually use now. But there are certain types of things that increase mutation rates. So they don't necessarily cause a mutation; they increase the rates that we have there. Yes. And so our environment plays with our DNA, if



that makes sense. And we know this: environment can actually be intricately involved with whether we even have a disease or we don't, because they interplay.

Carl Cincinnato (10:19): Is that what epigenetics refers to or is that something else?

Professor Griffiths (10:23): Epigenetics is probably the best known way to look at the interplay of environment and what's actually happening with your DNA. We're doing some epigenetic studies now looking at migraine to see whether there are some epigenetic changes for us to actually try and correlate — things like diet, or food, or hormonal changes, or things in your environment — and how it might change your DNA. Epigenetics normally doesn't measure changes in the underlying DNA base sequence. It measures the way that the structure of the DNA (it's called chromatin) can change with time or with environmental changes and methylation, which is patterns that overlay the DNA bases and can cause changes in the chromosome structure. And we know that these methylation changes can be directly related to changes in your environment, particularly things like different foods that you may eat, etc.

Carl Cincinnato (11:20): Approximately how much — and you might have covered this a little bit earlier — how much of migraine is genetically predetermined for the average person?

Professor Griffiths (11:27): There's been a number of different studies, and it does seem to vary slightly, but in general it's thought that migraine is probably between ... probably around about 50 to 60% of it would be genetic and the other part would be environmental. And these are the common types of migraine; this is not the ones where there's known causal mutations.

Carl Cincinnato (11:46): Do you think our genes affect our severity, frequency or threshold of migraine?

Professor Griffiths (11:53): Well, we certainly know that the monogenic forms of migraine — the ones that I've mentioned where there's three known genes — they absolutely and totally affect whether you do or don't have migraine. They also, particular genes and particular mutations in those, affect how severe it is and how frequent it is as well. It's quite possible that genes will also play a role in the more common types of migraine in exactly the same way. So it could be that it's not a single gene. It could be that there's multiple interacting genes that will affect things like that.

Carl Cincinnato (12:26): Does that mean that the frequency or the severity is set in stone because of our DNA? Or can we modulate it? Can we manage our migraine?

Professor Griffiths (12:35): Well, I really think, for the common types of migraine, for these you're looking at probably multiple genes that interact in an individual, and you're probably looking at the interplay of things like diet and environment. And I think being able to modify or identify things like your triggers and being able to modify that in your diet or even look at modifications of things like hormones — all of that is going to affect your severity, your frequency, and how severe your migraine is.

Carl Cincinnato (13:05): What is glutamate and what role does it play in migraine?

Professor Griffiths (13:09): So glutamate is a neurotransmitter ... so it's a chemical that's expressed in the brain. And it's been shown that glutamate levels are actually normal in



people who suffer from migraine; it tends to be increased in people who suffer from migraine, particularly when they're having a migraine attack. It's also implicated in animal studies: it's been shown that there's some abnormalities in glutamate levels. We also know that glutamate can affect a number of other neurotransmitters in the brain, as well. So, there's some potential role for what's actually happening in the brain of a person living with migraine and potentially it might play a role therapeutically down the track, too.

Carl Cincinnato (13:49): Does glutamate come from gluten?

Professor Griffiths (13:52): They're actually totally different things. So glutamate, as I said, is a neurotransmitter. It's not gluten at all. So gluten is something that is found in food and it's specifically from wheat, and it's actually a particular protein that has absolutely nothing to do with glutamate.

Carl Cincinnato (14:09): That's good to know. What are ions and ion channels?

Professor Griffiths (14:14): OK, so they're usually something that ... they're called an ion because they actually have a charge that's associated. So they tend to be a particular chemical that has a charge on it, such as magnesium, or such as copper, or such as sodium. If you have them in a form where they're linked to something else, they're not an ion because they haven't got a charge. But if they're on their own in a liquid form, they have a charge on them. So they're called an ion.

Professor Griffiths (14:43): What is an ion channel? An ion channel is a pore that's created in the cell surface that allows ions to move in and out of the cell. Probably doesn't sound terribly important to you, but it is frightfully important for a cell to function normally and to respond to what's happening in its environment by being able to control the level of ions of various sorts that are in its environment. In particular, I mentioned before that there are three known genes that cause particularly severe types of migraine, and they're all ion channel genes. And by this, they are something that affects the movement of ions in and out of cells and, in particular, neuronal cells in the brain. So the first one is a calcium channel gene, the second one is an ATPase gene, and the third one is a sodium channel gene. And all three of those have mutations in them. That means that the level of the ions — whether it's a sodium or an ATP one, or whether it's a calcium one — are not normal.

Carl Cincinnato (15:50): And how might that affect a person who has migraine?

Professor Griffiths (15:53): So ... if someone has a mutation inside the calcium channel gene ... that ion channel — that calcium channel — doesn't function normally in a certain type of neuron in the brain. And so the levels of calcium going in and out of that are not normal. And that actually affects a lot of neurotransmitters. So things like serotonin, things like glutamate — things like other sorts of normal levels of neurotransmitters in the brain — are no longer normal and that brings on very severe migraines.

Carl Cincinnato (16:25): So you can start to appreciate just how complicated this is when you're talking about the cells and the DNA and the interaction between all of these things. It's no wonder that we haven't quite cracked a cure just yet.

Professor Griffiths (16:36): Well, we have got a few cures. So there are some very good treatments and a lot of that has come by determining what are the differences that you find in people with migraine versus non-migraine. I don't think we've got all treatments and I



don't think we've got all genes yet. I think there's definitely ... a lot more genes to identify, which will give us some great ideas about what new sorts of targets we can have in order to develop new treatments.

Carl Cincinnato (17:01): Well, we'll come back to those cures then. Before we do, can you tell us what vascular function is?

Professor Griffiths (17:06): So, vascular function just means normal blood flow that you find throughout your body. It's been shown for migraine, as an example, that it's probably not just the neurotransmitters — the chemicals that you have in your brain — that are playing a role in migraine. There's another theory that there's also changes that happen in your vasculature; so your blood flow across the brain and throughout your body. That can also play a role in migraine too.

Carl Cincinnato (17:33): Does that mean that the vascular function could be ... well, migraine could be a primarily a vascular disorder?

Professor Griffiths (17:41): Well, there's some discussions and a few arguments about whether it is vascular or whether it's neurological. And I prefer to think that it's probably not going to be so simple as being one or the other; it's probably going to be a mix of both of those. And also potentially there could be differences in one individual to the next. I don't know whether we always need to expect everybody to have exactly the same thing.

Carl Cincinnato (18:06): What is MTHFR?

Professor Griffiths (18:08): So, that's a particular gene for a particular enzyme. It stands for methylenetetrahydrofolate reductase — quite long! So that particular gene ... and I mentioned a little bit before about epigenetics. So it's a gene that plays a role, potentially, in methylation, which is something that affects epigenetics — so the interplay of the environment with your DNA. It's also a gene that's been shown to be a susceptibility gene for common types of migraine.

Professor Griffiths (18:39): And there's quite a number of susceptibility genes. But this is one. And it also is considered to be a vascular related gene because it plays a role in various cardiovascular or vascular type disorders as well. So if you have a particular mutation in that gene, it increases risk of things like stroke or cardiovascular disease, and also migraine with aura.

Carl Cincinnato (19:00): Are mutations in the MTHFR gene common?

Professor Griffiths (19:04): So probably about 9% of the normal population would have a mutation within that gene, a double mutation. So, everybody has two copies of every gene, and if you have both copies with a mutation it would be double. That's then called a homozygote because they've got both copies of the gene that are actually abnormal. If you have that, it results in abnormal levels of the gene product, which is the enzyme that I mentioned. And in fact about 50% of the gene is actually produced. So you only produce half of the normal enzyme level if you have that.

Carl Cincinnato (19:40): So how would you know if you have that?



Professor Griffiths (19:43): You can actually test for it like most gene mutations. If you know which particular gene you're looking at — you know what particular mutation point — you can do DNA sequencing methods to identify that particular one.

Carl Cincinnato (19:55): And is it worth doing it — trying to identify that gene for the average person that has migraine?

Professor Griffiths (20:01): Well, not everybody who suffers from migraine is going to have that. As I've mentioned, there's an increased number, and that's why it's called a susceptibility. So it does go up, but not everybody will have it. And it really only plays a role as a susceptibility gene in migraine with aura; so it's not all types of migraine, as well. If you do have it, you can test it by DNA. You can also test it because the product of it will be homocysteine levels, which is something that you find in the bloodstream, will actually be increased as well.

Carl Cincinnato (20:30): Let's say for example, you discover you do have the mutation. Is there anything you can do about it?

Professor Griffiths (20:36): Well there's a couple of things you can do about it — in actual fact you can make the enzyme work faster even though you don't have as much produced if you have the double mutation. You can actually make it work faster and better by either taking supplements that increase certain types of B group vitamins, or else even just increasing those B group vitamins in your diet as well. So you need to really increase folate and vitamin B levels in your diet, and that can actually make it work faster and that will most likely drop down your risk of things like cardiovascular disease. But also we've shown in some trials, as well, that it has a good impact on your migraine with aura, as well. So ... if you have the mutation, it can drop the frequency, and severity, and the pain associated with your migraine with aura episodes, too.

Carl Cincinnato (21:27): So if you have migraine with aura, you could just eat these foods and, whether you have it or not, you might get benefit.

Professor Griffiths (21:34): Correct. I mean I actually think they're quite good foods to eat anyway — so things like green, leafy vegetables, etc., can actually help as well. But I think, from the trials we did anyway, the dose needs to be pretty high, too, if you have the double mutation. If you just have a single one, I think perhaps diet could have some good impact.

Carl Cincinnato (21:53): So leafy greens would be good. Are there any other foods that people should be thinking about?

Professor Griffiths (21:57): Anything with vitamin B's in it. So it tends to be, you know, peanuts and things like that; but it's mostly leafy green vegetables. So, I always believe green vegetables are great for you.

Carl Cincinnato (22:06): Super foods. So then, if you have the double mutation, what type of supplements should you be looking at?

Professor Griffiths (22:12): Again, they're vitamin B related; so folate and vitamin B related ones are the best ones. But people should always make sure that they consult their specialist or their GP, as well, before doing that because sometimes taking extra supplements can interact with other things you might be taking as medication — so,



important to talk to somebody first rather than just start willy-nilly taking all sorts of vitamin B's.

Carl Cincinnato (22:37): So you mentioned earlier about potential cures. Can you tell us about what you were referring to?

Professor Griffiths (22:42): Oh, there's a number of new treatments around for migraine, and probably the really interesting ones at the moment are the monoclonal antibody ones — and so they tend to be directed to neurotransmitters. We've mentioned some of those before, but CGRP is one of those. And the ones that are directed to that have produced some really good results and they're now out there for people with migraine to try. Not saying that some of the other treatments, particularly the triptans that we've had for a number of years, aren't effective for everyone but I just think different people might need different types of drugs. But there's some great ones around at the moment.

Carl Cincinnato (23:18): But these aren't necessarily cures that cure everyone who takes it?

Professor Griffiths (23:22) No, I think this is exactly what it is: So I think there are different genes that play a role in migraine and different genes in different people. And so to think that everybody is going to respond exactly the same way to the same treatment is probably a little bit silly. I think we're going to have to start making sure that we target the treatment to the actual genes that make up the profile of a person. And I think that's where we're going in the future.

Carl Cincinnato (23:47): So with the monogenic migraine conditions like hemiplegic or familial hemiplegic migraine, because we know the gene, have we developed a cure for that type of migraine? Or certain types or subsegments of that migraine?

Professor Griffiths (24:00): So, we currently do diagnostic testing, and a lot of clinicians will now get diagnostic testing to try and determine whether their patients with hemiplegic migraine have one of those three known mutated genes. And that sort of testing is actually, I think, very beneficial to try to work out which particular patient you've got here, because there are different treatments depending on which gene it is. And so there are some good treatments, if you know which it is, but you've probably needed to do some testing to actually do that. But I will point out that we've just done a study that has looked at about 200 — it was actually 183 — diagnostic cases referred to us. And we looked at all of those known mutation genes and looked at all points of them during DNA sequencing; and from that we picked about 25% of our cases would have mutations in one of those three genes.

Professor Griffiths (24:56): So, that's good for the patients for diagnosis and then for treatment choice. But it also means that 75% of people that are being referred for diagnostics and have symptoms don't actually have mutations in those known genes. So it means that there's probably other genes to identify. So, we're currently doing a project where we're looking at whole exome sequencing, meaning we're looking at the whole genome in those patients. We know that they have severe symptoms, we know that they have families that are affected, but we also know that they don't have mutations in the known genes. So now we're testing about the 20,000 other genes.

Carl Cincinnato (25:36): A little bit of work ahead of you.

Professor Griffiths (25:37): Just a little bit!



Carl Cincinnato (25:37): Talking about your work, can you share some of the things you've been doing around the genetics of concussion?

Professor Griffiths (25:45): Yes, concussion genetics is a new project that we've started looking at. And the reason that we started looking at it is: one of the known causes of familial migraine is a calcium channel gene. And as I said, we do some diagnostic testing and we've been doing this for quite a number of years for all of Australia and New Zealand. For that particular calcium channel gene, there is a specific mutation point that occurs in that gene, and people who have that are highly prone to concussion after very minor, in fact very trivial head trauma. And it's not just concussion, it's very severe concussion. So as an example, we've got cases of small children who maybe hit their head on a table. Normally small children hit their heads on tables all the time but they tend to bounce or scream a little bit and then they get better.

Professor Griffiths (26:37): But people who have this particular mutation point ... very trivial head trauma like that results in severe concussion that can go on for days. It can result in severe coma that can go on for even months, sometimes cerebral edema and sometimes even fatality. These are severe responses to fairly minor head trauma. We've noticed, looking at our cases referred to us, that quite a number of people are starting to actually notice this concussion in people with familial hemiplegic migraine. And so we started to look at, "Well maybe there are other genes that might be playing a role." That is one gene — it's an ion channel gene, it's a calcium channel — and it results in severe responses to trivial head trauma. So we started looking at some of the other cases that we have, and we found, in particular, that patients who have mutations in the second FHM2 gene — it's an ATPase gene — about 35% of those with mutations in that gene actually have severe responses to concussion and notable multiple concussions, and even concussions through a number of family members.

Professor Griffiths (27:51): So we believe that that might also be playing a role in response to concussion. So that's led us to start thinking maybe there are other ion channel genes that play a role in, not just response to concussion, but maybe susceptibility to concussion as well. And if we can identify what genes are playing a role, I think that might help in starting to think about, well how do we treat it and how do we manage concussion? And maybe we don't manage everybody exactly the same way if there's different genes involved.

Carl Cincinnato (28:21): Are we talking about concussion within the population who have migraine or is this just within the general population?

Professor Griffiths (28:26): So our original results came from looking at the population with severe forms of migraine. But as you know, concussion affects all sorts of people. And if you look at, as an example, football players, some people sort of get hit on the head. And in fact, football players get hit on the head a lot, don't they? Some of them seem to respond quite well, whereas others don't respond nearly as well to similar sorts of levels of trauma. And so we think that maybe ion channel genes are playing a role in this response. And in fact, you can actually see that a lot of the damage that occurs, whether it's in animal models or even in humans, shows that neurotransmitters are abnormal. And that there are ion differences and homeostasis is quite different and abnormal after concussion.

Professor Griffiths (29:14): So we're currently looking at, not just people with migraine, but actually starting to look at a broader population of people that could be affected and



particularly looking at those who have things like post-traumatic migraine, which is the most common symptom following head trauma.

Carl Cincinnato (29:31): If you have migraine, are you more likely to have a more severe concussion, as a result of an injury?

Professor Griffiths (29:41): I don't think people have looked at that enough. And really this has only come about because we were looking at our severe hemiplegic migraine cases and as I've mentioned, it's been known that there is one of those hemiplegic migraine genes that does play a role in response to concussion and response to head trauma. But I don't think anybody's really looked at migraine in general and whether that makes you more prone. I think to do this, you actually need to be looking at the trauma as well. So, not all migraine patients play football or whatever. So yes, I think we probably need to be looking at bigger and better populations, so we're starting to do that now.

Carl Cincinnato (30:19): If I had hemiplegic migraine and I had a child, then I would be wanting to find out whether my child is going to have this gene because I'd be far more protective of them and maybe limit some of the sports if it was that great of risk. Is that something that people with familial hemiplegic migraine should consider?

Professor Griffiths (30:39): Well, I don't think people really have been considering it very much and that's probably the impetus for why we started working on concussion genetics. You can do diagnostic testing and you can sequence for those genes, but I don't think, again, that that would cover all of the genes involved in concussion. That's really just the ones involved in a hemiplegic migraine. But certainly you could test for that now. So if you had a child who wanted to play football, and you were worried about it, and you had familial hemiplegic migraine, it is definitely something that you could be looking at.

Carl Cincinnato (31:09): Would you suggest doing that test for anyone that has migraine and has a young child?

Professor Griffiths (31:14): I don't think I would suggest it for everyone. What we're talking about here is the more severe and the rarer forms of migraine. So hemiplegic migraine is not a common type of migraine; it's a subtype of migraine with aura and it is rare. So, I don't think I'd suggest everybody doing this. Give us a bit further time to actually work out how many more genes are involved before you'd start screening everybody.

Carl Cincinnato (31:37): I think that leads into the next question. And the final question is: What else do you hope to discover in the research that you're currently doing?

Professor Griffiths (31:44): Well, again, my passion is really to look at migraine genetics. It's something we've been working on for quite some time and clearly we haven't identified all the genes involved in migraine yet. We do it for two reasons. One is so that you can diagnose people better, and I really think that really helps if people know what is their specific gene problem. But more importantly, it then helps with treatment choice. And so ultimately I'd really like those two to go hand-in-hand and to become a lot more personalized in terms of individual's migraine, what's causing that, and how should they treat it?

Carl Cincinnato (32:18): Well, it was fantastic to have you at the Migraine World Summit and it was another fascinating discussion, as always. So thank you very much for joining us.



Professor Griffiths (32:24): You're most welcome, Carl. I enjoyed chatting with you. Thank you.