

**Alzheimer's Talks
with Dr. Gregory Jicha
March 17, 2017**

Note: This Transcript has been edited for content and clarity

Debra Lappin: Good afternoon and welcome to [Alzheimer's Talks](#), a free monthly telephone conversation presented by [UsAgainstAlzheimer's](#). My name is Debra Lappin and today I am standing in for your regular host, George Vradenburg. As you know, UsAgainstAlzheimer's is an entrepreneurial and innovative organization dedicated to transforming the fight against Alzheimer's. Today our guest is [Dr. Gregory Jicha](#). Dr. Jicha is Professor of Neurology and the holder of the Robert T. and Nyles Y. McCowan Endowed Chair in Alzheimer's Disease at the [Sanders-Brown Center on Aging at the University of Kentucky Alzheimer's Disease Center](#).

Dr. Jicha came recommended to us by a couple of our regular listeners, and we really want to say thank you. This is just the kind of interaction we hope to have with our audiences and with all of you. We saw immediate value in contacting Dr. Jicha and we really are looking forward to our conversation with him today. He will speak to us today about the impacts of genetics on Alzheimer's risk, how research might help identify key targets for disease modification, and whether a treatment for Alzheimer's might in fact become part of what we see today in an increasing focus on personalized medicine.

Before we start, just a few reminders: If you have a question during our call, please press *3 on your phone. By pressing *3, you will be placed in a question queue, you'll share your question with a member of our staff, or if you're listening to us online, you can simply type your question into the question box, and we hope to get to as many questions as possible after Dr. Jicha's presentation. And, a final reminder: Dr. Jicha, like all of our guests, is not able to answer personal medical questions.

Now, let's get started. And thank you for joining us today, Dr. Gregory Jicha.

Dr. Jicha: Fantastic, and thank you Debra for having me on. I'm sorry that George couldn't make it today but the work that he's doing is incredibly important and not just in education but in transforming the entire landscape of how we look at Alzheimer's as we push closer to a cure.

Today, this is one of the topics that I find that my patients and family members are frequently asking me. What is my risk for the disease? What are the genetics behind it? Mom has this disease, my spouse has this disease, what does this mean for me, what does this mean for our children? And I think this is really important. Most folks, when they look at genetics, think of it either as science, that's so far out from our understanding what people are doing in the laboratories, all the way down to, "Are you going to give me a Yes/No about my risk for Alzheimer's disease?" And many other folks think, "Well, who cares anyway, because there's nothing you can do about it." Genetics really has contributed in some very important ways to how we can think about Alzheimer's disease and how we can use that knowledge to really advance our efforts at both diagnosis as well as treatment, and so, I'm going to present my thoughts on this, from my understanding and the work that I and many others have done in the field today. Before we get into some of the specifics of genetics, I'd just like to cover a few basics for everyone out there.

We know that there are many genetic, as well as environmental, risks for Alzheimer's and these have been really hard to parse out over time because Alzheimer's is so prevalent. There's so many of us that get it, and age is really the number one risk - it by far overshadows any kind of genetic or familial risk. So, right there, we're starting to look at things that may differ, so I want everybody out there to be thinking, just because you have a family member who may have been affected by Alzheimer's or another form of a degenerative disorder, one of the related disorders to Alzheimer's, does not mean in the vast majority of cases that you are definitively doomed to come down with a disease like this, and so that's important.

Now with that being said, there are some types of genetics that can lead to increased risk for Alzheimer's, and the first that I'd just like to get out of the way is what we call autosomal dominant risk. That is risk that is carried in a gene and it's inescapable. I often tell people, this is what I call blue-eyed genetics. If Mom has blue eyes and Dad has blue eyes, well, all the babies better have blue eyes or Mom's in big trouble, because if you inherit the gene,

you're going to have the trait. And this type of Alzheimer's exists, and many of the folks on the line may have watched the [60 Minutes special](#) a few weeks ago where they talked about a rather large family in Colombia, South America, where we're working to try to treat Alzheimer's disease before it presents. This type of family has this kind of Alzheimer's disease; autosomal dominant, we call it.

That means that an affected parent is going to have one normal chromosome, and one chromosome with an Alzheimer's mutation, and they are going to pass down one of those two copies to each of their children. So in essence, each child will have a fifty percent risk of coming down with Alzheimer's, that is inescapable. And so one of the reasons why we're in Colombia, South America, while there are other major studies like [DIAN](#), which is the Dominantly Inherited Alzheimer's Network, doing exactly the same thing here in the United States, and in many other countries, in Europe as well as Australia, is that if we identify those folks, we understand if they carry the mutation, they will inescapably come down with Alzheimer's, 100 percent certainty. And that's scary.

Now the good news for most folks out there is, this is very rare. It's probably less than one percent of Alzheimer's disease worldwide, only carried in about five hundred family trees, these types of mutations. They are informative for the disease, because we can predict who's going to come down with the disease and moreover, with these types of genes, universally, we have early onset disease. These are people that are coming down with Alzheimer's in their forties. And we can pretty much predict on the basis of when a parent may have come down with the disease—if they came down with it at age forty-two, the children that inherit that same mutation are going to come down with it at about age forty-two as well.

So this is a rare circumstance, and I'm not going to dwell on that today because most of the genetic risk that we see in the vast majority of patients involves a number of other genes that are what we call risk factor genes. What that means is that if you inherit one of these genetic mutations, you're at higher risk for Alzheimer's. But it's not a definite. If you have low environmental risks, you may be able to escape that. Sometimes it's just happenstance that one may inherit these risk genes and not come down with the disease. Likewise, one can come down with the disease and have none of these risk genes whatsoever. So, these genes cluster, and in 1992, we

discovered the first one of these genes. It's called apolipoprotein E. Many of us know this as APOE, and APOE comes in three different types or three different flavors, as I always say, like Neapolitan ice cream (chocolate, vanilla, strawberry) but for APOE, it is APOE 2, 3, or 4. And those that inherit this number 4 copy of that APOE-4 gene, that doesn't mean four copies of it, but the number 4 version of it, are at higher risk for disease. If you inherit one copy of APOE-4 you're at several fold higher risk, and if you inherit two copies, your risk may be as high as ten fold higher than somebody without that genetic risk.

These risk genes explain why Alzheimer's seems to run in families, and we all know that this runs in families, partially because if we come from a long-lived family, our family in and of itself without any genetic risk is going to have a higher number of people in it that will come down with Alzheimer's. Over the last several years, there has been a lot of work done, both here nationally, as well as globally, to identify all of these risk genes. We've known that there have been many, and now we have about a dozen and a half of these identified in addition to APOE. These genes are really, really important for our understanding. So they tend to cluster, they tend to encode proteins, or changes in the cells in the brain and the body that are linked to cholesterol, cholesterol trafficking in metabolism. That doesn't mean if you have high cholesterol you're going to come down with Alzheimer's but how that cholesterol is trafficked and moving around in the body and in the brain may be playing a very important role and so those genetic discoveries have led to a whole branch of research into how cholesterol moving around in the body and the brain may increase risk for Alzheimer's in the hope that we could fix that problem.

Many of these genes cluster in what we call inflammation and so they may cause excessive inflammation in the brain, or they may reduce inflammation in the brain, in different ways, and that change in inflammation can greatly change what each of our risks are for Alzheimer's disease.

Other genes may cluster in areas that are involved in synapse formation, that is the connection between two neighboring nerve cells, how they talk with one another, and of course in Alzheimer's disease this inability of nerve cells to talk to one another is a fundamental problem that leads to the memory issues that many experience. Still others relate to brain development, or how the brain may function, in and of itself.

So each of these discoveries has actually taught us more about how Alzheimer's begins to take hold in the brain and more importantly, identifies for us kind of a road map of where we might be able to intervene with medicines to slow, stop, prevent, or perhaps someday even reverse Alzheimer changes in the brain. So, this is really the important aspect of what I'd like to get into today, it's not just the genetic risk that says, "Boy, I'm bumming here, I'm in a really bad place" or "Thank goodness I don't have any of this, I'm in a good place."

For years, we've thought that these genes may not yet be important in terms of our treatment of disease, and yet we've learned over the past five to ten years with study after study, and we hear this on the news and often it's dismaying—another drug failed in Phase III trials for Alzheimer's disease—and while we haven't hit pay dirt as of yet, we've accumulated some very interesting evidence. And some of that evidence relates to looking at people's genetic background, their genetic risk, and how they may have responded to one or more of these medicines.

So, [one of the first studies that was done in 2004, published, I think, in 2005, was donepezil, or Aricept, for mild cognitive impairment](#), mild memory disease, impairment that does not yet meet criteria for Alzheimer's disease, and that study failed, it did not show that over a three year period, we could prevent Alzheimer's with Aricept, or donepezil, which is the generic name. But when we looked back at that data after the fact, we understood that it may slow the progression of symptoms in some, and specifically, if we looked at whether or not somebody carried an APOE risk, we could see a profound difference in those with the APOE-4, the bad risk gene for Alzheimer's disease, the medicine donepezil actually was able to slow the process throughout the course of the study; for those that did not have that risk gene, the medicine did nothing. And there are many reasons for that, that I don't want to get into to complicate, but it was really one of the first demonstrations that genetics might influence the way people respond to medicines.

We've done a lot of work with amyloid-lowering compounds, antibodies and vaccines, and what we know from those studies is that people that carry the APOE-4 gene are at higher risk for some of the adverse side effects, some of the complications of that therapy, which can include swelling of the brain,

what we call vasogenic edema, but those without that APOE-4 allele, without that APOE-4 risk, are at very low risk for adverse events from these medicines.

So again, the genetics are telling us, not only about whether medicines might be beneficial, in certain people, but also telling us whether some of our medicines that we're developing may be risky in others. And so, knowing that genetic information in the future may be incredibly important for us to pick the right medicines for an individual person. We've seen this time and time again, studies of DHA, docosahexaenoic acid—boy is that a mouthful—but that is an omega-3 fatty acid in fish oil. Fish oil doesn't seem to have a benefit for Alzheimer's for all comers, but for those that don't carry the APOE gene, there may be a significant benefit of the omega-3 fatty acids in those individuals.

We've seen this again and again with different studies. [Recently, there were some reports, that just came out a week ago, looking again at the mild cognitive impairment donepezil studies](#), starting to look at different genes, genes that are involved in the way donepezil works, showing and suggesting that alterations in what we call the butyrylcholinesterase gene may be very, very important, and people that carry mutations in this gene may not benefit at all, as a matter of fact, the medicines may make them worse. For those that don't carry those gene risks, the medicine may work much much much better.

[Another study that came out just a little over a week ago was looking at statins, cholesterol-lowering medicines](#). We've had many studies that have looked at this. There's been a lot of suggestion that lowering cholesterol might reduce Alzheimer risk and yet, when we've performed these studies we've not shown benefit. It turns out that your APOE status may be the important determinant as to whether or not you're a responder to statin therapy. Those, depending on that profile, statins may be remarkably beneficial in slowing the progression of disease.

So, as we start to think about genetics, I want everybody to think about the two ways that we might use these in the real world. One is: Can they help us with diagnosis, with telling us what our risk is for developing the disease in the future? But the second much more important way to look at these genetics is: What do they tell us about the disease and how in the future might that genetic information help doctors pick a better medicine, a better medicine for you individually, a better medicine for your loved one individually, a medicine that has much lower risks for you, based on who you are uniquely as a person.

I'm going to sum up at this point and answer a few questions, but before I do, I wanted to set the stage. We're not quite there yet. We've accumulated a tremendous amount of information about these genes, about how they may work to increase risk for Alzheimer's, and about how they may influence a large number of medicines and how they work, but more work needs to be done before routine genetic testing really becomes a part of what we're doing in everyday practice, and more work needs to be done before we can definitively decide which medicines a person should be on, on the basis of their genetic risk. Currently the American Medical Association and the American Academy of Neurology does not recommend genetic testing unless you think you have true genetic Alzheimer's—family onset in the forties, half of every generation coming down with disease, like those in Colombia, South America. Having a risk gene in your medical record could pose potential ethical, legal, or financial repercussions that we're not ready yet as a society to entertain until we have a little more evidence in our hands, until we have a cure and are able to change those genetic risks.

That's a lot of material to cover in a short period of time, but there are many important questions out there and I want to make sure we have plenty of time to reach all of those.

Debra, I think I'm going to pause there. If there are any aspects of what I've talked about that we should discuss or clarify in more detail, please let me know and I hope they do come up in the question session of the program today.

Debra Lappin: Well, thank you. I'm going to give a reminder to our listeners. If you have a question during the call, please press *3 so that we can connect you immediately with one of the members of our staff and get your question to us; or if you're listening online, please type into the question box.

I want to begin personally by saying it's really clear to us why you were recommended, Dr. Jicha. This was an amazing presentation with just such clarity, and I think you're going to find that we have a wealth of questions. So, let's get started. Do certain ethnic or racial groups worldwide have a higher prevalence of APOE, and APOE-4 in particular?

Dr. Jicha: That is a great question. Let me start by answering a preface to that question. The preface is in my own mind but I think it's important to state outright that the incidence of genetics is fairly uniform across the globe, so your racial or ethnic background is not going to influence your overall risk of Alzheimer's disease and of coming down with it. Now, from there, we can hone in to the actual question which is APOE and yes indeed, we know that APOE comes in those three flavors, the 2, 3, and 4, and the 4 is what's risky for Alzheimer's. We know that people of European descent may have a higher frequency of APOE-4 positivity than folks with their heritage placed in other areas of the world. But I will say APOE in all of its forms, the 2, 3, and 4, is found throughout racial and ethnic groups, so again, the APOE-4 risk may be slightly higher in those of European descent, but it exists for all of us.

Debra Lappin: So I'm going to give a question framed by Anne Wormley in Colorado. She said her husband has early onset Alzheimer's since his mid fifties. There are at least four people in his family diagnosed later in life with Alzheimer's; a father, a brother, an aunt, a cousin. There may be more that haven't been diagnosed, we just don't know about them. Are our two daughters at a higher risk for developing Alzheimer's? Is there a test that can determine if they will get it? How accurate is the test? And then, I think it opens up the questions that you just suggested, in that case, and in many of the cases of our listeners, you alluded to the social and legal implications of getting the test. So I know this is going to drill back into things that you said, but really pinning them down for the personal lives of some of the people who are listening.

Dr. Jicha: Absolutely. So, these are really important questions. I was hoping that we'd hone down on some of what we had talked about as well. First off, let me say when we're looking at familial risk, yes, we can look at larger pedigrees, we can look beyond, but when one is looking at their own personal risk, it is best to stay focused on first-degree relatives: Mom, Dad, brothers, sisters, children. Unfortunately in some instances we have many parents who still have normal cognition and are actually caring for their children who have already come down with Alzheimer's; what a horrible thing. But we look at first-degree relatives. So the question to pose is, we've got one parent in this scenario, one of two parents who came down with the disease, that's important, and we have one sibling. Now it might be a little bit different if that's the only sibling in the family; then we're looking at, "Uh, oh, could this be one of those true genetic forms of Alzheimer's?" Or is it just a familial

genetic risk? Now if there are twelve siblings in the family and only one of them has come down with Alzheimer's, we would say, well it's not really likely that this is true genetic Alzheimer's. So we can use those first-degree relatives to start to stratify that risk.

The fifties is kind of a grey zone, so I would say if somebody makes it into their sixties or early seventies, the likelihood that they carry one of those true genetic risks is very low. If they come down in their forties, the likelihood of one of these genetic risks is quite high. But in the fifties, we could be talking about either. Most likely, this is genetic risk, and Dad may just have two copies of the APOE-4 gene or some of the other of the eighteen genetic risks, and this is really important to sort that out. Your doctor should be able to sort that out from their understanding of genetics as to what that likelihood is when a family pedigree is truly drawn out, so if you have questions, really specifically about your individual risk and your family, it is a good idea to raise those with your doctor or neurologist and/or ask about consultation to a genetic specialist. Most medical centers will have a genetic specialist on staff, that can help explain and work through some of these things.

Now there are some clinically available tests to test for the rare genetic mutations, what I call the blue-eyed inescapable genetics of Alzheimer's; those are available. And who might those be important in? Well, perhaps, there are questions from children as to whether or not they should have children if they are carrying that risk gene. And those questions may differ. Maybe it's about preparing for the future, although I'd like to remind everyone that each and every one of us is at risk for Alzheimer's, not one of us is spared that risk. And it's best for us all to be prepared and to assume we're all at high risk, and that we're doing everything we can for our brain health.

Typically, the points that I've touched on so far really focus on first-degree relatives; when it comes to cousins, aunts, and uncles, your own personal genetic risk is less impacted by those second-degree or further relatives. The younger the age of onset, of disease that runs in your family, the higher the likelihood that there is some genetic component to that risk of disease. So those are important and it certainly sounds, in this case, like we've hit on both of those, a possible high number of first-degree relatives with disease and an earlier onset of disease.

Now, if one does decide to pursue genetic testing, there is genetic testing available for the APOE gene as well, although the seventeen other genetic risks, as far as I'm aware to date, do not have a certified genetic test. Their testing is still largely in the research realm. But we can test for APOE, and some doctors do choose to do that, despite the AMA and ANA statements that right now, it's not going to change our management of the patient. It's not something that's recommended. Now, if one does decide to pursue that testing or goes for something like 23andme, where you send in a little swab from your cheek and they send you back all your genetic risks, I actually have a young friend who lives in Florida who did this, and it came back showing that they had two copies of the bad E-4 gene. And that's problematic; this person is in their early fifties and they're looking at, "Oh my goodness, I have this increased genetic risk."

And I always tell them, well, there's still a possibility, despite the genetic risk, that you're not going to come down with Alzheimer's disease. If you are tested, you should know that there is something out there called [GINA, the Genetic Information Nondiscrimination Act](#), and that is a law that carries some protection. It carries protection against certain forms of discrimination on the basis of genetic risk, so if you were tested for APOE and found to carry a risk gene, you can not reveal that information, when folks ask you, "Have you ever been genetic tested or do you have a genetic risk for a known disease like Alzheimer's?" You're able, in many cases, to say no. And that's kind of a white lie, if you know you're positive, but it's an act and a law that's been developed because of the uncertainty of these genes, to try to protect people from being discriminated against. Now there are a lot of nuances to GINA that do need to be discussed, if there are specific questions about GINA and how it would protect you individually if you decide to seek out genetic testing, this is something that your doctor or a genetic counselor can answer for you individually, because it's going to vary person to person and by specific state

Now I will make one other comment for those that feel that they're at risk, and for those that understand where we are in developing medicines to prevent the disease. We're actually looking for folks who are still normal in memory and thinking, but carry these genetic risks, and we are right now working on several studies across the globe giving them experimental medicines that may prevent Alzheimer's from ever appearing. If you're genetically tested through a research program, that information can be protected by a certificate of confidentiality and never make it into your medical record, but most often,

you will not be told the results of that genetic testing. There actually is a mail-in program called GeneMatch and if you Google (or Yahoo or Bing) GeneMatch and fill out a brief questionnaire, they will mail you a cotton swab that you swipe the inside of your cheek with; they will process to see if you have genetic risk and if there is a study in your area that is right for you based on your genetic background, they will point you in the direction of that study. This is a resource. When we say that there's nothing we can do about our genetic risk right now, well, that's not exactly true. We could get involved with some of this research, we could potentially get our hands on an experimental medicine that might help us, but more importantly is going to help us move closer to better treatments and the cure that we're looking for. Great question. Sorry my answer was so long, Debra.

Debra Lappin: No, this is so great. If you go into a clinical trial and you just mentioned this, you may be genetically tested in the course of research, can you as a participant in the trial, say, "I want to know my genetic status rather than having it kept from me."

Dr. Jicha: That's a great question—you certainly can, and different studies approach that in different ways. We have some clinical studies here at the University of Kentucky, and this is the same for many of the other major Alzheimer's centers nationwide, there are some studies where disclosing genetic risk, telling people what their genetic risk after we test it, is actually part of the protocol and it's always done. There are some studies where it's seldom if ever done, or not done at all, and the only way to know is to talk with the doctors and ask them; there is no harm in asking the question.

We have had instances here before where we have had folks in research studies where the study says, we're not going to reveal that genetic information. But the patient has really wanted that genetic information, we then have submitted to what's called the institutional review board, the regulatory board that watches what we do in research, to make sure that we're helping and not harming people and weighing things in that favor. We've applied to them and said, for this person, there is a need to know and we would like to disclose that information, and we have been given that opportunity in some of our studies. In some of our studies the answer has been no. Almost always before we reveal genetic information, though, that's a time to really sit with a doctor or genetic specialist that understands the meaning of those genetics, that can help us really understand what those

results mean. This is not like a strep throat test, where “Yes, you have strep” or “No, you don’t have strep.”

This is something that’s a little more cloudy and one should always remember, when you’re being genetically tested, and if that information is being revealed, it’s not just about you. It’s about everyone that shares your bloodline. And if there are potential ways to link that information to others within your family, we need to be really really careful and protective of them, while we’re trying to maximize our understanding of where we may each be individually. I think that’s going to change in the future, Debra, as we develop these medicines that may be dependent on what your genetics are in terms of whether they work or not or what your risks are. I think it’s going to become routine in the future, for some degree of genetic testing and to reveal that to people, because that’s how we’re going to pick their medicines, but again, we’re not quite there yet.

Debra Lappin: You said that genetic testing is good for diagnosis, it’s good for picking your medicines. I want to raise another area. Would it not be good for supporting what is needed today, and that is to get pre-clinical people before they have Alzheimer’s, into trials? So we have a woman who’s asked: With my family history (I’m assuming it’s a family history along the lines of what we’ve just discussed), can’t early detection start with a baseline? Would I not want to get it ten or twenty years maybe before I’m going to get Alzheimer’s? And I’ll add on to that, would people with a family history not want to think about genetic testing as a motivator for them to enroll in trials and to become part of this new legion of Americans that we need to recruit into trials before they have symptoms?

Dr. Jicha: Yeah, I think that that is a great question and I think it spans both genetics as well as routine assessment. I’m a firm believer in establishing a baseline for each of us, as a matter of fact, even if there’s not a family history of risk for Alzheimer’s. I think that everyone, when they turn age sixty-five, should be evaluated for any early signs of memory loss, with memory testing, perhaps an imaging of the brain to make sure we’re not seeing any early changes in atrophy or shrinkage of the brain that could be signaling or heralding a future onset of Alzheimer’s disease. I think that that can be useful; that makes us much more accurate if a memory problem develops in the future. I use sixty-five as a cutoff for those without family risk, for those with a family member, I typically say, whenever your loved one began coming down with memory problems, so if it’s somebody like our last example whose dad

came down with it in his mid fifties, it's a good idea to get a baseline in your mid fifties. If a family member came down with it in their forties, it's a good idea for you to get a baseline in your forties.

Now when it comes to the genetic testing, we still have all these caveats, but you're right, we need a lot of people, and there are a lot of studies that are being done in pre-clinical Alzheimer's, that's people who are still normal but at risk for disease in the future. And many of these studies are basing that on genetic risk and many of them are relying on GeneMatch and other programs like that to help find these people. The number of folks out there, out of every 100 here in the United States, there are two that carry two copies of the E-4 gene. So, that's what we call a homozygote, they have E-4/E-4, two copies of that gene, and they are, as I said earlier, at least at ten times the risk of Alzheimer's as someone else. We're specifically looking for over 1,000 of those folks to participate in ongoing trials currently. And it's hard, that means we really need to do genetic testing on 100 people to find the two. And if we're going to test this on 1,000 people, then we're actually going to have to do genetic testing on 50,000 people to fill a single trial. Folks that have a strong family history are really in a position, you can assume that you might have one of the genetic risks, and if you've seen Alzheimer's create trouble, if you've seen one of your loved ones come down with this disease, I think that is a call to arms. That's a call to stand up; your increased risk may make you one of the most important people out there, in our battle to find a cure for Alzheimer's.

Debra Lappin: Right. Thank you for that. You know, I'm here in Washington, DC. So we have followed major levers in the policy arena, and one of them has been the [Precision Medicine Initiative](#), that has been launched by the National Institutes of Health, with the blessing of the prior president, and certainly with funding that came from a recent bill called the [21st Century Cures Act](#). That effort hopes to recruit one million Americans who will be genetically tested, so would that, will that effort incorporate genetic testing for Alzheimer's, and is this going to be a pathway that you're going to be working with and seeing as a potential to offer great promise for us?

Dr. Jicha: Yeah, that's a fantastic question and description for the folks that are on the line with us today, about where this is going. You are right, the Precision Medicine Initiative and the 21st Century Cures Act is designed to collect genetic information on tens of thousands, or more, Americans. This is going to grow over time and we'll be looking at genetics not just of cancer risk

or heart disease risk or diabetes risk, we will be looking, in those folks that are part of that, we will be looking at Alzheimer's risk as well, and be following those folks over time. Likewise, we have many folks here and across the nation at the leading Alzheimer's centers, funded by the NIH, where we are already collecting genetic information and sharing it through what is called the [NCRAD, the National Cell Repository for Alzheimer's Disease](#), it's being used by what's called the [ADGC, the Alzheimer's Disease Genetics Consortium](#), and it's all being placed in databases. One of the problems that we've run into, in the area of Alzheimer's disease, is, frequently the genetic material is given up for the purpose of studying Alzheimer's but not for studying anything else. And that's a real limitation, you know, if we're going to get our genetics out there in a protected way where we're de-identified, nobody can trace it back to us, to help cure diseases, well, you know, myself, I've donated my genetic material, I want that to help find cures for as many different diseases out there. I would like that to help people with Parkinson's, I'd like that to help people with ALS, I'd like that to help people who come down with cancer in the future or who are at high risk for stroke. I just finished a small study here polling about 1,000 people in the community as to what their wishes were, and you know, we found exactly that. We are altruistic at heart as human beings. I think it's just part of who we are. We can pretend to be Scrooge, or Scrooge-like at times, but really, I think everybody wants this. What the 21st Century Cures Act, and what the Personalized Medicine Initiatives really mean is, let's figure out genetic risk across all diseases including Alzheimer's disease, and let's use that information to find cures and better medicines. So, Alzheimer's is definitely part of that, Debra.

Debra Lappin: Let me understand a little better. If I were to get my genetic testing done, how do I then make it available, just in the way you have? From GeneMatch, am I given an option, to make it available?

Dr. Jicha: Yes, as a matter of fact, some studies will already have incorporated into them the ability to share widely across disease states, and with other researchers nationally and internationally. Some studies may have limitations, so it's really, really important, when you get involved with a research program, to take a look at that, to really ask. And you have the right as a research participant to say no, I'm only interested in having my DNA used for Alzheimer's disease. But the greater good is to make sure that the way that you get involved is the way that's actually going to increase the benefit for each other, here on the line today, for all of our children, and for generations

to come, in my opinion. I think that if they're going to use my genetics to help find a cure for Alzheimer's, I hope that they use it to cure all those other diseases as well. But that's something that's going to be very study specific, Debra, and people are going to want to make sure that they ask.

Meanwhile, I really think we should be placing pressure on the scientific community for open sharing of this type of information; I think we need to tell researchers, and we need to tell ethicists at the level of the NIH and at the level of individual institutions that we not only want but we demand this kind of sharing, because it's only through large numbers, tens of thousands or hundreds of thousands that we're going to make these discoveries. The more that we can share, the quicker we're going to come up with the answers we all desperately crave.

Debra Lappin: Right and you just said that the sharing was study-specific, and this is a question from James in Idaho. He said, "There are many of us listening today [we have over 1,000 people listening today], many of them in rural areas. If this is study-specific, how do we equalize access to the opportunities to take advantage of all that is happening today in Alzheimer's?"

Dr. Jicha: You know, that is a fantastic question. Let me say first off that folks in rural areas, and remember, I'm in Kentucky and Kentucky has a very sparse population and I appreciate those comments because I do, indeed, I have folks that may be driving from Appalachian Kentucky down to Lexington. It may be five hours each way for them to come for study visits and participation in research and not everyone can do that, I understand that. We're working in many different ways to do this, and the initiatives occur at the local level so here in Kentucky we are using telemedicine, video Skyping, to not completely eliminate trips to Lexington where people have to do ten hours round trip to participate in a study, but to eliminate a number of those visits and make it more doable for family members. I think that we're going to grow in this regard.

One of the areas where we've run into trouble is in making sure that we have networks set up that really span the nation. So George himself has worked to develop right now what is called GAP-Net or the [Global Alzheimer's Platform](#) and that really is growing, just in its infancy, it's designed to link together sites like a net so that we can catch everybody and that we can really mobilize those that are ready to take up arms in this fight against Alzheimer's and other

related dementias. I think we need that kind of network, so we're working on multiple levels. Investigators in individual regions are coming up with ways, many of our research studies will offer reimbursement for travel, hotels to stay overnight, if people are coming, and then I think the vision, part of the vision, that George and others have, that have been developing the GAP-Net program, is that we have a net, we have a net that not only catches everyone but allows everybody to take up arms and fight the disease. I think that this is important.

Idaho is beautiful country, I know there's not a lot around, but I think if you look, and if you're interested in getting involved with clinical studies, the best way to do it is to hop on clinicaltrials.gov, search for clinical trials in your area. That is a website run by the federal government, by the NIH. The Alzheimer's Association has a trial match program. Many of the universities use something called [ResearchMatch](#). There is a [Brain Health Registry](#) that one can sign up for, to actually find out and have other people do the ground-work for you. If you get yourself on these lists, they know that you're interested and people will try to reach out to you, and making sure that we know that you're there is the first step towards us overcoming those barriers, that right now, do unfairly exclude many folks that may live in rural and underserved areas of the nation. But we're working on this, James.

Debra Lappin: We are working on it, and speaking for UsAgainstAlzheimer's because you've just opened the door to the very mission of UsAgainstAlzheimer's, is to build legions of people working together and one of the resources that UsAgainstAlzheimer's has launched in the last year, and you many not know about it, Dr. Jicha, but I'm going to take the time at this moment to talk about it, is something called the [A-List](#). And you can go online, look at the A-List and we're going to send information to everybody on the call today. The A-List will allow people, wherever you live, to come together in the digital environment and learn about clinical trials. There is a tool on there, where you can walk through "[Is a clinical trial right for me?](#)" and you can find out if in fact you're really ready for a clinical trial, and if there is one, and then there is another tool that kind of demystifies clinicaltrials.gov, it's called [Antidote, and it really helps you understand the trials](#), where they're taking place, and I think one of the bottom lines from the conversation we're having today, is that the people here, the thousand people that are on this call, if they can become part of the A List and part of what UsAgainstAlzheimer's is doing, we will all be contributing to research, and we'll all be getting faster glide

paths into becoming part of research, and that is going to be one of the biggest changes that we need to make in our fight against Alzheimer's. It needs every one of us. And I personally know that I may get genetically tested, because of the confidence that you have given me today, that this would be something that is much safer than I thought it might have been, before our conversation.

And along those lines, Jamie Tyrone, I hope, if you're still with us, you have a call about, I think, genetic counseling and disclosing of your APOE status. If you're there, Jamie, jump in.

Caller: Hi! I have to tell you that this has been one of the most fabulous calls that I've been on, and I really appreciate UsAgainstAlzheimer's and Dr. Jicha to be a part of this. I am APOE homozygous; I found out my genetic status kind of accidentally, and I've been doing a lot of advocating for the need of, the role of the genetic counselor and disclosure especially as you're looking at these trials. I know that GeneMatch has done a wonderful job of including genetic counseling as a part of this. If someone wants to participate but doesn't want to know their genetic status, that is a very safe place to be. I think you answered a lot of the questions I had, regarding how do you see the role of the genetic counselor. But I will have to tell you, being a homozygote, that for me, if you want to know, get your financial house in order. Get your long term health insurance, get your life insurance. There isn't anything you can do, knowing your genetic status, with the exception of research participation. So to me, that's a huge motivating factor. I'm actually a lab rat for Banner Alzheimer's Institute and I can't tell you how rewarding it is to be a research participant. When I go there, I feel like a rock star lab rat, the researchers are so appreciative to have people that are willing to participate in research —and it's not necessarily altruistic, I definitely get something out of it, but from a perspective of, you know, that's kind of smart. Because as George Vradenburg says, the first person that's going to be cured of Alzheimer's is going to be a research participant.

Dr. Jicha: Absolutely.

Debra Lappin: Jamie. This is phenomenal. And I'm being told that we are at the end of our time, can you believe this? Your question just kind of brings it all home. Dr. Jicha, if you want to make one last sentence or comment, I want to give it back to you and say thank you, we're going to follow up with

everybody who is on the call, please come to the UsAgainstAlzheimer's website, and Dr. Jicha, I'm going to give it back to you for a closing comment.

Dr. Jicha: Very good. I think those were fantastic comments to really close the talk today. I know that there's a lot more out there, that everybody wants to ask, and we could go on for hours and hours, but I'm sure that we all have other things that we need to get to. I think it's important, without being condescending, I'm really proud and incredibly respectful of everybody that took this hour out of their day today. The fight starts with education. Understanding this disease is where it all begins. We're all ready, hopefully, to enter the ring. I appreciate you all, more than you can know. Debra, thank you so much.

Debra Lappin: We appreciate you. You have been a star. And thank you to everybody who has been listening. We look forward to our next conversation with you. So, thank you so very much, one and all.