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Alzheimer's Talks Transcript
Boosting the Brain's Immune System
with Dr. Katrin Andreasson

Thursday, June 25, 2015

Note: This transcript has been edited for content and clarity

George Vradenburg: Welcome to Alzheimer's Talks, a monthly teleconference series presented by USAgainstAlzheimer's to connect you with the leaders in research and policy working to stop Alzheimer's.

My name is George Vradenburg. I'm Chairman and Co-Founder of USAgainstAlzheimer's, which, as all of you know, is a fearless and disruptive organization trying to transform the fight against Alzheimer's, changing business as usual.

Thank you for joining us today to hear about fascinating new research from Dr. Katrin Andreasson.

We have been very busy since last month's Alzheimer's Talk.

Just two quick updates on legislative developments:

Key House and Senate committees in Congress are proposing a $300 million increase in base Alzheimer's research funding from basically $586 million a year to $886 million a year, obviously a pretty significant increment. There continues to be a fair fight about how or whether we can afford those increases, and so there will be negotiations that will go on through the month of July on exactly what the budget caps ought to be this year and whether or not we can afford that money. So I just want all of you to know that all your voices actually are being heard and that the efforts we are making have emphasized to both parties, the need to highlight and to prioritize Alzheimer's research investments, so thank you all for helping us advocate for that increase. Please continue to call your

members of Congress and respond to our action emails as we continue to press for that increase in research funding.

Second is the 21st Century Cures Act, which is now moving through the House of Representatives. It is designed to improve the drug approval process in order to speed it up and get treatments to patients faster including efforts to continue to emphasize and prioritize Alzheimer's treatments. So this is going through the House now, and there will be a Senate bill that will move through the Senate in the fall, and this particular bill, which we are quite supportive of, will be, hopefully, passed by the end of the year. So we very much appreciate your support for those.

We are also hard at work on our own Women's Summit, September 30 and October 1 in Washington, DC, bringing together national and international leaders in the fight against Alzheimer's. Women, as you all know, are disproportionately affected by the disease, both as victims and as caregivers, so if you would like more information or to participate in any of the activities on September 30 and October 1, please let us know at 202-459-0870 or WomensSummit@linderglobal.com.

In all cases, to get the latest updates on the movement and updates on research and policy, please go to www.usagainstalzheimers.org and sign up if you haven't already. I hope you'll join us because we need everyone involved. That's why we named our organization USAgainstAlzheimer's. It's going to take all of us.

Now to today's call.

We have over 500 people registered today for the call from 47 states and the District of Columbia, as well as several countries including Canada, Russia, and Austria. Another almost 2500 people who can't make the call requested the recap materials which we will send to everyone who provided an email address and we'll do that about a week after the call.

As a reminder, if you have questions during the call please press star 3 on your phone. By pressing star 3, you will be placed into the question queue. Please have your question ready to share briefly with a member of our staff. We'll try to get you on live as soon as possible, when we open it up for questioning. If you're listening to us online you can type your question in the box and we'll get to as many questions as possible after the opening presentation. Unfortunately, we do not and cannot answer personal specific medical

questions during this call, out of respect for Dr. Andreasson and the other members and participants on the call. We'd like to keep this to levels that relate to the conversation that Dr. Andreasson will shortly lead us through.

It is my pleasure to introduce you to Dr. Katrin Andreasson. She is Professor of Neurology at Stanford University Medical Center. She has received the Pfizer/AFAR Innovations in Aging Research Award from the American Federation for Aging Research. Her recent research has literally made headlines around the world so we are honored that she is joining us today. So, thank you so very much for joining us today, Dr. Katrin Andreasson. We appreciate your willingness to spend some time explaining your research and answering questions today.

Dr. Katrin Andreasson: Thank you so much. It's a great pleasure and honor, actually. I'm very humbled to be speaking with all of you today. I think this is an amazing organization, from what I know about it. There is definitely some progress being made, at least at the political level, so we'll just keep our fingers crossed.

So I've been asked to tell you all a little bit about our research and what is probably different from what others are doing in the field of Alzheimer's research. I'm a physician scientist, and a trained neurologist, but what I do mostly at this point is that I do basic disease research, trying to figure out what are the fundamental things that go wrong to lead the brain to develop Alzheimer's disease.

There are a couple of very interesting concepts that have crystallized over the last couple of years. The first one is that the development of Alzheimer's disease now is thought to begin in early- to mid-adulthood, which is somewhat of a frightening thought. There are limited pathologies that start to arise in the brain, and that remain clinically silent for many years to decades before the onset of memory loss. And, in fact, many people will go through life with these changes and never develop dementia. But then, there are people who have these incipient pathologies who then, at some point, since Alzheimer's is really associated with aging, so at older ages, seventy and above, will begin to develop the initial signs of memory loss, etc.

This is a very interesting concept and one that's really now being appreciated in a new light. It's actually very good news, because what that means is, that if we were able to figure out who is at risk with good biomarkers, we have plenty of time to intervene, therapeutically or preventively.

So that brings me to the second point, which is where we started thinking about this. There is a reproducible preventive effect of a class of medications called NSAIDs or non-steroidal anti-inflammatory drugs. You all probably know about many of these—Motrin, indomethacin, Naprosyn—all these are in this class of NSAIDs. And there have been different studies around the world, from the Netherlands to the U.S., that have shown that, with normal aging, folks who are aging normally with no cognitive issues, if they are taking NSAIDs, will have a significantly lower risk of developing Alzheimer's disease later on in life.

This is a very interesting phenomenon and it suggests that there is something going on as we're getting older, and that if we take NSAIDs for our aches and pains, whatever prodromal process that is going on is somehow prevented from getting worse. NSAIDs, we know, are anti-inflammatory agents. They block inflammation throughout the body, including the brain. That suggests that one component of this long development to Alzheimer's that is an inflammatory response that is suppressed or just decreased somewhat with NSAIDs.

What we've been doing over the past 17 or 18 years is trying to pick apart this preventive pathway at a biochemical and cellular level, in order to figure out what are the inflammatory mediators that are being blocked if you take NSAIDs. We are trying to identify the inflammatory mediators, what receptors they bind in the brain. Our research has been funded continually by the National Institutes of Health and I'm putting a plug in: please call your Congressmen and Congresswomen and make sure that the NIH is well funded because it is definitely not at the moment, with scientists not being able to continue their research, and with many promising scientists leaving research. Our work has been supported by private organizations including the Alzheimer's Association and Bright Focus and American Federation for Aging Research, so it's thanks to all these funding agencies that scientists like myself can actually make some headway.

We've been working on this question for quite some time. The brain actually contains not only neurons, or nerve cells, but a couple of other cell types. One of them is an immune cell called the microglial cell. Micro- for small, and -glia, is a name for a cell that's not a nerve cell. We actually have immune cells in all of our organs: lungs, heart, liver, etc. The brain has these specialized immune cells as well, and they are called microglia. There's a lot of recent and exciting research on microglia as they really were not high on anybody's radar decades ago. Microglia are very important—they help keep

the brain humming along, and they make sure that there are no infections, they clean up any kind of debris that's made by other cells, and they support nerve cell function. And the reason that's very important is that your brain really has to be squeaky clean in order for the nerve cells to fire and everything to hum along normally.

Normally in aging, immune cells lose a little bit of their ability to do all their basic functions, but generally they do all right. However, in Alzheimer's disease, the microglia really start to decline and they cannot keep up with the pathologies that are developing.

The two big pathologies, some of you may know. The main one is amyloid deposition and the second one is neurofibrillary tangles. The neurofibrillary tangles actually start accumulating quite early in adult life, but then it's in a very limited distribution, and these tangles generally do no harm. Amyloid deposition can be actually quite extensive. It's has been confusing because even with very extensive amyloid, a person may not have any cognitive deficits at all. In the field, there's been a huge emphasis on amyloid-lowering agents, and until now, most pharmaceutical and academic efforts have focused on amyloid.

But we're focusing on something entirely different, which is the quality and nature of the microglial immune response. This response indirectly includes amyloid, because part of what microglia do is that they clear the amyloid and they also clear the abnormal tau that leads to tangle formation, and they also control the inflammatory environment of the brain. And finally, the last thing the microglia do is they actively participate in nerve cell function. They provide good factors to keep neurons healthy, and they also help form synapses or clear synapses, so they're very involved in neuronal function.

So we have discovered that an inflammatory receptor called the EP2 receptor, that functions in microglia in the setting of Alzheimer's pathology in our experimental models, does a lot of harm. It suppresses the good and healthy functions of microglia, and when we remove it—either in cell culture or in mouse models of Alzheimer's disease—we can improve a number of critical microglial functions. We can improve the inflammatory environment of the brain, and that's very good for nerve cells and neurons, they can work much better.

If you remove the EP2 from the microglia, the microglia are also better able to get rid of the amyloid. Without EP2, microglia also make beneficial factors that support neurons and synapses. The one that we particularly were interested in was IGF-1, insulin-like

growth factor, which in the brain is a factor that helps with many things, including nerve cell survival and control of inflammation. So with the EP2 receptor suppressed, you now you have a brain with an army of very healthy and effective microglia that are cleaning things up and getting things back to normal so the nerve cells can function normally.

That's what we found. It brings up a new concept where if we could somehow change our microglia so that they're behaving in a more healthy and effective way, that might go a long way to slowing down the process leading to Alzheimer's disease. And so that's where we're at right now. We're trying to understand how EP2 suppresses all these important processes in microglia.

We do not have a compound yet to target EP2. I know there are a number of questions on this. Hopefully with some funding, an inhibitor could be developed that would block the EP2 receptor on microglia, thereby restoring microglial functions to healthy states. To develop a safe and selective compound generally takes about four or five years, before one can go to the FDA and get approval for Phase One trials. That's assuming everything works. From there, the time it takes from Phase One through Three trials really depends on how well the new drug candidate works. If there's going to be more funding for Alzheimer's research, development of new interventions will be accelerated.

George Vradenburg: Thank you very, very much for outlining your research. I am going to try to understand the logic here and then we can ask some questions. So the presence of this EP2 receptor causes a reduction in microglial function, which causes the immune system not to be able to basically use the body's basic processes to clean out the brain, right?

Dr. Katrin Andreasson: That's it.

George Vradenburg: So, tell me, this is a really stupid question. What do you mean by inflammation?

Dr. Katrin Andreasson: That's a very good question. Inflammation is an area that has been getting a lot more attention recently. Inflammation actually is a good thing. It protects us from infections, so that is a very important thing. So there is a normal, healthy function of inflammation. In the brain, microglia are on the alert, they are migrating around, they are cleaning up cell debris . . .

George Vradenburg: They are the trash collectors.

Dr. Katrin Andreasson: Essentially yes, they are very important in establishing what we call "homeostasis" in the brain. So if you have equilibrium, or a stable and good environment, the brain will work much better, and that's what the microglia do. That's good inflammation. Now bad inflammation is what we think is driving progression of Alzheimer's disease, and with bad inflammation, microglia, instead of making growth factors for nerve cells, start to make proteins that are inflammatory and that irritate and even harm the nerve cells. One class of inflammatory proteins are called cytokines. There are good cytokines and there are bad cytokines. Bad inflammation is characterized by production of cytokines that can harm nerve cells.

A microglial cell that's not behaving well and eliciting a lot of bad inflammation will also generate a lot of free radicals. The brain can't tolerate free radicals. So, to get back to your question, there's good inflammation and bad inflammation. What we're doing with the EP2 receptor is basically eliminating the bad inflammation but preserving the good inflammation. What we found, interestingly, is that when we removed the EP2 receptor from microglia in the brain, not only did we get rid of the bad inflammation but somehow the good inflammation came roaring back - the microglia generated healthy factors to support neurons, amyloid was cleared more effectively, and inflammation was more benign. So the way we think about the EP2 receptor is that the EP2 receptor puts the brakes or suppresses healthy microglial function. You remove the brakes and now the microglia can do what they are supposed to do.

George Vradenburg: So essentially the presence of the EP2 receptor is inhibiting the normal defensive functions of the brain that basically protect us, and so the presence of this receptor is inhibiting our natural defense mechanism. So where does this EP2 receptor come from?

Dr. Katrin Andreasson: The EP2 receptor is part of a family of receptors and there are four of them. The EP2 pathway actually is very highly preserved in many different organisms. So I would imagine it probably has some very important function. But, when you have something that induces a lot of inflammation like amyloid, or tangles, the levels of the EP2 receptor go way up. So under normal circumstances, there would be normal levels of EP2 and you'd probably be okay. However, if you're starting to accumulate some amyloid, if you're starting to have a too many tangles, because these proteins are very inflammatory they may drive microglia to make a lot more EP2. The high levels of EP2 we

believe are what disrupts healthy microglial function. The idea, then, would be to drive the EP2 down so we can restore the normal function of microglia.

George Vradenburg: That's a great description. We do have a question from Big Sandy, Texas, from Cassandra Brenton, which is a natural follow-on to this line of inquiry. Cassandra?

Question: Hi, yes. I was wondering if you've actually come up with a therapy or substance or something that will actually get rid of the EP2?

Dr. Katrin Andreasson: That's a great question. To do that, we have to develop compounds to block EP2 that are deemed to be safe and effective by the FDA. With a safe and effective compound, a Phase One clinical trials which test the the safety of the compound in people would be the next step, followed by Phase Two and Phase Three trials. This process can take many years.

George Vradenburg: We have a question online from Loretta Hollingsworth who asks: Is it your opinion that an anti-inflammatory diet, over a period of time, would help stave off Alzheimer's, perhaps by some of the processes you're describing?

Dr. Katrin Andreasson: Yes, ok, that's a very interesting concept. An anti-inflammatory diet would be a diet where you would be eating less sugar, lower levels of fats and saturated fats, so essentially a very healthy diet like what we're supposed to be having. And definitely that will help many different things, including propensity for diabetes, and obesity, that contribute to metabolic syndrome. Metabolic syndrome is intimately tied to Alzheimer's disease. So, for my patients, I always stress diet; Mediterranean diets are very good, they are high in olive oil and garlic and tomatoes and all that good stuff. Anything with a lot of color, berries, grapes, blueberries, raspberries, all those things are very, very good for you.

But the one thing I would add, in addition to diet, is exercise. A regular exercise regimen is probably the one thing that has been shown to slow things down and there have been some recent and very exciting studies in mild cognitive impairment, just simply looking at people who exercised and people who didn't. The people who did exercise did a lot better. Exercise is known to drive inflammation down. If you have a good diet, an anti-inflammatory diet, and exercise—in moderation, don't overdo it—those two together will help a lot.

George Vradenburg: Good question, good answer. Next question here from Carol Stewart, who asks about another behavioral issue.

Question: Hi. Can microglia in the brain do its function in people with sleep disorders, which may lead to limited hours of sleep, frequent wakenings, etc., and not remaining in the various brain wave states for significant periods?

Dr. Katrin Andreasson: Yes, that's another great question. You guys are hitting all the right points. So, it's known that sleep apnea is a risk factor for lots of things, heart disease, strokes, and all of that will influence the brain's health and the health of all the cells in the brain, including the microglia.

Sleep is extremely important. Microglia during sleep do one very important thing, which is they clear amyloid that is produced normally during the day. So whenever we're thinking, we're actually producing a little bit of amyloid. To clarify, this is not amyloid but it's the small protein that forms the amyloid, called A-beta protein. A-beta is actually released from our nerve cells every time our nerve cells fire, and it's a normal process. But the A-beta is usually taken back up by the microglia, and so it disappears. During sleep, the interesting thing is that microglia get to work. They're patrolling around, they're clearing all the debris, they're clearing all the A-beta that they can. So, if someone is not sleeping well, and is not going through the normal stages of sleep, that's probably going to impact negatively on microglia's ability to clear the A-beta. Sleep apnea is something we always ask about. It's very common, and there are definitely ways to fix it, with a CPAP machine, for example, and if you can get used to it, it can be a lifesaver.

George Vradenburg: So far, we've heard a good diet, exercise, and fix your sleep disorder.

A couple of questions online here. How much does genetics factor into Alzheimer's? This is from Mary Justice, and in the context of this call, is there a genetic influence on the presence of EP2?

Dr. Katrin Andreasson: Yes, there's definitely a genetics component in Alzheimer's disease. The most well-studied one is the APOE e4 allele, which many of you might be familiar with, and it's actually particularly important in women, from very recent studies from a colleague of mine here at Stanford. But more recently, there have been some very

nice genetic studies with Alzheimer's patients that have discovered that there are some genes that can be slightly different, they are called "variants", and these genes, interestingly, are immune genes. They're microglial genes.

So that has taken the field by surprise, because in general the field was not thinking that inflammation or microglia were a driving force in the development of Alzheimer's. However now there are half a dozen of variants that are associated with increased risk of getting Alzheimer's disease that are immune genes or microglial genes. So what this means is that the microglia in these subjects with these variants are not able to behave properly. They're not healthy microglia so there is an increased risk of developing Alzheimer's later in life. So yes, there's definitely a genetic component, but the feeling is, I will be an optimist here, with good modification of diet and exercise, you really could decrease your risk; if you live a healthy lifestyle, this has a very beneficial effect on your immune system, and on your microglia in particular.

George Vradenburg: We have a question online here from Deb Legel: How do you know if you have the EP2 receptor?

Dr. Katrin Andreasson: Everybody has the EP2 receptor. How do you know if it's too high in your microglia? At this time, I don't know how we would determine that. That's a very interesting question; I'm going to have to think about that one.

George Vradenburg: I've got a question here that just came in at the same time as I was asking the online question. Karen, you asked the same question, but you also mentioned something else. Would you like to go ahead and ask your question?

Question: Yes, I was wondering if this EP2 is affected by the COX-1 and COX-2 pathways, or do you know which, whether it's COX-1 or COX-2, and is that why the non-steroidals may be effective in preventing Alzheimer's?

Dr. Katrin Andreasson: Yes, yes, you've got it! That has been our logic all along. NSAIDs block COX-1 and COX-2, and by doing that, you don't make very much of the prostaglandin E2, PGE-2, which is the inflammatory molecule that binds to the EP2 receptor. So you're absolutely right, by blocking COX-1 and COX-2 with NSAIDs, we're reducing PGE-2, and hence EP2 activity. Our approach over the last ten or fifteen years has been to systematically go through the PGE-2 pathway, one step at a time to get to

the place where we're getting a very specific effect, and that would be EP2 suppression of healthy microglial function.

George Vradenburg: Karen, can I just ask you, are you yourself a researcher or are you just following this like a hawk after a mouse?

Question: I'm following this like a hawk. I have my own inflammatory issues and I am a nutritionist so I'm a bit of a professional. But I also have a mom who has this disease and so I try and put together everything and these talks have been so beneficial to me; the opportunity to speak to top people like this is unbelievable.

Dr. Katrin Andreasson: Thank you.

George Vradenburg: Thank you, Karen, for your observation and for following this so closely on behalf of your family. Thank you.

A question online here from Saurah Litzky; would you like to ask your question?

Question: Yes, thank you. In terms of taking NSAIDs to help inhibit the inflammation, how much?

Dr. Katrin Andreasson: That's a good question too. So, the dose to take has not been determined. There's a good side to NSAIDs and there's a bad side. On the good side, the epidemiology studies that have shown that taking NSAIDs are preventive if you're aging in a healthy way, and have normal cognition, those are very, very solid. The down side of NSAIDs is that as you get older, NSAIDs can have side effects like kidney and stomach toxicity, because downstream, like we were just talking, downstream of the Cox 1 and Cox 2 pathway, there is a whole family of prostaglandins, and some of them are actually good guys, that you don't want to eliminate, and actually a lot of our work has been identifying those as well. So that's the one problem with NSAIDs.

If you're younger, healthy, and you have no issues with your kidneys or your stomach, or blood pressure issues, it's probably fine to take NSAIDs—with food and water. In terms of the dose, it's very interesting that one of the first studies—they didn't actually examine what dose people were taking- the study just recorded whether subjects took NSAIDs or not. So what could be happening is that we all have a little bit of inflammation and as we get older, unfortunately that level rises. If you take an NSAID, the level of inflammation

drops down, and that's probably good. It will then gradually come back up again and you drop it down. My gut feeling is that it's probably not good to take NSAIDs around the clock, and you should take them if only you need them. Therefore, since NSAIDs can ultimately block beneficial prostaglandins as well as toxic ones, we are looking at pathways downstream from where NSAIDs act, for example at the EP2 receptor. If we could block the toxic pathways, but preserve the beneficial pathways, we would be much less likely to have side effects.

George Vradenburg: I've got a question here from Lori Pollack online. Do microglia and EP2 act differently in women versus men?

Dr. Katrin Andreasson: That's a good question. We haven't investigated that. My guess is, given the differences with APOE e4 (APOE e4 incidentally is very tied in to the inflammatory response as well), we know that response in APOE e4 is very different between women and men. It would be very interesting to look at that, but I don't know the answer.

George Vradenburg: Is there any correlation between—how to put this question? There are female and male mice; are there differences between female and male mice correspondent in any way to the differences between female and male humans?

Dr. Katrin Andreasson: This is a challenging area, because mice are not humans and in fact mice will not actually develop full Alzheimer's pathology, so we have to develop a model where we can look at Alzheimer's in a mouse; we actually have to introduce a gene and make what we call a transgenic mouse. Now, if we look at the differences between male and female mice that have this transgene, in some strains there are differences and in some, there are not. The NIH has actually recently come out with a policy where they would like researchers to look evenly at both genders; that's a great policy. I hope they will follow it up with a more funding because those kinds of studies are prohibitively expensive.

George Vradenburg: Question online from Bob Carrico. Are the current findings of an important role of microglia cells in pain processes related to your research in any way?

Dr. Katrin Andreasson: Yes, that's very interesting too. I'm not an expert in mechanisms of pain, but the inflammatory response is increasingly taking center stage there as well. I think in many of these diseases, where microglia or inflammatory cells are not behaving

normally, that would be a very interesting area to study. Pain is a very complex process, not just where it hurts in your arms or legs but actually, there are changes that occur all along the spinal cord up into the brain where circuits are actually changed. And microglia will likely have a lot to do with changing those circuits, because microglia can remove synapses or help synapses form, and my guess would be that this receptor may be involved in pain perception.

George Vradenburg: We have got a question online from Lois Lutz who asks about other anti-inflammatory nutritionals like cat's claw or others that may have the same effect as NSAIDs.

Dr. Katrin Andreasson: I'm out of my depth here so I don't know. I'm guess I'm somewhat of a simpleton here. I take fish oil. And I take NSAIDs here and there, but I don't know enough about how these nutritional supplements work.

George Vradenburg: A couple of interesting questions here asking you to comment on other people's research if you are willing to do this; we'll just ask. One is from Laura, online: Can you comment on the recent research of Carol Colton, re: the immune system and arginine?

Dr. Katrin Andreasson: Carol Colton and arginine, yes. Arginine is supposed to be an anti-inflammatory compound and Carol Colton is a very well-established, very respected scientist. She's been working on microglia for a very long time, I think she's probably one of the first people to bring attention to microglia, so she's a real visionary. Arginine is anti-inflammatory; it suppresses inflammation, and it can be made by microglia. I'm actually not familiar with this recent study, I'm afraid.

George Vradenburg: Ok. Joan would like to ask your thoughts on the recent UVA study on new lymphatic systems in the brain.

Dr. Katrin Andreasson: That's really interesting, a very cool concept. Our bodies have a lymphatic drainage system, our lymph nodes, and for the longest time the brain was thought to be very unique in that it did not; but now there is evidence that there is lymph drainage from the brain, and it's very, very early days. This system allows us to flush out unwanted substances out of our brain into the blood vessels. And this is very important, and allows the brain to get cleaned out, and microglia and probably astrocytes, which are

another very important cell type in the brain, participate in this. So it's very early, it's a very interesting process, and I'm looking forward to hearing more about that.

George Vradenburg: Is there any difference in the presence of EP2, to the extent you know it, in those who are APOE e4 positive or negative?

Dr. Katrin Andreasson: We don't know that yet, but we want to look at that.

George Vradenburg: We have another question here from Cassandra. Cassandra Brenton, you are on live again.

Question: Thank you for taking this second question. With as little as we know about the origins of Alzheimer's, how dependable can study results be that are performed on mice who have been given this artificial form of Alzheimer's?

Dr. Katrin Andreasson: So you're asking whether the mice, the models that we use, whether they really replicate Alzheimer's, is that the question?

Question: Yes, because you say mice don't get Alzheimer's, so we are inducing kind of an artificial form of Alzheimer's?

Dr. Katrin Andreasson: Yes, you're absolutely right. So, normally, mice will live probably two to two and a half years, but they will not really develop the amyloid or tangles. So we have to help them develop these pathologies by introducing the genes that encode amyloid formation. This is not optimal, but on the other hand, it actually works much better than one would have predicted. There are a lot of different transgenic mouse models at this point and this is true not just for Alzheimer's but for other terrible diseases like Lou Gehrig's disease and Parkinson's disease. This is one way to at least start to get a handle on what happens in these diseases.

George Vradenburg: Dr. Andreasson, thank you so very, very much for being with us today. We've run out of time, and it was completely full, and I must say that I am impressed as heck by the quality of the questions you've gotten from the people that listened in on this call. It sounded to me like they were researchers themselves. It's very impressive, and your work is impressive and promising and so, thank you for what you do in the research field for all of us who are trying to fight against this disease, and thank you for spending some time with us today.

Dr. Katrin Andreasson: Oh, it was my pleasure.

George Vradenburg: Thanks to everyone on the phone and online, for participating in this talk today. In about a week, we'll have a copy of this recording and a transcript on our website for you to share with your friends, and anyone who has provided us their email will get a recap of the call.

Just as a tease, we have our next call on Tuesday, July 14, from 4 to 5 p.m. EST. We'll feature Dr. Michael Raffi. He's the Director of the Memory Disorders Clinic and Assistant Professor of Neurosciences at the University of California, San Diego. He's also the Medical Director of the NIH-funded Alzheimer's Disease Cooperative Study and Attending Neurologist at the Shiley-Marcos Alzheimer's Disease Research Center.

Mrs. Shiley is a contributor to US and, we thank her for that. She's also appeared in readings of my wife's play in various cities around the country, so Darlene Shiley is a great friend. She's also a great supporter of Masterpiece Theatre, so we're glad to see that.

Dr. Raffi will share with us, on July 14, information on the NOBLE Trial, for those with mild to moderate Alzheimer's disease.

As always, please stay on the line if you would like to leave us a message with a question or comment; we're particularly interested in what you would like to discuss on future calls.

Thank you all for joining us today, and thanks again to Dr. Katrin Andreasson from Stanford, and to all of you, have a good afternoon.