ERIC M. REIMAN, M.D.
1956 -

Honored as 2025 Historymaker
World Leader in the Fight Against Alzheimer's

The following is an oral history interview with Eric M. Reiman, M.D. **(ER)** conducted by Laurie-Sue Retts, Ph.D. **(LR)** for Historical League, Inc., and video-graphed by Leonardo Buono on Tuesday, June 10, 2025, at The Center for Positive Media in Phoenix, Arizona.

Original tapes are in the collection of the Arizona Historical Society Museum Library at Papago Park, Tempe, Arizona.

LR First I want to say congratulations to you on being selected for this honor, Dr. Reiman.

ER Thank you so much. It's a privilege.

LR Tell us a little about yourself. Tell us about your work, but also about your family and your wife, your kids.

ER Sure.

LR How long have you been in Arizona?

ER I am a brain imaging researcher and psychiatrist by background. I am currently CEO of the Banner Alzheimer's Institutes, which include Banner Alzheimer's Institute and Banner Sun Health Research Institute, and Director of the Arizona Alzheimer's Consortium. My colleagues and I are trying to make a difference in the scientific and clinical fight against Alzheimer's disease and contribute to research, care, and collaboration in other ways. My overarching goal is to prevent Alzheimer's disease as soon as possible, hopefully sooner than you think. I have a wonderful family and cherished friends. My wife Lori and I have four adult children, Rebecca, David, Nicole and Sammy, who are the joy of our lives. I have lived in Arizona since July 1988 and love being here.

LR Tell us about your growing-up years. Let's start with growing up with your family. Your parents, brother and sister, your friends?

ER I grew up in New York. I was born at Mt. Sinai Hospital, the very place where my father and mother met when he was training to be a pediatrician, and she was training to be a nurse. After spending three years in Forest Hills, New York, we moved to Port Washington, a small town on the north shore of Long Island, which I adored. We lived right on the Manhasset Bay, about 30 minutes from Manhattan. It was an idyllic place to grow up. We never owned a key to our front door. I recall walking to elementary school at a very young age. I cherished my friends growing up and continue to do so today.

LR Brothers and sisters?

ER I have a brother, Todd, who is a year younger than me and a sister, Beth, who is 3 ½ years younger than me. We all ended up choosing healthcare professions. I am a psychiatrist and brain imaging researcher by training. Todd was an emergency room physician, Beth was an occupational therapist, and her husband Michael is an infertility doctor.

LR And how about friends?

ER I have quite a few childhood friends, whom I cherish, and am extremely close to several of them. Despite living in distant locations, we're there for each other. Since the COVID pandemic, several of us communicate by Zoom almost every month. Last year was our 50th high school reunion, and we just loved it. I'm a fairly private guy, but through my work, my wonderfully social wife, who is responsible for the balance in my life, and other interactions, I have friends and colleagues here in Arizona and around the world, whom I deeply value. They include some of the of the finest people I know.

LR Wow. That's special.

ER Yup. I'm very lucky.

LR As far as special, is there a significant or fun event that you remember from your days on Long Island?

ER While I can't think of a particular event, I can tell you that I was flooded with memories during that high school reunion. One of my friends wanted me to know about a time that the two of us were walking home from school. He had assumed the leadership role in helping his family, helping his mom and siblings get through an extremely difficult time, had done so in an extraordinary way, and noted that it sometimes felt overwhelming. He recalled me telling him that I would always be there for him and wanted me to know that this memory helped to sustain him. As I mentioned, I'm a fairly reserved guy, and I look back on things that I could have done better to support the people I love. But those times that the people I care for have been there for each other, I for them and them for me in good times and bad, mean the world to me.

Until I went to high school, I had always thought of myself as an under-achiever. I remember being in class all day, watching the clock until 2:45 when the school day was over. I had difficulty focusing on the teacher and subject matter that required memorization, and I had little energy left for homework in the evening. That said, I had a proclivity for math and problem-solving that helped me get by. Things changed when I went to college and had only 2-3 classes each day. It was a revelation. I had time to think, I found my interests and strengths, and I ended up thriving. I think all students need the options and flexibility to find their passions, revel in their strengths, and find the self-confidence to move forward, whatever their goals.

My parents divorced when I was a freshman in college. It was harder on my brother and sister, who were still at home, and it introduced a little hardship when it came to paying for college and medical school. Based on some things I had done during my freshman year at Duke, I received a scholarship that covered only some of my college expenses due to my father's income, which was needed for other family expenses at the time.

One summer, my brother and I leased and operated an ice cream truck. Another summer, I drove into Manhattan at night to work on a skyscraper's freight elevator, hauling garbage from different floors. I also took additional classes throughout the year in order to borrow more money for my tuition costs and get through college and medical school in six years. It wasn't a hardship, just a required a change in plans.

While my parents' divorce was painful at the time, it worked out surprisingly well in the end. My mother moved to Arizona in the mid-'70s, soon after the divorce. My family and I moved to Arizona in 1988, and my father and stepmother moved to Arizona a few years after that. It turned out that my father, mother, stepmother, and in-laws became best friends. My wife, despite her full-time job and travel schedule, would have everyone over for dinner each Sunday. It was

really wonderful.

LR She kept family unity in spite of some…

ER Lori is amazing.

LR So, as you look back to your growing-up years, you said that you weren't much of a student. Were there other things that you really enjoyed doing with your friends, or some things that you were particularly good at?

ER I really enjoyed basketball, racquet sports, and other ball sports that required coordination. Activities that required particular strength or speed (I ran like a duck) were not my thing. I loved playing basketball with my friends, despite an inability to jump.

LR Tennis is big in Forest Hills, I think?

ER It was big in Port Washington, too, which included a well-known tennis facility, where I believe that kids like John McEnroe played for a time. I was on the high school tennis team, playing doubles, but not very good. There were so many things that I loved about growing up in that town.

Academically, there were subjects involving math and problem-solving that seemed to come naturally to me and I really enjoyed. I had several teachers over the years whom I revered. They inspired and challenged us, kindled our interests and strengths, and showed us how much fun problem-solving could be. They included my 4th, 8th, and 11th Grade math teachers Mr. Davis, Mr. Boyle, and Mr. Meystrik, my 8th grade science teacher Mr. Coppola, who reminded me that science was more about problem-solving than memorization, my AP English teacher Mr. Bogardus, who taught us how to explicate poetry, and my History of Philosophy Professor at Duke, Dr. Mahoney. Their dedication, approach to teaching, and joy in challenging us and bringing out our best had a profound impact on me. I also remember a particular book from one of my first college classes, entitled *Introduction to Philosophy.* I still have that old book and a couple of essays that I decided to write on my own about subjects like limitations in our perception of the physical world using Plato's Socratic method. At Duke, I majored in both Philosophy (for fun) and Zoology (which included many of my pre-med requirements).

Besides those things that came naturally to me, there were other things that I found challenging. I was never good at memorization, foreign languages, or playing a musical instrument. I was never comfortable writing papers—ironic, given that I'm an author of so many articles. While I write pretty well, I tend to obsess over the precise wording, making the writing process unduly painful and prolonged. Given that challenge, I would regularly select classes that required me to

take tests over those that required me to write papers.

Growing up, I had a fear of public speaking. During my residency training in Psychiatry, I decided to teach a weekly psychopharmacology course to medical students. While the students seem to value the lectures, the course also gave me a captive audience to practice my speaking skills and begin to overcome this fear. While that worked well for repeated lectures to smaller groups, I had more work to do. My very first research article was published in the journal *Nature,* and I was invited to give a short scientific presentation to about 3,000 people. Fortunately, I worked in a lab with a wonderful mentor (Marc Raichle, a father figure to me when it comes to my research career) and several incredibly smart and equally tough but supportive colleagues, who required me to repeatedly revise and present my talk until I got it right. In 1984, before the existence of word processors, I used a typewriter to draft my slides, photograph the printed pages, and repeat the process until the slides and my presentation were just right. My colleagues seemed to eviscerate every word until they were satisfied *[laughs]*. By the time I was ready to give that presentation, I was confident that I would get through that presentation *[laughs],* and my presentation skills continued to improve over time

LR So you never took a formal public speaking class? You were your own speech therapist?

ER Exactly. Self-help.

LR It looks like it worked.

ER Not perfectly, but better than I ever predicted. I think we all have our own strengths and challenges. Despite my own challenges, things worked out pretty well.

LR I'm wondering… when you say you weren't a very good student, but there were certain things you did like, strengths like math and things like that. A number of people who end up being quite creative in their professional life seem to be dreamers in school. They find themselves dreaming about something else instead of really focusing on school. Would you put yourself in that category?

ER I think I've been a lifelong daydreamer, partly due to my limited attention span. It became less of an impediment to me in college, and it turned out to become a real asset to me later on. Some of my dreams, including those that seemed to be highly unrealistic at the time, turned out to make a major difference in my work,

LR What do you think was the turnaround in college? You talked about some mentors and some classes you liked.

ER In college, I spent much less time in the classroom and had a lot more time to think, develop my interests, and leverage my strengths. Except for the teaching experiences I mentioned, classes were not my thing. During my freshman year, I did quite well in school; I wrote those essays for fun; I volunteered for the Big Brothers Program and became a longstanding Big Brother to two young boys who were living with their divorced mom. I played a lot of racquetball, enjoyed my college friends and found other interests as well. After that year, I received an A.B. Duke In-Class Scholarship. The funding turned out to be limited by my father's income level, so I needed to find other ways to cover some of my costs. But it included the chance to spend a summer at Oxford with some of the other Scholars, which was fantastic.

LR Wow. Okay. A summer in Oxford?

ER Yes.

LR And specifically studying what?

ER I was hoping they would offer a philosophy class, but they offered an English literature class instead. Still, I really appreciated Oxford's tutorial experience, the centuries-old buildings, traditions and surroundings, and the students I got to meet from around the world.

LR So, there's hope for kids that don't necessarily do well in elementary and even middle or high school, right?

ER Everyone faces challenges from time to time. They deserve the chance to learn, grow, and find the path that works best for them. It's never too late to find that path, even at my age. I like to encourage my students, trainees and younger colleagues to look around, seize their opportunities, and be open to the unexpected opportunities that will inevitably come their way—and I frequently call upon my own life experiences to underscore those points.

LR Tell us more about your educational experience after high school. You went to college…

ER My friends and I applied to many of the same schools, including a few Ivy League schools and some smaller schools in the Northeast. I can't recall how I learned about Duke, but it was located in North Carolina, it was beautiful, and it seemed a little different from the others. I ended up spending nine years at Duke: Three years in college, three in medical school, and the first three of my four years as a Psychiatry resident.

In 1983, family considerations led me to move to Washington University in St. Louis, where I completed my residency training, launched my research career and become a faculty member. In

1988, family considerations led me to move to Phoenix to chart my career path. In each case, I worried about the impact of the move on my career, and in each case, my concern turned out to be unfounded. The opportunities I chose to pursue turned out to be incredible.

LR Did you go into medical school thinking that you wanted to be a psychiatrist?

ER Based on my father's gentle but persistent prodding about the impact one could have as a physician, and based on a general sense that I would be able to find a role that I might find fulfilling, I always considered the idea of applying to medical school. At the time I applied, I was open to almost any medical specialty other than psychiatry.

LR Tell me a little bit more about those reasons.

ER One summer, I volunteered to work in a psychiatric hospital. After observing the psychoanalytic approach taken to the care of patients with severe psychiatric disorders, I thought the field had a long way to go to understand, diagnosis, and treat these disorders and engage concerned family members in more supportive ways. At that time, the idea of a career in Psychiatry wasn't for me. I changed my mind during my Pediatrics rotation in medical school. I helped care for two children with terminal diseases--a small boy with cancer and a teenage girl with cystic fibrosis, who would spend the last months of their lives in the hospital. I was struck by the grief these children experienced being away from their family in the hospital, the grief their parents experienced knowing their children would not be returning home, and the impact their feelings had on all of them. I thought I might contribute to the treatment of unresolved grief and decided to become a psychiatrist after all. Even though I ended up pursuing a different line of work in my psychiatric career, I saw a career path with the potential to make a difference.

Although Duke medical school was designed to introduce students to research early in their education and training, I was a late bloomer in this respect. I didn't work in a research laboratory until I was a fourth-year resident in psychiatry, and that wasn't until I left Duke for Washington University in St. Louis in my last year of psychiatry training. Before leaving Duke, I asked my Psychiatry Chair for advice regarding a research career—and I have shared his advice with my own students ever since. "Choose a mentor based on his or her cutting-edge methodological skills, track record of productivity and impact, and genuine interest in you and your career development. Do so even if your mentor's line of work is different from what you had in mind at that particular time, for you'll be able to capitalize on those skills to pursue your own interests later." He also encouraged me to look into PET when I got to Washington University, noting that they invented it there.

When I arrived at Washington University to complete my Psychiatry residency, become a faculty member in the medical school, and launch a research career, my new Psychiatry Chair invited me to spend at least 80% of my time during my fourth year of my residency and then on the

faculty to develop my research career. While I missed seeing patients more frequently, the opportunity to conduct research, develop my research skills, and learn from greater people was an incredible gift.

When I talked with my Chair about my interest in PET, he wasn't sure that this technology would be relevant to Psychiatry. When another resident explored this possibility, it didn't work out that well. Undaunted, I met with the person in the PET laboratory who turned out to be my mentor. Marc Raichle would become the father of human brain mapping and a professional father figure to me. At the beginning of our conversation, Dr. Raichle, wasn't sure it made sense to have another psychiatrist join the lab, which included several neurologists and a neurosurgeon. After talking about some mutual interests, he eventually relented and invited me to give it a try. The next day, I entered the small office that I would share with two young neurologists in the lab. Without looking up, they said, "We want you to know that we had a vote about whether to permit another a psychiatrist to work in the lab. It was unanimous against you, and the only reason you're here is that Marc Raichle is a pushover." When I laughed, they asked me what was so funny. I replied, "Given your low expectations, there's only one direction that I can go from here!"

My mentor and lab mates were incredible, given their intellectual curiosity, methodological rigor, high expectations, and collaborative spirit. It was a perfect place to start my research career, and I treasure the experience to this day. Dr. Raichle had a boyish enthusiasm for our work and not only supported but encouraged us to find new ways to address challenging problems.

When I joined the lab, I was assigned to a project that involved the study of patients with panic disorder. Patients with this condition experience anxiety attacks, characterized by the sudden onset of severe apprehension, fear and related symptoms, that would occur at unexpected times. In this project, I would use PET to measure regional cerebral blood flow, an indicator of brain activity, to study patients with panic disorder and healthy volunteers before and after the intravenous infusion of sodium lactate, which would commonly induce an anxiety attack in the patients but not in the healthy volunteers. By the time I joined the lab, PET images had already been acquired in some of these volunteers.

So, I had this data that we were collecting in people before and during panic attacks to see the brain function; to see parts of the brain that light up when they had panic attacks. I'm looking at this data, my first, my very first project. And it's very noisy data. It's hard to see subtle changes. A couple of my colleagues were working on some ways to know where in these blurry brain images you were, in a standard brain atlas that people had developed based on autopsy. I said, "What I'd like to do is figure out a way to mold everybody's brains into the same size and shape and put them together and superimpose them. The noise will cancel out and you'll see these subtle changes." And as my mentor wrote in this history of brain mapping, he says, "This young

psychiatrist proposed this idea and everybody scoffed and said the result would be mush." But as soon as we saw the results, the students and a colleague who helped with some of the programming, it was amazing. So that image averaging and standardization has changed the

study of the human mind and brain. It has been used in a range of ways outside of my own interest then in panic disorder …for a range of things and I'm very proud of that.

What struck me at the time was, there's no way I could've done that without my colleagues who had these complementary strengths to address that question. One step after the other in my career, I can tell you what we've been able to accomplish working together that none of us could accomplish on our own and that was great. So at that time, I thought, well, I'm going to do brain mapping research and I'm also an expert in anxiety disorders, so it will help in that regard. That's when I came to Arizona, again for family considerations. My mother was there. We had young kids. The medical school was in Tucson, not Phoenix. I was commuting. I was one of two individuals. The other was Robert Spetzler, the Director of Barrow Neurological Institute. We two were full-time faculty from Phoenix. I would travel two days a week there and see what we could do. The medical school wasn't here. And there were no universities that had the cyclotron, radiopharmacy lab, or imaging system needed to perform PET scans in the research or subsequent clinical setting. The predecessor to Banner Health, Samaritan Health System, decided to make an investment in PET, a big expensive piece of equipment called a cyclotron and a PET scan. I said, "I don't think this is going to be ready for clinical use very soon." But they said, "No, we'd like to give it a try." And that turned out to be a great opportunity. So, I knew what I wanted to do in mapping the brain involved in anxiety disorders. I thought I could figure out a way because of this underused scanner and other opportunities, I could develop a mechanism where we would work on ways to see subtle changes with greater power and use them to study the human mind and brain.

My very first paper was in the journal *Nature*, which is considered the leading scientific journal in the world. It was described at the end of the standard neuroscience expert on the history of psychiatry ended with this finding which kind of came and went in panic disorder. People [in St. Louis at Washington University] thought, "well you're moving to Arizona. We don't understand." We understand the importance of family. I've always thought family comes first. So, when I was leaving, another mentor, a well-known person in neuropsychology, a fellow named Michael Posner, said, "Eric, don't feel so downtrodden about this. At the University of Arizona they have world leaders in cognitive science, the study of the human mind and brain. World leaders in the study of memory, emotion, speech, consciousness. Go out and meet with them." So, when I moved here, I ended up deciding out of desperation to figure it out – I knew what I wanted to do in my own area, but I had opportunities to advance this emerging area of brain mapping research. To figure out brain regions that are involved in normal behavior as they conspire to produce psychiatric disorders. For instance, I would reach out to leaders in the fields and lure them into brain imaging research, even though they didn't necessarily want to do that.

At ASU, they had a wonderful program in what we call computer-aided geometric design. The mathematical description in three-dimensional analysis and visualization of images that we can work on. So I ended up forging these relationships and in addition to the work we were doing in anxiety, we did the very first studies to show regions of the brain in normal human emotion, happiness, sadness, disgust, positive and negative emotions.

LR So which parts of the brain light up?

ER Which parts of the brain light up during those emotions?

LR Using Positive Emission Tomography (PET)?

ER Right. And then we ended up doing maybe the second or third studies of brain regions involved in normal memories, working with a leader named Dan Schacter, brain regions that are involved in the unconscious recollection of events where your performance gets better, but you don't know consciously that you've learned something. False memories. The first studies. we have a neuroimaging program associated with NIH in Phoenix, an NIH program related to the study of obesity and diabetes in American Indians. We did the first studies to show brain regions involved in hunger satiation, taste and the predisposition to obesity. We first showed the brain regions involved in the illusion of pain.

LR Was this after you were at Banner? How did you come to be associated with Banner Institute? Were these all after you joined the Banner Institute?

ER When I was at Wash U, my family wanted to move to Arizona. So, I said, well, I'll look. We'll explore opportunities, but I thought it would be a loss in terms of my traditional career. I first looked at Barrow Neurological Institute. There was a terrific head of neuroradiology then, Burt Drayer, and he said, "You know, it doesn't sound like we're going to invest in PET, but Samaritan is thinking about it." I explored that. I then developed a good relationship with them and then a very supportive relationship with the psychiatry department. So, I told psychiatry, "I'd like to join the psychiatry department." I had a grant that would cover me. "Don't worry about paying me. I'll just use my grant for a relatively low salary." And I think $30,000 is what I was getting on the grant. And I just wanted to have the time to do what I wanted to do, but I also wanted to see patients a day a week. They said, "It will probably cost us money for you to see patients." I said, "No, I have to be able to see patients and I need to teach." So I had established a very good relationship with my psychiatry colleagues in that department and was the scientific director of the PET center there. And while I was there forging these relationships, we ended up figuring out a way to get some funding to pay for free PET scans. And my team's ability to analyze data for folks then lured them in for collaboration. The first grant we got in the

1990s was from the Flinn Foundation, a highly competitive grant. My colleagues at U of A, the associate dean for research said, "You know, you can apply through the U of A, but all these grant applications are going to go in through the medical school. You have this relationship with ASU. Why don't you apply through ASU and still have us involved?" Which was that collaborative spirit. I just love that collaborative spirit. And that small grant and that opportunity led to a range of things.

Well, as we're getting this work going on, one of the pilot studies we decided to do was on Alzheimer's disease. It was after I had been asked in around 1991 or 1992 to join the local chapter of the Alzheimer's Association. I still don't know why they asked me. I was a general adult psychiatrist. However, I would occasionally evaluate people for memory and thinking problems in a consultation fashion, to rule out reversible memory problems, but it wasn't my area of expertise. I thought it was important to show my young kids an investment in the community that had nothing to do with my work. And I thought this would be a good example. So, when we got there, I met some really wonderful people, including a couple of physicians from other institutions, Rick Caselli at Mayo Clinic and some others. Some I hired when we established Banner Alzheimer's Institute. I was embarrassed. I didn't realize, as a physician, what a terrible toll Alzheimer's took, not only on the patient, but on the entire family. Something all physicians should know. We wondered if we could figure out something we could do to help in that regard in addition to working on the board with addressing community needs.

After I joined the Alzheimer's Association board, researchers at Duke, as it turned out, discovered a common susceptibility gene known as APOE4, which is found in one out of four of us, but is found in about 60% of people with Alzheimer's disease. This is the major genetic risk factor for developing the disease. And I'm reading this paper about the guy who became a friend of mine who was the head of the neurology then in the *Wall Street Journal*. If it wasn't in the *Wall Street Journal*, I may have missed it actually. So I was reading the *Wall Street Journal* and half the article was on what an amazing finding this was and that APOE4 is associated with Alzheimer's. The rest of the article was on how much the field was upset that it was this guy who was the one who discovered it because he was such a contrarian. A great guy, as it turned out. But a real contrarian. And they were saying, "we don't know if we believe this finding. We need to study people who are in middle age, follow them over many years before we know this is a risk factor." I thought, "that's ridiculous." Then I thought, if we wanted to address this problem, it would be nice to have a way to prevent Alzheimer's disease. And if we want to prevent it, it had been suggested back then that blood pressure lowering treatments, cholesterol lowering treatments, and hormone replacement therapy might have a benefit if started in middle age. I did a rough calculation. I thought to myself, "How many people would it take to do a prevention trial, waiting for people to go on to develop Alzheimer's dementia, enough people in the placebo group getting a sugar pill to know if the treatment actually reduced it?" I estimated that would take 50,000 people over 25 years. So, imagine if you had a prevention therapy that

could work and no way to evaluate it. What if we could use imaging, not to figure out how the brain works, but to see if I could detect and track some of the same brain changes we see in patients with Alzheimer's? And then set the stage to develop a paradigm that could be used to make it possible to evaluate prevention therapies, including lifestyle interventions now and investigational disease slowing drugs when they become available.

LR So you really took a very circuitous path…

ER To say the least.

LR …a circuitous path to get to your Alzheimer's research as your primary focus. Tell us more about the disease itself. You've used some adjectives to describe it. Tell us more about the disease.

ER Alzheimer's Disease (AD) is a terrible problem. It's the most common form of memory and thinking problems. It accounts for about 60% of individuals who develop disabling cognitive impairment. The term we use for cognitive impairment that interferes with your activities of daily living is dementia. And AD accounts for about 50% of individuals who have mild cognitive impairment at older ages. Like many other kinds of memory and thinking problems, it can cause people to have serious problems with their memory, their judgment and reasoning and their language skills, their ability to perform routine tasks like dressing and/or cooking, doing their finances. In its most severe stages, people can lose their ability to control their bladder or bowel functions, lose their ability to mobilize very well. People can lose their ability to swallow. The swallowing problems and other complications with reduced mobility make Alzheimer's disease indirectly, possibly the sixth leading cause of death in older adults through those indirect causes. In addition to those losses along the way, Alzheimer's disease can introduce distressing symptoms like repeating the same thing over and over, which can be very frustrating for family caregivers. "Where's mom?" It can cause some individuals to become agitated, anxious, sometimes violent, sometimes apathetic. It can cause hallucinations, paranoid delusions. And it turns out these non-cognitive behavioral symptoms are a more common cause of distress in family caregivers and long-term care placement than the loss of the memory and thinking abilities. We don't have great treatments for that as well. So, we have these conditions with progressive losses and there is a common misconception there's nothing you can do about it. While there was nothing for many years that we could do to slow the progression of symptoms, there are things that one can do to make a difference in people's lives, both by helping the caregiver and the patient themselves; things that play to a person's existing strengths throughout the course of their illness that they can thrive on and go with their own reality, as opposed to confronting their reality. When somebody says, "Where's mom?" over and over, the typical response is "Well, you know, mom died." So one has to relearn that again. It's no good for anybody. And there are other strategies. "You know, I was just thinking about mom the other day," and going with their reality and then distracting. There are a bunch of tips that I've had the

chance to learn from my colleagues along the way that are difference makers, even while we're finding more effective ways to address the problem.

LR Looking at the disease itself, have they identified any environmental toxins that contribute to AD? You talked about the genetic component, which we'll talk more about in a few minutes. But any environmental toxins? With this or other neurodegenerative diseases?

ER At the moment we believe that about 70% of a person's risk is due to inherited genetic factors. But that leaves about 30% of a person's risk to other non-genetic factors that are potentially addressable in a number of ways. The best studied non-genetic risk factors for Alzheimer's disease are – well, let me turn this around and suggest another way. I'm often asked because of the work I do, what can I do to reduce my chance of developing memory and thinking problems? And the short answer is, we don't know for sure because those rigorous prevention trials haven't been done. We have suggestive evidence that several things can be helpful. So, aerobic exercise, even modest aerobic exercise, social and mental stimulation may be helpful, maybe not as helpful as exercise, but helpful for the particular areas that are being stimulated, cognitive domain stimulated. Healthy diet, a cardiovascularly healthy diet or Mediterranean or MIND diets, have been suggested in numerous studies to actually be helpful in promoting cognitive health as we get older and reducing the risk of dementia. Not smoking. Managing one's high cholesterol levels, high blood pressure. Treating one's diabetes can be helpful. Getting a good night's sleep. Those are some of the lifestyle and dietary and medical interventions that have been suggested to make a difference. The effort to understand toxic environmental factors has been a bit better studied with Parkinson's disease. For instance, pesticides, and other risk factors, although they still need more work than with Alzheimer's, but we can't rule them out. We just can't rule them in for Alzheimer's just yet.

LR So, further studies are needed?

ER Further study is needed. And what will happen is, we'll have better ways to study it. My area of research is involved in developing biological measurements of the disease, biomarkers, starting with PET scans that can measure amyloid plaques and tau tangles that are used to define the disease at autopsy. And now more scalable blood tests. To be able to do that. And once we have biological measurements of the disease, we can do a range of things. We can detect and track it before the onset of symptoms. Evaluate the ability of prevention therapies to slow those changes without waiting to see who goes on to develop symptoms. That's an idea that I've been interested in for a long time that's turned out to work out well. But you could also use those biological factors to look at a bunch of risk factors and re-purposeable medications to see whether they change the biological features of the disease. For instance, using legacy blood samples with blood tests. So, we're going to see now that we have blood tests for Alzheimer's. We're going to learn a lot more about risk and protective factors that we couldn't get up until

now. So that's important.

LR So, you've really shifted to the focus on prevention?

ER We started with the idea of prevention, but to get to that, we needed to show that we could detect and track in people at different levels of risk. We started before we had these biological measurements of plaques and tangles in living people. So I reached out to a colleague, Rick Caselli from Mayo Clinic, and together we launched a paradigm of setting people at three levels of genetic risk: those with two copies of APOE4 they inherit from both parents, those with one copy from one parent , and those with no copies, and we were able to show over the years, starting in 1996, that we could detect and track Alzheimer's disease in people at different levels of risk and inform the design of our future prevention trials. That was a big deal for us.

LR You've talked about the importance of certain voices that have steered your path or changed your path throughout your career. You've also talked a lot about the importance of collaboration with people at Mayo and other places. Talk a bit more about why you see that as an important thing in your area of research or in medical research in general, specifically Alzheimer's…about that collaborative piece that seems to be of strong value in you.

ER I think our competitive advantage is the recognition of our own, my own, limitations and recognizing that science is a team sport and that we can better address my questions, somebody else's questions and shared goals in a more effective way by working together, capitalizing on our complementary strengths, than we could on our own. I think that's our competitive advantage here in Arizona, in part because we're less well developed with a smaller critical mass of research within any one institution. We haven't developed that illusion of self-sufficiency that can sometimes happen when researchers become very busy.

LR It's a common perception of doctors also, I think. You seem to be more humble in that respect in terms of your own self, and the importance of identifying your own strengths and your own areas where you need complementary help.

ER I'm sure there are other limitations I have that I don't recognize, but I am keenly aware of many of my limitations and the need to figure out opportunities to compensate for them. With this learned helplessness model, so to speak, it's worked awfully well over the years, and it's been a joy. The idea of bringing people together to address an ambitious goal that most people think will not be possible and then to accomplish it, which we've had the opportunity to do in a number of different ways, has been a great joy.

LR I want to go back to that, because this is a message of hope. You mentioned in one of the articles, your hope and prayer is the possibility to end Alzheimer's before we lose another generation. Are you still feeling positive about that?

ER I could not be more excited about the possibility. As we wrote in the leading neurology journal last year entitled, "*A Chance to Prevent Alzheimer's Sooner Than You Think,"* we believe that recent developments in the legwork that was done since 2012, have a chance to find the first effective secondary prevention therapy for Alzheimer's. A treatment that is started in unimpaired individuals with blood test evidence of Alzheimer's disease, which is about a quarter of healthy people over the age of 65, and intended to avert, the further biological, cognitive and clinical manifestations of Alzheimer's. Avert the onset of cognitive impairment. We are collaborating on prevention trials which would not have occurred if we didn't launch that new year of Alzheimer's prevention research back in 2012. It could have weeded out a trial of a treatment that has now been demonstrated to have an effect in impaired patients, mildly impaired patients, in unimpaired individuals with blood test evidence of Alzheimer's. Our thinking from the beginning of this is that by the time people have cognitive impairment of any kind, the disease is already extensive. Amyloid plaques have plateaued, some of these downstream. The fire that really causes brain cells to die is now raging. And if we could intervene before this disease becomes metastatic, so to speak, by preventing it, we could have an effect. So, I think we have a realistic chance, I would say today, a better than even chance of finding that first secondary prevention therapy to significantly reduce the likelihood of becoming cognitively impaired within the next year. If that trial works….

LR You're hopeful.

ER Very exciting. And that'll be a monthly intravenous treatment. If that works, we've suggested a strategy by which you could quickly then find better treatments. So we think we could find a self-administered subcutaneous treatment a year later, if these first treatments work. And then our hope is to use these same amyloid plaque-reducing treatments as infrequently as once per year … to find a treatment that prevents it dramatically, if not completely, prevents the biological ensuing clinical onset of Alzheimer's disease within four years. That would be amazing.

LR That would be amazing. What would you say to those people that say, "I just want to live in the present and I really prefer not to know what my future is." ?

ER I think people deserve a chance to make informed choices about benefits, risks and what makes sense for them. The more we can arm people with information and resources. If it was a family member of mine and somebody had biological evidence of Alzheimer's and I knew that it reduced the onset of impairment by 70% , and I knew what the side effects are of the severity

that I think they're going to turn out to be in these trials, I'd be strongly encouraging them to consider that option. But I believe people need to be able to make an informed choice about benefits, risks, and treatment options.

LR So, tell me about the breadth of services the Banner Alzheimer's Institute provides to families that are dealing with that possibility.

ER So, if I can go back for a second, we were at Banner Health for a long time and in early 2000s, I approached the CEO of Banner Health, Peter Fine, with the idea of establishing the first center of excellence for the entire health system. The idea was if we could focus on a couple of things, maybe Alzheimer's and then cancer research, cancer centers, and create these so-called centers of excellence where there would be greater investments leveraging the resources of the community and philanthropy we could raise, we could do some breathtaking things. And I talked to him about what we could do with prevention. And his response, was, "You know, Eric, our mission and the mission at Banner Health is to make a difference in peoples' lives through excellent patient care. What are you going to do to create a new standard of care?" I love that question. I said, "We have a woefully inadequate standard of care. This will cost a lot of money, but we can better address the medical and non-medical needs and we will create a place where people could go that will provide the kind of care we would want for our own families. It will take much longer than that to find a scalable financially self-sustaining standard of care, but that should be the goal. That everybody should be asked about memory and thinking problems, understand what they are, rule out reversible problems and empower patients and family caregivers with treatment and prevention." So we could do that. So we embraced this idea of this marriage between research and care, help and hope. Our first goal when we opened our doors in late 2006 was to find and support the approval of a prevention therapy in 20 years. And at the time, there weren't the drugs and there wasn't a paradigm to evaluate treatments and now we have a realistic chance, I would suggest maybe a 70% chance, to meet that goal next year.

LR That was an ambitious goal.

ER It's an ambitious goal. Trials often have surprising results. There's no guarantee until we see the results of those trials. But those trials, other trials, are very important. And then the third goal was to forge models of collaboration in biomedical research and that's been a very important priority for us.

LR The Arizona Alzheimer's Consortium?

ER The Arizona Alzheimer's Consortium. We've been working in these other ways with all these other institutions, and I knew them so well. We brought together a bunch of institutions to do

that. So, since 1997, our researchers have published more than 10,000 papers, they've generated pioneering findings that have changed the field, Alzheimer's and brain aging research. We generated directly and indirectly two billion dollars in new investments to Arizona. Well, not all coming to Arizona, new investments in Alzheimer's and aging research that have a chance to make a real difference. So we're very excited about that. And it's a testament to the wonderful people we have working on the problem. We had those three goals at Banner Alzheimer's Institute, and it's really been a joy to be able to serve the needs of our patients and families. From the beginning we wanted to figure out how do you launch a new era in prevention research? We had these ideas about the first two prevention trials. We wanted to study one in people at highest risk for the more common form of Alzheimer's disease that occurs late in life. People with two copies of that APOE4 gene. I had a couple of cousins I was following after we discovered what we could do to track the disease, who had a rare misspelling of the gene. We call it an autosomal dominant Alzheimer's mutation which makes them virtually certain to develop Alzheimer's. Their children have a one in two chance of inheriting the same gene and getting AD and become cognitively impaired typically in their early 40s. So, we devised a plan to convince a range of stakeholders, including NIH, to embrace this idea of prevention trials.

Our first prevention trial turned out to be in Colombia, home to the world's largest extended family known to carry one of these rare mutations. That was an example of a collaboration that's turned out to be a dream come true to us. We figured that if we could launch the first prevention trial, and get industry to come to the table, other companies would follow suit and say, "Look, they did it." And we would have then, not on our dime, on the industry's dime, access to the most promising treatments and the funding needed to have a range of prevention trials and find one that works. And that's exactly what's happened.

LR I would imagine there was a particular challenge in cross-border research and collaboration, as you set up those trials and made relationships with the people in that community. How did you approach them? Was there someone already doing research there?

ER We had two trials in mind. The first one we decided to put our money on was in, individuals who had these autosomal dominant Alzheimer's mutations in Antioquia, Colombia, a state that includes Medellín in it. There was a colleague of mine who just passed away last year, Dr. Francisco Lopera, a Colombian neurologist and a really heroic figure, who had identified about a thousand of these family members and a certain percentage of them who had the mutation. We thought it would be a good idea to do that. So, I was introduced to him by a mutual friend, Ken Kosic, and then Ken said to me, "You know Eric, we have people wanting to collaborate with Francisco all the time, but this is the first time anybody's proposed a collaboration that could help those families." He's a remarkable person. With our financial support and encouragement, we said, "Well, we can find more than a thousand of these family members each. Will you think about it?" He said, "Well maybe." We encouraged him and over time we found 6,000 of these

extended family members, 1,200 of whom are certain to develop Alzheimer's disease based on this mutation. It was a life-changing experience going down there. What connected us across cultures, countries and languages, was a demonstrably common priority of care, this marriage between research and care.

So, when we flew the first 50 family members and their loved ones up to Phoenix, before we had a cyclotron and PET in Colombia, we offered caregiver training. They loved the program and it was just amazing. My first time in Colombia. That was 700 family members. I met with one family in the home in which sadly six out of seven, bad luck, it's one out of two, six out of seven siblings living together in a small area have dementia and their children are caring for them. I wanted to figure out how do we go about this? I have a couple of colleagues on my team on the Alzheimer's Prevention Initiative we established who've been wonderful and critical to this endeavor. Before we went there I asked, "What can we do to provide some help along the way?" To a person they said, "Well, could you provide more adult diapers." Heartbreaking. So, we go down there and they're just amazing, these family members are heroic to me. We were thinking when we go down to Colombia, we need to figure out who's going to invest in a cyclotron and PET and a 3T MRI system, create an infrastructure for clinical trials, infusion therapies. We met with a lot of leaders in the community, and we were able to figure that out. We were able to figure that out on their dime actually.

We convened a group of leaders, thought leaders in the field at NIH, stakeholders in Phoenix, to have this discussion back in 2010 about these two prevention trials we wanted to do. Could we apply for funding? NIH was broke at the time and Alzheimer's wasn't getting a lot of funding. I said, "I'd like to apply for a $15 million grant. And if we get the grant, we will match it with $15 million in philanthropy." Banner didn't have a track record of raising money, but the champion for this new Banner Alzheimer's Foundation for our Institute was Jerre Stead. I said, "I want to raise the first $30 million and spend it on two trials." Most people would say, "Are you out of your mind?" I said we'd raise this money. And then after we had the trial and the philanthropy, then we would have a competition among industry. We would be like Tom Sawyer getting companies to paint the fence, as I told one of my volunteers who has an autosomal dominant mutation. I promised him that and that's exactly what happened. We had a competition and that worked. So, we ended up having a group, including Francisco, and we go around the room to decide is this something that is feasible? And most of the researchers are saying it may be a little early to do this, maybe not. They get to Francisco and he says, "My families are waiting." And that was the decider. So NIH had to go back and decide whether they could entertain a grant application for us. Eight months go by and I get a call from the leader of the dementia program there, who just passed away a couple of months ago. He said, "Eric, I have bad news. You can apply for the grant, but you have to get a great score on the grant. And you would have to have the philanthropic and industry contributions by the time of the notification of grant award." So I said to him, "Neal, so the bad news you're telling me is that I could have the endorsement of my peers and I have a deadline to raise the money. Is that right? The bad news?" And that worked

great. So, we ended up getting funding for that. The NIH and Congress got together and announced a new national plan to address Alzheimer's disease, which was the big difference made in 2012. What happened was, Congress took it, they took a little extra time, they took an extra year to provide funding. So, the Director of NIH, Dr. Francis Collins, took the dollars from the other institutes. He made this giant announcement and the whole announcement was based on $20 million. He gave the first 15 of the $20 million, announcing our prevention trial as the cornerstone in the national plan to address Alzheimer's. It's gotten a lot of interest and attention along the way, you know, covered in the *New York Times*, *60 Minutes*, other things. It's a double-edged sword sometimes the media exposure, except that it really highlighted the urgency of the problem in these amazing family members. When we were down in Colombia, while I'm negotiating a cyclotron my colleague, Pierre Tariot is going to each of these little towns. In the center of these towns is a beautiful little church, no matter how poor. They're visiting a church in which they have the remains of a priest who is undergoing this canonization process. One of them turns to my colleague and says, "We think you being here may count as one of the miracles," which was a reminder to us that we want to be able to do this in a way that doesn't lead to unrealistic expectations.

We were aware when AIDS/HIV treatments were first introduced in Africa it led to a sense among people who were receiving investigational treatment that they were being experimented on. We spent a lot of time thinking about what we could do to ensure that we're able to look at an experimental treatment in healthy people, vulnerable people from a developing country in ways they would value. Our response to that was to design the study, think about the kinds of drugs we would consider, the interventions, how much safety data in partnership with them. We described in general details these different elements, got their input and they felt like partners from the very beginning. So, imagine a study, that was this first study, it turned out to be a drug that failed to work. Over a course of eight years, people were studied from five to eight years where during a civil war in Colombia, with a lot of kidnappings to start. This was in healthy people including women of reproductive ages. If they get pregnant, they're no longer allowed to be receiving the treatment. Traveling great distances sometimes to get to us for the procedures we had. After eight years, 94% of the people were still in the study. And when the study failed to work, they pleaded with us to talk about the next study. In addition to that information, what we did was to provide philanthropic support to the community, irrespective of their participation in the study for them to use in ways that they wanted to use for social support and that which they valued and we continue to provide along the way. Last year we got a new $75 million grant from NIH for the next prevention trial, which I think is a very important trial. But the most important trials are the ones that are going to weed out the more common form of Alzheimer's that we see in older adults and that we're very excited about. So, no guarantee, but a real opportunity to make a real difference.

LR The *Scientific American* recognized as one of the most world changing ideas in 2012 was your

prevention study there in Colombia. It's not always true that you have a sample size that large in the contained population. Am I right in understanding that there is one particular woman that is in her 70s, who has survived in that family group, and that there's been some research as to what kind of a protective factor she might have in her DNA and in her biological makeup?

ER Yes, thanks for asking. As we're preparing for the prevention trials, there were a lot of things we could do in that kindred. They know that they'd develop mild cognitive impairment at 44 and dementia at 49 on average, plus or minus a couple of years. We could use our different biological measurements to figure out when they occur, how many years before mild cognitive impairment and dementia, and we did that. There's another group that has done a wonderful job called the Dominantly Inherited Alzheimer's Network, in a complementary way in folks outside of Colombia or studying different groups. What they've done is they've changed the field in knowing when these biological changes occur in relationship to census to inform the design of prevention trials and give them more information about their risk. But unfortunately, everybody who has this particular mutation that leads to an overproduction of amyloid gets these dementia symptoms at 49 plus or minus 5 years. This woman, however, was in her 70s and she was unimpaired. So, we and our colleagues were interested, our colleagues in Colombia and Harvard were interested in seeing if we could find a genetic protective factor that accounted for her not developing symptoms, and we also wondered why she didn't develop symptoms. If you get amyloid plaque and tau tangles, which one of these things might be protective? We ended up finding a gene that turned out to be a rare form of the common APOE4 gene that's a susceptibility gene that was very protective, very protective. She had two copies, which is probably like a one in a million chance to find people with two copies of this rare mutation that we believe protected her.

LR She had an extra copy of that?

ER Well, most people don't even have one copy of this rare form of APOE. So, it was important in several ways. One way was, they'd found a protective gene that if we can replicate how it works, could come up with an effective way to prevent Alzheimer's or treat and prevent it. We developed an antibody therapy that is being studied based on that discovery. We also showed that APOE itself has effects that go beyond amyloid plaques. Because most people thought it was just due to amyloid, most people haven't really been trying to develop APOE modifying treatments because we have other plaque-reducing treatments. Now we know it has effects on tau tangles, too. So now we see an effort to develop APOE modifying treatments, all based on this wonderful volunteer. She's since passed away and donated her brain, but she was really remarkable. It's a good reminder of what a difference even one volunteer can make. You know, we have Banner Alzheimer's Institute in Phoenix, but we also have another part of our program, the Banner Alzheimer's Institute/Banner Sun Health Research Institute in Sun City and Banner Alzheimer's Institute in Tucson. Banner Sun Health Research Institute, which started as part of

my consortium, started before it was part of Banner. We had this wonderful brain donation program that we've been able to learn a lot from. We had these incredible volunteers in the Sun Cities community who agree to have these detailed cognitive and biological assessments every year and then donate their brains and other body tissues after they die. By being within a 5-mile radius of Banner Sun Health Research Institute, with a 24-hour autopsy program, my colleagues have been able to retrieve and conduct an autopsy within, on average, three hours after they pass away. So, it's the highest quality brain tissue in 2,500 people that actually passed away and donated their brains. The main resource to advance the research for Alzheimer's around the world is the human brain.

LR In addition to brains…..

ER In half of the individuals, it's the leading resource for Alzheimer's and related memory and thinking problems, Parkinson's and other movement disorders, and then half of these amazing volunteers are unimpaired neurologically. A colleague who set that up, Joe Rogers, often told the volunteers that if we can't find the answer to this disorder in Sun City, who will find it in a Sun City brain? And I just think of our research volunteers in heroic terms. They're amazing. We've been able to learn some amazing things in the brain donation program. New ways to detect and track the pathological changes. We introduced ways to get PET scans approved to measure amyloid plaques and diagnose Alzheimer's in life. And now tau tangles. And then since then, blood tests. We're actively involved in the blood test space. We've just recruited a world leader in this space, so when you watch what happens when you see new blood tests for these disorders developed. To develop them, you have to compare them to the standard of truth. Now we have those in life for Alzheimer's. But for other causes of memory and thinking problems and motor problems, like Parkinson's, we need to compare it to the autopsy measurements. So, we have this remarkable resource to be able to do that. And it's just a very exciting time for the field.

LR So, you co-founded and advise a company called ALzPath, to advance the role of blood tests in the fight against Alzheimer's. You developed the key blood test that you just referred to. *Time* magazine recognized it as one of the most important inventions in 2024. That's impressive!

ER So, yes. So, it's very exciting in a different way. I'll start with my academic head. Because we were following people in Colombia, a colleague from Sweden wondered whether we could study a new blood test for something called p-Tau217 that measures amyloid plaques and can diagnose Alzheimer's. He wondered how early we can see it before the onset of symptoms. I said, "We can study that in our Colombia blood samples, but we have an even better group to study. Use our autopsy measurements to see how accurate it is." So, we provided two of the three cohorts for this study that was published in *JAMA* in 2020. On the cover of the *New York Times*, the title of the article describing this finding was, "Amazing, Isn't It." Which is a very frightening title

for a biomarker researcher because biomarkers tend to come and go. It was a fairly large number of individuals there, but it turned out to have legs, this finding. We ended up using an assay that was developed by Lily actually to do that, but it looked very good. I had mentioned to our champion at Banner Alzheimer's Foundation, Jerre Stead, who has just been an incredible advocate and champion philanthropically for Alzheimer's and a very successful businessman. I said I thought there would be ways in which blood tests would change, transform research and care. I said, "I'm no businessman, but I think it's going to have a great impact. And you're so philanthropic, we could come up with a nimble organization that's a non-profit to do this. That you contribute through philanthropically, or we'd create a company that probably is going to lose money but have a great impact. But you're going to provide those dollars to us anyway." And he said, "You're absolutely right, Eric. You're no businessman. This will be fun. Let's create a startup." And he did that. He's kind of amazing that way. And we started this startup. What we had in mind originally was the idea of what if we could just license a blood test from somebody and have virtual nurse practitioners who know all of our care model and do the heavy lifting for primary care providers so that more people are asked about memory and thinking problems and get the care we need. We started that. That has some advantages, but we decided we can do that in the non-profit space. When we couldn't license that particular assay, we said well, " let's develop one of our own." And somehow we got lucky with the assay we developed. And we developed the key ingredient known as a capture antibody for p-Tau217 and an assay that was now on most of the commercial systems that'll be used in the clinical setting and research systems and that works very well. It seems to be about 95% accurate compared to autopsy measurements. It's already changed research, these assays. We don't have the only one, but one that is pretty widely available. And it's beginning to change care in impaired individuals. And as soon as we have an effective prevention therapy, you can imagine using a preventative screening test in everybody, say over age 55, to know. This is how I think we would want to change – in addition to having an inexpensive blood test to make prevention affordable. PET scans will not be affordable to screen everybody for it. So it helps us with prevention. I think it'll change care. I think up until now, the roadblock has been getting primary care providers and other busy physicians to do memory and thinking tests. That's asking a lot. What if you can do a blood test, an easy to do blood test, and if it's positive, here's what you can do for prevention. Here's the benefits and risks and if you're impaired. We're working, we and Collins are working on automated ways, using AI agents to actually automatically do, in a very compassionate way, memory and thinking tests or provide information about blood test risk.

LR Did you say Collins? Francis Collins at NIH?

ER Oh, Francis Collins was the former director of NIH. And he was really key, he oversaw the human genome project.

LR Which also was competitive. Kind of like your work?

ER Correct, correct, correct.

LR To get the competitive challenge going.

ER What I think is going to happen, what I am hoping for, even though prevention is easier than treatment, we don't ever want to lose sight of our impaired patients and their family caregivers. And we have the first disease modifying treatments. We have non-medication strategies to address needs of patients and family caregivers. We need combination therapies that target different elements of the disease in patients. And I think what we're going to end up having with a care model is we're going to end up – first of all, we're going to have more success with treatment development now that we know which biological changes are associated with the clinical benefit. This work that has happened is just going to make development of treatments more informed. But in patients, we need to figure out how everybody gets asked about memory and thinking problems, everybody. And we need to be able to provide resources in ways that overcome the paucity of specialists that are not large enough to address those needs. What I think is going to happen is blood tests, established treatments, and these AI agents to ask questions about memory and thinking to provide information, where we have a paucity of genetic and biomarker *data*, tell them what the risk means to them and then AI agents to address their everyday questions while they're on some wait list to get in to see somebody. That will be a game changer. And that is not far away and how wonderful is that?

LR Yes. And blood tests are seen as not as invasive as some of those other things.

ER Right, right. So we're very excited about this blood test and one of the things we're working on right now is thinking about ways to actually have a way, rather than having somebody go into the lab where they get blood drawn and centrifuged and analyzed, sent out, is to have a home test. A pinprick-like test. Because there are a number of people who might be a little shy about going in and having somebody know that they might have biological manifestations of the disease. There's some stigma associated with it. They might be afraid that they would lose their life insurance, disability insurance, long term care insurance.

LR Right.

ER So, we've got work to do in that space. We have prevention therapies I'm hoping will begin to destigmatize it a bit. But I do think the idea of a home test is doable. The colleague I recruited to Sun Health, a world leader in this space, believes it's all workable. We just need to find a device to be able to collect their blood in a more reliable way.

LR So it's sounds like being a researcher, you've a multi-faceted focus to your career that includes patient care and not just working in a research lab. It sounds like it requires a lot of patience and

a lot of persistence. The other thing I'm interested in is this. As I've looked at your bios, you have a lot of jobs and titles. With the U of A, TGen, ASU, Banner Research. You've talked about some of those. Two of our Historymakers, Dr. Jeff Trent and Dr. Von Hoff, work at TGen. What have you done in collaboration with that biomedical research facility?

ER Well thanks for asking. Before I – before I get to that particular question, you mentioned that it takes a lot of patience and persistence. It does take persistence, but I don't think I'm known for patience. I have a heightened sense of urgency. But what helps keep us in the game are all the things that we can accomplish along the way in a range of areas while we're working on hopefully an audacious goal. And that's worked out well. We've just been lucky. I have a bunch of job titles. I feel like a title hoarder, mainly because of the collaborative nature of the research I do. I have affiliations with the University of Arizona, and ASU, our Consortium and other organizations where I've wanted to be helpful in more modest ways. My parent organization is Banner. TGen is a special place. I first was approached by TGen not in my researcher hat, but in my philanthropic hat. I'm a longstanding board member of the Flinn Foundation and Chairman of the Board now. We were approached by Jeff Trent, who had just completed the human genome project at NIH and was interested in returning to Arizona potentially and Dan Von Hoff, the world leading investigator of new treatments for untreatable cancers, amazing people. They came to the Flinn Foundation to talk about what they were doing with stakeholders in the community like Dick Mallery and others to make an ambitious investment in this crosscutting methodology. It would not only do things at TGen but help to advance the research interests of other institutions. Flinn is very interested in collaboration, and we decided to foster it. And along the way, Jeff learned that we were with our Alzheimer's Consortium and other things. We were very strong in neuroscience. The original TGen goal was to be a cancer research institute. And they decided, because of our strengths in that area, to create a neurogenomics division. Dietrich Stephan was the first director of that, and Dietrich and Jeff asked me to be the clinical director of the neurogenomics division. I didn't know the first thing about it. I knew something about APOE, but I didn't know a lot about genetics research. I'm pretty good at thinking about killer applications of the tools. We ended up fostering that relationship. About 5% of my time in addition to other collaborative efforts is really in the interests of helping to advance those goals. So, the first studies that we ended up doing there was getting the first funding for what we call a genome-wide association study of Alzheimer's disease. The first study of its kind. Not a geneticist, but I joined the genetics community by coming up with a finding that was hard to replicate. The impact of that finding turned out to be rather remarkable. One of my colleagues, a well-known geneticist in the field, John Hardy, who came up with the amyloid hypothesis said, "You know, if you want to make a difference, why don't you just share that data with everybody when you publish it." "Sure, we'll share it." We had this TGen data set and shared it, but that was not the paradigm to share data. People were very protective of their own data. If you have a shared resource, you're really having a greater impact and lots of people have used it. Initially the geneticists were pretty upset with us with sharing that data. They'd say, "Why are they upset with you? We're sharing data." They said,

"When we write a grant application and we show preliminary data, they're going to say, what did you find in the TGen data set with that?" But it turned out that resource and then showing the first genes that are turned on and off in the brain, that shared resource turned to be invaluable. I ended up proposing to the NIH, the idea of creating an Alzheimer's disease genetics consortium where we would not focus so much on getting the genetic studies done, just getting the DNA for a hundred thousand people. And the geneticists thought it would ruin their career. It turned out it was great for their careers. They're the ones who lead it as I don't know the first thing about genetics. I co-founded that. We now have 80 confirmed susceptibility genes for Alzheimer's and while most of those genes don't really add to information about your individual risk beyond APOE, they do give us targets at which to aim new treatments. So, the opportunities to advance drug discovery has turned out to be very important and that's a part of the many things that TGen does.

So, let me just say a word about Jeff and Dan. Jeff has just been so supportive and so thoughtful in collaboration. There's been an interest from the beginning. It is the galvanizing impact that TGen has had in Phoenix, in Arizona, and research has been enormous. We'd like to think about other breathtaking goals where we're leveraging shared resources. Maybe in AI or blood test proteomics, things like that along the way. Dan is a remarkable figure. I can tell you on a personal level as well as a professional level, I've had a couple of experiences with cancer in my family. Dan reaches out to you any time of the day or night. Reaches out to other individuals to be able to figure out how to get care- he's an exemplar for remarkable care. I'll give you a personal example. My brother, Todd, got diagnosed last Memorial Day with mantle cell lymphoma, very life-threatening cancer. He was going to see somebody, but I asked Dan what he could suggest. He says, "Let me find the right person for you to see." So he spends his Memorial Day weekend arranging on that Monday for somebody, my brother lives in Richmond, in Alexandria, Virginia, to see him. My brother goes in and sees him and gets very good help. And the physician, the oncologist there said to my brother, "Do you know what it's like getting a phone call from Dan Von Hoff?" That's Dan to a tee. And they're amazing, remarkable people. It's really a privilege to be associated with them through this – this nice honor, the Arizona Historymaker's honor.

LR So, Dr. Reiman, some of the recognitions you've received were the Potamkin Prize, Rock Stars of Science and Arizona Historymakers. Are there any that stand out? We're curious about the Rock Stars Award!

ER Well, I'm very grateful for this Historymaker recognition. I love Arizona and I love the idea that maybe we've made a little bit of a difference here. The Potamkin Prize is considered the Nobel Prize in medicine, in Alzheimer's research, and it was just really a thrill. It was not only a thrill to be recognized for our contributions to the early detection study and prevention of Alzheimer's, but to be recognized with two close colleagues and friends who've had an amazing impact. That was really a thrill. And then this other recognition, was the Rock Stars of Science thing. It was

unusual, but fun in a number of ways. I was approached by the Geoffrey Beene Foundation that developed a marketing strategy to encourage young people to go into science research. It was to develop careers in scientific research. Something we need now more than ever, given the current threats we're experiencing on the federal level. Their thinking was that most researchers like me aren't that charismatic. If they could have a marketing campaign where they would have these *GQ Magazine* photos on large billboards primarily in airports and some other places for a few years, where three researchers would be connected to a rock star. It would give off a flavor that this is an attractive thing to go into. We went for this photo shoot with all these pictures taken and now looking at those pictures, I can understand. They don't look quite like me, I would say, but it was a lot of fun to do that. I got more comments from people who see the billboards, than I did for anything else!

LR Who was the rock star you were associated with?

ER I'm embarrassed. Who is the lead singer from Poison who happens to live in Arizona? You know who I'm talking about?

LR The singer for Poison?

ER Michael?, this fellow was really lovely. It'll hit me in a second, but he became very well known on the medical side. He had a subarachnoid hemorrhage.

LR Oh, he was treated at Barrow. Yes.

ER He was treated at Barrow. That's the person.

LR Oh, Brett Michaels?

ER So interesting. So that's the person. You had the three of us researchers and this rock star. You would have no problem, based on charisma, knowing who the rock star was among the four of us. What was interesting is he says, "You know, I would like to fly you back on a plane with me to Arizona." But I was visiting my son in Los Angeles, and I didn't want to leave my son, it would've been fun, but that's what we did. And it's obviously a very different kind of recognition that was kind of fun.

LR So, on a personal level, what gives you the most joy in your life?

ER Well, first is my family and friends. Also, the joy of getting the chance to work with and support great colleagues and students. That gives me a lot of joy. I think those things probably…

LR I'm not sure how you even have any time outside of your work, but are there things you enjoy doing outside of your work?

ER I'm mainly following my wife's lead and enjoying Arizona, not yet enough. Pickle ball, things like that. The other thing that I find gratifying is this role on the Flinn Foundation Board. We are the recipient of funding that we've benefited from, but it's a special joy to be able to invest in other people, invest in other great people. So the Flinn Scholars Program, the civic leadership program, great researchers, finding and working with the other academic or health system institutions, what leaders would get a gleam in their eye. I love small investments that would give our institutions the courage to pursue a goal and leverage it in ways that would be valuable. The Flinn does a remarkable job doing that thanks to a remarkable staff. All of my board member colleagues, board colleagues feel the same way about them.

LR It's a longstanding institution in Arizona, that foundation.

ER Yeah.

LR Benefits a lot of students. Looking back, are there people you'd like to acknowledge or thank? You've mentioned a number of people. Anybody else in particular?

ER Well, I appreciate your saying that. My worry now is leaving some people out. So, if you don't mind, I'll mention a few people. It was the CEO of Banner, Peter Fine and Jerre Stead who gave us this opportunity with Banner Alzheimer's Institute and a number of other stakeholders; leaders like Marc Sklar, a remarkable person in the history of Arizona. My fellow researchers in the Alzheimer's Prevention Initiative, Pierre Tariot, Jessica Langbaum and Bob Alexander. My close collaborator at Mayo, Rick Caselli and Francisco Lopera in Columbia. I also want to just take a moment to acknowledge the patients' families and research participants we see who make such an important difference. You know, they say, "success has a thousand parents and that failure is an orphan." In this particular case, if we were able to find a prevention therapy, all those parents, all those individuals should feel and share a sense of pride and ownership in that success. We can't wait to see what happens in the next year for the first prevention therapy and other developments along the way.

LR There was news today about the Bethesda Initiative and you've talked a great deal about how important NIH funding has been in a number of your projects. How important grant funding is in continuing research. How do you see the impact of the current cuts impacting your research?

ER Well, let me start by putting it in a positive way. You know, when we were in Colombia, we had the House and Senate Appropriations Committees chaired at the time by fiscally conservative

Republicans, Roy Blunt, former Senator Blunt and current House Appropriations Chair, Tom Cole, who are passionate about Alzheimer's disease. I look back at that. We have a prevention therapy, in the National Plan to Address Alzheimer's. When we announced this, it was we'd find it in 2025. There would be no chance without that support to have a prevention therapy. And those individuals share in that success. And we need to be able to share in that success going forward. It breaks my heart to see wonderful federal officials attacked for their motivation and their work ethic, people I know have been wonderful stewards of this funding. It breaks my heart to see the threats and uncertainties to research, to ongoing research and the next generation of researchers. It breaks my heart to see us discouraging rather than actively inviting the best students in the world to come here and stay here so that we can achieve our goals. And it breaks my heart to see reduced investment in our scientific partners from other countries who are critically needed. There were complementary resources and strengths in all of them. It is again a team sport. And it is my hope that eventually we will recognize how important this is. It will have long-lasting effects, but I'm hoping we will eventually double down and remind people that the United States will play the leadership role in this effort that will encourage other countries to do the same and we will make this the priority it deserves.

LR It is, indeed, heartbreaking how it will impact our next generation of researchers like you in the future. How would you like to be remembered? What would you like your legacy, if you will, to be?

ER I think my primary legacy, I'd like is a valued husband, father and friend. Somebody who wanted to make a difference and tried to work with others to make that difference. And hopefully helped to prevent Alzheimer's disease.

LR Is there anything else that we haven't talked about? Did we miss anything?

ER Did a pretty good job. I really appreciate your letting me talk about all those things and all those people.

LR Well, thank you so much, Dr. Reiman, for your time and your thoughtfulness in this. Thank you for the legacy that you're leaving. Obviously, you've led not only with your head, but with your heart and with your entire person. I think that's why you've had such an incredible career, and will continue to have an incredible career and impact on families and generations to come. Thank you so much.

ER Thank you, I really appreciate it.

LR From the Historical League, from me personally, from all of the people of Arizona, I would like to speak on their behalf. Thank you and congratulations on this honor!

ER My deep thanks to all of you for taking the time.