

I'm not robot!

Adam: We're approaching Alzheimer's disease from a slightly different approach than that the work that we're doing in my lab and in our center is really targeted at the idea of preventing the onsets of dementia or Alzheimer's disease, or at least attempting to offset when you might develop these diseases. And so the approach we take very often involves evaluating different types of novel interventions, and when very non-invasive interventions, that have the potential to alter the brain's function and improve the brain's function and potentially enhance some of those thinking and memory problems we see in later life. Now, the underlying concept for that is to change that trajectory of decline, and that's the trajectory of decline that we experience naturally as we get older. As we get older, even starting as early as our 20s, we see a slow decline in thinking and memory skills. That decline gets much sharper in the sixth, seventh, eighth decade and beyond. If we can take that trajectory and move it up, recover some of that lost function, we have the potential of changing that trajectory towards future decline. Development of things like mild cognitive impairment, this stage before Alzheimer's disease or, ultimately and eventually, Alzheimer's disease. As Todd had said very well, this is not something we feel like everyone is going to get. We feel like this is a preventable disease. So, our group isn't so much in the business of treating Alzheimer's directly. We're more in the domain of attempting to prevent the onset of Alzheimer's. And some examples of what we do are noninvasive interventions like cognitive training. Very often you hear these referred to as brain games, computerized games that are targeted towards enhancing certain domains of cognition that decline as we get older. But we don't just do these brain games or cognitive training. We also pair that intervention, which has shown some exciting efficacy — in fact, a recent study showed, using 10-year follow-up data, about a 25% reduction in MCR, or mild cognitive impairment, conversion rate in adults who had done 10 to 15 hours of this training 10 years in the past. So there's real potential here for this concept of prevention or offsetting the onset of Alzheimer's disease. But we also pair it with forms of non-invasive brain stimulation, like transcranial direct current stimulation. So the application of this weak, electric current to the brain by placing electrodes on the scalp, you feel a tingling prickling sensation on the scalp. But the amazing thing about this technique is that it actually allows us to noninvasively stimulate the underlying brain tissue to facilitate the neuroplastic response of that tissue. And what that means is learning at the neural level. When you take something that facilitates learning at the neural level, and you pair it with another technique like cognitive training, which also facilitates learning at the neural level, you have this potential synergy to enhance the overall efficacy of these kinds of interventions. These are just a couple of the interventions we're looking at. We kind of pride ourselves on doing bench to bedside research, where we start to try to understand the mechanisms of these novel interventions, and then convert those interventions into actual clinical trials and potential clinical applications with the end goal being to create a series of accessible technologies that can be deployed in the community to help prevent Alzheimer's disease. Todd Golde: As I said, I grew up in this, what we call the molecular age of Alzheimer's disease and was fortunate enough to be a somewhat naive MD-Ph.D student who helped to, I think, define causality in this disease. So taking, not doing genetics, but taking clues from genetics and understanding how they altered the biology to lead to Alzheimer's disease. And that really is the foundation, or was the underpinnings, of what we call the amyloid-cascade hypothesis of Alzheimer's disease, that the cumulation of this peptide we call amyloid in the brain triggers the complex disease. Over time, I've helped, I think, to guide and frame how anti-amyloid therapies might work or not. More recently, though, with this idea that we really need to turn our attention to the complexity and the brain organ failure that's contributing to Alzheimer's disease, we've begun to develop programs that are, for example, trying to target non-genetic factors that may promote risk. One that I'm particularly excited about is the impact of psychological stress and stress signaling pathways in Alzheimer's disease. And we've actually developed a therapeutic that impacts this pathway and, remarkably, it does amazing things to body physiology and we're still trying to figure out whether it will have effects in Alzheimer's disease, but we think this will end up, if we're lucky in the clinic someday, maybe not for Alzheimer's, but for something else. And that's one of the things that's sort of exciting about doing the sciences. If you keep your mind open, you never know where it leads. But ultimately the last thing that I'd like to do is the idea of figuring out how we impact the disease in the symptomatic patient. And that means, I think a combinatorial approach, and this is going to be really hard, but we don't really have what we call a preclinical roadmap for even doing this. There's no way, there are very few examples of people taking a multi-modal therapy and showing, hey, even in our mouse models, which are models of the pathology, not necessarily models of the disease, that we could completely cure the disease in the mouse model. And so that's what we want to try to do. And it may, whether it's in Alzheimer's disease or a related dementia model, that's where we'd like to go. Because ultimately, again, if you're symptomatic, you want to feel better, think better and not decline. And in order to do that, we've really got to do better than what we're doing. And it's going to take a little different approach. Nicci Brown: So we're really fortunate to have three leaders in your fields gathered around the table on the campus here at University of Florida, but how much interaction is there throughout the world between other countries and sharing of some of this research. And is that an impediment to you moving forward if there is not a lot of it? Todd Golde: I think one of the wonderful things that's happened in science in general is that there has been a, especially in the preclinical space, even in the private sector — so pharmaceutical companies, biotechnology companies — there's a much more willingness to exchange data before you get to a drug or an intervention or something that's going to make money. There's still the individual laboratories that don't want to get their work scooped by somebody else, so keep it relatively private. But I think everybody realizes that no single discovery or person will ever fully develop the cure. They might identify a target or some way to do an intervention, but it's going to take an army to translate that into something that actually impacts human health. And so I think we've all been humbled by how hard this journey is to go from. In my own world of when I began doing research some 30 years ago in this space, we were driven by these amazing genetic discoveries that laid the underpinnings of understanding causality in Alzheimer's disease. And most people in the field thought we'd have something in the clinic that was working 10, 12, 15 years later. And we're still waiting. And so it's been pretty humbling, I think, for everybody in the field to see how hard this disease is to tackle and we realize we're not going to do it this way and no one else should ever do this thing because you do that. And then we, over the last 10 to 15 years have really evolved into this concept of team science and team science is great at the local level, around different institutions, but what we're talking about in terms of Alzheimer's disease and other major diseases is a world scale of science. Not just the local team, not just the teams across universities, and efforts to share data, efforts to build worldwide partnerships, which there are a number of models for and there are, in fact, a number of foundations and other agencies working to facilitate this. We've had some experience with the McKnight Brain Research Foundation, facilitating multi-site studies to really understand what does the successful ager look like so we can create new intervention targets to bring us to that goal state. So there's no one answer to the question, but what we do know is that it is a worldwide scale that will be required with many great minds, not just those around the table or at the University of Florida, although we've got a good start here to really go after this and find that solution, as Todd said, we thought we would have many years ago already. Todd Golde: The other thing I like to say is ultimately science is the art of reproducibility. And something that makes the headlines and then never gets reproduced really isn't helpful to the field. And when you have large groups of teams working on it, it generally leads to a higher degree of reproducibility and not leading the field down rabbit holes and wasting time trying to pursue an observation that was made in a single lab and then is poorly reproduced outside of that laboratory, even though it sounded really exciting and that still happens, but it tends to be figured out a lot quicker. And so we don't go down dead-end roads. We tend to stay on the path that we think is likely to lead us to things more easily. Nicci Brown: What are some of the impediments that really challenge you right now? Todd Golde: Well, I think the biggest one that happened is we can't do true therapeutic discovery, not non-pharmacologic interventions, without pharmaceutical partners. We just don't have the infrastructure and the cost. Those trials cost somewhere between \$1.5 and \$2 billion at a minimum. That's a guesstimate. So you could imagine that there's a big gap between the kind of funding that's been remarkably increased in the Alzheimer's space over the last five years, recognizing that it was sorely underfunded relative to the unmet medical need and the huge societal, personal and economic toll it was taking. So that's likely been right-sized finally after 20-some odd years, but that's still not enough to really change or say we don't need the private sector to help us. We need them. And so I think that's one of the challenges and just getting the sufficient data to make that investment is challenging because a private sector looks at this and goes, "We put a lot of money in and we haven't gotten a return. So why do I want to gamble this huge investment for something that so far the track record isn't good for probability of success." Thankfully, some companies, not all, some have abandoned this, but some companies are still working very closely with academics and still have quite a bit of internal funding to make sure that this is still going on. And let's hope that doesn't change because it'll be not a good thing. There was a real retraction when some drugs failed in the around 2010 and many pharmaceutical companies basically stopped doing research on neurodegenerative diseases. They said it's too hard. And slowly they regained and rejoined. But academics really haven't lost steam. But I think the real bright spot is the public advocacy groups and people like the Alzheimer's Association and American Federation for Aging Research, increased I think it's almost a five-fold increase in NIH funding for Alzheimer's disease and related dementias that we've seen over the last six years. And that's bringing new people in the field, new ideas and it's enabling. Malú Tansey: I think another impediment has been really that perhaps we've thought about these diseases as very homogeneous and they're not. So the heterogeneity of the presentation of the diseases has been difficult. And without biomarkers until very recently, we just haven't been able to design a good trial. And a trial that's meaningful and that can inform a good Phase 2 trial. And so when you design a trial and you take all corners, your signal to noise ratio, you can't even test the hypothesis, right? And so it's very when I have good biomarkers to really know that whatever target you're shooting for in your trial that you've engaged with the target, as they say, that you've really hit it. If you don't have that, then it's really difficult to interpret negative results. Todd Golde: The other thing I would add is that there's been a dilemma of treatment versus prevention and what the biomarker studies have really taught us as well as autopsy studies is that there's a long, silent phase to Alzheimer's disease. So pathologies begin to accumulate in your brain 20 to 25 years before you show symptoms. And so there's a disconnect. And I think a lot of the reasons you might ask, well, "Why is this?" Well that's because brain reserve and resilience, your brain could withstand a lot of damage before you start showing true cognitive impairment that falls out of the normal range. And yet if we track those people earlier, some of the tests that Adam does and my colleagues within the Alzheimer's Disease Research Center, sort of cognitive stress tests, and you could begin to see that people even before they would be called symptomatic actually are having decline in function. It's just within the normal range. So you can't call it abnormal yet. But when you add that with the biomarkers and we get enough data now, maybe something will happen because we could say, hey, you're on the track to get the symptoms full blown, full minute Alzheimer's disease. Now we can intervene. But we're still in early days on proving that these biomarkers can serve as surrogates. Nicci Brown: Alzheimer's is a terrifying disease, I think, for a lot of people. We've seen the effect that it has on our loved ones. And so we're all, a lot of us, thinking of things that we can do to try and prevent it. And I think, Malú, you mentioned earlier about people going down a path that can even be dangerous because they're so desperate to head this horrible disease off. What are some of the dangers that you think people need to be wary of? Malú Tansey: Yeah, I mean, there's good reason to think just based on epidemiological studies, which really shouldn't draw any causation from them, that there are some associations between chronic inflammation during life and your risk for these diseases. That's just based on medical records. It's based on people with autoimmune disease that appear to have higher incidents. And if they're treated with blockbuster anti-inflammatory drugs that they have less incidents. But that's just an association and it's very tempting to infer causation on that. And then when you run the trials, the trials fail. Probably because it was too late to treat anybody with an anti-inflammatory at that point. So I think some of the dangers are that people may read those studies and say, "I'm going to take daily ibuprofen or daily whatever." Unlike the daily baby aspirin that has been associated with reducing the risk for heart attack or whatever, that's not the case here. And so you could give yourself GI bleeding or something. And so that's a problem. Other things, we know that a good diet and exercise and sleep are good for you, just like they are for lowering your chances of cancer. And they're good for your cardiovascular health. But you don't want to go in and, say, buy a lot of expensive probiotics and prebiotics and spend your money on that because there's no good scientific data really linking any kind of disease modification or slowing down of any of these diseases with any of those things. Whether they may change your constipation or your GI health, that's a different story. They may do that. And if you feel better, that's great. But in terms of changing the disease itself, there's no good evidence of that yet. Todd Golde: I would add that at a public health level and referring to the broader category of dementia, not Alzheimer's disease per se, there's pretty good data that says doing things in your mid-life, such as controlling your blood pressure, exercising, eating a Mediterranean diet, may have a benefit. So, there is a genetic component to this, there are familial risks, and you could do everything right and still get it. But just like with general public health measures, doing things to take care of yourself do influence your cognitive health. Even educational attainment is associated with protection from Alzheimer's disease. And we don't really understand that per se. The only way I conceptualize it — and this is just conjecture — is that it's like having a fit brain, you could withstand a lot more insult before you show signs of . . . Malú Tansey: Mental reserve. Adam Woods: Yeah. The cognitive reserve. And that's something that's education has been used as a surrogate marker for cognitive reserve and cognitive aging for a long time. And there is a protective value there, but I would like to circle back to that idea that we're getting at here. And it's a question I get asked constantly when I give community talks. And that's when I say, "When should I start doing these things? When should I start with this physical exercise? When should I start with brain exercises and so forth, so on." And my answer is always, "Do you have time right now?" Especially in the non-pharmacological, noninvasive space, many of these are accessible technologies that you can access today. Now we're still doing the science to provide definitive evidence of reducing Alzheimer's incidents and conversion of mild cognitive impairment. Once we obtain that data, it's something where, my hope is, we'll push into earlier and earlier ages where we're suggesting, "Hey, start exercising these systems." We always talk about exercising in the body. We rarely talk about exercising of the brain. Our research and research of many others around the world, demonstrate that there is significant value, whether it be educational attainment, whether it be different types of programs, behavioral interventions, or other approaches to exercise the system, because it is arguably one of, if not the most important, organs in the entire body. And so waiting until and at later disease state or what we still clinically call early Alzheimer's disease, we're not early in any fashion. There's a certain point where pathology can impact the system to a point of no return, where no matter what I can attempt to do, whether that be pharmaceutical, whether that be non-pharmaceutical, there's only so much gain I can get from these interventions. So pushing our approach to this to earlier in life, whether that be midlife or otherwise — I mean, in reality, we talk about seeing cognitive aging effects in our 20s. You're in your mid-20s, it's as good as it's going to get. From there, we're going to start slowly declining. Well, in many disease processes, we look at when do you start declining and we intervene at that point. Unfortunately, in systems of cognition, we just ignore that until your sixth or seventh decade of life. And then we get concerned. So a shift in our thinking and our mindset relative to how we can intervene more effectively is going to be very important in moving forward with better prevention of these diseases. Todd Golde: But that also is in my research, really focused on the root causes of the amyloid pathology. And now more recently, the tau pathologies that we know are significant drivers of the degenerative process within the brain. But the earlier you go in the disease process in an asymptomatic individual, the safer your drug has to be. So we've lost some really good promising candidates because they turn out to have unacceptable side effects. And that bar for safety is higher today than it ever has been. The second thing is that those trials cost a huge amount of money. And depending on the modality you're using, if you're using a typical, what we call small molecule drugs, something like a statin, there's no guarantee of exclusivity for a pharmaceutical company. If it takes 20 years to prove their drug worked, there are off patent by that point. And they probably will never regain their investment. In contrast, using something like a biologic, an antibody approach, they have exclusivity at least under current law. So they'll throw an antibody in there, even though it costs a lot more to treat people with an antibody. And it is really not a great public health solution even if it worked and typically involves an infusion or something, which is not convenient for a patient and, at least with the current antibodies, every month. So it's a real challenge. My thinking has actually changed a little bit and partly it's the recognition that you're late pathologically when you start to show symptoms. You're actually beginning to have what I call now brain organ failure. And if we do not approach the symptomatic patient as somebody who has brain organ failure and try to make that system work better with a multi-pronged approach, be it a non-pharmacologic intervention, a mixture of things or what we sometimes call a magic shotgun drug, something that does a lot of things and has a number of actions that actually can restore function, I think we're going to struggle. Because, at the end of the day, even if you have a disease-modifying drug, unless it's amazing and completely stops a disease in its track, an individual on a certain trajectory won't really know that they're not getting better, you're just slowing their decline. That's a tough one for a patient to stay on that regimen. They want to restore their memory and if you can't do that, it's going to be harder. So the field has turned away from simply trying to make the brain work better. And I think we need to turn our attention back to that. We have amazing what we call magic bullets — gene therapies or RNA vaccines or ways to more precisely and more safely target things. And I think we need to be bolder here and try to change the way that we do these trials so that we're looking for bigger effects. Adam Woods: Well, in leveraging off something Malú said and then Todd alluded to as well, this concept of precision and precision in medicine and the approach that we realize humanity is individual variability. We treat it like it's all the same when it comes to a treatment and intervention, we might slightly titrate the dose, maybe. But we know that that isn't the most effective approach. We know that we have to drive further into addressing just the milieu of individual variability. Each individual, each patient that walks in is completely unique. Their backgrounds, their premorbid medical history, genetic factors, yet there's a lot of information there. And it's really hard to parse that information into actionable items for intervention. I think one of the things we hope to do as we forge forward with newer technologies, like the AI and our artificial intelligence initiative at the University of Florida, is drive these technologies that are incredibly well-equipped to take this robust, deep, dense data and start to parse out actionable patterns and targets from what is ultimately the individual variability of the patient. Patient to patient. And so we're not there yet, as was being said, we have to do better. We have to drive forward in terms of both our approach and our mindset and the technologies we apply, to really leverage these skills that cross multiple, multiple domains of expertise and pull that information together to titrate the approaches. As Todd was saying, we're going to have to take multifaceted approaches to addressing this disease. It's not going to be a one and done. It's not going to be the magical drug most likely. And so in that case, as you said very well Todd, we have to do better and we have to do more. Todd Golde: I would also just to your individual variability, I'd like to call a little kudos to my colleague, Dr. Tansey, because she's been a real champion of diversity and inclusion in Alzheimer's disease and neurodegenerative disease research and women in science. In general, we do a really bad job of including diversity in our trials. What we should say is we know a heck of a lot about the natural history of Alzheimer's disease in Caucasians or Northern European descent. There's also lack of just diversity — socioeconomic and educational diversity. And that's partly because these trials are pretty challenging. If you agree to one of these, you're going to go through extensive neuropsychological batteries that last hours. You're going to strap yourself in an infusion chair for a few hours, you're going to get multiple radionuclide PET scans, you're going to get multiple MRI scans. They might ask you to have a lumbar puncture. This is a big burden to place on somebody, and so it takes a lot of processing. We have a lot of people who are rightfully a little fearful of the medical system and we're seeing the consequences of that with some of the lack of vaccination rates and things in the country. You could imagine the hurdles to try to get more diverse enrollees in these trials. I'll give a shout out, mostly to my colleagues in South Florida. I lead the NIH-funded 1Florida Alzheimer's Disease Research Center [ADRC]. It's a consortium of universities and institutions throughout Florida. We were refunded for another five-year cycle. But in that first period, we had the highest percentage of Hispanic/Latino participants of any ADRC in the country, out of the 30 networks. And it wasn't that high of a burden or hurdle because most of those did not have very many Hispanic enrollees. And they would lose them when they would enroll them. And we were actually able to retain them and continue to follow them for many years. And now our colleagues at the University of Miami are actually doing a great job of bringing in African-American participants. So we probably will end up with one of the more diverse research participants in our Alzheimer's Disease Research Center. And it's not me. It's my colleagues, Drs. Ranjan Duara, David Loewenstein, Rosie Curie and Melissa Armstrong, who were really leading that clinical effort. And I'm sort of the ringleader. But it's really remarkable to see, and you don't really understand how bad we've been until you look at the data and go, okay, we have 5,000 brain scans on people with Alzheimer's disease and 100 from African-Americans and 125 from Hispanics. It's not quite that bad, but it's close. Malú Tansey: That's exactly right. We know very little about how dementia affects people of color. Not just because of the demographics, but just lifestyle and access to care. And it's a complex picture. And then getting them enrolled in trials is very difficult because of cultural differences and outreach and things like that. But I do agree with Todd. I think the University of Florida does a remarkable job. I think Emory does a really good job as well. They have a really good ADRC that does outreach. Whitney Wharton out there, Allan Levy, they do a lot of African-American populations, they'd go into the churches and they seek them out. But yes, there's a lot that we need to do better to understand the effect of diverse genetic background. Adam Woods: And in my mind, because I'm leading four clinical trials at present and have worked on numerous clinical trials over the years, when you see a trial finish and it's five, six, 10% in minoritized participants, that is a failure of science because that is doing science for the majority and not science for everyone. And so we have to do more. And then here we work very hard. I mean, we just finished the enrollment in a Phase 3 trial and across the University of Arizona and University of Florida main campus we ended with 16% minoritized participants. And while our data safety monitoring board and others were really excited by this, I was disappointed. I wanted 25% and we invested heavily — we paid for transportation for every single participant from point-to-point at every time, provided remuneration that was appropriate for the study, provided any kind of accessibility issues and tried to address them one-on-one. We had full-time recruiters, out in the community, that are in the churches, at these events in the community, literally every weekend, every day they happen, and that's literally what we have to continue doing. We have to do more because we can't continue having these drug trials finish to where it's not representative of the U.S. population. That is a failure. Nicci Brown: Resources, websites people can go to? Todd Golde: So just for some local information, there's some data on the research that's going on at the University of Florida that's updated at the McKnight Brain Institute. So mbi.ufl.edu. Nicci Brown: Our brains helping yours? Todd Golde: And there's also a website for our 1Florida Alzheimer's Disease Research Center. And then I think one of the better websites on the larger scale is the national Alzheimer's Association website that really lays out in lay language the disease, its impact and how you could go to get — we didn't talk about things like caregiver burden and other kinds of things. And caring for a loved one with this disorder is a huge burden and a real challenge. And there are resources and links to support groups, ways to manage that, et cetera. So I think the national Alzheimer's Association website is probably the one that I would most strongly recommend if you just want to figure out how you're going to cope with this disease. Adam Woods: And then probably the CTRND [Center for Translational Research in Neurodegenerative Disease] website. Nicci Brown: The CTRND website, yeah. Adam Woods: And Center for Cognitive Aging and Memory website would make sense to include that as well. Nicci Brown: Yeah. Todd Golde: Well, and a final one would be their clinicaltrials.gov. And so if somebody does want to enroll in trials, and if they're hearing that someplace besides the state of Florida, these are run nationally and there are many sites and one could look at trials in your area. Pretty much if you are running a clinical trial, whether it's non-pharmacological or pharmacologic, it has to go on that site now. Adam Woods: And I get emails all the time from people who have gone on ct.gov or clinicaltrials.gov, and they'll reach out and say, "Hi, I'm at this location, are you running a site here? I'd like to participate in your trial?" And so it is a resource that people use to find trials that can fit. We have local research registries and other things of that nature, but clinicaltrials.gov would probably be a nice one to add in. Nicci Brown: So we've spent a good amount of time and I think we've barely scratched the surface because there is so much to talk about, but for our listeners, are there any things that you would say they should be on the lookout for in the next few years, any breakthroughs that you might see coming or developments that we should be on the lookout for? Todd Golde: Well, I think it's a really exciting time. There is a renewed interest in pharmaceutical companies, and I think whether you think this new drug [Aduhelm] worked or not, at least for some people, this will mean that there is a path to getting some financial reward for investing in therapeutic development in this space. And so I think that will bring about a continued investment in the pharmaceutical sector. But we were beginning to unravel the complex biology of this disease in ways that I think we wouldn't have really anticipated a few years ago. And I think that with the novel technologies around, be it RNA vaccines, I'm not sure if that's applicable to Alzheimer's disease, but somebody might find it, there are gene therapies, there's an ability to more rapidly identify novel traditional small molecule drugs or make new antibodies. So I think there is hope. I think we need to learn from our failures or not complete successes. And I think the field's willing to do that. We've eaten enough humble pie that we can say, "Hey, we need to change the dialogue." And when we think of developing a therapy or an intervention, we need to align it with the stage of disease, be it even clinical or preclinical, where it's most likely to show an effect. These prevention studies that are going on, on people with genetic risk for Alzheimer's disease, that are really heroic efforts, mostly from the participants who are really probably doing this more likely for the next generation, rather than for themselves because the likelihood that they're going to receive a drug that will prevent them from getting Alzheimer's disease, as we go on I think is higher and higher, but in the early days, they're not getting optimal drugs, but we're learning about the natural history of Alzheimer's disease. And that's ultimately how we're going to figure out how to prevent this disease is in those people initially. And then we're going to figure out ways to intervene better in people who have the symptomatic phase of the disease. I fully believe that, it's not going to be easy, but we're going to roll up our sleeves and get to it. Nicci Brown: Anything to add from anyone? Malú Tansey: Yeah. I think people should be on the lookout for acknowledgement that while it is a complex disease, we are getting a better handle on the biology. We are understanding how the gene and environment interactions in the immune system, how you respond to your triggers outside — stress, sleep, diet, all those things come together to dial up a dance card of your predispositions and your likelihood. And while you can't necessarily control your genetics right now, there's probably an opportunity to potentially do a lot of things about the other factors as soon as we find out more about them. I'm extremely excited about the potential for modulating the immune system to understand risk and lower those risks over a lifetime and develop new therapies. Adam Woods: I don't have really much to add in that. I think my colleagues have said it very well. I think the one thing I would like to reiterate is the heroes in this aren't the scientists. It's not the clinicians. It is the participants, it's the participants in all of these trials that come in day after day, and you talk to these participants and they say, "I know this probably isn't going to help me directly or maybe it'll help me a little, but if I can help move this forward, if I can help my children, my grandchildren" that to me, is the sign of a hero. And that's the people we're working with. Those are the people who are going to break the bow in this and move this forward. We're just going to be there to help them facilitate. Todd Golde: Even those, I mean, much of what we learned beginning with Dr. Alzheimer and Dr. Oscar Fisher, who was a contemporary scientist, basically they looked at the post-mortem brain. And so we do have brain donation program here at the University of Florida and having access to brain tissue is a gift that is huge because we would be nowhere in this disease without the access to the human brain and understanding the proteins. In fact, it was in the 1980s that what I call Alzheimer's disease entered the molecular age. It wasn't until that. So, we had these descriptions of what went on in the brain and the clinical features. But they purified the proteins that we still work on today, amyloid and tau, from the post-mortem human brain. And then both were linked in different ways to genetics of dementing disorders in the 1990s. And that really served as a framework for our modern understanding of this disease. Though, in some ways we also oversimplified it at that time. And as Adam said and Malú, there are so many factors that influence your cognitive trajectory. It's not just about amyloid and tau, and we need to embrace the complexity and move beyond that. Nicci Brown: Well, I want to acknowledge all those people who have participated, but also thank you all for your time this afternoon and also for your work and your research and that of your colleagues. Todd Golde: Glad to do this. It's important to get the message out there. And the only thing I'd add just at the end is that the increase in public support funding at the national level, and even the state of Florida level, has been tremendously important to what's happening at UF and across the country. And so one thing you could do, which doesn't involve participating in a trial, is to contact your representative or state Legislature, and just tell them how much you're concerned about Alzheimer's disease and continue to support it. And we're not going to do this without that, funding is key. And it sounds a little self-serving, but we've been paupers in the world of relative levels of funding to medical impact and that's changed. And we need to keep it that way in order for us to really move this from where we are to get the next one. Malú Tansey: To the next generation too, really. I think it's important well we might have the resources and the ideas, the next generation of people in our labs that are already here, they have even better ideas than we do, hopefully. Adam Woods: Yeah, that's right. I mean, we're looking at a tripling of the population afflicted by Alzheimer's disease by 2050 and economically our health care infrastructure isn't well equipped to handle that level of care. And so what we're looking at now is trying to find solutions to address this now, not when it becomes a catastrophic level of economic impact. And so everyone has a role to play, whether that be participating in a study, participating in reaching out to representatives to help support future Alzheimer's funding. But at the end of the day, go Gators! Nicci Brown: Listeners, thank you for joining us from Florida, a University of Florida podcast where we share the stories of faculty, researchers, students and administrators whose thought leadership is moving our state, our nation and our world forward. I'm your host, Nicci Brown, and I hope you'll join me for our next story of innovation from Florida. Collapse September 14, 2021 Welcome to From Florida, a podcast where you'll learn how minds are connecting, great ideas are colliding and groundbreaking innovations become a reality because of the University of Florida. I'm your host Nicci Brown and on each episode, I'll be talking with UF faculty, researchers, students and administrators — thought leaders from Florida — who are moving our state, nation and the world forward. The University of Florida is one of America's leading public research universities, recognized for innovative discoveries and advances in a broad range of fields — from agriculture to artificial intelligence — for educational excellence and for our major role as an economic engine in our state. Our impact, though, extends around the globe. We have many stories to share. I hope you'll join us. Collapse

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