

Transcript –Dr. Kim Season 7

A new *Voices of UMass Chan* podcast episode

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Thank you for listening to the voices of UMass Chan, featuring the people, ideas and advances of UMass Chan Medical School.

JENNIFER BERRYMAN

Welcome back to the voices of UMass chan I'm Jennifer Berryman. Today, our guest is Dr Jason Kim. Dr Kim is a professor of molecular medicine and an expert in metabolism and Type two diabetes, which affects millions of people around the globe. He's here to talk about a new three and a half million-dollar grant from the National Institute on Aging that will allow him to explore the connection between type two diabetes and Alzheimer's disease. Dr Kim, thank you so much for making time to talk with us.

JASON KIM

Thank you for having me here.

JENNIFER BERRYMAN

So, we were just saying before we started recording that your career has been so fascinating, and you've done work literally all around the world exploring Type two diabetes, the causes and the pathogenesis of it. Tell me about how you first got into this. Why did you choose to research this?

JASON KIM

That's a great starting question, and many have actually asked me about that. We all have different paths to how we develop passion for the work that we do. For me, it was a personal cause. This was when I was graduating in college. I was at UC Irvine, and I had a very young aunt, young, meaning she was only about seven years older than me, but she was my aunt who I really known quite well, and grew up very close with. And of course, at the time, she lived in South Korea. Now that's where I was born. And then I came to the U.S. with my parents when I was young, about 12 years of age. And then I grew up in Los Angeles and and what I found out, and she seemed very healthy. And again, we spent so much time whenever I visited Korea. Then all of a sudden, I got news from my uncle saying

that my aunt had passed away. Oh, that was shocking and puzzling, because this was a wonderful, beautiful young woman full of life, whom I just met. And that time, wonderful time only, the past summer, and then all of a sudden, she died. So, when I asked about it, it turned out she had undiagnosed diabetes, and that progressed to some major complications leading to a kidney failure. She was hospitalized for just about three days, and then she passed away. Now I was devastated and at the time, and this goes back to very early 1990s, I had no idea what diabetes was, and I wanted to find what this disease is and how such a disease can take away such a beautiful young life. And that's where my passion began.

JENNIFER BERRYMAN

Oh my gosh, I'm so sorry. And she was in the prime of her life, it sounds like when she passed.

JASON KIM

Yes, indeed. And the disease has really transformed over the past 30 years, since I began the work to affect more and more young people. We're talking about, even teenagers are being diagnosed with type two diabetes and have to be put on medication, which, as we know that this is a chronic disease that we still do not have a cure for the disease, so one often has to be on medication for lifelong.

JENNIFER BERRYMAN

So just to give our listeners some perspective as a reminder, type two diabetes effects, is this number? Could it possibly be right? 550 million people around the world? That's a staggering number, and you're saying so obviously.

JASON KIM

That's correct.

JENNIFER BERRYMAN

Now, decades later, three decades after you suffered that personal loss, scientists and physicians know more about type two diabetes, but we still don't really have we have effective treatments, but we don't have a cure. So, you went into the lab and what were you trying to unearth?

JASON KIM

Yes, that is absolutely true. Over the past 30 years, the work of our lab and many others, we know a lot more of type two diabetes than we have ever known before. So, the first of

the advances in the understanding of the disease is certainly has been traumatic, especially over the last two decades, because type two diabetes, which is closely, causally associated with obesity. And of course, we know obesity has been an epidemic event that it affects globally and the populations in skyrocketing over the years, and that almost explains why type two diabetes prevalence has also been rising at an equal rate, and this field has gone through really an important and exciting paradigm shift, type two diabetes that was once perceived as a disease of an abnormal sugar metabolism, therefore causing imbalance glucose levels and elevated glucose levels in your blood, the hallmark of diabetes. But over the last two decades, we've come to understand that obesity as a cause of type two diabetes is a chronic inflammatory state, and that inflammation may be the important link between obesity and and type two diabetes, and in that in that spectrum, we're learning a lot more every day about how this new paradigm is shaping the new understanding of type two diabetes, and hopefully a new ways to treat the disease in the future.

JENNIFER BERRYMAN

That that is still, though, uh, aspirational, right, in terms of finding a new treatment that treats the inflammation. People with type two diabetes are still taking insulin for the most part, right?

JASON KIM

That's correct, yes. So, inflammation definitely plays an important role, but it is somewhat different than what most of us consider kind of inflammation to be an important and beneficial event for our body when we have to fight these common infection. So it's a little bit different kind of framework. Those that develop the inflammation that develop in response to an infection, is a huge, a massive inflammatory response that immune cells are activated and respond to any source of invasion, by toxins or outside Asian like viruses. But the obesity, the inflammation that that develops in obesity, is more of a kind of a low-grade inflammation that is much more chronic in duration, of course. So, so my laboratory has really been studying what you know, what causes that, that low grade, chronic inflammatory response in our body, and then what type of cells are involved in this process, and then how they then cause what is known as insulin resistance, which is the major characteristic of type two diabetes, where our hormone insulin is unable or less able, to regulate our blood glucose level. To understand how inflammation leads to this event.

JENNIFER BERRYMAN

Fascinating. So, I want to talk now about this new realm of research that you're going to be diving into. So it's so interesting as a non-physician, the correlations between that have been discovered, and so there's not only a strong correlation between Type two diabetes and obesity, but there's also a strong correlation between type two diabetes and Alzheimer's disease.

JASON KIM

That's absolutely correct. The studies have shown that about 80% of people with Alzheimer's disease have type two diabetes. And this cannot be just purely coincidental. There must be a biological connection between these two common human diseases.

JENNIFER BERRYMAN

Tell us more about that 80% of people with Alzheimer's disease have type two diabetes.

JASON KIM

That's correct. So, to tell you a little bit, since I've had a chance to introduce to all of you about type two diabetes, I want to give you a little bit about the Alzheimer's disease. Now the population is equally striking. It affects about seven million Americans, or globally, more than 40 million people around the world. Now, Alzheimer's disease, as we all know, is an aging disease that affects more than 70% of those 75 years old and older. It is also an irreversible neurodegenerative disease with declining memory and cognitive function and personality changes. Now, just like diabetes, there are three currently FDA approved drugs for treating Alzheimer's disease, but none is intended to cure the disease, as they simply slow the progression of the disease. So there's no doubt there is a strong need to better understand this disease. Now this is where it gets really interesting. Okay, Alzheimer's disease, diabetes and obesity are rising throughout the world, and we all ask, why is that the case now? Just like how I described how type two diabetes has gone through its share of changing, kind of evolving paradigm, we call it. The Alzheimer's disease has gone through a similar kind of phenomenon. Now, traditionally, it involves a loss of brain function and brain cell death, and the well-known hallmarks include formation and accumulation of these undesirable protein deposits that are famously known as amyloid plaques and neurofibrillary tangles. And I know these are kind of a lot of scientific terms, but these are basically protein aggregates that accumulate, and they spread throughout the brain as the disease progresses and they affect the brain function and eventually cause neuronal death. Now, traditionally, people have thought that the Alzheimer's disease has really as a disease of dying neurons as a result of this protein aggregation, but it's quite possible that that these events that we all know so well may simply be a manifestation of disease, not the actual causality. And what's really exciting is that some recent studies are

indicating that in Alzheimer's disease, their brain is also developing inflammation. We call it neuro inflammation, and that may possibly occur in the early stage of the disease and may contribute to disease progression. So you begin to see some similar features between Alzheimer's disease and type two diabetes, and that's what we are keen to investigate and try to understand more.

JENNIFER BERRYMAN

So what will that research look like, and who will you be collaborating with?

JASON KIM

Yes, so very important questions. So I have to admit that the NIH, the National Institutes of Health, the government agency that funds our research really recognize this important trend and connection between these two human diseases that are very common, Alzheimer's disease, and type two diabetes. So that actually was the goal when the NIH and the National Institute on Aging released a notice of special interest aimed at improving our understanding about age associated metabolic changes in peripheral organs or in the brain, affect the onset or progression of Alzheimer's disease. So when I saw that last spring now I, as a leading expert in diabetes and metabolism, found out who might be the right neurobiologist at UMass Chan Medical School campus to join me in this exciting collaborative venture, and that's when I found and teamed up with Dr. Dory Schafer, a bright, young, neuroscientist who's making a name for herself as a leading figure in dementia research as a co-investigator on this grant to put forth an exciting and innovative paradigm that could potentially explain this important connection between type two diabetes and Alzheimer's disease.

JENNIFER BERRYMAN

What will the study look like? What will you and Dr. Schafer do?

JASON KIM

Yes. So, the premise of our investigation is really in two folds, again, the notion, and really the new, newly perceived notion, that Alzheimer's disease involves this inflammation in the brain and connecting that to type two diabetes is also a disease of an inflammatory state. So we want to understand, and of course, we've been studying, that important notion on the role of inflammation as a cause of type two diabetes. So, our goal is to bring these two together to ask a fundamental question, whether peripheral inflammation that develops in obesity and type two diabetes and insulin resistance may contribute to brain inflammation leading to Alzheimer's disease, and how changes in peripheral metabolism may be an early event in the progression of both of these diseases. And this is where I find this grant to be

also timely, because last year I received another NIH grant to study metabolic liver disease, which is a major comorbidity of type two diabetes. And it turns out that one of the key features of the metabolic liver disease is also inflammation and insulin resistance that leads to a common liver disease known as Metabolic Dysfunction-Associated Steatohepatitis known as MASH. And this is where it gets really even more exciting, there is also a strong correlation between this metabolic liver disease and Alzheimer's disease. Really bringing these things all together with a central theme being inflammation at the center of a potentially maybe these three common immune diseases.

JENNIFER BERRYMAN

So, are there biomarkers that you'll be looking for, or how do you go about figuring out what comes first and what's causing the inflammation?

JASON KIM

Yes, that's an outstanding question. Of course. Discover new biomarkers that can help us identify and early diagnosis these diseases is always key, and that's something that is certainly in kind of a downstream path of our current research. But what we at this time want to understand is this biological timeline of event, as you alluded right there, when it comes to a chronic and progressive disease, it's important to understand what happens early on as opposed to what simply shows up later on, because often time what happens early tends to be causally related to what happens when a disease is fully onset. So, we are using mouse models. These are known as transgenic or genetically engineered mouse models, that mimic the human Alzheimer's disease condition. And we are studying them as the animals age at different ages, from young to middle age, and as they get older, as the Alzheimer's disease pattern begins to show. We want to know what happens during the early stage when it comes to the changes in inflammation and metabolism in peripheral organs, meaning organs outside the brain as well as within the brain.

JENNIFER BERRYMAN

That is fascinating, and as we said earlier, timely research that potentially has implications for a half a billion people or more around the globe. So, we will certainly be watching closely to see what you and Dr. Schafer are able to learn and congratulations on this new grant.

JASON KIM

Thank you. It's been a great pleasure to talk about this exciting grant, and of course, I have to thank and really be grateful to the support of the NIH to help us pursue our investigation and conduct our research, which we think that we may be able to uncover a new pipeline

of exciting therapeutic strategies to treat Alzheimer's disease and possibly targeting outside of the brain. Let's imagine that we may be able to target Alzheimer's disease. A disease of the brain, but outside of the brain, thereby minimizing the undesirable effects of CNS targeting drugs.

JENNIFER BERRYMAN

That public investment in science and discovery is so critical. It's really the foundation of so many health discoveries that have been made over the past century. Dr. Jason Kim, Professor of Molecular Medicine at UMass Chan Medical School. Thank you so much for making time to speak with us.

JASON KIM

Thank you, Jennifer. It's been a great pleasure to tell you all about all about our research, and I especially do want to thank the UMass Chan Medical School for giving me the place and all the excitement and support to continue our exciting research.

JENNIFER BERRYMAN

Thank you, and thank you for joining us. If there is a specific topic you'd like to hear about on the voices of UMass Chan, email us at UMass chan communications@umassmed.edu I'm Jennifer Berryman. We'll see you next time.

Voice over artist

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Music

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