

Interview with Leonard Guarente Resveratrol

KYLE JENSEN: Welcome to SAGE Crossroads, the premier online forum in issues of human aging. These podcasts feature lively discussion with the experts on the ethical, political, economic, scientific, and societal implications of aging related science. Thank you for listening.

I'm speaking now with Dr. Leonard Guarente. Dr. Guarente is a researcher and the Novartis professor of biology for the Massachusetts Institute of Technology.

Dr. Guarente, can you briefly describe the field of Sirtuin biology?

LEONARD GUARENTE: Yes. We found a gene that was an anti-aging gene that extended lifespan in yeast about 15 years ago. We've been pursuing it ever since, and that gene is called SIR2. The term sirtuin refers to all the genes that are similar in sequence to SIR2 from many different organisms. What we think is that these genes function to slow down aging and in mammals, diseases of aging when they are activated.

KYLE JENSEN: How does resveratrol fit into this equation?

LEONARD GUARENTE: So resveratrol was identified...so one of the most basic properties of sirtuins and in particular, SIRT1 which is the major human sirtuin, is it has an activity as an enzyme which has a technical term of NAD dependent acetylase, but you can assess how active it is. People screen for small molecules and chemicals that can activate it even more and identified resveratrol and other natural products of this general class which are called polyphenals. What these molecules do is evidently they bind to SIRT1 and increase its activity, so they are sirtuin activators.

KYLE JENSEN: What do you hope resveratrol will be able to do?

LEONARD GUARENTE: I think resveratrol has a good chance of having benefit in people. It's being tested now in human trials, and phase one trials are completed and clearly indicated safety. Secondarily they showed that it's likely that it reduced blood glucose which means that immediately may have applications for metabolic diseases like diabetes.

KYLE JENSEN: A lot of headlines have been coming out of NIH studies that you've been involved in that state resveratrol improves health in mice but not longevity. Do you think there is a chance that resveratrol can increase human longevity?

LEONARD GUARENTE: Absolutely. I think we aren't going to know that for a very, very long time. In mice so many things have been approved by sirtuin activators, and the fact that longevity hasn't been observed yet I think it just a matter of time before one has the right strain. If you have a strain of mouse that's dying from some idiosyncratic

reason like a particular cancer which most mouse strains die of and that happens not to be treated by the resveratrol, you won't extend the lifespan.

KYLE JENSEN: Do you all plan to do clinical trials in areas other than type II diabetes?

LEONARD GUARENTE: Not yet but I think that's on the horizon. Over the next decade I think you will begin to see a pretty wide swath of diseases fall under this regulation, so it's an exciting time right now. I think the sky seems to be the limit, and we'll see whether there are disease we group as treatable this way or preventable this way or disease that won't.

KYLE JENSEN: Now do you think this approach, going after drugs like resveratrol, will hold the key to defeating age-related disease and increasing lifespan?

LEONARD GUARENTE: I don't think we will defeat them, but I think we have a chance to hold them at bay longer and increase the period when we are healthy and disease free. Perhaps as much by a decade. Which, you know, will make a huge difference.

KYLE JENSEN: Lastly, the audience of SAGE Crossroads is made up of scientists, policy makers, and curious consumers. If there is one last statement that you could make to them regarding resveratrol and the potential it has, what would it be?

LEONARD GUARENTE: I think what I would say for policy makers is this finding about sirtuins which we made 10 to 15 years ago came as a result of basic research on aging. There may be a lot more things out there that would be very, very important in aging and diseases that haven't been discovered yet. So my message would be that it is a very good idea to increase funding for the basic biology of aging.

KYLE JENSEN: Thank you. On behalf of SAGE Crossroads, I'm Kyle Jensen.