

Interview with Dr. Richard Sprott Biomarkers

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 joined now with Dr. Richard L. Sprott. Dr. Sprott is a former director of the NIA's Biology of Aging Program and the current executive director of the Ellison Medical Foundation.

Dr. Sprott, what is the NIA Biomarkers of Aging Program?

RICHARD SPROTT: Well it was, it doesn't exist any more, it was a 10 year effort to try to find biological markers of aging that are different than chronological markers of aging. I assume as part of your larger overall conversation here you have some discussion about what the differences are. In any case, what we did was to create a very large colony of a variety of mice, inbred mice and inbred rats, as a source for studies looking for biomarkers of aging. All of the animals were raised in a single place with controlled diets and so on and then shipped to investigators around the country when they reached the appropriate ages. That was intended to eliminate differences in laboratories that arise from differences in husbandry. All together of a 10 year span we had, if I remember right, 14 different laboratories involved and the biomarker research spanned the scientific spectrum from cellular and molecular model searches to whole organism behavior and sort of everything in between looking at all of the physiological systems and along the way characterizing the pathology, the normal pathology, of animals at different ages from 6 months of age to in some cases roughly 50 months of age for the longest lived animals in the program.

KYLE JENSEN: What were the setbacks that you all encountered there?

RICHARD SPROTT: Oh, ok well. As I said, we offered a large array of mouse genotypes. When we started there were 7 different genotypes, and both inbred strains and F1 hybrids between the two, we provided equal numbers of males and females. Half of the animals were calorically restricted because that's the one intervention we knew produced an increase of lifespan, and half of the animals were fed ad libitum. One of the things that happened, which was a great surprise to us, was that most of the investigators did not avail themselves of this great genetic diversity that we provided. That was a real opportunity that was missed. Most of them used the most commonly used mouse strains, C57 black 6, few used EBAs and the F1 hybrid, and with the rats they used the Fisher 344 rat even though we had 3 other genotypes available, and that was a real loss. It was an opportunity that was lost to get much more diverse information than we were able to get. Whether that was part of the explanation that we were not able to find any viable biomarkers, I'm not sure, but of course, the major setback was that we didn't get a panel of biomarkers that was useful. Such a panel has not been developed. We did get very

valuable information about the normal pathology of animals of this kind throughout their lifespan and a demonstration of something we expected but were not sure of in that the diseases that these animals show or the conditions that they might show at various ages, are not necessarily the things that kill them in the very end. That is terminal pathology might be quite different from results we got in cross sectional pathology. We also found that there are putative biomarkers, things that might turn out to be biomarkers, that are only predictive at all at a particular age. We couldn't find any kinds of biomarkers that stay stable throughout the lifespan of the organism. Perhaps we were naïve when we started it thinking that we might turn that up. We also found that it was much more difficult to pull together results from disparate set of laboratories in the end. So we have a very, very large number of individual studies but a rather restrictive set of information that tries to pull all of those studies together.

KYLE JENSEN: What is your outlook for biomarkers of aging? How long do you think it will be until we have these validated biomarkers?

RICHARD SPROTT: I think right now, perhaps this is indicated by your interest in it as well – we recently had a meeting in New York back last fall, I think there is much renewed interest now. It's been 20 years since that NIA effort started, and we have a lot of different tools available to us now then we had then. We know more about the genome, we have some molecular techniques which allow us to make different kinds of progress, we know a whole lot more about the genome, so I think we are going to find that those kinds of approaches perhaps will allow us to make a different kind of progress for biomarker research than we were able to do then. We know more about the physiological systems I think.

KYLE JENSEN: 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 about biomarkers of aging, what would it be?

RICHARD SPROTT: I think it will be that while the popular press right now and in particular the purveyors of anti-aging products would have you believe that we have a set of biomarkers of aging that are useful for humans, in fact we don't. And so one should listen to that kind of information with great skepticism and look the promise of current science to produce such a panel biomarkers or sets of panels of biomarkers for different systems. That might turn up in the next 5 or 10 years.

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