



## Living Longer, Living Better: Dr. Christian Sell

Christian Sell, Ph.D., associate professor in pathology and laboratory medicine at the College of Medicine, has received national attention for his research into aging. His current discoveries may have implications for many diseases that plague old age, such as dementia. Ironically, despite this academic interest in aging, he is also invested in youth – his graduate students and their scientific contributions.

Dr. Sell's research is built upon a multipart study investigating the role of insulin-like growth factor (IGF) as it relates to animal longevity. It is for this work that he has been featured on "60 Minutes" and in Philadelphia Magazine. He is currently examining the mitochondria's relationship in this process, a development predicated upon his earlier studies of IGF.

For the ongoing study, Dr. Sell and his team (including collaborators at the University of Texas, San Antonio, and Penn State) reduced the levels of IGF in mice. Those mice (known as "midi" for their mid-size) had a longer lifespan when compared to a control group of normal mice. Other studies have shown, however, that IGF can be a boon to older neurons, helping them recover from injury. This paradox concerning IGF levels highlights the complexity of these cellular processes.

The midis were also found to have an increased ability to clear damaged mitochondria, a discovery that has potentially huge implications. Dr. Sell says, "We think that's another part of the mechanism that contributes to their long lifespan, because mitochondria damage and dysfunction...are a big deal [as we age], especially in muscle tissue and potentially in neurons, like in Parkinson's disease or ALS."

The mitochondrion has its own DNA and reproduces independently within the cell. This chemical reaction may contribute to lost muscle function as animals age. The fact that the midis have a better ability to eliminate damaged mitochondria as they age is significant for Dr. Sell's research. "That's one of the new things we've [learned] with the animals that I think is good...it seems as though the damaged mitochondria are selectively targeted, but we don't quite know how that works. So we'd like to understand how that works and how this hormone system... impacts that." Dr. Sell posits that this discovery may help illuminate many age-related problems, such as ALS, Parkinson's, Alzheimer's, and sarcopenia, as well as many degenerative diseases and, potentially, cardiac failure.

IGF seems to regulate the mitochondria as well as the proteasome system, both of which clear



damaged proteins. The balance between these two processes is most likely important to the cell's overall homeostasis. Dr. Sell explains, "There's a balance between two clearance mechanisms that's probably important to maintaining the homeostasis...in the cells. Maintaining the normal balance...is important because what happens as we get older – basically the real underlying cause of all the problems – is that you can't maintain proper homeostasis...in any of your organ systems.... So that's why we think the mitochondria thing is really important.... The balance between [the two systems] is probably critical to cognitive function late in life."

Dr. Sell's research has attracted national attention precisely because people are concerned with the physical and mental implications of growing older. This is even more important now that, as a nation, the population is aging.

Dr. Sell acknowledges, "If you go to a nursing home, and say you try to study aging or extend life, most people say, 'Well, why?' I think the reality is you really want to extend function more than lifespan, right? It gets complex. We're really at the start of this."

In Dr. Sell's lab, he and his colleagues are just as interested in maintaining cellular functions as they are in extending them. A long life in itself is not terribly promising without quality of life. To this end, the midis "have better cognitive function. They have better muscle function during aging. That's why, again, we like the mitochondrial clearing thing so much because it probably is important in maintaining proper function of, let's say, the muscular skeletal system.... It's the same with cognitive function. We really want to understand how to maintain cognitive function."

Dr. Sell continues, "How do we preserve function as we age? ... Some of these mechanisms will allow us to potentially maintain normal function as we get older and protect ourselves from some of those imbalances that progressively occur as we age.... That's why the mitochondria thing is so exciting. You can envision that being tied to multiple different diseases, from cardiovascular disease to dementia to sarcopenia."

Dr. Sell's discoveries, exciting as they are, are only one component of the wide-ranging research being conducted under the auspices of the Aging Initiative. The Aging Initiative, a multi-departmental research collaborative, traces its origins to a program at the Medical College of Pennsylvania (MCP). Dr. Sell describes its revival as "a phoenix story."

Sell's early mentor, Dr. Vincent Cristofalo, started the Center for Gerontology at MCP with an endowment from the Mars Foundation. When MCP began to experience financial challenges, the program fell by the wayside. At Drexel University College of Medicine, Dr. Sell; Dr. Ken Simansky, vice dean of research; and Dr. Jim England, then chair of the Pathology and Laboratory Science Department, reestablished the center as the Aging Initiative. They were able to re-appropriate the funds from the Mars endowment and use it to help establish new labs concerned with aging research. Investigations are now being conducted into the relationship between aging and the brain in menopause, for example.

Dr. Sell began his career studying cancer, examining IGF as it functioned in that disease. He says that he transitioned into aging research once it became clear that scientists could "really start to ask real questions about it." In addition to his work at MCP, Dr. Sell was an associate investigator at the Lankenau Institute for Medical Research in Wynnewood, Pennsylvania.

Student research, however, is considered the "cornerstone" of the Aging Initiative. Dr. Sell explains that their research is a priority because, "in the end...the students who are really coming in with new ideas and enthusiasm, kind of running with the ball, are often the ones who come up with the new stuff. They're the engine of the labs, especially here." Although the Aging Initiative has been in place for about only a year, three graduate students are currently conducting research under its guidance.

While Dr. Sell and his team are ever closer to leaning the secrets of longevity – and prolonged cognitive function – it is perhaps fitting to entrust the future of the field to the continued zeal of youth.

*To listen to Dr. Sell's medcast on "Answers About Aging" visit:*

<http://www.drexelmed.edu/Home/AboutTheCollege/MonthlyMedicalPodcast.aspx>

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