SPEAKER 1: We together with colleagues at Mayo a couple of years ago found that clearing senescent cells-- these are cells that came late with aging and various diseases and a period of damaged tissues that clearing these cells from genetically modified animals resulted in improvements in what we call health span. The period during life when people can live-- or in this case animals-- independently and free of chronic disease. Now, this was in genetically modified mice.

Obviously, what we want to do if we can, and this is the step that we've taken now, is to develop drugs that will selectively kill senescent cells in non-genetically modified individuals so that we can eventually take these beyond mice and into people for a number of applications. A single dose of these drugs, even after the drugs were long out of the animals bodies, resulted in improvements in cardiac function in old mice, and vascular function in old mice, in mice that had a leg radiated much like people have radiation treatment for cancer. One of the things that happens is that the senescent cells accumulate and even the hair on the leg turns gray and the animals have difficulty walking. We found that a single dose of these drugs resulted in improved exercise endurance and walking ability and that this single dose had a persisting effect for seven months after they were given just one dose for one day.

I think it's very hard to predict how long it will take to translate these kinds of interventions into people. Obviously, we don't study lifespan and health span in people, but there are some indications that we can see these drugs could be used for early on in humans. Those would include targeting multiple problems within the same person.

As you're aware, there are elderly individuals who are perfectly healthy and play 36 holes of golf a day. There are other elderly individuals, and I as a geriatrician often see them, who have 10 or 15 different problems or are on 20 different drugs. The question is whether these kinds of agents, these kinds of interventions that target fundamental aging processes could delay or perhaps even alleviate multiple problems within the same person at the same time.

We also found that in animals with an accelerated aging like state that we were able to alleviate a number of things that occur with these animals with increasing age, including brain and neurological dysfunction, and also including bone dysfunction-- osteoporosis and problems with the disks that separate the vertebra and the spine and lead to back pain. So these drugs appear to have multiple effects, many of which we didn't suspect, but we had an idea that we would get extended changes because of the previous work that we and other groups had done at Mayo showing that clearing senescent cells from the genetically modified individuals works. So it looks like these drugs are having multiple effects in animals, and the hope is to move these into various applications so that one day we can use drugs something like these in people.

It helps that these drugs are in human use. It also helps that these drugs can be given by mouth. It also helps that we know a lot about the safety profiles of these drugs. They've been used for many years. So all of those things will help us in getting to initial clinical trials.

I think it's important though to realize that these drugs are prototype drugs. People in the general population should not start taking them, and physicians should not start prescribing them off-label. We don't know enough about them yet. We don't know what the side effects are likely to be, and we need to do a lot of work in animals to do this. Furthermore, by knowing how these drugs work, we may be able to figure out the actual underlying fundamental mechanisms through which they're clearing senescent cells that may lead us to even better drugs with less side effects and sharper profiles so that we can eliminate senescent cells in particular parts of the body, for example, or in particular cell types and tailor this to the individual patient.