THE ELLISON MEDICAL FOUNDATION– PAVING A NEW PATH FOR AGING RESEARCH

BY AIMEE DINGWELL

Larry Ellison is a speculator. He is also a visionary. Not afraid of risk or ridicule, this maverick mogul of Silicon Valley built his Oracle software empire (and his $39.5 billion net worth) with less than $2,000 in savings on a philosophy that dismisses convention; and it is exactly that philosophy that he is betting on to change the face of aging and age-related diseases.

Some may know him for his high-dollar, daredevil lifestyle, like owning the fastest sailboat in history and racing it and Team Oracle to a 2010 World Cup victory, flying his Italian F-16 fighter jet for fun or owning the largest private yacht in the world. But few will know he has a serious philanthropic side that is just as focused as his business acumen.

The Ellison Medical Foundation is the largest private funder of research on aging, and the second largest overall funder—second only to the federal government's National Institute on Aging. Since its inception in 1998, Ellison's Medical Foundation has provided more than $300 million to fund basic biomedical research on aging relevant to understanding life span development processes and age-related diseases and disabilities, including stem cells, telomeres, longevity genes, DNA and mitochondrial damage, Werner Syndrome, Alzheimer's disease, neural development, degeneration and cognitive decline, and cellular response systems to aging and toxins.

It is said the research foundation began not so much from altruistic origins but from the confluence of Ellison's interest in science and an aversion to mortality. Cancer killed Ellison's adoptive mother when he was in college and Oracle co-founder Robert Miner in 1994.

A chance encounter with an equally visionary scientist, the late Nobel laureate Dr. Joshua Lederberg led Larry Ellison to understanding the therapeutic and market potential of biotechnology.

After hearing Lederberg, an icon of molecular biology and artificial intelligence, speak on the topic at a Stanford University symposium in 1990, Ellison was so intrigued by the scientist that he invited him to his home for a weekend. That weekend turned into a lifelong friendship. In 1994, Lederberg returned the favor with an invitation to vacation with him for two weeks—in the lab. Never one to pass up a challenge, Ellison took Lederberg up on the offer, likely to explore his own interests in molecular biology and science.

During those 14 days, pushed by his own interest to challenge himself, Ellison starting asking questions that altered the course of Lederberg's experiments, and would change the face of aging research in this country for years to come.

Thus over the next several years, the beginnings and mission of the Ellison Medical Foundation focused on aging emerged. Lederberg, who was then President Emeritus of Rockefeller University, was tapped as director of the Scientific Advisory Board, and Dr. Richard Sprott became the new Foundation's Executive Director, after years directing the National Institute of Aging's Biology of Aging Program.

"One of the problems with philanthropy is that people think that once they've written the check they're done," noted Ellison when asked about his charitable activities. "I believe that in order to be a successful philanthropist, you not only have to write the check but you have to spend enough time with these projects to make sure you are getting results."

And for Ellison, the road to results is often the one least traveled by others. Not surprisingly, the Medical Foundation's approach is different, innovative, and bold. As Lederberg once put it, "Our job is to fund the new, the unconventional, and to take chances that others won't. Our only criterion will be the best science and the best of scientists."

CUTTING-EDGE AGING RESEARCH STILL UNDERFUNDED

Fifteen years later, Larry Ellison's Medical Foundation continues to "fund people, not projects," according to Sprott, looking for scientists with track records of creative, productive work and unique ideas, while favoring basic research that may be too risky or speculative to attract mainstream funding. This year, the Ellison Medical Foundation will fund a total of $40 million to 25 Senior Scholars, and 25 New Scholars, each for four years. "At the moment, that means that at any point in time we are funding 200 laboratories," says Sprott. And the funding levels are significant. Senior Scholars are awarded about $1 million for 4 years of research, according to Sprott.

New Scholars receive approximately $400,000 for four years of research.

"My reason for coming here could be summed up with the notion that basic biologic research on aging was the least well-funded research at the National Institute on Aging," says Sprott, "And it still is."

While all of the degenerative and proliferative diseases of aging are related to basic biological, genetic and molecular processes, "no Congressman believes that he or she or his constituents die of basic biology—they die of diseases," says Sprott. "And so it doesn't sound very sexy. It is very hard to attract research dollars for basic biology," Sprott frustratingly notes. "Even in the view of Josh and Larry and the advisory board, the only long-term solution to age-related problems is to prevent them. And you can only do that with basic biological research. Anything else you do is playing catch up. Unfortunately, most of the money is going to fixing diseases that are already in place. So the Ellison Medical Foundation particularly wishes to stimulate new, creative research that might not be funded by traditional sources or that is often underfunded in the US," says Sprott.

And despite his personal losses from cancer, there are no specific diseases that motivate Ellison or drive the Medical Foundation's work, according to Sprott. Ellison is so devoted to basic aging research that the foundation started to focus exclusively on identifying and funding research opportunities that could lead to "quantum leaps" or "paradigm shifts" in scientific understanding that greatly impact human health.

"Larry is one of those people who truly understands the need for basic science, and clearly understands the need for focus. We focus very sharply," says Sprott. "If we funded a broader variety of things we would have much less impact on any of them. And I think he appreciates that's the way you really get something done."

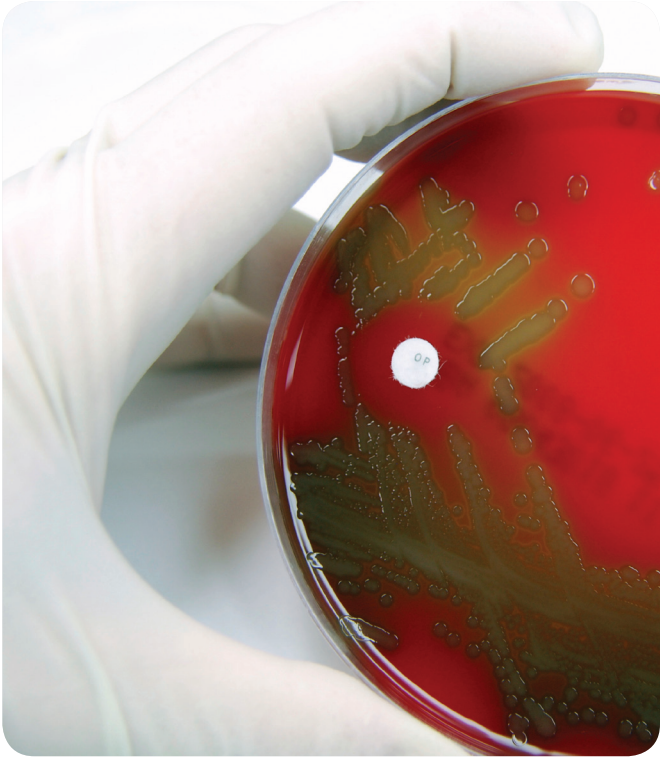
THE EMF FILLS A GAP, ADVANCES SCIENCE

Such sentiments are echoed by veteran researcher and EMF Senior Scientist Scholar Dr. Judith Campisi. The current research climate "is the worst I have ever seen it," says Campisi. "And it is particularly bad for basic aging research right now, as opposed to other aspects of aging research, and certainly as opposed to other fields," notes Campisi. "It is really terrible right now. And what I think Ellison has done is helping to fill a gap that is a real need."

Campisi, who is a professor and has her own lab at the Buck Institute for Research on Aging in Berkeley, California, knows first-hand the difficulties of securing research funding from the standard government sources like the National Institutes of Health (NIH), including onerous application procedures and extensive oversight once funded. "The Ellison Medical Foundation, I believe, has striven to break the NIH mode of requiring extensive preliminary data and really encourage people to even go outside their fields or to bring people who have not worked in aging to begin to apply what they know in other fields to the problem of aging," says Campisi, who studies the relationship between cancer and aging. "And in my opinion they have been very successful in doing that."

This is exactly what Ellison and Sprott want to hear. "What we think we can do that is not necessarily done very well by NIH is that we can take a chance on an investigator based on what we know about them in their application or what we know about them from their existing research and track record," Sprott explains. "If they have a really good idea, we can take a risk because we are not doing it with taxpayer dollars."

Campisi is a perfect example of this. "Cancer is very different than most other age-related diseases," says Campisi. "Most age-related diseases are degenerative. Your kidneys stop working well, your heart doesn't work well, your brain stops working well. But cancer is very different," she says. "In order for a lethal tumor to form, cells have to acquire new functions, new phenotypes, and so we've been thinking for years about whether this is coincidence that cancer goes up with age and all these degenerative pathologies go up with age or whether there is real biology that connects them."



ENTER TELOMERES

Telomeres are small units of DNA at the end of our chromosomes. As our cells divide, telomeres progressively shorten until they become dysfunctional, causing aging and age-related diseases, including cancer. But if telomeres can remain intact, they protect the genes inside the cell. Still, while Campisi knew about new theories surrounding telomeres at the time, she had never done research in them.

The funding from the Ellison Medical Foundation allowed her to blend her cancer research with telomere research. "At the time I got my Ellison funding the major paradigm for understanding this potential link was this idea that telomeres, these structures that cap the ends of chromosomes, get shorter with each cell division. And they also get shorter with age. And when they fail, when they get so short that the telomeres fail to function, the cells become senescent. But when cells become senescent they change their function so much that they can begin to alter the tissue and cause degenerative changes," says Campisi. "But I had never worked in telomeres. I was just dabbling."

"So the link between telomeres and degenerative changes was extremely obscure. And it was through the Ellison Medical Foundation that we were able to do some really interesting molecular studies and sort of close that loop to help us understand how it is that telomere failure related to all of the other inducers of senescence and then how senescent cells can change the tissue marker environment."

The Ellison funding, Campisi says, was a crucial link that really allowed her and her lab to go outside the box of traditional NIH funding. "It was something we had suspected for many years, and now we have proof, but at the time we only had a suspicion."

While Campisi is no longer funded by Ellison, those advancements have allowed her to continue to make "enormous progress." Not only has she been able to confirm many of the early, very speculative ideas about how senescence might link to degenerative diseases of aging with cancer, but she also has recently been able to identify that senescent cells may be responsible for chronic inflammation in the body.

"Very often aged tissues are said to have 'sterile' inflammation, meaning a pathologist will look at that tissue and see low-level, chronic inflammation, but there is no evidence of a pathogen. It has nothing to do with infection," says Campisi. "But we now know that senescent cells have the capability to create that kind of environment," based in part on an evolutionary need, Campisi believes, for the compromised cell to communicate with the immune system to clear the cell. "But if that damaged cell doesn't go away it becomes a chronic situation and we think this is a major reason why senescent cells might drive multiple pathologies, because every major pathology associated with aging has a component, either a cause or an exacerbating factor we now refer to as chronic inflammation."

BASIC RESEARCH MEANS SAVING LIVES

With this type of knowledge, scientists and researching physicians affiliated with groups like the Ellison Medical Foundation and Life Extension Foundation® are able to do much more to extend our healthy life spans and prevent needless deaths.

The Ellison Medical Foundation has also funded major initiatives in **longevity genes** and **life span extension**. In 2000, Dr. Nir Barzilai at Albert Einstein College of Medicine of Yeshiva University also became a Senior Scholar in Aging. His research focused on identifying longevity genes and biological factors associated with long life span in humans based on Ashkenazi Jews and Old Order Amish populations. He found that both groups had significantly larger high-density lipoprotein (HDL) and low-density lipoprotein (LDL) particle sizes than control groups.

As many *Life Extension* readers may already know, in terms of cardiovascular health, this characteristic is associated with lower prevalence of hypertension, cardiovascular disease, and metabolic syndrome. Dr. Barzilai's research identified two genetic alleles seen with increased frequency in the centenarians and their offspring. His research even found that one of the genetic mutations also conferred better cognitive function in the centenarians.

"What we're doing is investing philanthropic dollars in basic research that has the potential to have a very large impact on everyone's lives," notes Sprott. "When you look at the website and look at the projects we fund, you see a lot about life span extension. But we don't fund them for precisely that reason. We fund them to understand the basic processes so that we can improve the quality of the latter part of the life span. So we are more interested in quality rather than quantity," notes Sprott. "And our underlying theme is that if we can eliminate the diseases that are age-related that will translate into a big effect for people's lives."

WHAT'S THE FUTURE OF AGING RESEARCH?

Going forward, Sprott's goal for Ellison's Medical foundation is to "stay on top of what is cutting edge research at any point in time and make sure that we are leading and providing the funds for those cutting edge scientists to get far enough down the road that they are successful for funding from more traditional sources."

And come late summer and early fall, Ellison, Sprott and the foundation's Scientific Advisory Board will have funded a new round of New and Senior Scientists. Still, the Medical Foundation only funds a researcher once, which means there is still a tremendous unmet need in aging research. "We have a firm policy that no one gets a second award," Sprott says flatly. "When we first started out, we thought we would run out of bright people fairly fast. But in fact, we get more and more good applications every year. We have been at this 14 years and we are finding more and more really good people. But if we give people second awards—we've funded 800 so far—there would be another 800 people standing in line looking for an award. And we wouldn't fund anybody new."

CONCLUSION

Larry Ellison and **David Murdock** (described on following page) are examples of what ultra-wealthy individuals should be doing to fund **research** aimed at eliminating the horrific consequences of **aging** and its associated pathologies. They are not the only philanthropists supporting aging research, but they remain in the tiny minority.

Unlike any other philanthropy, the fruits of aging research benefit virtually every human on the planet. Even if one were to find a cure for all cancers, this would only benefit those stricken with cancer. Aging, on the other hand, strikes every human who lives long enough.

Based on what you are learning in this month's issue of ***Life Extension Magazine***®, scientists are discovering enough about the mechanisms of aging to make significant strides…but only if enough **research dollars** are intelligently allocated to perfect methods to control and ***reverse*** it. ●

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