RESEARCH AT MERRIMACK

INSIGHTS AND INNOVATIONS

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CHIRP: MitoCure Lab

Aging in our cells (and ourselves) **Unlocking the secrets to longevity**

PRINCIPAL INVESTIGATOR

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Research Interests:

- Age-associated metabolic dysregulation
- Mitochondrial function
- Inflammaging

To Assistant Professor of Health Sciences Leena Bharath, a single cell is endlessly fascinating: "With electron microscopy, we have the ability to visualize the tiny organelles in cells, and it's a universe in itself. Mystery lives in the cells. It's like detective work, figuring out how things work." In her laboratory at Merrimack College, Professor Bharath may be contributing to the answer to one of the greatest mysteries facing humankind: how to extend life. And she's not interested in just living longer; Professor Bharath wants to extend the "health span," increasing the number of healthy years we enjoy.

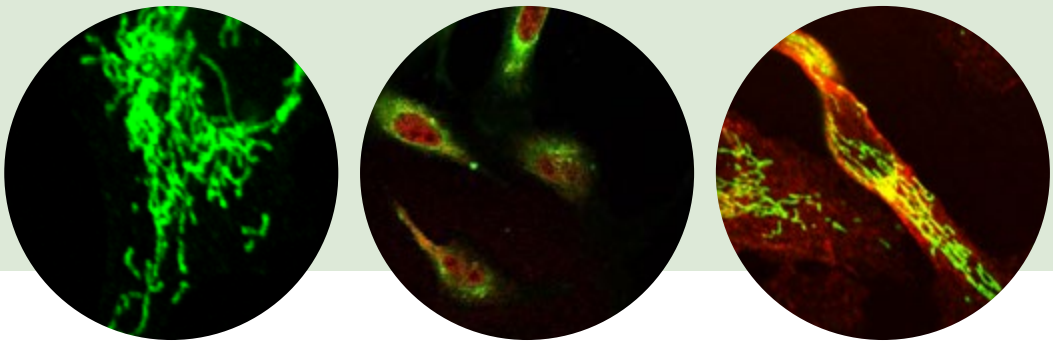
We spoke to Professor Bharath about her National Institutes of Health (NIH) funded research in cell biology and about the pharmaceutical drug Metformin.

Q: How did you come to focus on this particular research?
A: I started at the micro level examining cellular pathways. Sometimes something can go wrong in this tiny cell, and it then perpetuates and brings down the entire organism. It made me curious to understand what was happening at the cellular level. How can we prevent some of these changes, or fix them, so that the macro level is functional and there's no harm from aging?

Q: Tell us about the cellular aging processes you're studying.
A: "Inflammaging" is a chronic state of inflammation that happens as we age. It eventually results in cellular tissue damage, which then propagates or accelerates biological aging. Inflammaging seems to be related to the fact that as we age, we accumulate excess organelles in our cells, damaged dysfunctional proteins and so on. That's where autophagy comes in. Autophagy is our cellular cleanup system, a way to take out the recycling. Cells put all that excess and misshapen material into an autophagosome, which is like a trash bag, and bring that to a recycling bin called the lysosome. As we age, autophagy slows down. This decline has been linked to conditions such as dementia, Alzheimer's, Parkinson's and other neurological conditions. In my lab, we are focusing on how autophagy relates to diabetes, obesity and immune cell aging.

Q: What's an example of a "mystery" you've found in studying cells?
A: When I was looking at the immune system, at white blood cells, I compared samples from people around 30 years old to those of people over age 60. Our immune systems decline as we age, so I was expecting the mitochondria from the older people's samples would be slower and not as efficient. To our surprise, there was demonstrably more mitochondrial activity in the T-cells from older subjects than from younger subjects. So that was a mystery.

When you find something contrary to your expectations, the first thing you have to do is run more experiments to prove that what you're seeing is true. Once that's confirmed, as it was here, you need to broaden and reframe your research questions.



Images from the MitoCure lab of microscopic endothelial cells.

That's an exciting part of doing science.

So, what was happening? The older group, because they were using their mitochondria so much, they were actually creating an imbalance within the cell, overproducing something called reactive oxygen species.

Remember, for older individuals their autophagy is lower. They were making more reactive oxygen species, but with lower autophagy, there was less clearance of those molecules, leading to inflammaging.

Q: Can you tell us about the so-called "anti-aging drug" Metformin?
A: There's a popular book by Harvard Professor of Genetics David Sinclair, "Lifespan," that suggests Metformin has the potential to extend the human life span to 120 years. Nir Barzilai, the director of the Institute for Aging Research at the Albert Einstein College of Medicine, is leading another study to examine Metformin's effects.

We are kind of testing this drug backward. Already on the market, Metformin is a prescription drug for diabetes management. That said, nobody really knows the mechanism of action of Metformin. It's not metabolized in the body. You take the medicine and when it gets excreted from the body, the molecule is still intact. But somehow it produces all these beneficial effects in the human body. We think that Metformin is promoting autophagy.

All the research points toward the possibility that Metformin could be taken to improve health span, but I'm not involved in those medical studies, I'm just focusing on the cell.

Q: What can we do to promote autophagy and slow the effects of aging?
A: That's a great question. There are lifestyle changes we could make to naturally enhance autophagy in our cells and the first one will sound very familiar: You could exercise more! Exercise is a great promoter of autophagy and I would encourage more people to work out. A second habit that seems to help is calorie restriction, like you would experience with a pattern of intermittent fasting. The logic of calorie restriction is pretty straightforward: If you deprive your cells of a constant flow of energy from food, they will try to clean up and recycle what they have — that's autophagy — and it promotes overall health.