Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/heart-matters/examining-tissue-in-transit-micrograviy-and-the-heart/12256/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Examining Tissue in Transit: Micrograviy & the Heart

Dr. Sorrentino:
Our heart undergoes changes throughout our lives, but it might go through even greater change during and after time in outer space. One recent study that explored those changes is the Cardinal Heart Study which sent 3-D engineered heart tissues to the International Space Station to study microgravity's effect on aging and weakening of heart muscle cells. So, what exactly did this study find and perhaps, more importantly, what might we learn about our own heart health here on Earth?

Welcome to *Heart Matters* on ReachMD. I'm Dr. Matt Sorrentino and joining me to discuss the Cardinal Heart Study is Orlando Chirikian, a research scientist at the University of California, Santa Barbara, who utilizes human-induced pluripotent stem cells to understand mechanisms and cardiac development. Orlando, welcome.

Mr. Chirikian:
Hello. Thanks for having me.

Dr. Sorrentino:
Let's start by setting the stage. Orlando, can you explain what has previously been known about the effects of microgravity on the heart, both at the organ level and maybe even at the cellular level?

Mr. Chirikian:
So, prior microgravity research observed some interesting changes in cardiovascular system of astronauts by monitoring cardiac activity before, during, and after space flight. For example, cardiac atrophy, or weakening of the heart muscle, is seen after space flight. There are some hypothesis of why this phenomenon comes about; however, most of these changes are poorly understood and their mechanisms are truly unknown. From the cellular aspects, Joseph Wu, one of the lead PI's on this project, performed two-dimensional studies of cardiomyocytes derived from induced pluripotent stem cells on a 2-D culturing platform that also spent some time on the ISS and came back down. A lot of the assessments spear-headed a lot of the transcriptomic differences that we hypothesized early on and this current study utilizes three-dimensional tissues to further our understanding of how these mechanisms or these phenotypes come about.

Dr. Sorrentino:
Just so I understand this little bit better, in a microgravity environment muscles do not have to work against gravity, and I presume because they're not working against a higher load, they become weakened. Is this the theory of what happens to heart muscle cells, as well, that because they are not in a gravity environment, they don't work as hard and over time they can weaken?

Mr. Chirikian:
Yes. So, the current hypothesis is that this unloading effect causes drastic changes within the function of a heart, particularly the myocardium and the ventricle now has to work less hard and produce less force, which, over time, may weaken. And these are a lot of the questions that we have on the molecular scale, and looking at the mechanism of why this happens and why this is detrimental to heart function. In addition to this physical unloading of the ventricle, we also see changes in the metabolic of the cells within the heart. So, this is something that we're also interested in looking at, too.

Dr. Sorrentino:
With that background in mind, what were some of the key questions you and your team set out to investigate in the Cardinal Heart Study?

Mr. Chirikian:

So, the Cardinal Heart team is particularly interested in characterizing one of the phenomenons observed in the microgravity, which is this cardia atrophy. Many believe that atrophy is induced by this mechanical unloading that we just stated, and the number of metabolic changes within the cells of the heart may also contribute. However, its mechanism is truly unknown. So, previous space flight studies, biologists at the Wu Lab started the process of investigating these changes, again in this two-dimensional culturing platform; however, this current study builds upon the previous work and better represents the multi-cellular tissue of the heart using the three major cell types, epithelial cells, cardio fibroblasts, and cardiomyocytes, as well as provide this three-dimensional space complete with extracellular matrix proteins. So, if these tissues were able to mimic and this heterogenous cell communication and assess changes in contractile function, calcium handling dynamics, changes to tissue size, weight, as well as characterize things like sarcomere organization, metabolism, and the transcriptome.

Dr. Sorrentino:
And if I understand how the study was done, you utilized 3-D engineered heart tissue. Can you explain the makeup of this engineered heart tissue and some of the logistical considerations that you needed to take into account so that these tissues can be brought up to the International Space Station and stored in space?

Mr. Chirikian:
Absolutely, so the engineered heart tissues are made up of human-induced pluripotent stem cells, derived cardiomyocytes, cardiac fibroblasts, and endothelial cells imbedded in a fibrogen network, ECM network. These cells are derived from these pluripotent stem cells, which have been reprogramed from healthy patient blood samples and the beauty of working with induced pluripotent stem cells is you're really able to coax them into almost any cell type of the body. Here we have differentiated these cells into cardiomyocytes, endothelial cells, and cardiac fibroblasts. These tissues, once formed, stay alive and continue to stay alive throughout the launch, the stay at the ISS, and return back to the Earth. And then these tissues will continually be investigated for functional perimeters as well as transcriptome and the metabolic activity of these tissues.

Dr. Sorrentino:
For those just tuning in, you're listening to *Heart Matters* on ReachMD. I'm Dr. Matt Sorrentino, and I'm speaking with Orlando Chirikian about the Cardinal Heart Study, which sent 3-D engineered heart tissues to the International Space Station to study the effects of microgravity on human tissue. I think we have a better understanding of how the Cardinal Heart Study was put together, but I wanna shift gears a little bit and talk about what you anticipate from the results of the study and how it could be applied to our own hearts here on Earth. What might we learn from these cells about how our hearts function down here in gravity?

Mr. Chirikian:
Interestingly enough, these phenotypes seen in space during space flight, and their return are also seen in a number of cardiovascular diseases here on Earth, whether it be atrophy, hypertrophy, or cardiac remodeling. So we aim to really understand the mechanism of action and perform large drug screens to identify potential candidates that may slow or rescue these known phenotypes to benefit those on Earth, as well as those performing space-type conditions.

Dr. Sorrentino:
So, in a sense, I get an understanding that muscles weaken when they can't work and that's sort of what we're seeing with heart cells, as well; they weaken if they can't work.

Dr. Sorrentino:
This may have some more timely considerations 'cause I understand that Space-X plans to send an all-civilian mission into orbit by the end of 2021 and although these civilians will be in space for only a few days, it really, I think, raises the question about can space tourism become a real market? How long can individuals stay in space? Can we safely have people fly to Mars without weakening their heart? What do you see is the future with having people in prolong times in space?

Mr. Chirikian:
I think, long-term space travel is inevitable. And again, our health is crucial, and specifically the health of the heart, whether it be short-term or long-term space travel, so if this is going to become a thing, which, I really hope so, and I hope that it is in my lifetime, we really need to understand the mechanism behind a lot of these phenotypes that we see with cardiac tissue coming back to Earth.

Dr. Sorrentino:
Lastly, I know that there are only so many different things that we can learn from one experiment, and there's so much more to learn about cardiac myocyte mechanics. Are you planning another trip of your 3-D myocytes up into space any time in the future?

Mr. Chirikian:
Yeah. I mean these funding programs continue to grow and I just really hope that our work here on Earth continues to inform

generations of scientists and engineers who have this dream of commercial space travel will come to reality but also we can take what we learned from these return tissues that have these phenotypes and apply them to a lot of cardiovascular diseases here on Earth. Will we have another flight in the future? Absolutely. It is part of this multi-milestone based grant that we send tissues once more up to do a larger drug screen to identify if we can slow the progression of a lot of these phenotypes or rescue them completely.

Dr. Sorrentino:
Well, I think this is a fascinating way of studying cardiac mechanics with cardiomyopathies, and with heart failure becoming such an important disease in the country, learning about how heart muscles weaken and hopefully coming up with different therapies to prevent that weakening and bring back strength to our myocytes is such an important area. I would like to thank you, Orlando, for joining me to discuss the Cardinal Heart Study and this fascinating research on 3-D engineered heart tissues in space and how it may help us here on Earth. Thanks for joining the program.

Mr. Chirikian:
Thank you for having me.

Dr. Sorrentino:
I'm Dr. Matt Sorrentino. To access this and other episodes in our series, visit ReachMD.com/HeartMatters where you can Be Part of the Knowledge. Thanks for listening.