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Insights from the Network

Macrophages, Mentors, and Mysteries of the Cosmos: An Interview with Dr. Slava Epelman, the 2024 Till & McCulloch Award Recipient

Till & McCulloch Award Q & A, Dr. Slava Epelman

This month's Insights Blog features an interview with Dr. Slava Epelman from the University Health Network, recipient of the 2024 Till & McCulloch Award in recognition of his contribution to global stem cell research through his paper published in *Nature Cardiovascular Research* entitled, Primitive macrophages induce sarcomeric maturation and functional enhancement of developing human cardiac microtissues via efferocytic pathways. Dr. Epelman recently had the opportunity to engage in a conversation with Joanna Valsamis, SCN's Director of Knowledge Mobilization. Their discussion delves into his career, the life lessons he's learned, and his forward-looking predictions for the sector.

Thanks for talking with us today and congratulations on your award! Tell us about how your career commenced. What initially attracted you to the field of cardiology, and what inspired you to pursue the specific research path you're on today?

I completed my PhD in immunology before pursuing medical school, where I developed a keen interest in cardiology. During my PhD, I studied how macrophages are activated in response to bacteria. While undergoing clinical training, I discovered emerging research indicating that these same macrophages could be activated by sterile injuries, such as heart attacks. This revelation sparked my interest in understanding how the immune system not only contributes to cardiac injury but also plays a role in healing after such events.

Can you explain your recent publication, which earned you the T&M Award? Can you give us the highlights of the paper and what impact you see the work having on future research?

Our paper focuses on cardiac microtissues containing stem cell-derived cardiomyocytes (heart muscle cells) and aims to address two key gaps in regenerative medicine. First, traditional cell therapy approaches, such as injecting stem cell-derived cardiomyocytes into scarred hearts, typically rely solely on cardiomyocytes, which is insufficient to fully restore heart function. We previously demonstrated in mice that macrophages play a crucial role in healing after injury. Building on this, our collaborative team developed stem cell-derived macrophages and showed that they enhance the function of cardiac microtissues by clearing stressed or dying cells. This suggests that incorporating macrophages into current therapies could significantly improve outcomes. Second, most research on macrophage function in healing has been conducted in mice. Our study extends this understanding to human macrophages and explores how we can program them to support regeneration, potentially impacting not only cardiac repair but also the healing processes in other organ systems.

Over the course of your career, you must have encountered all kinds of interesting situations and met many people that made an impact. If you had to pick one, what would you describe as the most significant moment in your career?

It's hard to pinpoint a single defining moment, as my journey has been shaped by a series of impactful experiences. One pivotal period was during my time at Washington University, when I was a senior post-doc and early-career cardiologist. I faced the challenging decision of choosing between several offers to establish my lab, each in a different city. This was a critical crossroads for me, and the support and guidance from my colleagues, friends, and mentors were invaluable. Their advice ultimately led me to choose Toronto, which has been the most significant inflection point in my career so far. It's a testament to the profound influence that a strong support network can have on one's professional path.

The universe is full of unknowns. What mystery do you wish you knew the answer to?

In a universe filled with unknowns, the mysteries I'm most eager to unravel all relate to the nature of the universe itself and our place within it. How did life originate on Earth? Was it merely a statistical inevitability on a planet with the right chemistry and conditions? And, if so, can we predict the emergence of life on other planets with similar characteristics? These are the questions that captivate me, as they hold the potential to redefine our understanding of existence and our role in the cosmos.

What is something you think everyone should do at least once in their lives?

That's a tough question, as everyone's journey is unique. I'd say take big risks, embrace failure, and remember that it's all part of the process. Even when things don't go as planned, you'll be okay—and you'll likely learn something invaluable along the way.

What advice would you give to medical students or trainees who are considering a career as a clinician-scientist? What skills or experiences do you think are most crucial for success in this dual role and how do you see the role of clinician-scientists evolving in the future?

A key aspect of success is surrounding yourself with mentors who have already walked the path you aspire to follow. By building a diverse network of mentors, you gain a variety of perspectives to help you stay focused and navigate the inevitable challenges of a career that is as rewarding and inspiring as it is demanding. Their collective wisdom can guide you through obstacles and keep you on course towards achieving your goals.

Innovations are always around the corner. For the sake of speculation, what are your predictions for stem cell advances in the next 5, 10, 20 years?

I believe we will soon be able to create stem cell-derived tissues that contain multiple cell types, replicating the complex cellular interactions that nature has already perfected. These multi-lineage tissues will enable us to study how different cells communicate and self-organize, significantly advancing our understanding and application of regenerative therapies. Looking ahead, I see immense potential in both cell therapy, through direct cell transfer, and the reprogramming of endogenous cells as promising future approaches that will ultimately have a profound clinical impact.