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**ANDRE TERZIC:** Well, we need to realize there is a major unmet need worldwide and this is the growing pandemic of chronic diseases. Chronic diseases such as heart failure, diabetes, cancer, pulmonary disorders, they all represent a major, major challenge for global health. Despite advances in medicine and surgery, we have not been able really to tackle these chronic conditions. So new technologies and new solutions are on the horizon and regenerative medicine is being recognized as at the very, very core of the future of health care.

**SPEAKER 1:** Cardiovascular regenerative medicine uses both natural and engineered reparative tools to restore damaged tissue and function caused by heart disease. Clinical application of regenerative biologics has emerged as a tool that can be tailored to augment existing therapeutic strategies and offer a possible cure for otherwise incurable diseases, including heart failure.

**ANDRE TERZIC:** It's a field that really aims to restore the function and structure of a failing organ. So in essence, it's a fine example of reparative medicine. And to that end, we rely on various technologies, stem cells being one example.

But as the field moves forward, we are increasingly learning what is so magic about stem cells, why they are so useful in terms of repair. For example, we are decoding what they secrete and maybe this factor that they secrete can ultimately be the regenerative cocktail of the future, the regenerative pill.

**SPEAKER 1:** The Mayo Clinic Board of Governors has established an enterprise-wide, first of its kind center for regenerative medicine, whose purpose is to generate new knowledge of disease causes and cures, and bring next generation solutions to clinical practice.

**ATTA BEHFAR:** Our research focus is really to try and find regenerative solutions, either for people with end-stage heart disease, or people that come in with an acute event like a myocardial infarction, or heart attack.

**SPEAKER 1:** What was sci-fi truly is becoming reality, with a better understanding of how to use the healing power of stem cells or other regenerative technologies.

**ANDRE TERZIC:** One of the examples of clinical trials that are being built based on Mayo Clinic technology is the example of the SECURE trial that I will describe where so-called upgraded stem cells, stem cells that are being empowered, essentially, to repair heart muscle are being provided to the patient.

The SECURE trial is the first demonstration of the feasibility and safety of cardio reparative stem cells in patients with heart failure.

**ANDRE TERZIC:** The way we approach, initiate, is essentially a traditional approach of bone marrow harvest, a technique that has been developed by our colleagues in hematology, is being used to secure a bone marrow biopsy is a very, very first step. So in step two, essentially we now take advantage of various techniques that allow us to isolate specific stem cells. You can see here a variety of cell populations in the bone marrow. But those that we pick up are those that actually cluster, which are the mesenchymal stem cells, which are the cells that will be provided to these patients.

And rather than injecting them in the way we find them in the bone marrow, there is this unique step three, where we teach these stem cells to become actually reparative stem cells. What we do is we guide these stem cells to acquire specific properties associated with lineage specification. In other words, they become cell cardiologist of sort. In other words, they learn to become future potential tissue that may promote the repair of heart muscle.

And so when these nuclei have become green, they are ready to be used for the next step, which will leverage various delivery tools that have been developed in parallel. And here, through relatively minimally invasive approach, it allows us to go into the injured myocardium after a heart attack. We map essentially the area around the heart attack and rather than inject it into the scar, we inject around the scar which is safe to inject these lineage-specified stem cells that we call the cardiopoietic stem cells.

**ATTA BEHFAR:** Cardiopoietic cells do very similar things in the embryo. They can yield atrial muscle. They can yield ventricular muscle. They can yield conductive tissue. And they can yield vascular cells. So really all of the different cells that are involved in generation of heart muscle tissue comes out of this cell, hence the term, cardiopoietic. What's unique about cardiopoietic stem cells is that they highly express cardiac transcription factors. Those are Nkx, MEF-2C, Tbx, Mesp-1, GATA4, GATA6.

**ANDRE TERZIC:** And so this is the basis of this trial called SECURE, which now is moving to the next phase of exploration. It will be called the CHART 1 and CHART 2. And the reason why the regulatory agencies have allowed this next step is, on follow-up in these initial patients that we have follow-up in terms of, let's say, their heart function, here you can see the weak heart before therapy, but after stem cell therapy the ability, the so-called ejection fraction becomes improved and the volume also becomes improved of the heart. But beyond the heart itself, the overall fitness of these patients that have received health therapy has been improved. They can walk, essentially, here a whole football field.

Mayo Clinic has a built a very unique regenerative medicine blueprint and this blueprint gives us a goal to accelerate new knowledge and move this new knowledge for the express purpose of delivering new regenerative models of care. So collectively, where regenerative medicine is going, it's in many ways transforming the horizon of health care.

**ATTA BEHFAR:** I'm just absolutely fascinated by the science. I can't shut it off. It's just constantly in my head, night and day, dreams, everything. It's just like sort of in there. You give up hobbies just to do this. So it's sort of an obsession. It's an addiction. I don't know how else to describe it. Because it worked, you know. Because with every discovery, we actually end up helping somebody.

**SPEAKER 1:** Futures restored, lives preserved, health rejuvenated. That's the promise of regenerative medicine at Mayo Clinic.

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