## Stories of Hope: Pediatric heart disease

**Mary and Tony Goulart** didn't need to look at each other. They knew without any hesitation that they would ignore the doctor's advice.

Mary was four months pregnant and a pediatric cardiologist was confirming the worst. The left side of her infant's heart was undeveloped — and that was only the first of several devastating heart defects. The child's life was as uncertain as the next breeze. "Termination is a really good option in this situation," the cardiologist said. "He's unlikely to survive."

"We were like, no! No! We were unanimous right away. There was absolutely no way!" Mary says. They chose, instead, a difficult path: three traumatic surgeries to rebuild the baby's heart, the first one shortly after birth. Joshua's first years were like living on a knife-edge as he underwent surgeries then suffered a massive stroke and a life-threatening infection. He may never speak, they were told. He may never walk.

Today, **Joshua** is 12 years old. By age 2, he was walking. By age 4, he was putting sentences together. By age 6, he was in Little League. But his medical challenges aren't over. His repaired heart may not last far beyond his teens.

"I don't know what stem cells will be able to do for him," Mary says. "He will be here as long as he's supposed to be. But the impact that stem cell research has on so many different conditions, I will do whatever I can to support anything that offers hope."

- Watch the Spotlight on Heart Disease talks

## Toward a cure: Heart disease

Deepak Srivastava is making converts.

His starting material is fibroblasts, the support cells that make up the architecture of the heart. Unlike the contracting heart muscle tissue – which usually stops dividing shortly after birth - these fibroblasts readily divide to make new versions of themselves.

Why is that important? Because once muscle tissue is lost in a heart attack the damage is almost always permanent. So Srivastava, Director of the UCSF-affiliated Gladstone Institute of Cardiovascular Disease, wants to convert those fibroblast support cells directly into new muscle tissue, repairing damage caused by a heart attack.

The work builds on knowledge gained from studying how the heart muscle cells first develop. "We have worked to unlock nature's own secrets of how it builds a heart in the embryo," he told the stem cell agency's governing Board. "We want to deploy these same secrets."

Srivastava's work has revealed that a trio of factors can turn those abundant and self-replenishing fibroblasts into contracting, fully functional muscle cells.  He has already done this in mice but the technique still has some distance to go before it's ready to be tried in people. One of the reasons is that the number of fibroblasts that actually makes the switch is small. "We would like more," Srivastava says. And after using his technique on experimentally damaged mouse hearts, those hearts were better, but not normal.

Another challenge is how to get the transformative factors inside the heart. One approach is to use disarmed viruses to ferry those factors to the fibroblasts. However, to date the U.S. Food & Drug Administration has never approved a therapy using this kind of method.

Srivastava's team is now perfecting the fibroblast conversion method in pigs, which have the advantage of being closer to humans in size. Without CIRM funding, he said, this work couldn't go forward.

"This is the Valley of Death people talk about," he said. While the National Institutes of Health funds early-stage basic science, and private equity invests at the latter end of the research to bring a treatment to market, in between the two stages there is little money available.

"We're grateful to CIRM. It's hard to get funding for this work anywhere else," he says.

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