WHAT WILL IT TAKE TO CURE SINGLE VENTRICLE HEART DISEASE?

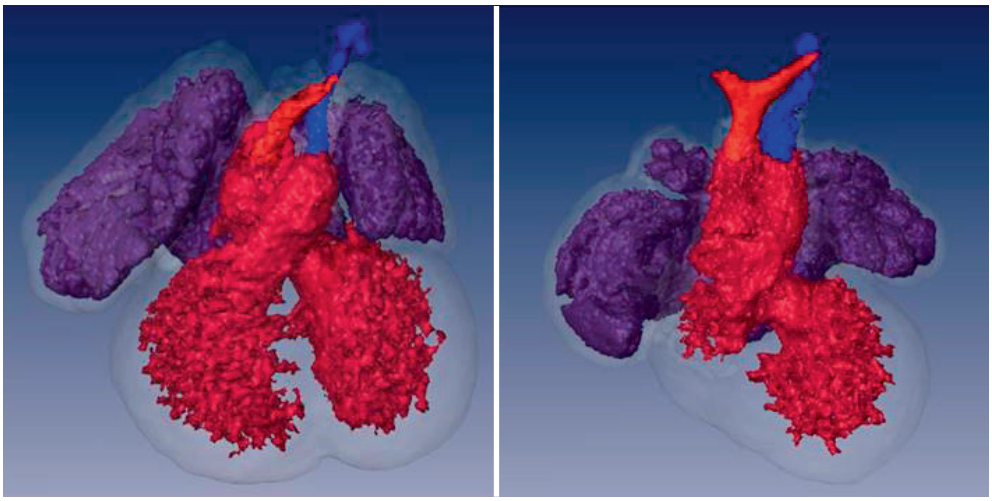
A significant basic and clinical research effort aims to develop curative treatments for this poorly understood family of DEVELOPMENTAL DISORDERS.

Babies born with otherwise-lethal single ventricle heart defects can gain decades of life from early surgical intervention, but their lives are still fraught with medical complications that significantly reduce quality and duration of life.

A healthy heart has two lower chambers, or ventricles: one pumps blood to the lungs, where it is infused with oxygen; the other delivers oxygenated blood to the rest of the body. But globally, roughly 9 in 100,000 babies is born with a structural defect in their heart that leaves only one functional ventricle[1]. "These children have chronic hypoxia, which can lead to all sorts of developmental issues," says Christopher Breuer, a paediatric surgeon at Nationwide Children's Hospital in Columbus, Ohio.

Structural heart defects can be detected during prenatal ultrasound, and many children born with single ventricle defects undergo a three-stage surgery that reroutes the circulatory system to ensure that the blood is adequately oxygenated. Breuer notes that patients who undergo this procedure can live to their forties or fifties.

But it is a risky and invasive procedure that can have long-term complications, thought to be linked to the increased venous blood pressure in the surgically altered circulatory system. The patients often experience severe organ damage or neurodevelopmental problems and some may require an organ transplant.



Takeuchi *et al*, 2005.

A healthy heart (left) has two lower ventricles, but some people are born with only one ventricle (right).

Knowledge gaps

Remarkably little is known about single ventricle heart defects, which comprise several disorders that produce a similar outcome. Kirstie Keller, vice president of programs at research funding organization Additional Ventures, says that most research to date has focused on clinical care rather than understanding biological causes and natural history. To fill this void, Additional Ventures recruited a team of experts to assemble a *Roadmap to Solving Single Ventricle Heart Disease*[2], which identifies key needs and concrete steps to address the challenges associated with single ventricle heart disease. The organization supports progress by issuing US$15–20 million in funding annually to researchers working on single ventricle heart disease and related topics.

One top priority is to understand the origins of single ventricle heart diseases. Breuer says that each form of single ventricle heart defect appears to arise from multiple genetic mutations, but adds there might also be "significant environmental factors". As part of the Roadmap, Additional Ventures is investing in whole genome sequencing of 5,000 patients to better understand the contribution of genetic factors, and will be making these data freely available to researchers.

Additional Ventures sponsors multiple annual grant programmes and has supported research on cardiovascular development, genetics, biomarkers of disease progression and development of functional cures. The organization also hosts numerous events, including an annual meeting that brings together a multidisciplinary roster of experts including scientists, engineers and clinicians to address this complex disease.

One important output of these efforts is the Cures Collaborative, a five-year programme with an annual budget of US$2 million, focused on developing tissue-engineered solutions to repair single ventricle defects. Breuer is one of nine investigators on this team, and although work is still at an early stage, he is enthusiastic about the long-term potential to develop engineered tissues that integrate seamlessly with the circulatory system. "This would enable us to go from palliative to curative treatments," he says, "so it's very exciting." ■

REFERENCES

1. Liu, Y. *et al. Int J Epidemiol* **48**(2), 455–463 (2019).
2. Keller, K. *et al.* (2020) https://www.additionalventures.org/research-roadmap

ADDITIONAL VENTURES