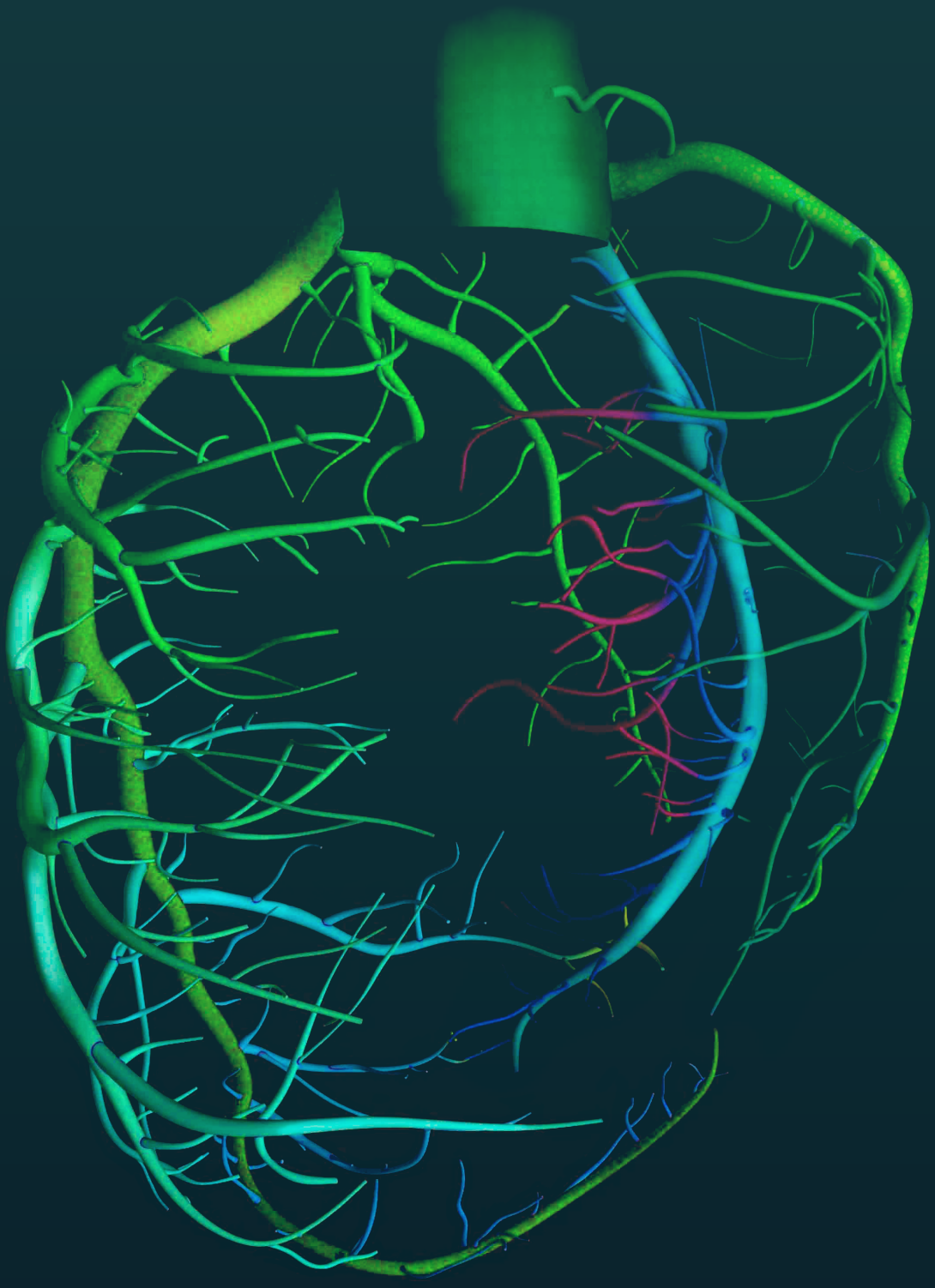
ADDITIONAL VENTURES

Enabling Discovery in Single Ventricle Research

Biomedical Research: Annual Report – July 2021 - June 2022



Front cover image: Mouse coronary anatomy, modeled in SimVascular created by the Marsden Lab at Stanford University

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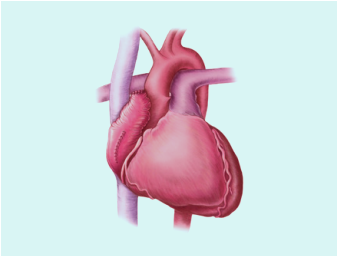

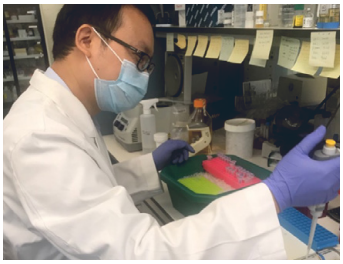

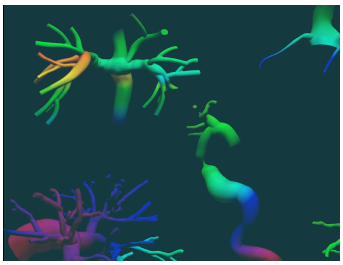

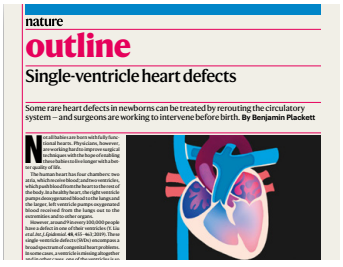

nature

outline

Single-ventricle heart defects

Some rare heart defects in newborns can be treated by rerouting the circulatory system – and surgeons are working to intervene before birth. By Benjamin Plackett

ABOUT US

A Letter from Our President

We believe that single ventricle heart disease is solvable – and with the right tools, ideas, and people, we can move towards a functional cure for our patients.

Our community of researchers has made great strides: deepening our understanding of single ventricle heart disease and identifying potential pathways to curative solutions. We are incredibly proud to be part of that progress.

We don't know where the next big breakthrough will be made – so our focus has been to create diverse programs that enable discovery through investment in people and projects.

In the past year, we expanded our grants programs to target new scientific areas critical to understanding heart development. We supported resources that capture patient history and outcomes. We developed a platform to elucidate genetic components of single ventricle heart defects. And we created new mechanisms for our scientific community to connect, collaborate, and share ideas. This Annual Report provides just a snapshot of what we have accomplished in the last year.

The single ventricle research community is **poised to make enormous leaps** in our understanding and treatment of single ventricle heart defects. The programs, projects, and people united by our mission are all critical to improving the lives of single ventricle patients and their families.

Our team is committed to removing barriers, responding to evolving needs, and incorporating burgeoning ideas to **accelerate progress with intention** so that we can find answers for single ventricle heart disease patients.

I am incredibly grateful to our network of research partners and collaborators for their work in service of our shared goal, and I am honored to continue to support this extraordinary community. I look forward to deepening our commitments to single ventricle communities and working with you all to amplify our impact in areas that need it the most.

Sincerely,

Erin Hoffmann
President and Co-Founder, Additional Ventures

Our cumulative work this year creates a launching pad to enable discovery in single ventricle research.

Image: Adapted from microscopy images of endocardial cells captured by the Srivastava Lab at the Gladstone Institutes

ABOUT US

An Overview of Single Ventricle

The human heart has four distinct chambers: two atria and two ventricles. In a healthy heart, the right ventricle pumps deoxygenated blood to the lungs and the left ventricle pumps the oxygenated blood to the rest of the body. Single ventricle hearts function differently.

What is a single ventricle heart defect?

Single ventricle hearts have just one functioning ventricle, and one ventricle that is smaller, underdeveloped, or missing a valve, resulting in functional loss of that pumping chamber.

How do we treat single ventricle heart defects?

Generally, single ventricle heart defects are treated through a **multi-staged surgical intervention** that ends in the Fontan procedure, in which the one functional ventricle pumps oxygenated blood to the body and deoxygenated blood passively returns to the lungs without a pump. **This palliative procedure is not a cure**; the Fontan circulation is correlated with long-term end-organ damage that significantly decreases patients' quality and duration of life.

What will it take to cure single ventricle?

In an emerging and complex disease area such as single ventricle, creative funding models and hands on methods are critical for progress. Nonprofit funders that act as a convener, invest in high-risk studies, and provide additional tools beyond capital are critical to unite a diverse space and catalyze rapid growth.

Through our funded work at Additional Ventures, we hope to **uncover new solutions for single ventricle** so that all patients, no matter their age, stage, or anatomy, live a long and healthy life that is free from major complications.

Here's what we know:

9 in 100,000 babies are born with a single ventricle heart defect

Single ventricle heart defects encompass a broad range of diagnoses, including:

- Double Inlet Left Ventricle
- Double Outlet Right Ventricle
- Hypoplastic Left Heart Syndrome
- Pulmonary Atresia with Intact Ventricular Septum
- Single Left Ventricle
- Tricuspid Atresia
- Unbalanced Atrioventricular Canal

Right now, there is **NO cure** for single ventricle heart defects

ABOUT US

Our Strategy

Our strategy is guided by our Research Roadmap and our Principles. It includes the following four parts:

1. **Making Targeted Investments:** We create impact-focused grant programs that respond to the evolving needs of the single ventricle field.

2. **Building Foundational Resources:** We generate comprehensive resources by integrating datasets and democratizing data to spur discovery.

3. **Supporting Team Science:** We employ creative models of integrated team science to launch new ideas forward, faster.

4. **Creating Community:** We develop platforms to enable learning, collaboration, and innovation across disciplines and institutions.

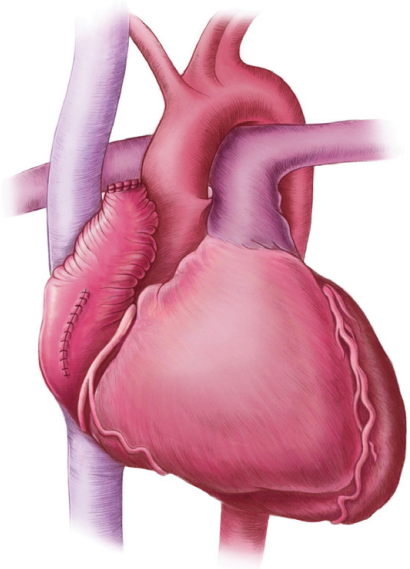

Image: Classic atriopulmonary Fontan, illustrated by Emma Scheltema, published in EMJ Cardiology 4(1)

Our Perspectives

With a scientific community poised to act and a defined roadmap for action, the single ventricle field is ready for investment. Curative solutions for single ventricle are achievable – when the right catalysts come together to build a creative environment.

Read more about our perspectives on solving single ventricle, published in the **Journal of Cardiovascular Development and Disease →**

Journal of *Cardiovascular Development and Disease*


MDPI

Journals / JCDD / Volume 9 / Issue 7 / 10.3390/jcdd9070220

Open Access Editorial

Catalysts for Change: The Role of Nonprofits in Solving Single Ventricle Heart Disease

by Kaitlin A. Davis *, Diane M. Pickles * and Kirstie E. Keller *

Additional Ventures, Palo Alto, CA 94301, USA

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J. Cardiovasc. Dev. Dis. **2022**, *9*(7), 220; https://doi.org/10.3390/jcdd9070220

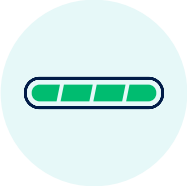
Received: 18 June 2022 / Accepted: 26 June 2022 / Published: 8 July 2022

(This article belongs to the Special Issue Hypoplastic Left Heart Syndrome: Etiology, Pathogenesis, Management and The Future)

Download Versions Notes

Our Approach

We collaborated with hundreds of investigators across disciplines to develop our **Research Roadmap** – a cohesive, central plan that communicates five key gaps critical to solving single ventricle. Our Roadmap is a launching point for exploration, uniting us all behind a common goal – and it will evolve with our community, expanding as connections are drawn between thematic areas, fields, and disciplines.



Resources

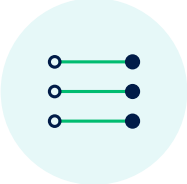
We know that **data enable discoveries**, but researchers currently lack the tools needed to ask and answer pressing questions about single ventricle. By building comprehensive, shared resources, we can springboard the field forward, faster.

Origins

Right now, **single ventricle origins are unclear**. Uncovering genetic factors related to the development of single ventricle and generating model systems to replicate the anatomical and clinical phenotypes could lay the foundation for why single ventricle occurs.

Outcomes

Origins, onsets, and trajectories of outcomes are not well defined. Linking biological factors with patient outcomes and progression from the surgical paradigm will move us closer to informed and improved care.



Care

Patients are surviving but not always thriving. With the development of evidence-based biomarkers, we can enter an era of predictive, preventative medicine and treatments to address the constellation of complications and comorbidities that these patients experience.

Cures

There is no cure for single ventricle. We must create and strengthen pathways for curative solutions that explore all avenues, including bionic, regenerative, and transplantation approaches so that our patients can live longer, healthier lives.

We're guided by four core principles that drive progress toward solving single ventricle heart disease: urgency, agility, collaboration, and impact focus.

Image: Adapted from microscopy images of cardiomyocytes cells captured by the Skylar-Scott Lab at Stanford University

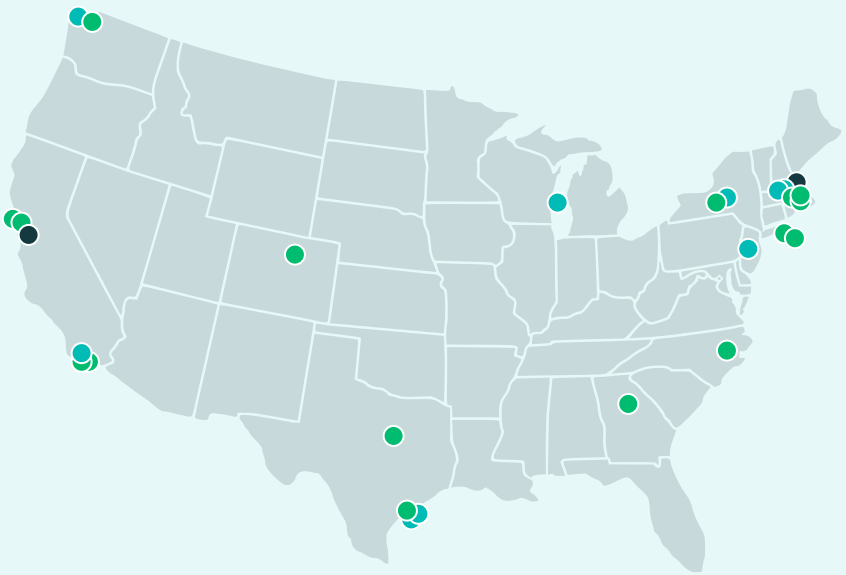
Image: Adapted from images of zebrafish larvae captured by the Mayes Lab at Seattle Children's Hospital

Targeted Investments

Funding great research begins with a focus on people and projects. We offer funding opportunities to support academic and clinical investigators to pursue topics relevant to single ventricle heart disease. Our programs aim to foster outstanding science across disciplines, fields, and career stages – and provide resources for our awardees to succeed.

Our Newly Funded Studies

In July 2021 - June 2022, we committed **$14M** in direct research support through our award programs - including support for 33 newly funded research studies.



Not Pictured:

- Edmonton, Alberta, Canada
- Oxford, England
- Paris, France
- Turin, Italy

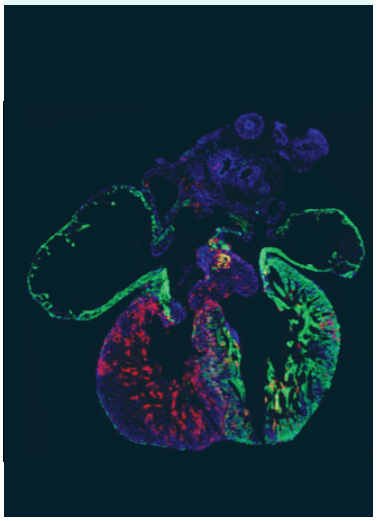
Award: Expansion Award · SVRF Award · Partner Program

TARGETED INVESTMENTS

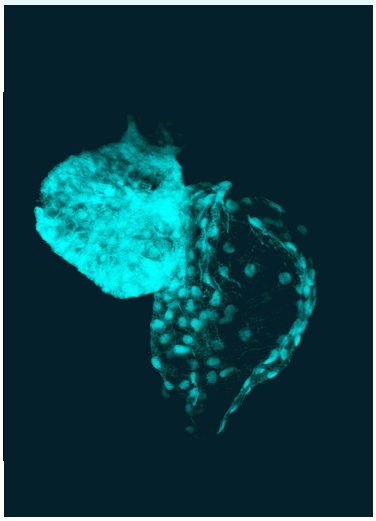
Our Grants Programs

Our grants programs are thoughtfully designed to maximize our impact. Diversity of science is required to move the needle in single ventricle, so our research award programs range in size, duration, and focus. This year, we launched our newest research award program: the Catalyst to Independence Award.

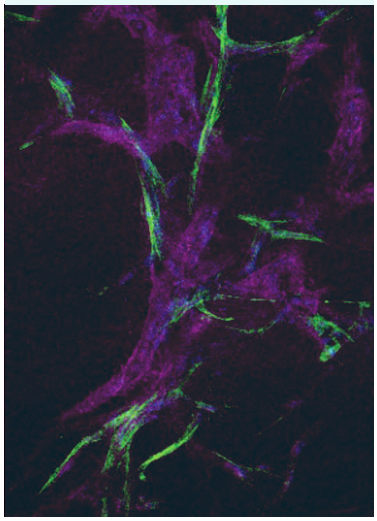
Expansion Award	Single Ventricle Research Fund	Catalyst to Independence Award
1-year Up to $50k Project-focused	3-years Up to $600k Team-focused	6-years Up to $1.2M People-focused



Developing heart, captured by the Bruneau Lab at the Gladstone Institutes



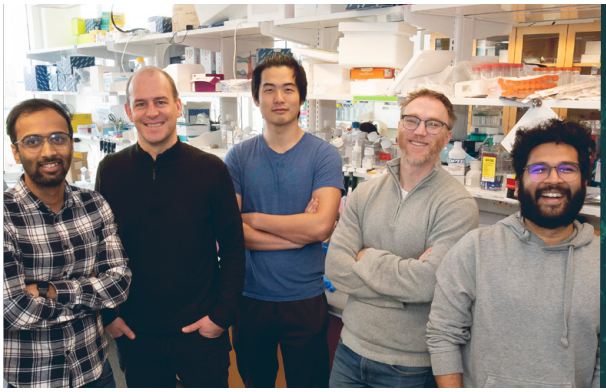
Zebrafish heart, captured by the Maves Lab at Seattle Children's Hospital



Differentiation of embryonic bodies, captured by the Skylar-Scott Lab at Stanford University

TARGETED INVESTMENTS

Expansion Award



10 Funded Projects
$492K Invested

Butcher Lab, Cornell University, Expansion Award Recipient (2022) and SVRF Recipient (2021)

Supporting Science

The Expansion Award enables teams to **add new single ventricle focused approaches and directions to their current work** by providing a one-time grant of $50,000. While the term of these awards is only 12 months, these investments will continue to offer returns in the long term – next generation equipment and technology housed in labs that are devoted to single ventricle research will outlive any single project and will continue to drive future discovery years beyond the limits of our initial support.

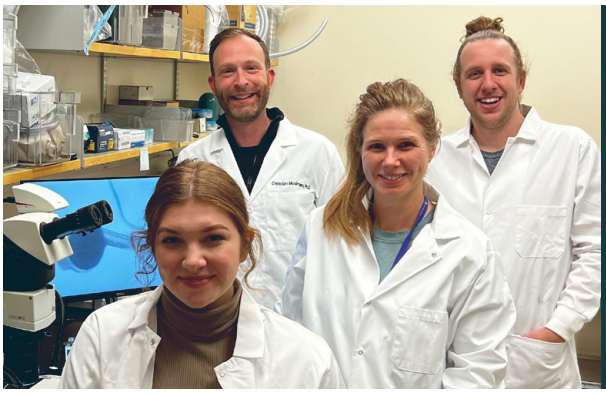
The selected proposals represent a broad spectrum of science, from microscopy to computation to molecular techniques, and demonstrate the myriad of ways in which this program can impact the trajectory of science. Among the 2022 selections, the Expansion Awards give our research teams the ability to bring new pharmacological treatments many steps closer to the clinic; test and validate brand new sequencing approaches that, for the first time, may allow researchers to assess all types of cellular RNAs at once; and, accelerate projects by up to a full year, increasing the potential impact of publications and freeing these teams up to explore their next great ideas in the single ventricle space.

"This expansion grant will allow us to purchase new equipment with advanced capabilities and software. These new capabilities will increase the rate, efficiency, quality and accuracy of the data we obtain and will further our research project positively in a faster fashion."

Muge Kuyumcu-Martinez, PhD, University of Texas Medical Branch, Expansion Award Recipient (2022) and SVRF Recipient (2021)

TARGETED INVESTMENTS

Single Ventricle Research Fund (SVRF)



18 Funded Teams
$11.8M Invested

Mosimann Lab, University of Colorado School of Medicine, Anschutz Medical Campus, SVRF Recipient (2021)

Supporting Teams

The **Single Ventricle Research Fund (SVRF)** supports bold and innovative research in single ventricle and adjacent fields. Each year, we review the needs of the field and select a topic that is poised to create an outsized impact in the single ventricle research space. This year, we designed the SVRF 2021 program to address important gaps in our understanding of the mechanisms that drive development, growth, and repair of both healthy and single ventricle hearts.

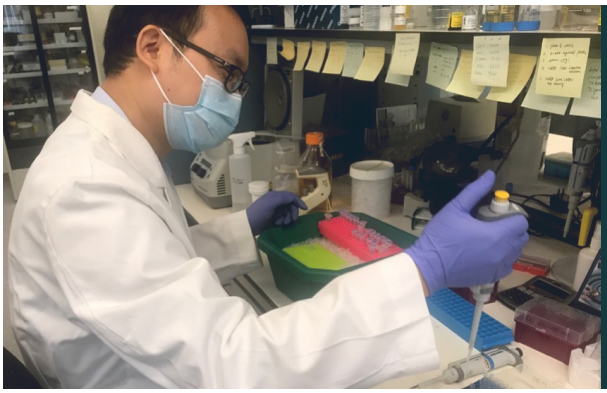
Our SVRF 2021 program focused on **identification and investigation of cardiac developmental pathways and mechanisms**. Fundamental knowledge of heart development is foundational to our understanding of single ventricle disease etiology – and may catalyze development of predictive measures of disease, risk stratification tools, preventative non-therapeutic strategies, and therapeutic interventions to correct developmental abnormalities. The awarded projects bring creative, cutting-edge basic science to the research landscape – including 10 research teams that are new to the single ventricle network.

Why fund cardiovascular development?

Fundamental knowledge about heart development is essential to our understanding of disease pathogenesis, and without a full picture of how a healthy heart develops, the causes of single ventricle heart disease remain incompletely understood. Recent scientific advancements in genomics, stem cell biology, and developmental mechanisms coupled with additional investment will move the needle towards uncovering the etiologies of this complex disease.

TARGETED INVESTMENTS

Catalyst to Independence Award



Anticipated funding: Up to 4 Investigators per cycle

Shijie Liu, PhD, Research Scientist in the Martin Lab, Texas Heart Institute

Supporting the Next Generation of Scientists

The future of the single ventricle field depends on the next generation of scientists, yet the transition from postdoc to tenure-track faculty is a hazardous bottleneck for early career researchers. In fact, less than a quarter of postdocs successfully make the leap.

That's why we created the **Catalyst to Independence Award**, an innovative new program that targets this critical window to provide a springboard for exceptional scientists to land in the single ventricle space. The Catalyst Award offers substantial financial support, community, and programming for advanced postdocs to jumpstart their own labs, catalyzing their careers and efforts to solve the biggest questions in single ventricle heart disease. The first cycle of this program launched in February 2022, with anticipated funding announcements in October 2022.

"Novel programs like [the Catalyst to Independence Award] will be a gamechanger for the investigator, the field, and ultimately the patients and families affected by single ventricle heart disease."
– **from 'Paying it forward: bringing innovation to academic funding' feature in ecrLife.** →

Catalyst to Independence Advisory Board

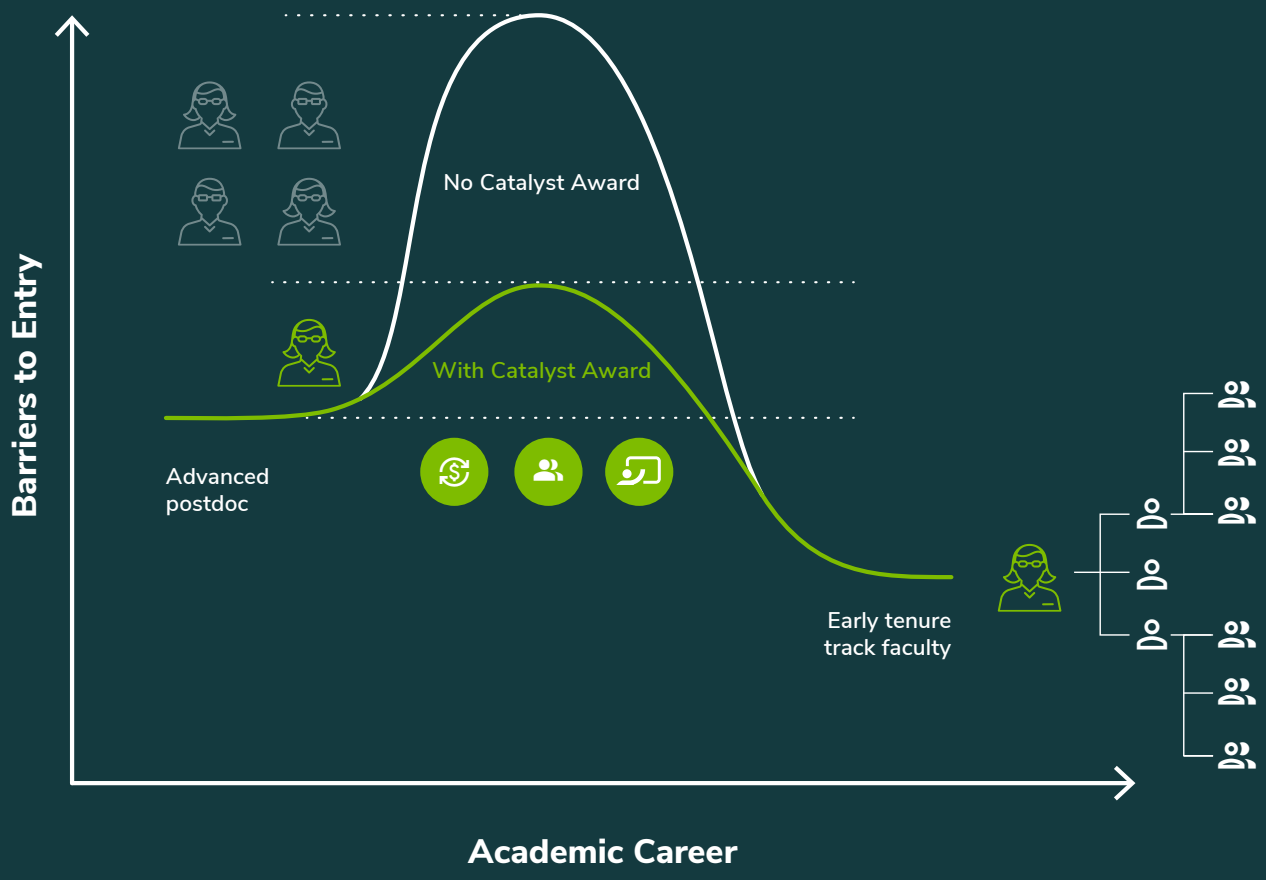
Nadine Kasparian, PhD
Professor, University of Cincinnati, Department of Pediatrics Director, Cincinnati Children's Center for Heart Disease and Mental Health, Heart Institute and the Division of Behavioral Medicine & Clinical Psychology

Oded Regev, PhD
Professor, New York University, Courant Institute of Mathematical Sciences, Department of Computer Science

Kyle Loh, PhD
Assistant Professor & The Anthony DiGenova Endowed Faculty Scholar, Stanford University, Department of Developmental Biology and Institute for Stem Cell Biology & Regenerative Medicine

TARGETED INVESTMENTS

Catalyzing the Pathway to Independence



Lowering Barriers to Entry for New Principal Investigators

Using a multi-pronged approach, the Catalyst to Independence Award provides generous financial and programmatic support to bolster the scientific and professional development of our awardees – truly putting the investigator first. Catalyst Award recipients will receive **up to $1.2M over 6 years** with funds including stipend, annual research expenses, salary support for technical staff, and a supplement that can be used for health or family care.

These unique layers of support are designed to equip our Catalyst Awardees with skills, tools, and resources critical to their success as leaders of outstanding independent research programs – effectively **lowering the barriers to entry for new tenure track faculty**, and priming our awardees for long and fruitful careers dedicated to advancing our knowledge of single ventricle science and medicine.

TARGETED INVESTMENTS

Partner Programs

In tandem with our Additional Ventures-led Grants Programs, we partnered with other organizations to support research within and adjacent to the single ventricle space – bolstering a robust and diverse research ecosystem in support of our mission.

Enduring Hearts

Enduring Hearts' mission is to fund research that increases the quality and longevity of life for pediatric heart transplant recipients. Together, we launched a funding opportunity to stimulate research focused on identifying, reducing, and eliminating pre- and post-transplant risk factors that affect outcomes of children born with complex congenital heart disease, including single ventricle heart defects.

$225K Invested in July 2021 - June 2022

Life Sciences Research Foundation

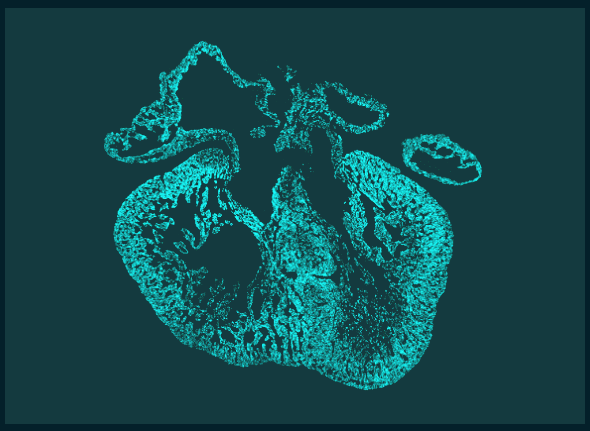
The Life Sciences Research Foundation (LSRF) supports exceptional postdoctoral researchers in all areas of basic life sciences discovery. We've partnered with the LSRF to extend our support to outstanding individuals that are developing tools and analyses that change the way we think about and incorporate basic science in our understanding of single ventricle biology.

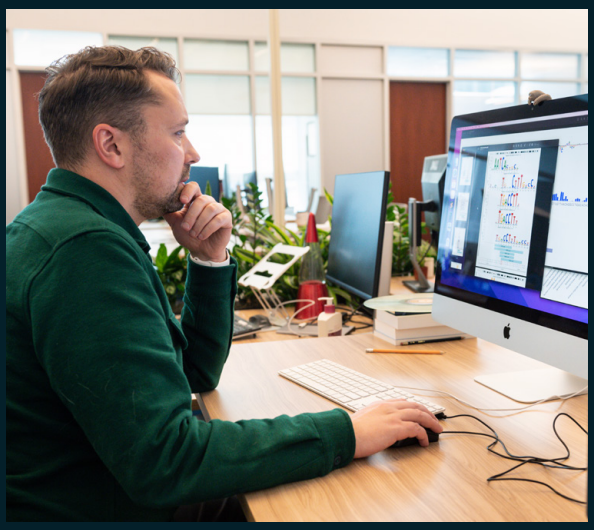
$210K Invested in July 2021 - June 2022

Additional Ventures Innovation Funds

In collaboration with five outstanding research institutions, we launched the Additional Ventures Innovation Funds in 2020 to seed high-risk projects that yield outsized, long-term impact in single ventricle research. While the partner institutions work together and share knowledge, each manages their funds independently – leveraging unique knowledge, infrastructure, and talent to accelerate discovery.

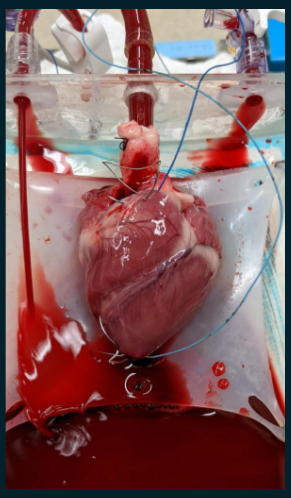
$1.2M Invested in July 2021 - June 2022

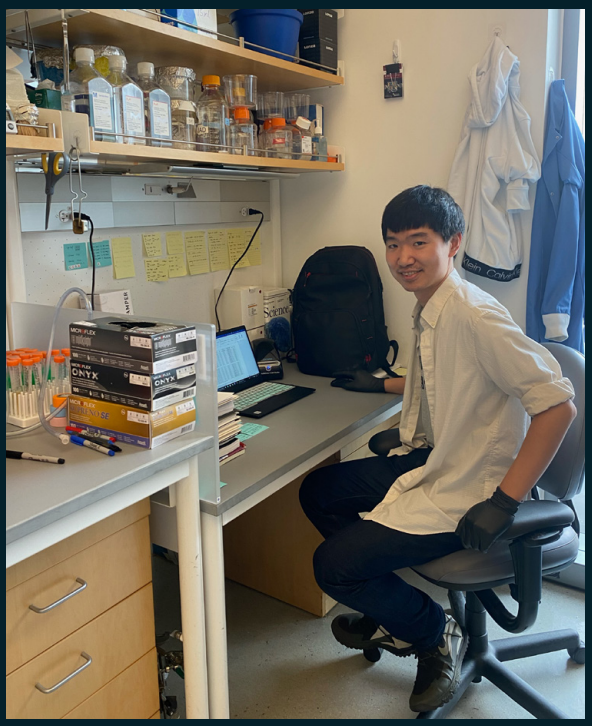


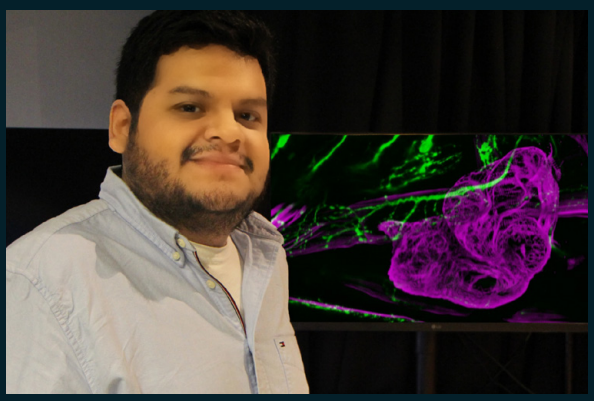


3 Funded Programs

$1.6M Invested







Images provided by investigators funded through our Partner Programs. Clockwise from top left: Developing heart imaged by the Bruneau Lab at the Gladstone Institutes; Sean Whalen, PhD at the Gladstone Institutes (photo by Michael Short); Perfusion experiments by Jennifer Conway, MD and Darren Freed, MD, PhD at University of Alberta and Stollery Children's Hospital; Luis Hernandez-Nunez, PhD at Harvard University, Kai Chen, PhD at University of California, Berkeley; Maureen Pittman, PhD and Katie Pollard, PhD at the Gladstone Institutes (photo by Michael Short)

Building Foundational Resources

Foundational resources are required to ask and answer the most pressing questions in single ventricle science and care.

In addition to the investments we make in individual researchers and research initiatives, we also devote resources to develop data infrastructure required to fuel scientific and medical research. We lead and support efforts to build critically important datasets and develop integrated, comprehensive, and open-access foundational resources available to the entire single ventricle research enterprise.

"Building the infrastructures and registries that support essential research is challenging but thinking about the patient and family perspective when establishing them is even harder. I strongly believe Additional Ventures' added efforts on this front are refreshing for the community and that they will make a difference in the way the research is done."

Arman Aksoy, PhD, Patient and Family Advisory Board Member

BUILDING FOUNDATIONAL RESOURCES

Infrastructure Development – Patient Registries

In an emerging and complex disease area that includes a range of structural defects and patient outcomes, our field must work together to develop integrated, robust datasets that, together, can provide a launching pad to understand single ventricle.

ACTION (Advanced Cardiac Therapies Improving Outcomes Network)

Housed at Cincinnati Children's Hospital, ACTION is a learning network and registry focused on improving care and outcomes for patients with heart failure, including those with Fontan circulation. Additional Ventures is funding initiatives to improve the timely referral of patients to transplant centers, stabilize the medical conditions of listed patients, and improve donor to recipient matching.

58 Clinical Sites
1,185 Patients Enrolled

FORCE (Fontan Outcomes Registry Using CMR Examinations)

Led by Boston Children's Hospital, FORCE is devoted to improving Fontan patient outcomes by using the power of imaging data and machine learning to identify which patients will do well and which will need more help as they grow older. Additional Ventures is providing startup funding for this innovative registry, which launched in 2021.

29 Participating Centers
2,725 Patients Enrolled

FON (Fontan Outcomes Network)

Coordinated by Cincinnati Children's Hospital, FON is a learning network and longitudinal registry for all single ventricle patients and those with Fontan circulation focused on improving physical health and functioning, neurodevelopmental outcomes, and mental health and resilience. Additional Ventures is providing funding to build the registry and learning network, which launched in 2022, and plans to integrate clinical data from FON with genomic data in Project Singular.

31 Participating Centers
Projected Enrollment: 10,000 patients in 3 years

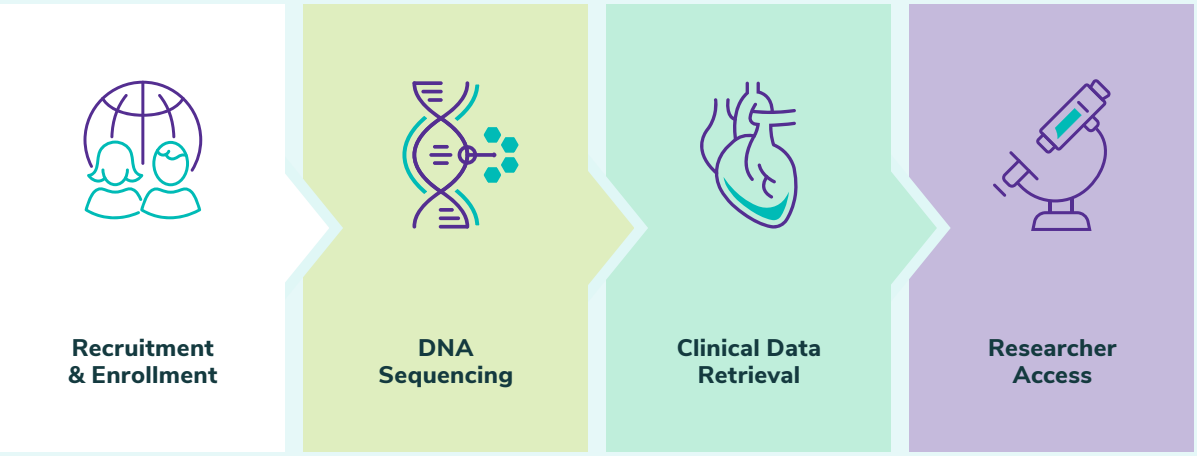
BUILDING FOUNDATIONAL RESOURCES

Project Singular

Project Singular is a large-scale genome sequencing initiative focused on **fueling research to discover the genetic causes of single ventricle heart disease** and genomic contributors to the many related comorbidities. Launching in 2023, Project Singular will work with other registries in the single ventricle space to share and integrate additional phenotypic data from patients to increase the power of the dataset.

PROJECT SINGULAR | Hope Through Research For Single Ventricle Hearts

Project Singular Workflow



Project Singular will use a direct-to-patient model with online consent and at-home DNA collection – lowering barriers to participation and increasing accessibility. Additionally, Project Singular will collect medical histories and detailed cardiac anatomies for patients and make deidentified phenotypic and genotypic data available for free to all qualified researchers – **fueling not just one research study, but many**.

BUILDING FOUNDATIONAL RESOURCES

Project Singular: Developing a Comprehensive Dataset

We are optimistic that this one-of-a-kind dataset will reflect the full picture of single ventricle heart defects, helping us understand why they develop and providing a clearer path toward a functional cure.

Involving patient and family voices

Project Singular can only be successful with patients and families as our partners. To honor our participants' generosity, we are directly engaging with patients and families as well as their trusted clinicians to develop patient-facing educational resources about our research and study progress.

Optimizing our workflow

We're committed to creating a platform that is accessible and effective – and puts the needs of participating patients and families first. This year, we piloted the Project Singular workflow, then implemented design and process changes to **improve accessibility** and overcome potential bottlenecks in our processes.

Projected Enrollment: 5,000+ single ventricle patients and their immediate family members

Democratizing data

We do not know where the greatest discoveries will be made. So we will allow **all qualified researchers** – within single ventricle and beyond - to utilize the deidentified Project Singular dataset free of charge. Moreover, researchers will be encouraged to make their codes and algorithms publicly available in Terra.bio, fueling additional research from other groups.

Supporting research

In addition to building the dataset, we are devoting additional resources to **drive research** utilizing the dataset. We will facilitate a cloud compute credit program to provide start-up funding for researchers to begin analyzing the data, organize data hackathons for early career investigators to compete as they investigate specific questions of interest, and initiate an RFP grant program that will provide funding for teams to leverage Project Singular data to conduct research.

Image: Vascular Model Repository, created by the Marsden Lab at Stanford University

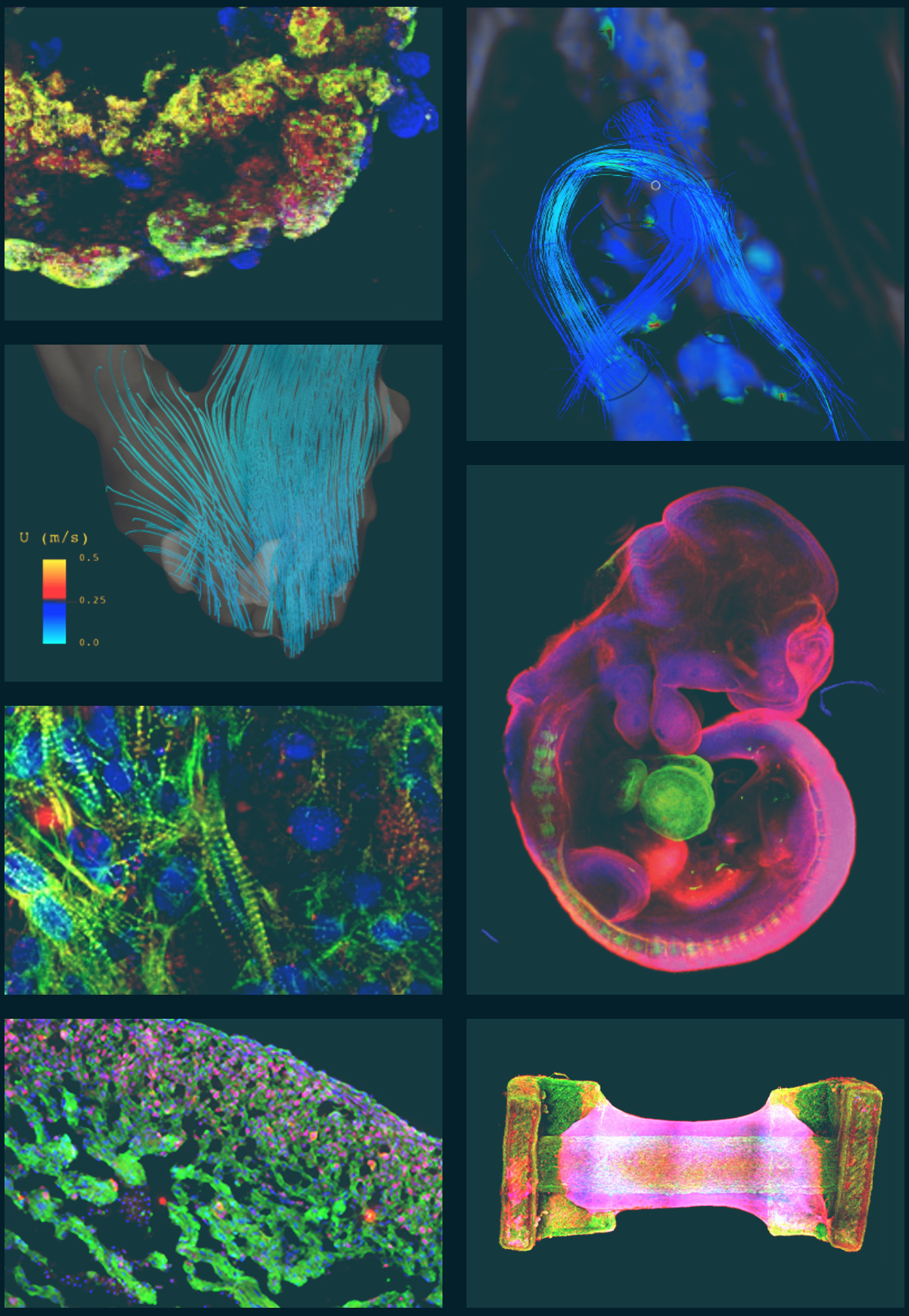
Supporting Team Science

The science of single ventricle is complex – no single scientist or lab can solve the multidimensional challenges that exist.

We recognize that funding individual efforts is not always sufficient to solve a complex disease like single ventricle, where there is a multiplicity of presentations and outcomes, and a lack of understanding of biological and clinical mechanisms.

We believe that creative models of integrated team science can launch new ideas forward, faster – an approach that is hands-on, coordinated, and laser-focused.

We currently support a collaborative network of investigators – called the Cures Collaborative – who are focused on finding a functional cure for single ventricle patients.



Images provided by members of the Cures Collaborative. Clockwise from top left: Perfusable SWIFT cardiac tissue; Cardiac output in Fontan sheep models; Whole mount immunofluorescence of mouse embryo; Confocal image of 3D printed heart tube; Cardiomyocytes in a mouse heart; Cardiomyocytes on heart tube surface; Fluid-structure interaction simulation

SUPPORTING TEAM SCIENCE

Cures Collaborative

We believe that supporting innovative team science is central to solving single ventricle. In 2021, we launched the Cures Collaborative as a model of integrated multidisciplinary research to develop a curative solution to single ventricle heart disease.

Our Mission

We hope to move from palliative approaches to a curative solution, eliminating the Fontan physiology by developing an external self-powered pump made of human cells.

Our Approach

Our group is split into two functional teams that approach our goal from either a top down or bottom up approach. All the research is intertwined, interdependent, and cohesive – it's team science at its best.

Our Team

Breuer Lab
Davis Lab
Dubois Lab
Feinberg Lab
Humphrey Lab
Marsden Lab
Rentschler Lab
Skylar-Scott Lab

With operational support by T-Y Hsia

Where are we now?

Our team is in their second year, with a lamb model of the Fontan circulation in refinement, small cellularized biotubes under construction, and novel approaches to scale cell production in development.

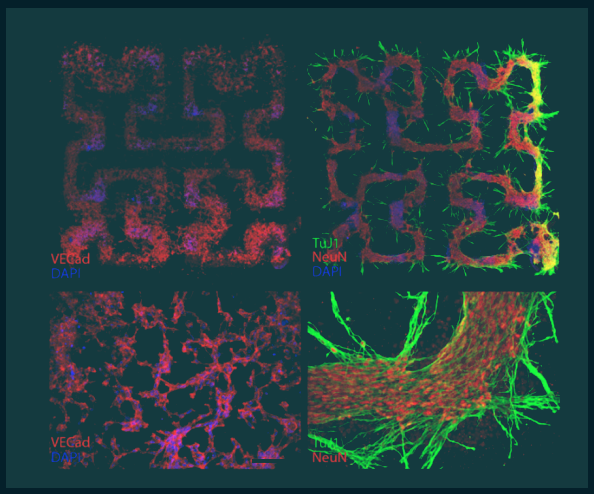
New Member: Nicole Dubois, PhD

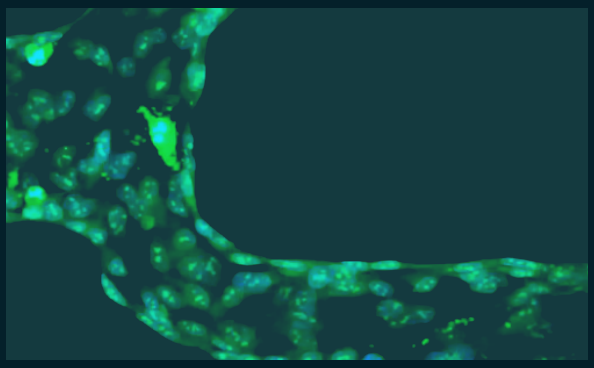
Dr. Dubois joins the Cures Collaborative as an investigator from the Icahn School of Medicine at Mount Sinai. She is focused on developing and testing critical cells types that support the function of the proposed pulsatile conduit.

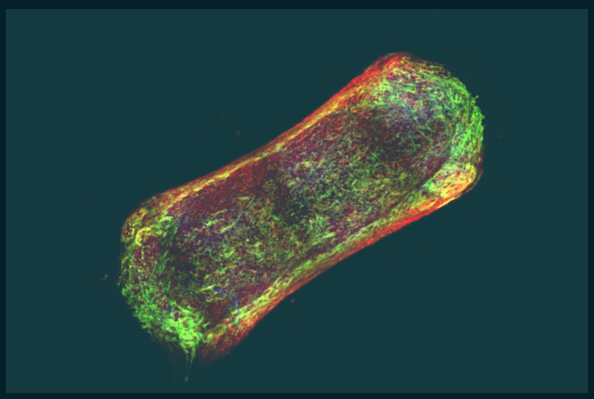
SUPPORTING TEAM SCIENCE

Cures Collaborative Retreat

In 2021, we convened the first annual retreat for members of the Cures Collaborative community – including PIs, postdocs, students, and support staff – to share research updates, identify gaps and challenges, refine study design, and develop future directions.

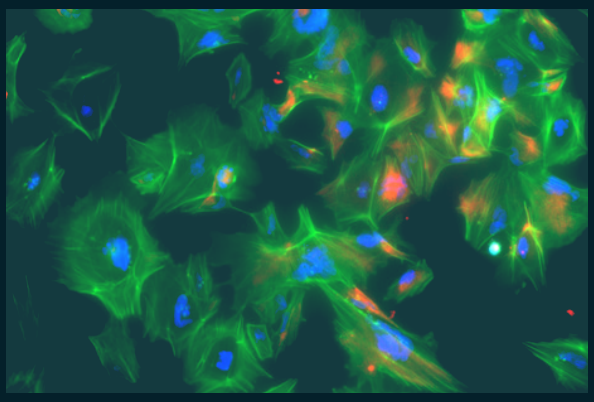






8 Labs

50+ Trainees



Images provided by members of the Cures Collaborative. Clockwise from top left: Differentiating iPSCs post 3D bioprinting; Endothelial cell-lining of patterned microchannels; Dr. Chris Breuer at the Cures Collaborative Retreat; Dr. Kuo-Chan Weng at the Cures Collaborative Retreat; Differentiated fibroblasts; FRESH 3D bioprinted heart tube

Image: Adapted from microscopy images of desmoplakin localization in mutant cardiomyocytes captured by the Feinberg Lab at Carnegie Melon University

Creating Community

It's clear that cross-cutting multidisciplinary research efforts are essential drivers for progress.

In our second full year, we worked to **expand our network** of investigators by engaging with researchers within and adjacent to the single ventricle field and **aligning these multidisciplinary investigators** around a common goal: improving our understanding and treatment of single ventricle heart disease.

Breaking down silos among single ventricle-related fields is critical to achieving this goal. That's why we developed platforms for our investigators to share knowledge, identify challenges, and exchange ideas – and we've partnered with other organizations to amplify our reach and bolster a united scientific community.

CREATING COMMUNITY

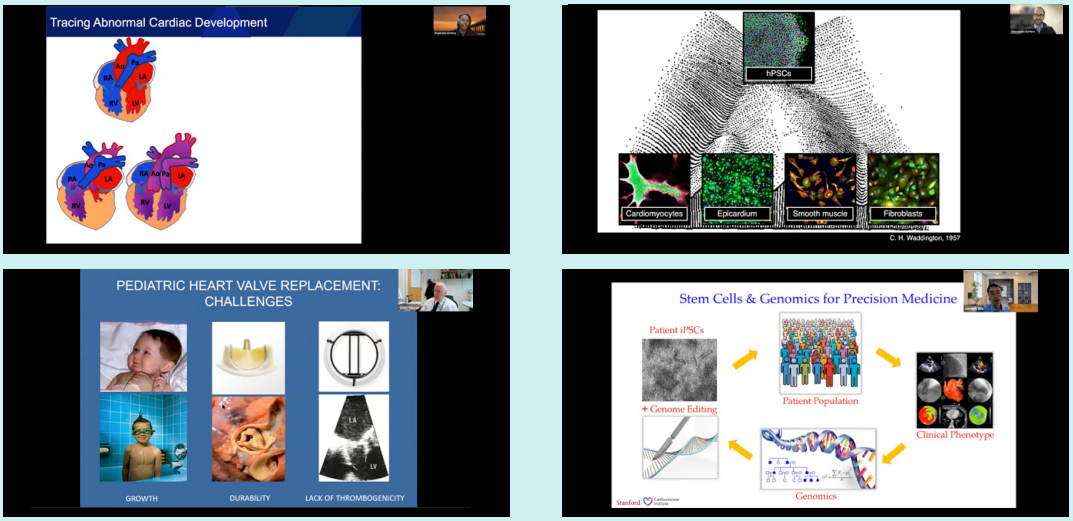
Speaker Series – Connecting Our Community

Back to Basics: Pioneers in Cardiovascular Science

Our multi-part virtual seminar series tackled diverse topics **through the lens of our investigators**. Each 4-week miniseries intersected basic, translational, computational, and clinical science – and connected the dots between multidisciplinary investigators using different approaches to achieve a similar goal, OR similar approaches with different goals.

In the past year, we heard from researchers using stem cells for precision medicine, disease modeling, and tissue engineering; investigators using computational models to predict growth and remodeling or structure-function relationships; and scientists leveraging machine learning to delineate genetic origins of disease or biomarkers related to disease outcomes.

Up to 115 Attendees per seminar



Clockwise from top left: Stephanie Lindsey, PhD, Alessandro Bertero, PhD, Joseph Wu, MD, PhD, John Mayer, MD

Spotlighting Early Career Investigators

The final session of each miniseries showcased work from selected early career investigators in Lightning Round presentation competitions. Meeting attendees voted to select two Outstanding Research Presentation Award recipients who received award packages to attend and present at the Single Ventricle Investigator Meeting in October 2022.

Our selected awardees highlight important topic areas across single ventricle science including heart morphogenesis, gene and transcriptional regulatory networks, and tissue engineering – bringing creative tools, workflows, and test platforms to the research landscape.

CREATING COMMUNITY

Strategic Sponsorships – Amplifying Our Message

In conjunction with our Additional Ventures-led programs, we engaged with partner organizations to in support of our mission to expand and sustain the single ventricle research community.

Weinstein Cardiovascular Development and Regeneration Conference

Weinstein Conferences are a mainstay in the cardiovascular development research community, making the organization a perfect partner in the space. This year, we brought single ventricle research to the forefront of Weinstein 2022 through sponsorship of single ventricle-specific programming and 30+ awards for early career investigators.

Cardiology 2022: CHOP Pediatric Cardiology Conference

This premier event in pediatric and congenital heart care brings together leaders in the space. To reach this important audience, we sponsored an information fair highlighting two game-changing innovations in the single ventricle space: Project Singular and Fontan Outcomes Network.

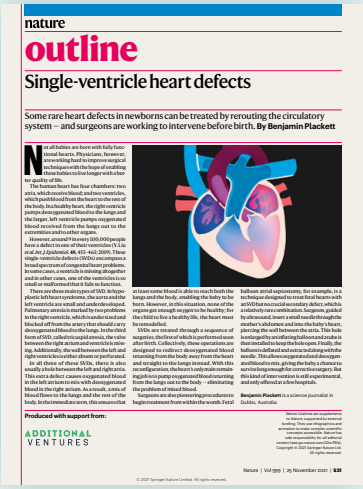
Academic Impressions

New this year, we partnered with Academic Impressions to provide opportunities for professional development, both virtually and in person. Career coaches hosted workshops and seminars tailored to our community – and covered topics like networking, impostor syndrome, leadership, and culture building to provide tools for success and create a community of practice.

CREATING COMMUNITY

Sparking Interest in Single Ventricle Research

We believe that more work and more focus is required to solve single ventricle heart disease, and the editors at Nature agreed! We provided financial support for Nature to produce a series of articles outlining the complexities of single ventricle anatomies and the staged surgical palliation to remodel the heart.


nature

outline

Single-ventricle heart defects

Some rare heart defects in newborns can be treated by rerouting the circulatory system – and surgeons are working to intervene before birth. By Benjamin Plackett

Produced with support from:

ADDITIONAL VENTURES

Nature Outline: Single ventricle heart defects

Written by Benjamin Plackett | Infographic by Alisdair Macdonald

Produced with support from Additional Ventures

Read the full collection →

Part I: The surgical solution to congenital heart defects →

A series of delicate operations can fix the damage and extend the lives of children with single ventricle physiology. 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.

Part II: How to repair a baby's broken heart →

The anatomy of each single ventricle defect differs, but they all result in a mix of oxygenated and deoxygenated blood being pumped to the body and lungs. This means that vital organs don't get enough oxygen. For the child to live a healthy life, the heart must be remodeled.

Part III: Video: Babies with misshapen hearts →

Babies born with one small or malformed ventricle can be treated with a series of surgeries, but new techniques could allow doctors to begin treatment from within the womb.

Part IV: What will it take to cure single ventricle heart disease? →

Remarkably little is known about single ventricle heart defects, which comprise several disorders that produce a similar outcome. A significant basic and clinical research effort aims to develop curative treatments for this poorly understood family of developmental disorders.

Progress

Image: Adapted from heatmap gene expression data from the Humphrey Lab at Yale University

This was a year of tremendous growth for our team and the single ventricle research community. By creating new programs and expanding on core initiatives, we've bolstered our efforts to engage, support, and connect the single ventricle research space – ultimately building a launching pad for enabling discovery in single ventricle research. Now, we're poised for outsized impact in service of our mission: to improve understanding, outcome, and treatment of single ventricle heart defects.

"I am hopeful that as so many work to gain a better understanding of the issues commonly (and not so commonly) seen with single ventricle heart disease, we will be able to better help all affected by single ventricle disease. I dream of the day they can live healthier lives filled with more quality than ever thought to be possible."

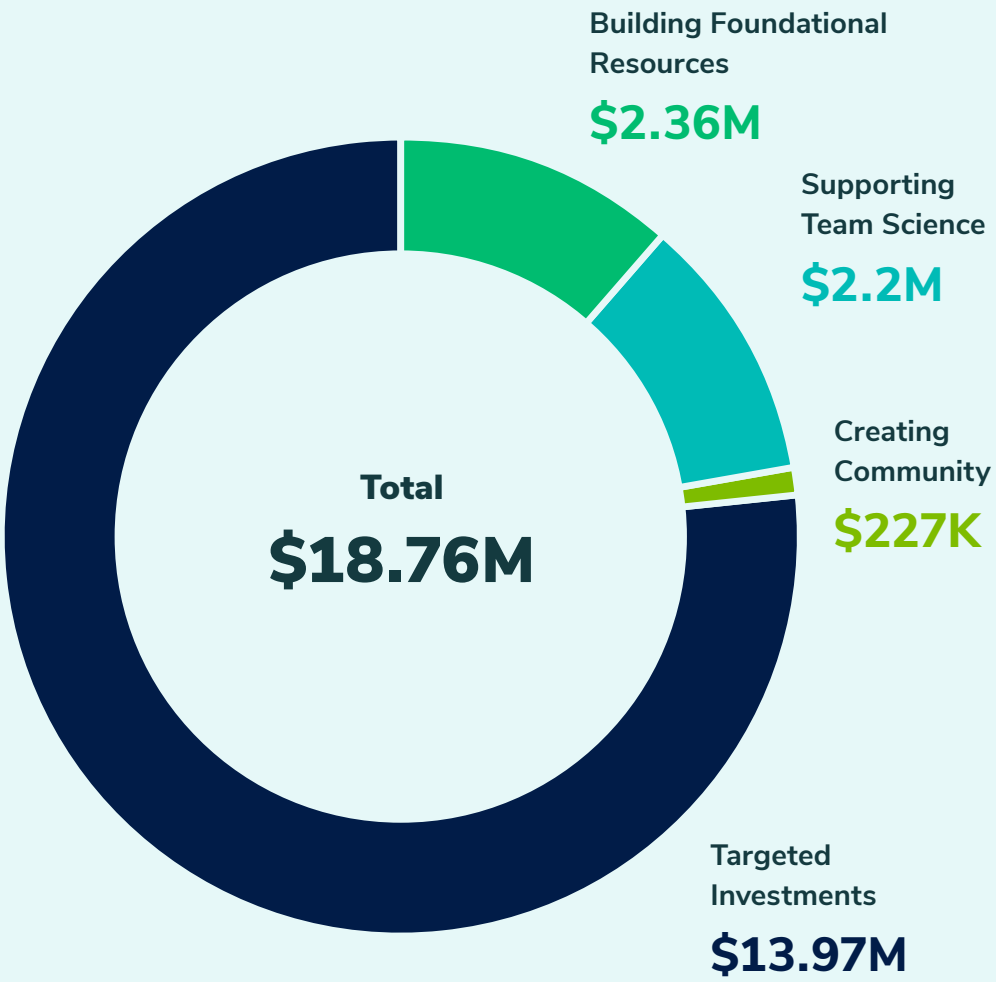
Karissa, Mother to a Single Ventricle Daughter

PROGRESS

Impact by the Numbers

Through coordinated interdisciplinary work, dynamic teaming, and flexible funding, **we can illuminate a functional cure for single ventricle heart defects.** In the past year, we committed over **$18.76M in funding** for research and infrastructure development, all guided by our strategic pillars.

Investments In Our Research Portfolio



PROGRESS

Roadmap Progress: By-the-Numbers

We use our Research Roadmap to strategically guide our investments. In 2021, we focused our annual SVRF program on cardiac development – but we take a balanced approach to seed research and development across our portfolio and bring our scientific community closer to finding a functional cure for single ventricle.

	July 2021 - June 2022	Cumulative Spend
	44 Studies Funded **$18.5M** Invested	**107** Studies Funded **$42M** Invested since 2020
Resources	**$2.3M** 3 Awards	**$5.3M** 9 Awards
Origins	**$7.9M** 18 Awards	**$10.9M** 30 Awards
Outcomes	**$5.9M** 12 Awards	**$13.9M** 32 Awards
Care	**$0*** 0 Awards	**$5M** 9 Awards
Cures	**$2.4M** 11 Awards	**$6.9M** 27 Awards

* In 2020, our annual SVRF program was focused on non-invasive interventions and biomarkers related to single ventricle outcomes, including clinical sequelae.

PROGRESS

The Additional Ventures Single Ventricle Team

Erin Hoffmann
President and Co-Founder, Additional Ventures

Kirstie Keller, PhD
Vice President of Programs

Kaitlin Davis, PhD
Senior Program Manager, Research and Grants

Diane Pickles
Program Director, Project Singular

Courtney Steger, PhD
Program Officer, Scientific and Community Engagement

Taylor MacLean
Program Manager, Project Singular

Elizabeth Ewen, PhD
Senior Program Manager, Project Singular

Hyunsoo Kim, PhD
Program Officer, Research and Grants

Patient and Family Advisory Board

With an unwavering commitment to improve the lives of single ventricle patients and their families, we recognize the importance of directly engaging individuals most impacted by the disease. In 2022, we convened our Patient and Family Advisory Board to provide critique, input, and guidance on our research priorities and directions, messaging, and communication strategies across initiatives.

B. Arman Aksoy, PhD
Father to a Single Ventricle Daughter

Computational Biologist

Jameson Rich
Post-Fontan Single Ventricle, Bi-Ventricular Repair

Writer and Filmmaker

Tawanna Williams, CPC
Mother to a Post-Heart Transplant Single Ventricle Daughter

Owner/Lead DEI Consultant, Race Equity Solutions, Podcast Creator/ Host, Broken Open

Taylor Houlihan
Single Ventricle Fontan Patient

3rd Year Medical Student

PROGRESS

Scientific Advisory Board

Our Scientific Advisory Board serves to provide scientific recommendations and strategic oversight to inform our decision-making processes. These members have a wide array of expertise within the single ventricle scientific and clinical community, creating a prolific sounding board for driving meaningful progress in single ventricle research.

Christopher K. Breuer, MD

Director of the Center for Regenerative Medicine and Endowed Chair in Surgical Research, Nationwide Children's Hospital

Director of Tissue Engineering, The Ohio State University

Rachael Cordina, MD, PhD

Clinical Academic Cardiologist, University of Sydney and Royal Prince Alfred Hospital

Clinical Senior Lecturer, University of Sydney

Anthony B. Firulli, PhD

Endowed Professor of Pediatrics, Indiana University School of Medicine

Tain-Yen (T-Y) Hsia, MD

Professor of Surgery, University College London

Professor of Surgery, University of Central Florida

Pediatric Cardiac Surgeon, Arnold Palmer Hospital for Children

Alison Marsden, PhD

Professor of Pediatrics – Cardiology and Bioengineering, Stanford University

Jane Newburger, MD, MPH

Commonwealth Professor of Pediatrics, Harvard Medical School

Associate Cardiologist in Chief for Academic Affairs, Boston Children's Hospital

Anthony Philippakis, MD, PhD

Chief Data Officer, Institute Scientist, Broad Institute of MIT and Harvard

David Rosenthal, MD

Professor, Pediatric Cardiology

Director, Pediatric Heart Failure and Transplantation, Stanford University School of Medicine and Lucile Salter Packard Children's Hospital

Deepak Srivastava, MD

President, Gladstone Institutes

Professor, University of California, San Francisco

Our relentless optimism and dedication to patients and families continue to power our quest toward a functional cure for single ventricle heart defects. We've made so much progress already – and we're just getting started.

Erin Hoffmann, President and Co-Founder, Additional Ventures

Photo 1: Elijah, 2 years old, HLHS; Photo 2: Gloria, 18 years old, HLHS; Photo 3: Zoey, 8 months old, Tricuspid Atresia, hypoplastic right heart

ADDITIONAL
VENTURES