MSCRF

MARYLAND

Stem Cell Research Fund

ANNUAL REPORT

2025

MSCRF
Maryland Stem Cell Research Fund

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About Us

The Maryland Stem Cell Research Fund (MSCRF) is focused on identifying and fostering cutting-edge research and innovation in the field of regenerative medicine in Maryland.

Our Accelerating Cures initiative comprises programs that help transition human stem cell-based technologies from the bench to the bedside as well as mechanisms to build and grow stem cell companies in Maryland.

MSCRF has supported over 700 projects to accelerate stem cell-based research, commercialization, and cures, in addition to building a collaborative stem cell community in our region. Learn more about us at **www.mscrf.org**.

Our Mission

Fund new medical strategies for the prevention, diagnosis, treatment and cure of human diseases, injuries and conditions through human stem cells.

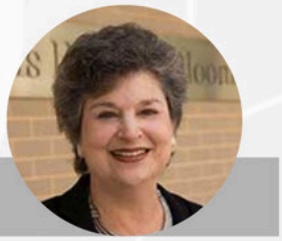
We strive to improve human health by advancing innovative cell-based research, treatments and cures to benefit patients with unmet medical needs.

Chair

Rachel Brewster, Ph.D.
Appointed by the
University System of Maryland

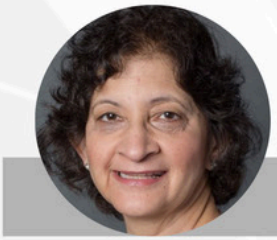
Vice Chair

Scott Bailey, Ph.D.
Appointed by
Johns Hopkins University



Margaret Conn Himelfarb, MPH
Appointed by the Governor

Rev. Christopher Dreisbach, Ph.D.
Appointed by the Governor



Mamta Gautam-Basak, Ph.D.
Appointed by the Governor

Diane Hoffmann, MS, J.D.
Appointed by the
University System of Maryland

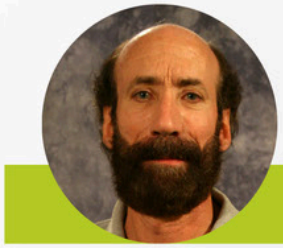
David Mosser, Ph.D.
Appointed by the
University System of Maryland

Barbara Nsiah, Ph.D.
Appointed by the
President of the Senate

Linda Powers, J.D.
Appointed by the
President of the Senate

Alan Regenberg, MBE
Appointed by
Johns Hopkins University

Rabbi Avram Reisner, Ph.D.
Appointed by the Governor



Ira Schwartz, Esq.
Attorney General's Designee

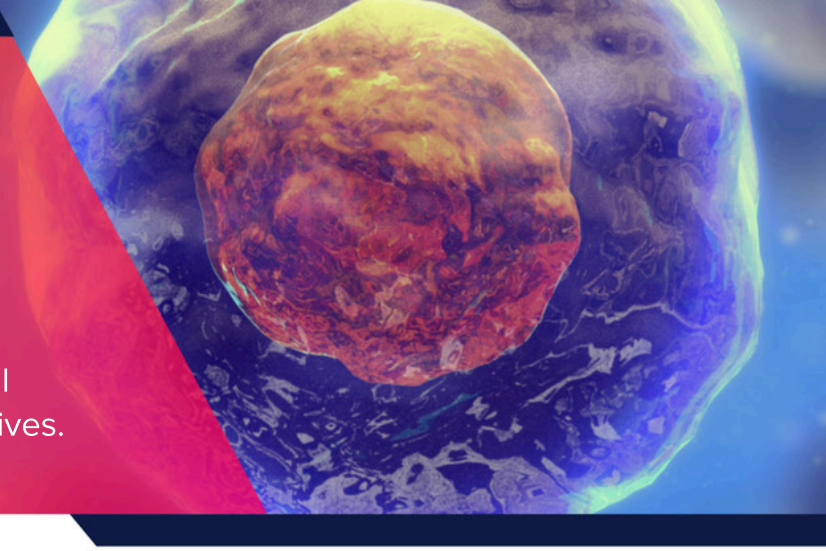
David Valle, MD
Appointed by
Johns Hopkins University

Curt Van Tassell, Ph.D.
Appointed by the
Speaker of the House of Delegates

"In today's challenging funding environment, the Maryland Stem Cell Research Fund plays a vital role in sustaining innovative research and commercialization efforts across the state. It is gratifying to see the impact of the projects we support, as well as the expanding range of institutions and investigators now under the MSCRF umbrella."

Dr. Rachel Brewster,
MSCRC Chair

MSCRF Grant Programs



MSCRF's seven grant funding programs support every stage of development—advancing stem cell and regenerative medicine to improve and save lives.

Clinical

Funding for clinical development of stem cell-based therapies.

Validation

Funding academic researchers for translational development.

Launch

Enabling new faculty members to pursue innovative stem cell research.

Post-Doctoral Fellowship

Support for post-doctoral fellows specializing in stem cell biology.

Commercialization

Helping companies transition their research towards clinical development.

Manufacturing Assistance

Funding to support manufacturing infrastructure / processes for stem cell therapies.

Discovery

Support for early-stage stem cell research projects in academia.

Second-Tier Funding : Additional support that catalyzes public–private collaboration, de-risks innovation, and accelerates regenerative therapies from the lab to patients.

MSCRF
Maryland Stem Cell Research Fund

A Complete Innovation Pipeline Support

From Discovery to Patient

What distinguishes MSCRF is its ability to support innovation across the full development continuum. Early-stage discovery funding enables scientists to explore bold ideas that may be too novel or risky for traditional funding sources. Commercialization and Validation grants support technology advancement to clinical testing, while Second-tier Funding bridges the gap between science and market readiness by incentivizing public–private collaboration. Clinical grants help move promising therapies into human trials.

The Manufacturing Assistance Program ensures that once therapies are ready to scale, they can be produced in Maryland.This integrated approach is deliberate. Breakthrough science alone does not deliver patient impact unless it is supported by commercial expertise, manufacturing infrastructure, and access to capital. MSCRF is designed to address those gaps — reducing risk, accelerating timelines, and keeping innovation rooted in the state.

> MSCRF Validation grant program is critical for aiding academic research through the transition phase into translation as there are few funding sources available for that type of research.

Dr. Warren Grayson
Professor, JHU

MSCRF

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EXECUTIVE
Overview

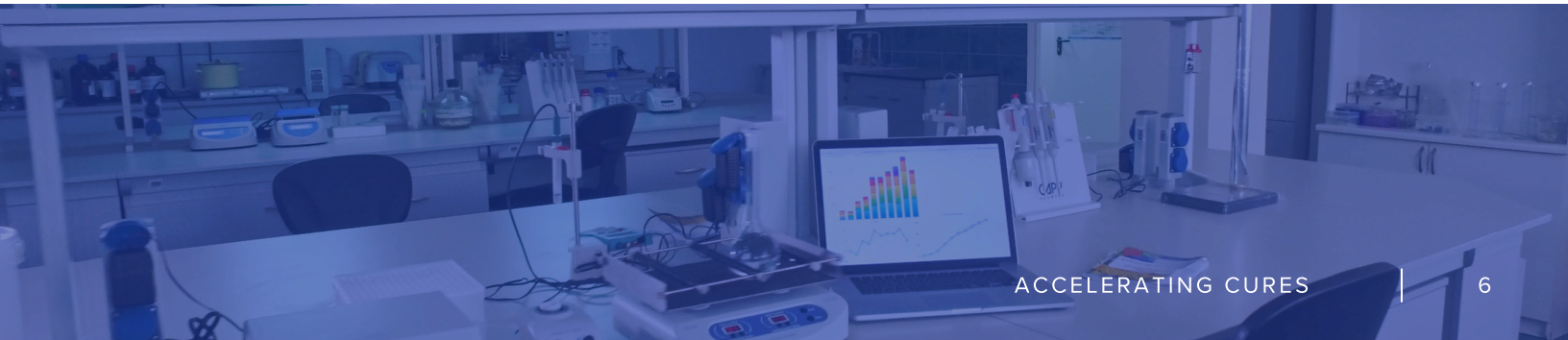
The year 2025 marked an inflection point for stem cell and regenerative medicine. Advances across basic science, translational research, and early-stage clinical trials showed that these technologies are moving beyond laboratory research—they are changing how complex and chronic diseases may be treated. **Development is moving toward therapies that are safer, more scalable, and more clinically meaningful for patients.**

Regenerative medicine continued to advance in tissue repair and modeling, with stem cell-based approaches showing promise for complex bone regeneration. At the same time, **next-generation organoids—developed using artificial learning (AI), machine learning (ML), and advanced robotics and imaging**—are increasingly able to mimic human organ function, improving disease modeling, drug discovery, and preclinical testing. This momentum was reinforced by the **NIH's launch of the Standardized Organoid Modeling (SOM) Center in September 2025,** the nation's first fully integrated platform dedicated to developing standardized organoid-based New Approach Methodologies (NAMs).

Across the field, regulatory wins accelerated therapeutic pipelines. More than 650 active trials are now evaluating engineered cell therapies in solid tumors, while regenerative treatments for neurologic, cardiovascular, and autoimmune diseases advanced into pivotal stages, bringing late-stage programs in wet age-related macular degeneration, multiple sclerosis, and Type 1 diabetes closer to approval. The Cell and Gene Therapy (CGT) field valued at roughly $26 billion this year, is projected to exceed **$119 billion** within a decade. The field outperformed the broader biotech market this year, driven by strong clinical data and early commercial success.

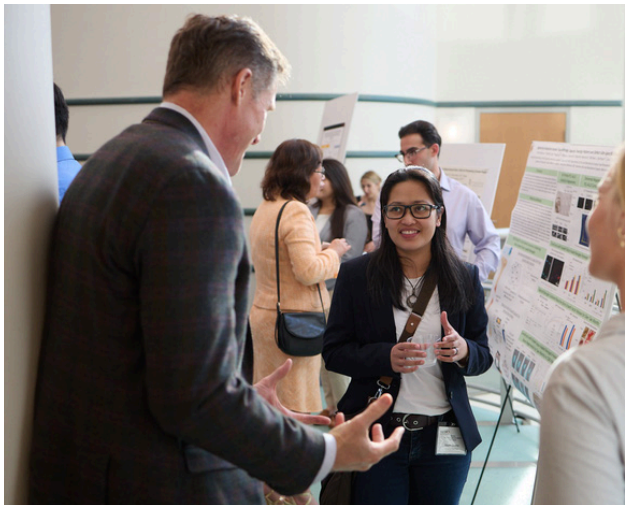
Maryland's Leadership in 2025

In 2025, Maryland strengthened its position as a national leader in stem cell and regenerative medicine—driven by sustained public investment, strategic partnerships, and a growing industry footprint. Through Maryland Stem Cell Research Fund (MSCRF), the state continued a robust grant-making agenda that infused tens of millions of dollars into scientific discovery, clinical development, commercialization, and manufacturing.



EXECUTIVE OVERVIEW

Momentum was visible throughout the year. High-profile convenings, hosted by MSCRF, including the second annual Maryland Stem Cell Research Symposium, Second Maryland Stem Cell Tech Showcase, Third MSCRF Felicitation Ceremony reinforced collaboration among scientists, clinicians, and industry leaders. These events highlighted the depth and connectivity of Maryland's regenerative medicine community and accelerated partnerships that extend well beyond state borders.



Maryland's leadership was further underscored by major corporate investment decisions. **Korean biotechnology company Nature Cell announced plans to establish a 100,000 square foot large-scale manufacturing presence in Baltimore, bringing an estimated 500 new jobs** and expanding Maryland's stem cell manufacturing footprint. The phased development of the Nature Cell BioStar USA Stem Cell Campus will support up to one million doses per year of stem cell therapies targeting knee osteoarthritis and Alzheimer's disease.

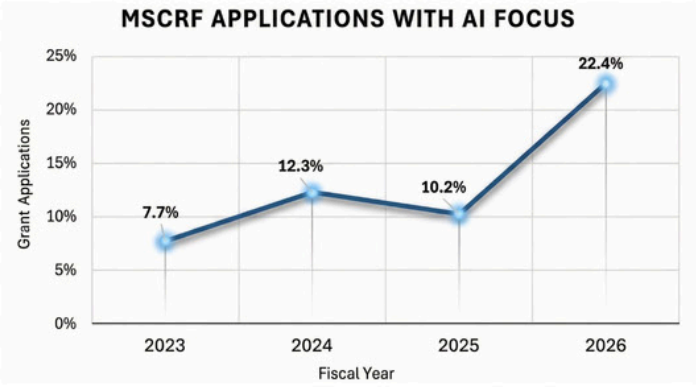
AstraZeneca announced a historic **$2 billion investment in Maryland**—the largest life sciences investment in the state's history—to expand advanced manufacturing in Frederick and Gaithersburg. The expansion includes AI-enabled production, automation, and new clinical manufacturing capabilities, building on AstraZeneca's long-standing presence in the state, including its recently opened CAR-T manufacturing facility in Rockville.

Dr. Jeong-Chan Ra
Chairman, NatureCell

> Maryland offers an abundant pool of highly-skilled technical talent that is critical to establishing global leadership and setting industry standards in stem cell therapeutics.

Maryland also demonstrated national policy leadership. Alongside 35 other states, Maryland joined a federal pilot program to test outcomes-based payment models for high-cost gene therapies under Medicaid. This effort aims to improve patient access to life-saving treatments. At the same time, FDA removed the REMS (Risk Evaluation and Mitigation Strategies) restrictions on CAR-T therapies expanding access to community hospitals—further accelerating adoption.

In 2025, regenerative medicine researchers and companies have been leveraging Artificial Intelligence (AI) and Machine Learning (ML) approaches at a faster rate than previous year. Since 2023, **the number of MSCRF applicants using AI/ML tools has risen nearly three-fold to 22.4% (from 7.7%).**



This momentum was underscored by a partnership between IonQ—a University of Maryland spinout and global quantum leader—and the Centre for Commercialization of Regenerative Medicine (CCRM) to apply quantum and **quantum-AI approaches to bioprocess optimization, disease modeling, and advanced therapy manufacturing.**

> MSCRF funding has enabled us to apply advanced machine learning techniques to analyze complex neurogenetic data in SETD1A-mediated regulation in stem cells, providing critical insights into the mechanisms underlying Schizophrenia and human neurodevelopment.

Dr. Arthur Feltrin
Postdoctoral Fellow,
Lieber Institute for Brain Development

MSCRF: Driving Impact

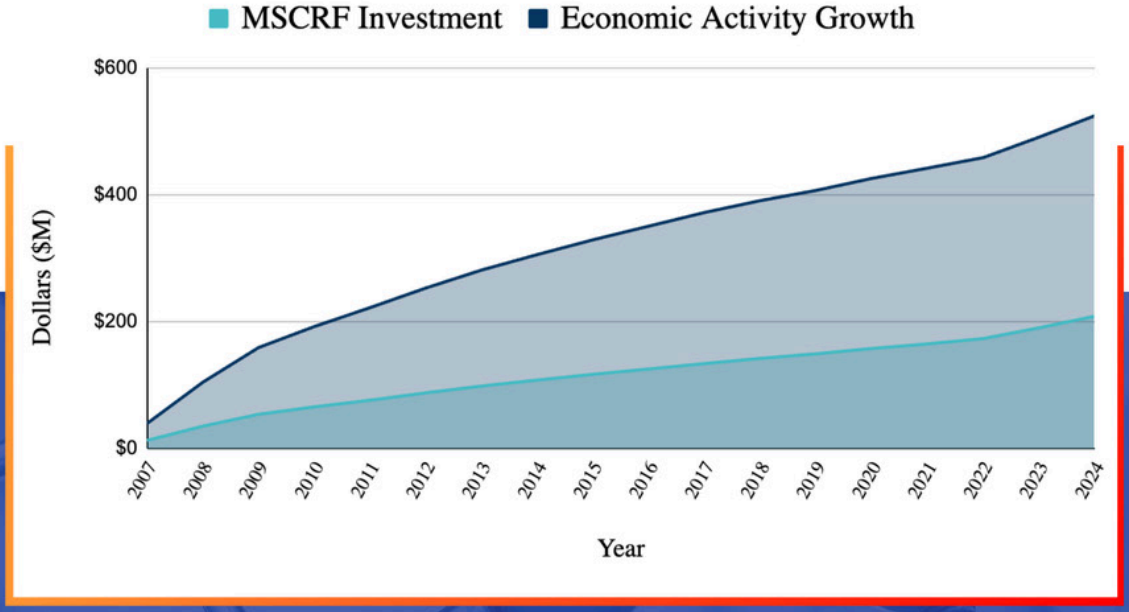
For nearly two decades, MSCRF has played a singular role in advancing regenerative medicine while strengthening Maryland's economy. Since its inception, MSCRF has allocated more than $235 million in grant funding to support research, clinical trials, commercialization, and more recently- advanced manufacturing.

Aligned with Governor Wes Moore's economic roadmap, which prioritizes life sciences, information technology, and aerospace and defense as **Maryland's lighthouse sectors**, MSCRF operates at the intersection of the state's highest-growth industries. By translating academic discovery into commercial therapies, **MSCRF aligns state investment with innovation, manufacturing, and patient impact — strengthening Maryland's innovation economy.**

Created to accelerate promising science into real-world therapies, MSCRF has grown into a nationally recognized model for how targeted state investment can deliver measurable returns for patients, for companies, and for Maryland taxpayers.

>$1B **Follow-On Capital Post-MSCRF Grant**

MSCRF Investment & Economic Activity



State's Each Dollar Attracts $79 in private capital

Economic Impact & Accountability

The results are measurable and well-documented. Independent analyses show that from FY2007 to FY2024, Maryland's investment in MSCRF generated over $525 million in economic activity, $200 million in labor income, and $19.2 million in state and local tax revenue, while supporting more than 2,000 jobs statewide. (2024 MSCRF Economic Impact Study, Sage Policy group).

MSCRF portfolio companies cumulatively raised more than $1 billion in follow-on private (venture) capital after receiving their first MSCRF award. MSCRF's portfolio demonstrates durability and discipline. Most notably, **MSCRF funding has proven exceptionally effective at leveraging private investment, with each dollar of state funding helping attract $79 in venture capital.**

Follow-on Funding MSCRF Companies (2007-2025)

89% percent of companies supported since 2007 remain in operation—outperforming typical venture-backed survival rates. Employment across most of the MSCRF-supported companies has more than doubled since initial funding, reflecting sustained growth.

Maryland is now home to about 150 cell and gene therapy companies, many of which began as small startups supported by early-stage public investment. Success stories such as Osiris Therapeutics and ACell illustrate the full lifecycle of Maryland-based innovation—from early development to major acquisitions—while newer companies continue to reach IPOs, global partnerships, and multibillion-dollar valuations. For example, **Kolon TissueGene, which received early MSCRF support in 2017, is now a publicly traded company with a market capitalization of ~$4.5 billion—demonstrating how early state investment can catalyze growth and long-term success in Maryland.**

$4.5M in Manufacturing Grants

Manufacturing: Driving Growth & Economic Returns

In 2023, MSCRF launched its Manufacturing Assistance Grant Program to tackle one of regenerative medicine's biggest challenges—scaling the production of complex cell therapies. Since then, **more than $4.5 million has been invested to help companies build GMP-compliant facilities, expand production, and hire specialized talent.**

89% of MSCRF Companies Still in Business

These investments are already paying off. MSCRF-supported manufacturers are growing facilities, creating high-wage jobs, and attracting out-of-state revenue—often 85–90% of company income—into Maryland. By bringing production in-house, companies have reduced reliance on external contractors and accelerated clinical and commercial timelines.

Patients at the Heart of Innovation

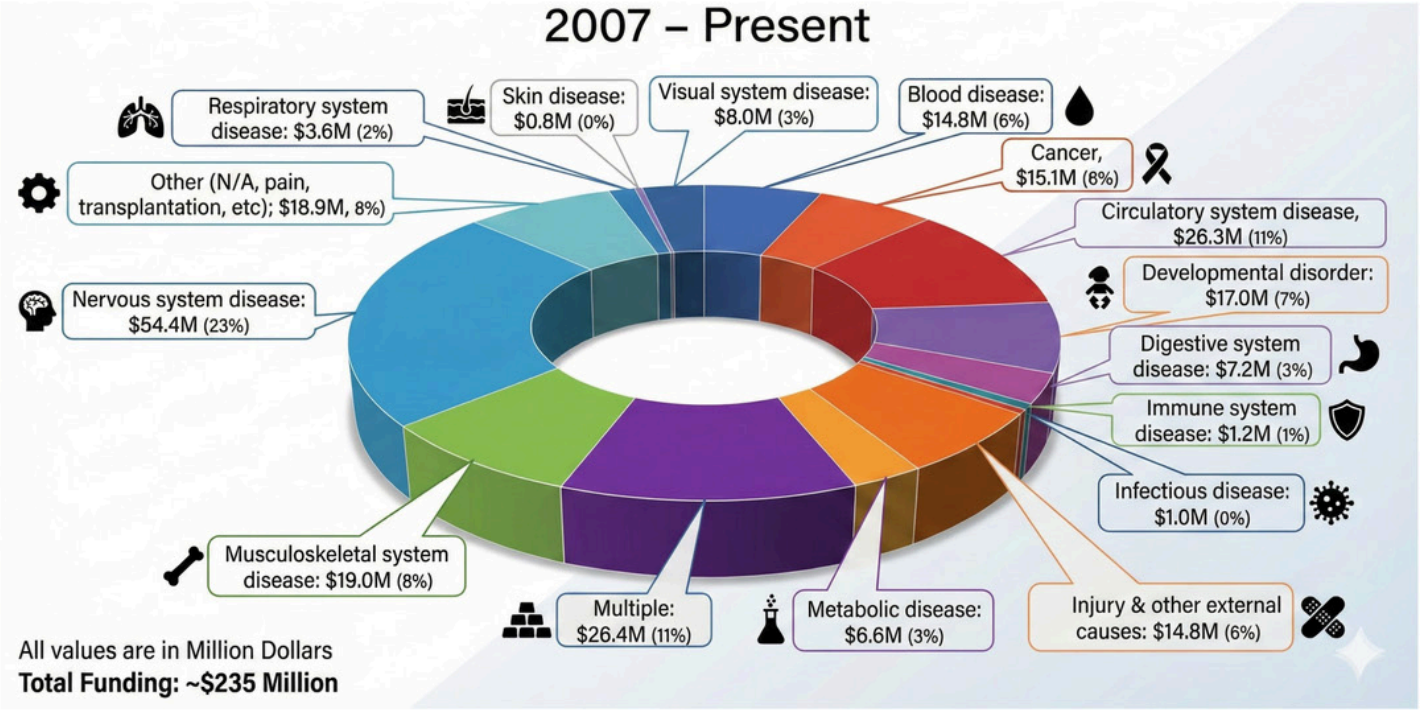
Every research funded, every facility built, and every job created by MSCRF serves a single purpose: improving lives. Research supported by MSCRF is driving therapies that cure sickle cell disease, reduce insulin dependence in Type 1 diabetes, restore vision, repair cartilage, treat cancer, heart diseases or conditions—from degenerative conditions to rare and life-threatening illnesses once considered untreatable.

716 Projects Supported by MSCRF

MSCRF to date has supported 716 projects spanning 197 disease indications. For patients and families facing limited options, this work represents not just innovation, but hope. The economic upside is equally compelling: **if technologies enabled by MSCRF grants save just 100 Marylanders, they generate more than $1 billion in economic benefit**[1], based on current estimates of the value of a statistical life. These investments helped maintain momentum, preserve talent, and ensure that promising therapies continued moving toward patients.

197 Different Disease Indications

Disease Categories Funded by MSCRF

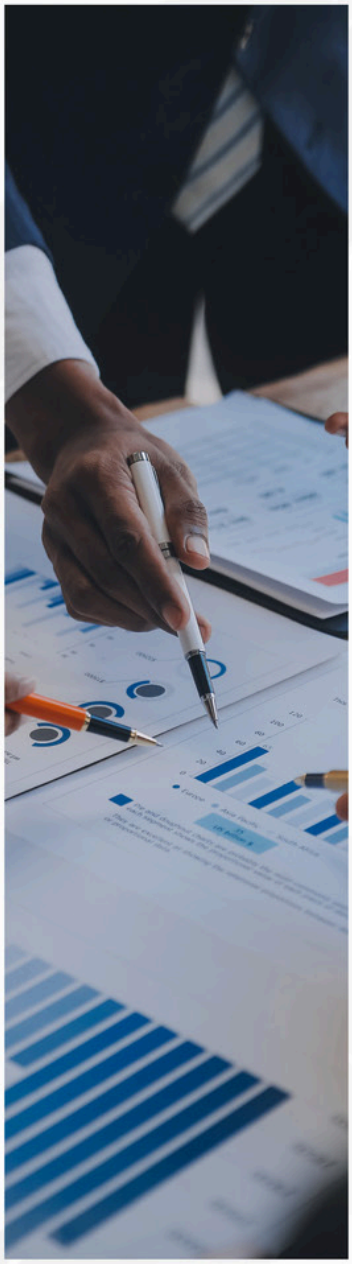


[1]*HHS Standard Values for Regulatory Analysis, 2024. Assistant Secretary for Planning and Evaluation, Department of Health and Human Services Office of Science and Data Policy.*

MSCRF

by the **Numbers**

(Since Inception)



716
Total Projects Funded

$235M
Total Funding Awarded

197
Different Disease Indications

$525M+
Economic Activity Generated

36
Companies Funded

$28M+
Grants Supporting Companies

47
Different Entities Supported

>60%
Postdoctoral Fellows Retained in Maryland

89%
MSCRF- Funded Companies Still in Business

>$4.5M
Grants for Manufacturing Support

>$1B
Venture Capital Raised by Companies Since MSCRF Funding

From companies to world-class academic labs, MSCRF awardees span the entire state of Maryland, tackling a vast array of diseases to revolutionize patient care. These researchers and companies are united by a single goal: turning cutting-edge science into life-saving treatments that improve human lives.

Looking Ahead: Sustaining Momentum in Regenerative Medicine

The future of regenerative medicine is promising. Breakthrough science, maturing markets, and growing confidence—bolstered by approved stem cell therapies—are converging to accelerate progress. Yet, with federal funding uncertain and cures at risk of delay, MSCRF's support is more critical than ever.

The story of 2025 is one of resilience, collaboration, and forward momentum. With sustained investment and strong partnerships, Maryland is poised to lead the regenerative medicine revolution — turning scientific breakthroughs into standards of care for patients around the world.

As we move forward, MSCRF will continue investing across the full innovation pipeline, with heightened focus on manufacturing, commercialization, workforce development, and public–private collaboration. Our mission remains clear: deliver measurable economic returns for Maryland while advancing therapies that improve and save lives.

With Gratitude and Purpose,

Ruchika Nijhara, Ph.D., MBA
Executive Director, MSCRF

Rachel Brewster, Ph.D.
Chair, MSCR Commission

Our vision for tomorrow is clear: to advance science with purpose - to shape a healthier and brighter future for Marylanders and beyond

MSCRF

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2025
At-A-Glance

MSCRF by the Numbers in 2025

~$22M
Total Funding

62
Grants Awarded

15
Different Entities Supported

MSCRF
Maryland Stem Cell Research Fund

159
Applications Submitted

$1.35M
Grants for Manufacturing Support

$5M
Grants to Companies

47
Disease Indications

2025: Advancing Innovation, Impact, and Growth

In 2025, the MSCRF solidified its position as a primary engine for regenerative medicine. By investing nearly $22 million across the full continuum — from initial discovery to large-scale manufacturing — MSCRF didn't just fund science, it accelerated the transition from lab bench to bedside.

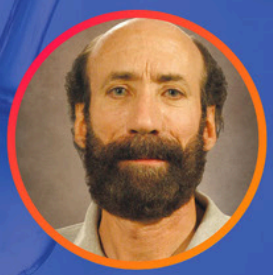
As federal funding faced increasing volatility, MSCRF provided the stability Maryland's life sciences ecosystem required to thrive. These strategic investments are currently fueling company formation, creating high-value jobs, and, most importantly, delivering life-changing outcomes for patients.

~$22M Awarded in 2025

Expanding & Strengthening Maryland's Company Pipeline

Company support remained a core focus for MSCRF in 2025. Nearly $5 million was allocated to Maryland-based companies, supporting both startups and more mature, clinical-stage organizations. Since 2017, when MSCRF expanded its grant programs to accelerate cures, both the **number of company awards and total funding to companies have increased more than fourfold**, reflecting the growing strength and demand of Maryland's regenerative medicine ecosystem.

> One of the most rewarding aspects of my job rendering legal representation to MSCRF is the related opportunity to also serve as one of the Fund's Commissioners. The chance to play a part in helping to fund cutting-edge, potentially lifesaving research in regenerative medicine, and help guide MSCRF policies advancing this important goal, makes me especially proud, as the work of MSCRF has such significant social utility. It is public service of the highest order, and I am fortunate to have this opportunity to help advance such a worthy cause.



Mr. Ira Schwartz
MSCRC

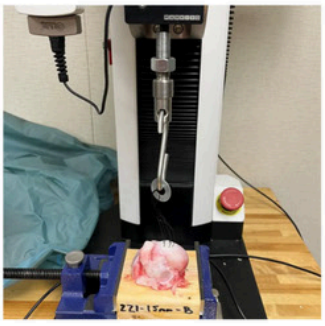
4.5X Increase in Funding to Companies

Since its inception, MSCRF has invested over $28 million in 36 companies, achieving an 89% survival rate—defying a sector where up to 80% of startups fail within five years. **By bridging the "valley of death," we provide the critical capital needed to move therapies from the lab into human clinical trials.**

The results are visible at every stage: early-stage startups are validating their first products, while established portfolio companies are scaling commercial operations and achieving successful exits. This proven track record has made Maryland a magnet for innovation. Several companies attracted to Maryland from outside the state including **Theradaptive, Caleo Biotechnologies, Nanochon and Stemora, cited MSCRF support as a key factor in their decision to build and grow their operations in Maryland.**

In 2025, MSCRF, through its manufacturing Grant Program allocated **$1.35 million** to enable companies build GMP-aligned infrastructure right here in Maryland. Through MSCRF's Manufacturing Assistance Grant, **Nanochon** will expand in-house 3D processing, validate its implant, and scale production—**shortening the path to commercialization for its stem cell product, chondrograft™ by up to two years**, while **Reprocell** will establish a centralized Contract Development Organization and **accelerate expansion of its offerings**.

NANOCHON



Rama Modali
CEO, Reprocell USA

> MSCRF-supported facilities will drive the development of breakthrough products and therapeutic approaches. By fostering collaboration among scientists, clinicians, and industry leaders, these facilities are positioned to translate pioneering research into real-world solutions that can address a wide range of diseases. Ultimately, it is all beneficial to patients throughout Maryland and beyond.

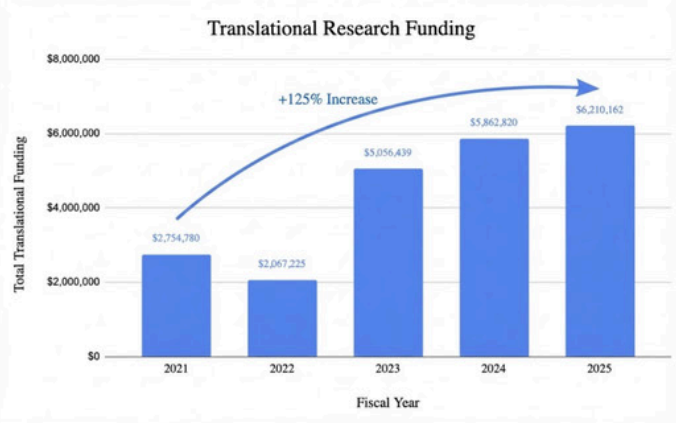
Increasing Demand for MSCRF Funding

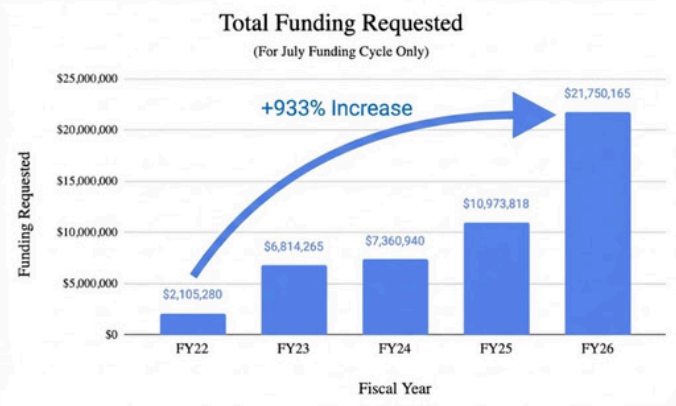
Translational research funding has increased 125% over the past five years, reflecting MSCRF's emphasis on bridging the gap between laboratory discovery and patient benefit.

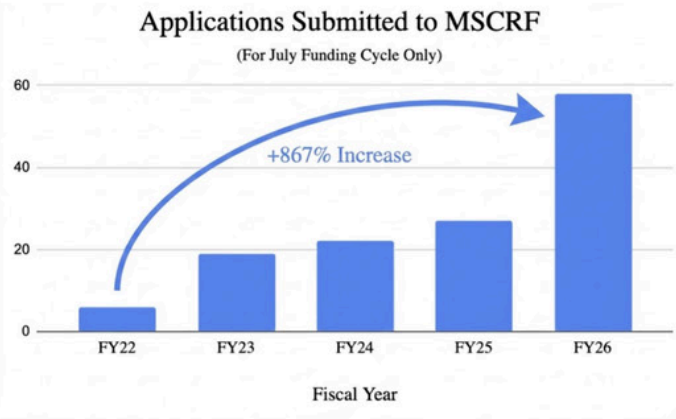
Demand for MSCRF funding continued to rise sharply in 2025. MSCRF received 159 applications, representing nearly a 50% increase over the prior year. Over the past five fiscal years (FY2021–FY2025), **total requested funding increased by 64%, reaching $44,562,649—more than double MSCRF's FY25 annual appropriation.**

900% **Surge in Funding Requests**

The scale of unmet demand became even more evident in the most recent funding cycle in July this year. **The number of applications** submitted in this funding round **increased by over 800%** compared to FY22 while the requested funding increased by over 900% to over $21M exceeding the Fund's entire FY26 state appropriation of $15.5 million. This increased need for MSCRF funding reflects both the expansion of Maryland's innovation pipeline and growing uncertainty around federal research support.







> Stem cell research is now central to identifying and treating genetic disease. Being able to contribute through the Maryland Stem Cell Research Commission feels like a natural next step.

Dr. David Valle
MSCRC

Collaboration & Translation in a Constrained Funding Environment

As federal funding grew increasingly uncertain in 2025, collaboration became essential. MSCRF's Second-Tier Funding initiative, launched in 2024, continued to incentivize public–private partnerships that stretch limited resources and accelerated translation

MSCRF also hosted several events to further collaborations. MSCRF's events including the Felicitation ceremony, Stem Cell and

Regenerative Medicine Tech Showcase and Stem Cell Symposium and Workshop brought scientists, entrepreneurs, and investors together sparking new collaborations. Through these efforts, **MSCRF engaged stakeholders across the public-private spectrum, strengthening a dynamic ecosystem where cutting-edge stem cell research can advance toward real-word therapies.**

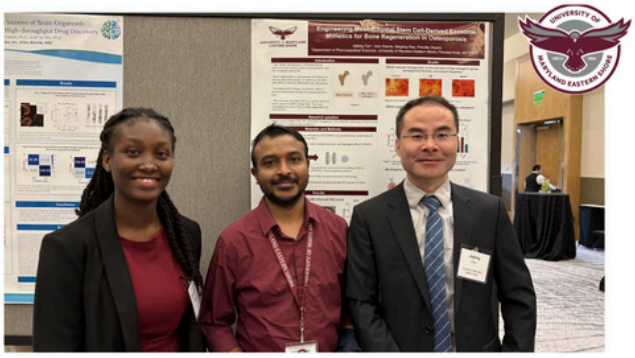
Select Collaborations in 2025

- **RoosterBio** & **Secretome**: Scaling production for stem cell-based therapeutics.
- **Reprocell** & **Dr. Elias Zambidis (JHU)**: Advancing GMP manufacturing for novel stem cells.
- **Caleo Biotechnologies** & **Dr. David Hackam (JHU)**: Validating an "organ-on-a-chip" platform for clinical use.
- **Diagnostic Biochips** & **Dr. Brady Maher (Lieber Institute)**: Developing AI-driven tools for brain organoid research.

Growing Statewide Reach & Research Impact

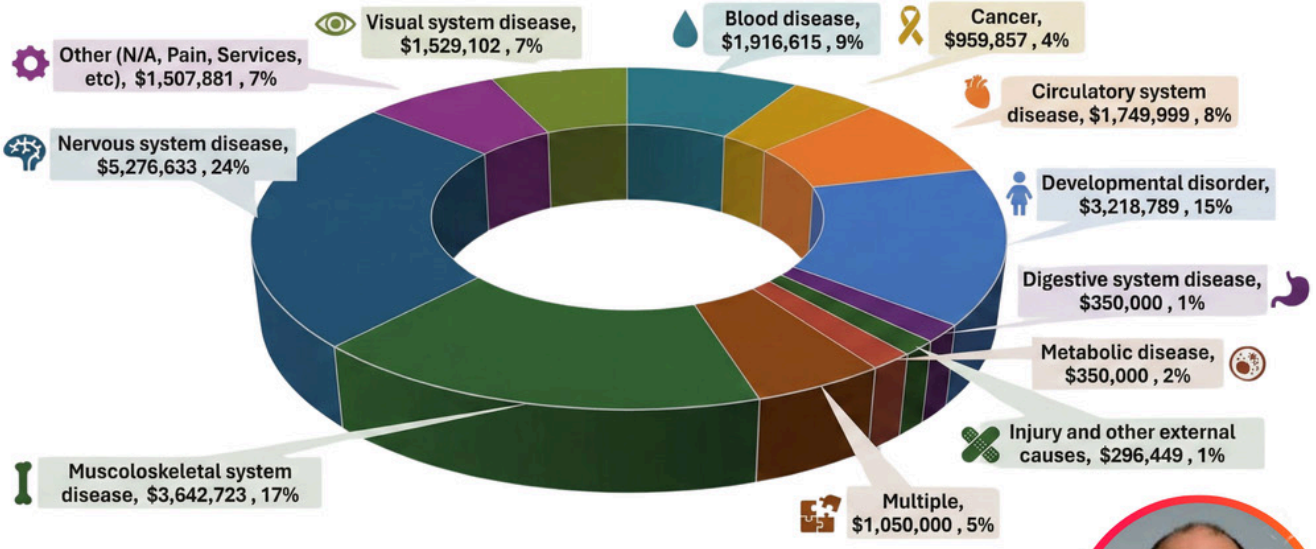
In 2025, MSCRF's impact continued to widen—reaching new institutions, attracting top talent, and strengthening Maryland's stem cell ecosystem. **For the first time, an investigator from the University of Maryland Eastern Shore received MSCRF funding**. Dr. Jiabang Fan, who relocated from California, pointed to Maryland's leadership in regenerative medicine and MSCRF support as decisive in his choice to build his lab in the state.

That extends beyond individual faculty hires. More than 60% of MSCRF-funded postdoctoral fellows go on to take employment in Maryland. **This concentration of talent has helped draw major investment, including Nature Cell's plan**



to establish a 100,000-square-foot stem cell manufacturing facility in Baltimore, creating more than 500 jobs. With this strong foundation, MSCRF-supported scientists and companies are advancing discoveries toward patients. In 2025 alone, funded projects targeted **47 disease areas** — led by neurological, musculoskeletal, and developmental disorders—with growing use of AI and computational biology to accelerate the development of new therapies.

MSCRF Funded Disease Categories (2025)



> MSCRF plays a critical role—not just in advancing stem cell science, but in ensuring that progress is ethically grounded and publicly accountable. That balance matters.

Dr. Alan Regenberg
MSCRC

Leadership & Governance: New Commissioners Join MSCRC

In 2025, the Maryland Stem Cell Research Commission (MSCRC), which oversees MSCRF's programs and funding decisions, welcomed **three new members** whose expertise strengthens the Commission's scientific and ethical leadership.

Dr. David Valle is a renowned geneticist and Professor at Johns Hopkins specializing in the identification and treatment of over 20 inherited disorders. He serves as the founding director of the Center for Inherited Disease Research and has been honored with the Victor A. McKusick Leadership Award. His research spans a broad range of conditions, from metabolic errors to inherited retinal degeneration.

Dr. Alan Regenberg brings deep expertise in bioethics and public engagement as Director of Outreach and Research Support and Senior Research Associate at the Johns Hopkins Berman Institute of Bioethics. His work spans stem cell science, gene editing, and ethical oversight, and he serves on both Institutional Review Boards and stem cell research oversight committees.

Dr. Christopher Dreisbach is the Associate Program Director and a senior lecturer at Johns Hopkins University, where he specializes in organizational leadership and ethics. An ordained Episcopal priest with a JHU PhD, he has taught in higher education since 1980 and holds a joint appointment with the Carey Business School. His work focuses on public philosophy and applied ethics, serving both law enforcement and religious institutions.

The milestones of 2025 make one thing clear: Maryland's preeminence in regenerative medicine is no accident—it is the direct result of purposeful, sustained investment. **The following pages profile the MSCRF awardees, including our 2025 academic researchers and emerging companies, who are turning state support into clinical breakthroughs and economic momentum.** These highlights illustrate how MSCRF is doing more than just funding science; these investments are accelerating the journey to patient cures and scaling the local enterprises that drive Maryland's innovation economy.

> 2025 demonstrated the full scope of MSCRF's impact—from supporting early discovery and companies to investing in manufacturing infrastructure that keeps innovation and economic returns in Maryland. As demand for our programs continues to grow, MSCRF remains committed to advancing science, strengthening companies, and ensuring that breakthroughs are discovered, scaled, manufactured, and delivered to patients.

Dr. Ruchika Nijhara
Executive Director, MSCRF

MSCRF

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MANUFACTURING

Grants Impact: Powering Growth

Strengthening Maryland's Economy via Regenerative Medicine Manufacturing

Manufacturing transforms scientific discovery into real-world solutions, driving innovation, creating high-value jobs, and fostering long-term economic growth. This sector accounts for over half of all private-sector research and development, making it vital for U.S. competitiveness.

According to the National Association of Manufacturers, manufacturing delivers one of the strongest economic returns of any sector: **Every $1 invested generates $2.64 in economic impact.** These are high-value jobs—averaging $106,691 in annual pay and benefits—and **each manufacturing position supports nearly five additional jobs** across the broader economy.

Stem Cell and Regenerative medicine manufacturing presents both extraordinary promise and unique challenges. Producing cell- and gene-based therapies requires specialized infrastructure, rigorous cGMP compliance, and highly skilled talent to manage variable biological materials. These complexities create significant barriers for early-stage companies—often before private capital is available—underscoring the need for targeted public investment.

Under Governor Wes Moore's leadership, Maryland has prioritized "lighthouse sectors" that will define the state's future economy. **Life sciences in particular depend on advanced manufacturing to scale breakthrough research into therapies that reach patients.**

MSCRF's Role in Advancing Manufacturing in Maryland

MSCRF's Manufacturing Assistance Grant Program was established to address this critical gap. Since the grant program's launch in 2023, **MSCRF has allocated over $4.5 million to support regenerative medicine manufacturing in Maryland**.

Through these grants, MSCRF has enabled companies to establish and expand Good Manufacturing Practice (GMP) facilities, optimize production processes, validate quality systems, and prepare therapies for clinical trials and commercialization.

These investments accelerate timelines, reduce manufacturing risk, and allow companies to retain high-value operations in Maryland rather than outsourcing them elsewhere.

>$4.5M in Manufacturing Grants

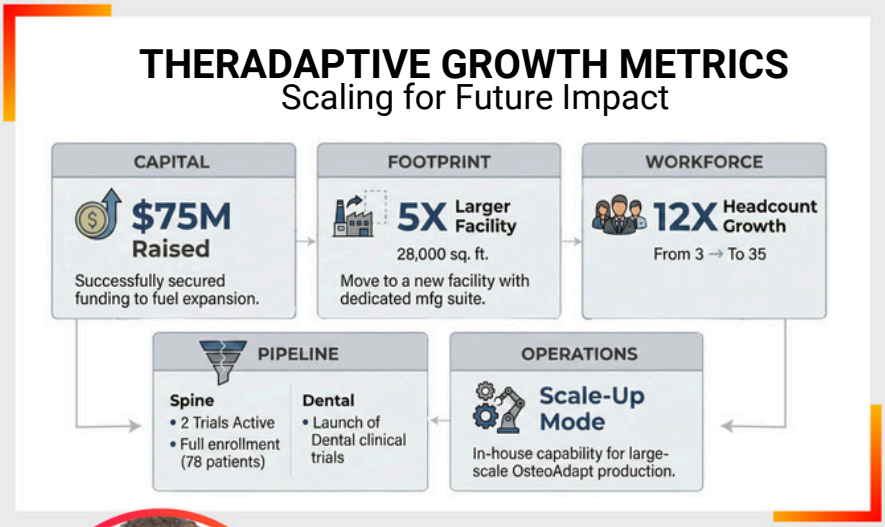
The following pages in this section highlight MSCRF manufacturing awardees to date and showcases the tangible impact these grants have already had in Maryland—and will continue to make—for companies, workers, and patients.

MSCRF manufacturing assistance grants drive high-skilled jobs, attract capital investment, and help growing companies scale in Maryland—strengthening the state's reputation as a global hub for discovering, developing, and manufacturing advanced therapies.

Theradaptive : Scaling Manufacturing to Advance Regenerative Orthopedics

As one of the first recipients of the Manufacturing Assistance Grant in 2023, Theradaptive used this support to scale manufacturing capabilities and advance its lead regenerative programs toward commercialization.

Founded by Luis Alvarez, Theradaptive is developing OsteoAdapt™, a regenerative biologic designed to enhance bone healing in orthopedic and dental applications. MSCRF support enabled the company to bring critical manufacturing capabilities in-house, accelerating development across multiple programs. In September 2024, Theradaptive expanded its Frederick facility from approximately **6,000 to 28,000 square feet** to build manufacturing and development capacity. **Internal manufacturing eliminates reliance on CMO availability, ensures on-demand production, faster clinical timelines, and GMP-capable internal testing that improves product quality and process control**. The company grew its team from **3 to 35 employees**, reflecting its rapid expansion. As the company builds out U.S. manufacturing capabilities in Maryland to support commercialization, Theradaptive expects to hire up to 50 additional employees. In June 2025, the company raised $26 million Series A to expand OsteoAdapt into additional indications bringing total funding raised to approximately **$75 million** —underscoring strong investor confidence and the leverage created by early MSCRF support. **These manufacturing investments are driving clinical progress.**



Following the full patient enrollment of its Phase II OASIS clinical trial for spinal fusion and the planned initiation of a Phase III study in 2026, Theradaptive has further extended OsteoAdapt's reach into dental repair via the RESTORE Phase I/II clinical trial. Growing clinical demand is increasing the need for robust, GMP-compliant manufacturing infrastructure.

Dr. Luis Alvarez
CEO & Founder, Theradaptive

> MSCRF's impact has been from day one. It allowed us to exist, and as we advanced product development, it enabled us to scale. The Manufacturing Assistance Grant bridged the gap between innovation and production—accelerating our therapies toward patients.

RoosterBio

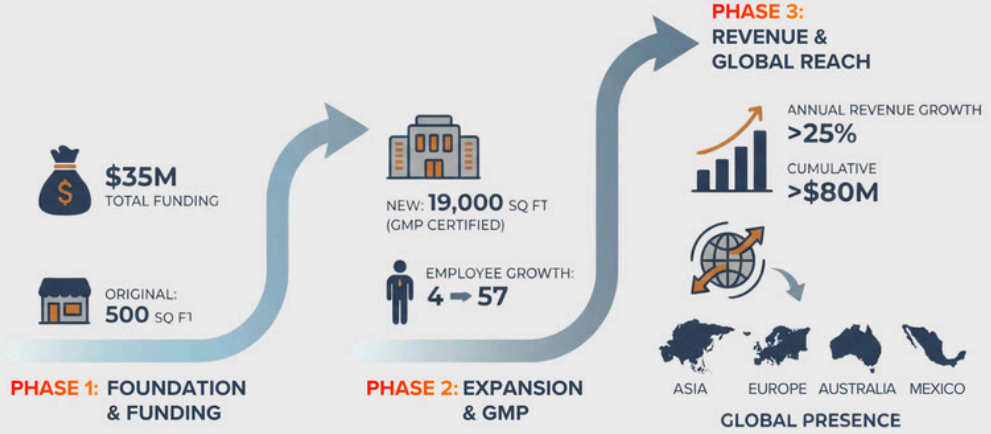
Building Scalable Backbone for Next-Gen Therapies

Based in Frederick, Maryland, **RoosterBio enables industrialized stem cell manufacturing.** They supply high-volume human mesenchymal stem cells (MSCs), engineered media, and scalable bioprocess templates to help move from bench to clinic. Manufacturing grant awarded in 2023, supported the build-out of a commercial-scale, cGMP-compatible manufacturing infrastructure, including a 50-liter bioreactor platform and bioprocesses systems for MSC-derived extracellular vesicle (EV) and secretome products. The manufacturing grant has led to significant economic impact. Founded in 2013, RoosterBio has expanded into a four-fold **19,000 square-foot facility** with manufacturing space and grown its workforce from **4 to 57 employees. RoosterBio has generated more than $80M in revenues** growing at over **25% annually** and has created high-skilled jobs while partnering with **global distributors** across Asia, Australia, and Latin America. They are strengthening its trajectory, by scaling up iPSC and EV production creating next-gen therapeutic platforms. **"A decade from now, I want the industry to look back and say, 'Cell and EV therapies became widely accessible because RoosterBio made it possible to manufacture them at the scale the world needed,'" says Jon Rowley.**

By investing in scalable, reproducible manufacturing solutions, MSCRF has helped transform RoosterBio from an early-stage innovator into a global manufacturing partner that can fill a critical gap in regenerative medicine.

ROOSTERBIO: SCALING FOR SUCCESS

Key Growth Metrics



"MSCRF funded the manufacturing backbone that allowed us to move beyond incremental improvements. This strengthened our growth trajectory and positioned RoosterBio as a global leader in scalable manufacturing systems."

Dr. Jon Rowley
CPO & Founder,
RoosterBio

REPROCELL

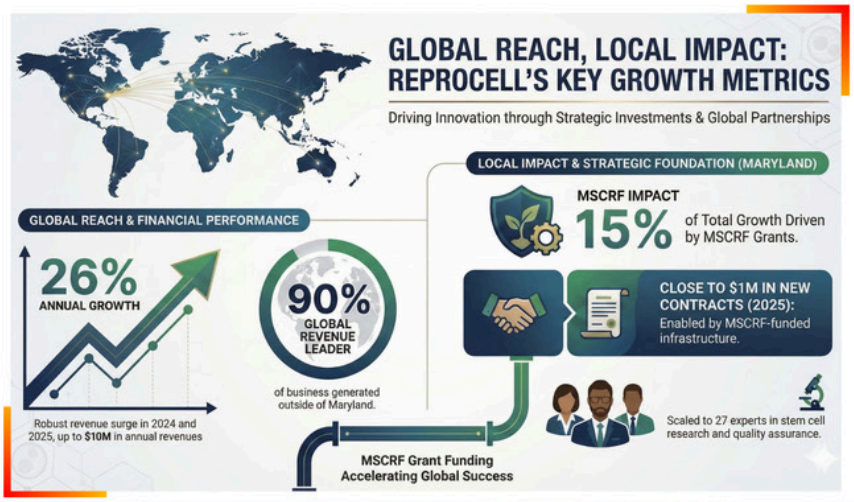
Scaling Stem Cell Manufacturing

MSCRF Manufacturing Assistance grant to Reprocell Inc., a Beltsville company, enabled optimization of the Biospherix Xvivo system to produce clinical-grade master stem cell banks, a critical step in advancing therapies toward the clinic.

Building on this foundation, a new MSCRF manufacturing award is supporting the construction of a GMP-grade cleanroom facility designed to house bioreactors and expanded incubator capacity. This expansion will enable large-scale production of iPSC and iMSC therapeutics, support exosome manufacturing, and facilitate the development of new products.

The impact of MSCRF's investment is already evident. In FY2024, Reprocell achieved 26% revenue growth, with annual revenues reaching nearly $10 million. Approximately 15% of this growth is directly attributable to products developed through MSCRF grants.

They currently employ **27 staff**. Within just months of receiving its MSCRF manufacturing award, Reprocell secured two new contracts totaling approximately $800,000. **Notably, 85–90% of Reprocell's revenue comes from outside Maryland, bringing external capital into the state while anchoring high-value biomanufacturing jobs locally.**



Rama Modali
CEO, Reprocell

> We have been in Maryland for the last 35 years, and we are building the future here. Maryland is a strategic hub for biotechnology, and we are excited to develop cutting-edge products and services that can generate transformative therapies across a broad spectrum of diseases. Creating therapies that offer hope where few options exist is deeply motivating and a privilege to be part of.

New Manufacturing Awardee: NANOCHON

Baltimore-based medical device company Nanochon is developing Chondrograft, a 3D-printed, fully synthetic, bone-sparing knee implant designed to regenerate lost cartilage and subchondral bone—a "pre-knee replacement" solution that could delay invasive surgery for the 32 million Americans with osteoarthritis. As Benjamin Holmes, CEO of Nanochon puts it, **Chondrograft aims to achieve the "holy grail" in orthopedics, the regrowth of loss cartilage in a joint.**

Founded in 2016, Nanochon, a spin-off from George Washington University, moved its seven-person team to Launchport in Baltimore in 2024, boosting its 3D manufacturing capabilities. **Holmes notes that when it comes to implanted devices, 3D printing is a specialty practice. "Setting up shop in Launchport and receiving the MSCRF manufacturing assistance grant provided a path to holistically support the 3D processing."** said Holmes**.** MSCRF Manufacturing Assistance Grant will support Nanochon's in-house 3D processing, implant validation, and scaling, enabling faster commercialization and reducing development timelines by up to two years, according to CEO Benjamin Holmes.

Animal and cadaveric studies demonstrate the implant's efficacy, strong fixation, and ease of surgical use. The implants are attracting the animal patient's own stem cells, which are regenerating the tissue, Holmes says.

Nanochon plans to begin a small **ten patients** human safety study in January 2026, followed by a larger randomized trial of ~200 patients. **The grant will also support workforce growth and help position the company for a Series A funding round in 2026.**

> "I can't understate how essential MSCRF's manufacturing grant is. It's taking two years off the cycle to get to commercialization. It takes a long time for companies like ours to reach value inflection points for potential investors. These funds allow us to do things beyond what investor dollars will allow us to do."

Dr. Benjamin Holmes
CEO, Nanochon

MSCRF

PATIENT IMPACT

Measuring Success by
Lives Improved

Patient Impact: Measuring Success by Lives Improved

Maryland Stem Cell Research Fund has jump-started a wave of promising clinical testing across the state and beyond, turning cutting-edge laboratory discoveries into tangible scientific advances for patients in need. By funding translational research, fostering collaborations between university labs, biotech startups and health systems, and underwriting early-stage trials, **MSCRF has helped move novel stem-cell therapies from bench to bedside** by accelerating safety testing, refining delivery methods and generating clinical data that attracts further investment. This has resulted in a growing portfolio of ongoing stem cell clinical trials that not only offer **new hope for patients with difficult-to-treat conditions** but also strengthen the state's reputation as a national hub for regenerative-medicine innovation.

Advancing a New Regenerative Option for Knee Osteoarthritis

Osteoarthritis (OA) of the knee affects hundreds of millions of people worldwide and more than 30 million adults in the United States alone limitingmobility, independence, and quality of life. For patients with mild to moderate disease, treatment options are often frustratingly limited—conservative therapies may no longer work, yet major surgery such as knee replacement feels premature. Importantly, there are currently no approved disease-modifying osteoarthritis drugs capable of slowing or reversing disease progression.

With support from MSCRF, a new **first-in human clinical trial i**s working to close this critical treatment gap by evaluating BRC-OA, a promising regenerative therapy designed to slow disease progression and improve function before irreversible joint damage occurs. Frederick-based biotechnology company, Britecyte's lead asset, BRC-OA, is an off- ct currently being evaluated in a First-in-Human Phase I/IIa clinical trial for the treatment of knee osteoarthritis.

BRC-OA, developed by Frederick-based biotechnology company, **Britecyte, Inc**., as an off- the-shelf, allogeneic adipose-derived stem cell product offers a regenerative solution that is accessible, straightforward, and designed to intervene earlier in the disease process.

The therapy's off-the-shelf nature is a key advantage. Because the product is cryopreserved and stable, it can be administered when it best fits a patient's life, without the need for tissue harvesting or complex scheduling. **The injection procedure itself is similar to a cortisone shot, something many patients already understand and tolerate—without the same concerns about long-term joint damage**. The clinical trial is a multicenter, randomized, controlled, single-blind, dose-finding trial conducted under an FDA-cleared Investigational New Drug application.

Dr. John Ferrell, III

"By focusing on outcomes that matter most to patients—staying active, social, and independent—the clinical trial reflects a broader shift toward biologically focused, patient-centered care. If we can slow or alter the progression of osteoarthritis earlier, we may one day look back and say, 'Back in the old days we used to replace knees. Now we use regenerative treatments so they never get that bad. - Dr. John Ferrell , Managing Partner, ROSM & Founder of ORI"

Approximately **36 participants** will be enrolled across multiple clinical sites, including locations in Maryland. Patients receive a single intra-articular injection of either BRC-OA or placebo and are followed for six months to assess safety, tolerability, pain, function, and biological markers of joint health. At the Maryland clinical site, the trial is led by **Dr. John Ferrell,** Managing Partner at **Regenerative Orthopedics and Sports Medicine (ROSM)** and **founder of the Orthobiologics Research Initiative**. Currently, 10 patients have been enrolled in Maryland, with additional participants expected by the end of 2025. "**This trial is a key step in moving regenerative orthopedics from a promising concept to a true standard of care."** said Ferrell

Patients enrolling in the clincal trial share a common story. **Many have exhausted conservative treatments such as physical therapy, cortisone injections, hyaluronic acid injections, and anti-inflammatory medications**. They remain in pain, yet are not ready—or are not ideal candidates—for knee replacement surgery. For these individuals, **the trial represents hope for an option that fits between failed conservative care and a major operation.**

While the clinical trial rigorously tracks pain scores, functional outcomes, and safety data, it's impact is perhaps most clearly seen through patients' personal goals. **One participant, who had already undergone multiple surgeries and was determined to avoid knee replacement, defined success in simple terms: being able to play nine holes of golf with friends without knee pain dictating the day.**

Dr. Ferrell credits MSCRF with playing a critical role in bringing this potential therapy to patients in Maryland. By supporting innovative clinical trials like this one, MSCRF is helping to advance regenerative medicine solutions that aim not just to manage symptoms, but to fundamentally change the treatment landscape for chronic, debilitating diseases such as osteoarthritis of the knee.

"MSCRF support took this from a strong scientific rationale to a trial that is treating real patients," Ferrell noted. "MSCRF grants help bridge the gap between innovation and patient access, **especially for technologies that may not yet attract large-scale commercial funding**." For Maryland patients, this support provides earlier access to cutting-edge regenerative therapies.

Dr. Alla Danilkovitch

> The MSCRF clinical award to Britecyte represents a significant step forward in the treatment of OA by advancing our adipose therapy, marking a turning point for the health of patients impacted by this devastating condition.
> - Dr. Alla Danilkovitch, Founder & Chief Scentific Officer, Britecyte, Inc.

A Potential Turning Point for Patients with Degenerative Disc Disease

For millions of people, degenerative disc disease is more than back pain—it is a daily barrier to work, mobility, sleep, and quality of life. As spinal discs break down, abnormal motion and nerve compression can lead to chronic pain that often leaves patients with few options beyond spinal fusion surgery. **Yet today's standard approach does not always succeed; in 5–20% of cases, the bones fail to fuse properly, resulting in persistent pain and the need for additional surgery.**

A Maryland-born regenerative therapy, OsteoAdapt™ SP, developed by Theradaptive, could help change that trajectory. **OsteoAdapt SP is now showing early promise in the ongoing Phase I/II OASIS clinical trial for patients undergoing lumbar spinal fusion—research made possible through support from MSCRF.**

OsteoAdapt SP combines a synthetic bone graft with AMP2, Theradaptive's next-generation engineered protein derived from BMP-2. Unlike conventional bone-forming therapies that rely on high doses and can stimulate unwanted bone

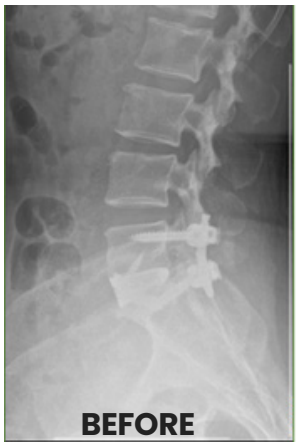
growth, AMP2 is designed to bind precisely to the graft material and promote bone formation only where surgeons intend. MedStar Southern Maryland Hospital Center is among the first clinical sites evaluating this approach**. Dr. David Weiner**, lead investigator for the OASIS trial at MedStar, sees significant potential for patients.

Dr. David Weiner

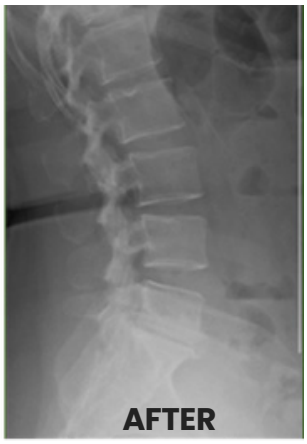
> OsteoAdapt is a revolutionary product. If this trial confirms what we are seeing so far, it could make major waves in orthopedic medicine and fundamentally change how we approach spinal fusion.
> - Dr. David Weiner, MedStar Southern Maryland Hospital Center

Patients enrolled in the trial also recognize the significance of their participation. **Many express pride in contributing to a therapy that may improve outcomes for future patients**—even without knowing whether they received OsteoAdapt SP or standard treatment.

"People are excited to be trailblazers," Weiner noted. "They understand they may be helping create a better option for patients who come after them." The OASIS trial has completed enrollment of 78 patients across U.S. sites, with MedStar serving as one of the largest contributors. Patients are being followed for two years, with successful fusion expected between six and eighteen months. For the approximately 1.5 million patients who undergo spinal fusion each year, **the potential impact is substantial. It could reduce the need for revision surgeries and give many patients lasting relief from back pain.**



Treatment



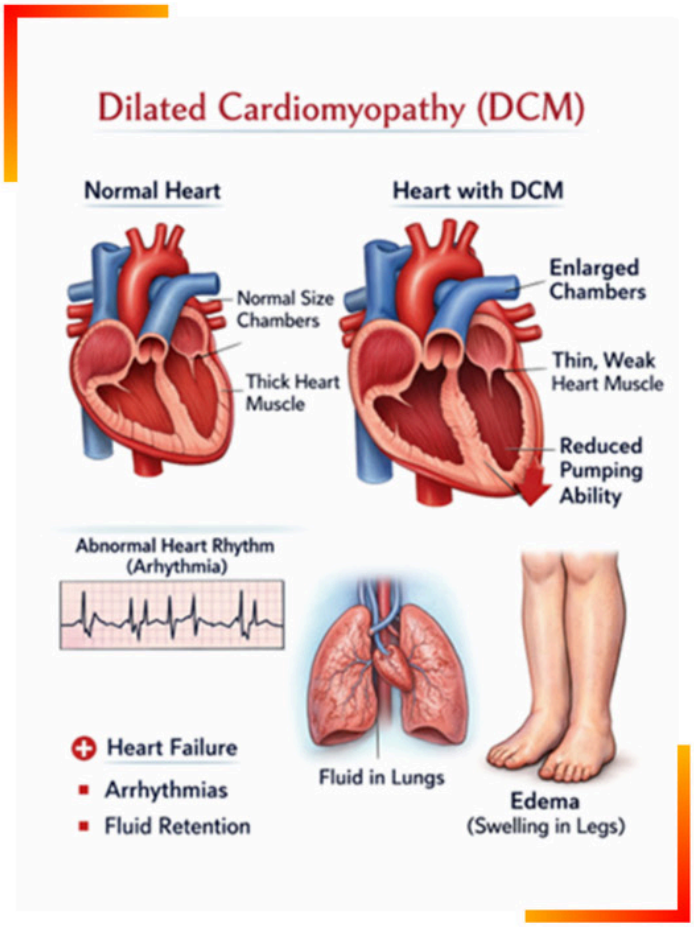
Treatment

Through MSCRF's investment, OsteoAdapt SP has moved from promising science to clinical evaluation—bringing innovative regenerative medicine closer to patients in Maryland and offering new hope for those living with degenerative disc disease.

Advancing Stem Cell treatment for Rare & Life-Threatening Heart Disease

For children and young adults living with dilated cardiomyopathy (DCM), treatment options are extremely limited. **DCM—characterized by enlargement of the heart chambers and weakening of the heart muscle—is a leading cause of heart failure and accounts for approximately half of all pediatric cardiomyopathy diagnoses**. In children, the disease is often diagnosed early in life and carries a poor prognosis, with many patients facing limited survival without heart transplantation.

Managing DCM in pediatric patients presents unique challenges. While some cases are inherited, many are believed to arise from autoimmune or inflammatory responses to viral infections. Progressive ventricular remodeling, inflammation, and fibrosis drive worsening cardiac function over time. Currently available therapies for DCM—including ACE inhibitors, ARBs, beta-blockers, and mineralocorticoid receptor antagonists—can improve heart function and survival but do not offer a permanent solution. Device-based interventions like implantable cardioverter-defibrillators and cardiac resynchronization therapy provide more precise management but come with surgical risks, potential malfunctions, lifestyle restrictions, and psychological burdens. Further, these current treatments do not address the underlying disease processes, leaving morbidity and mortality rates high. Heart transplantation remains a last resort for some patients yet carries significant long-term risks, underscoring the urgent need for new, disease-modifying therapies.



With support from the Maryland Stem Cell Research Fund (MSCRF), Secretome Therapeutics is advancing a novel therapeutic approach designed to target these core mechanisms of disease. The company's lead investigational therapy, STM-01, is an exosome-based, allogeneic product derived from human neonatal heart–derived medicinal signaling cells, developed to activate the heart's intrinsic repair pathways and counter inflammation, fibrosis, and myocardial cell loss.

Dr. Sunjay Kaushal

Preclinical studies led by Dr. Sunjay Kaushal formerly at the University of Maryland, Baltimore and Dr. Michael Davis at Emory University and Georgia Tech demonstrated marked improvements in cardiac function in both adult and juvenile models of heart failure—key findings that helped move STM-01 toward clinical testing. **STM-01 is now being evaluated in multiple Phase I clinical trials,** including an investigator-led, dose-escalation study assessing safety in adults with DCM, with plans to advance to pediatric DCM if the therapy is shown to be safe and well tolerated.

In March 2025 STM01 was granted Fast Track designation by the FDA for heart failure with preserved ejection fraction (HFpEF). Early safety data from the HFpEF Phase I trial are encouraging, with seven patients having received escalating doses of STM-01. Although final trial results are not yet available, Vinny Jindal, President and CEO of Secretome Therapeutics reports that t**he data to date demonstrate a "more than adequate safety profile," providing confidence in the therapy's continued development.**

In parallel, Secretome is preparing a Phase II clinical study in Duchenne muscular dystrophy (DMD), a devastating genetic disease in which cardiomyopathy is the leading cause of death and effective cardiac therapies are lacking. "Early safety data from STM-01 give us confidence as we move toward a Phase II study in Duchenne muscular dystrophy, where the need for effective cardiac therapies is profound," said Jindal.By supporting early-stage, high-risk research, MSCRF is accelerating the development of a new class of regenerative therapies while bringing hope to patients and families facing life-threatening heart disease.

Mr. Vinny Jindal

> Our goal is to develop treatments for patients who currently have none. With MSCRF support and encouraging early safety data, we are moving forward with a program that could fundamentally change how we treat heart disease in rare and underserved populations. - Mr. Vinny Jindal , CEO & President, Secretome Therapeutics

Restoring Sight and Quality of Life: A New Hope for Patients with Ocular Graft-Versus-Host Disease

For many patients who undergo allogeneic hematopoietic stem cell transplantation (HSCT), survival is only the beginning. Although HSCT can cure blood cancers, up to 50% of patients develop graft-versus-host disease (GVHD), a chronic autoimmune condition. When GVHD affects the eyes—known as ocular GVHD—it becomes one of the most painful and debilitating complications patients face.

Ocular GVHD causes severe inflammation of the eye surface, leading to chronic dry eye, burning and stinging pain, excessive tearing, discharge, and progressive damage to the cornea. **For patients, these symptoms interfere with daily activities such as reading, driving, and working, dramatically reducing quality of life.**

There are **currently no therapies that specifically target the underlying disease.** Standard treatments—including artificial tears, immunosuppressive medications, scleral lenses, and lifestyle modifications—offer limited relief and do little to repair damaged tissue or prevent vision-threatening complications.

Paul Dela Vina knows these challenges firsthand. In 2009, he was diagnosed with acute lymphoblastic leukemia and received treatment at the University of Maryland, including a bone marrow transplant that successfully put his cancer into remission. In 2023, after a relapse, he underwent another transplant. While the cancer treatment succeeded, he soon developed ocular GVHD.

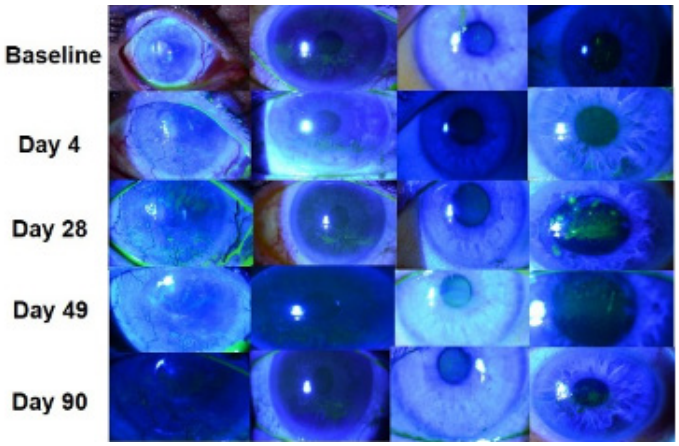
Mr. Paul Dela Vina

> This is a very good thing for the patient. It's a lot of help. To know that there are people behind this—the researchers and state-funded programs like MSCRF — it's a good feeling to know that people like me are being seen and cared for. It's good knowing there are people helping us out. - Mr. Paul Dela Vina

The condition caused persistent pain, burning, stinging, excessive tearing, and discharge—symptoms that proved difficult to manage despite visits to multiple physicians. Ultimately, Dela Vina was referred to Dr. Sarah Sunshine, an assistant professor at the University of Maryland, Baltimore, who specializes in corneal and ocular surface diseases, particularly complications arising from cancer therapies.

Dr. Sunshine is leading for the **first time a clinical trial investigating the use of mesenchymal stem cells (MSCs) to treat severe ocular surface damage** caused by oGVHD. MSCs are known for their anti-inflammatory and regenerative properties, offering the potential not only to relieve symptoms but also to promote healing and prevent harmful scarring. Sunshine holds an FDA-approved Investigational New Drug (IND) application for this therapy and received, making the trial possible.

With support from an MSCRF Clinical Grant to Dr. Sunshine, Dela Vina enrolled in the blinded study. While he does not know whether he received stem cell therapy or a control treatment, he is already noticing encouraging changes.



"It's kind of crazy not knowing what treatment I actually got," Dela Vina says with a laugh. "But my eyes are getting stronger, and I'm hopeful things will keep improving." **Beyond the physical improvements, participation in the trial has given Dela Vina something equally important: hope.**

The primary goal of this MSCRF-supported clinical study is to evaluate the safety and effectiveness of MSC therapy in patients with non-healing corneal epithelial disease and severe ocular surface injury due to oGVHD. The clinical team headed by Dr. Sunshine is measuring epithelial healing, scarring, and visual acuity over a three-month period, with the primary efficacy endpoint assessed at Day 28. To date, **six patients** have been treated, with additional participants expected before study completion in May 2026.

For patients like **Paul Dela Vina**, each visit represents more than a data point—it offers the possibility of restored vision, reduced pain, and renewed independence. For patients facing the long-term consequences of life-saving cancer treatments, MSCRF-supported research offers something profound: the possibility of healing beyond survival.

MSCRF

Annual Report
-2025-

COMPANY AWARDEE
Spotlight

COMPANY WINS IN 2025

BIOCARDIA

- Initiated 250-patient Phase 3 trial (May 2025) in ischemic heart failure, looking into major cardiac events to support approval and adoption.
- An autologous cardiovascular cell therapy developer.
- 34 employees, $119M raised to date.

Britecyte

- FDA-cleared BRC-OA (adipose allograft) for osteoarthritis. 10 patients enrolled in MD; expanding enrollment through 2025.
- Established in 2020, focuses on cell and tissue regenerative therapies for metabolic diseases.
- Raised ~$11M in capital and has 6 employees.

Cartesian therapeutics

- In Nov 2025, Descartes-08 (an outpatient CAR-T therapy) showed strong Phase 2 Systemic lupus erythematosus results, and is advancing into myositis in 2026.
- A clinical-stage cell therapy autoimmune company.
- 66 employees, $202M raised to date.

elixirgen THERAPEUTICS

- First clinical use of telomere elongation to age-normal range, with improved neutrophil counts and no treatment-related adverse events.
- A clinical-stage gene therapy company targeting rare telomere disorders.
- 14 employees, $29.4M raised to date.

KOLON TISSUEGENE

- Completed its Knee Osteoarthritis product TG-C, strong Phase 2 efficacy (55% lower knee replacement rate).
- Developing first-in-class allogeneic cell and gene therapy for musculoskeletal disease.
- 58 employees, $403M raised to date.

LONGEVERON

- Completed Phase 2b (June 2025) enrollment for laromestrocel in treating hypoplastic left heart syndrome.
- Focused on aging-related diseases.
- 25 employees, raised to date.

COMPANY WINS IN 2025

MaxCyte®

- Acquired SeQure Dx ($4.5M) in Jan 2025; adds revenue generating gene-editing safety assays to bolster end-to-end cell & gene therapy platform.
- Maxycte, platform providing CGT tools, technology, and services.
- 114 employees, $174M raised to date.

NANOCHON™

- Received Health Canada clearance for a first-in-human knee feasibility trial in late 2025 to evaluate safety and performance in patients with cartilage lesions.
- A medical device company developing stem-cell based orthopedic solutions for cartilage repair.
- Spin-off from George Washington University.

RoosterBio®

- RoosterBio announced a collaboration with Thermo Fisher Scientific in April 2025 to pair MSC/exosome media systems with Thermo's CDMO/GMP capabilities.
- Roosterbio, provides scalable cell and exosome manufacturing tools for regenerative medicine.
- 57 employees, $41M total raised to date.

Secretome THERAPEUTICS

- Initiated 2 clinical trials in 2025 for heart diseases.
- Partnered with MD-based RoosterBio, Inc. for Scaling up their Product.
- Focuses on stem cells from neonates.
- University of Maryland spin off with $32 million raised and 8 employees.

SereNeuro THERAPEUTICS

- Generated proof of concept animal data in 2025 data showing chronic osteoarthritis pain relief and slowing cartilage degeneration.
- Baltimore- based Johns Hopkins University spin-off.

Theradaptive

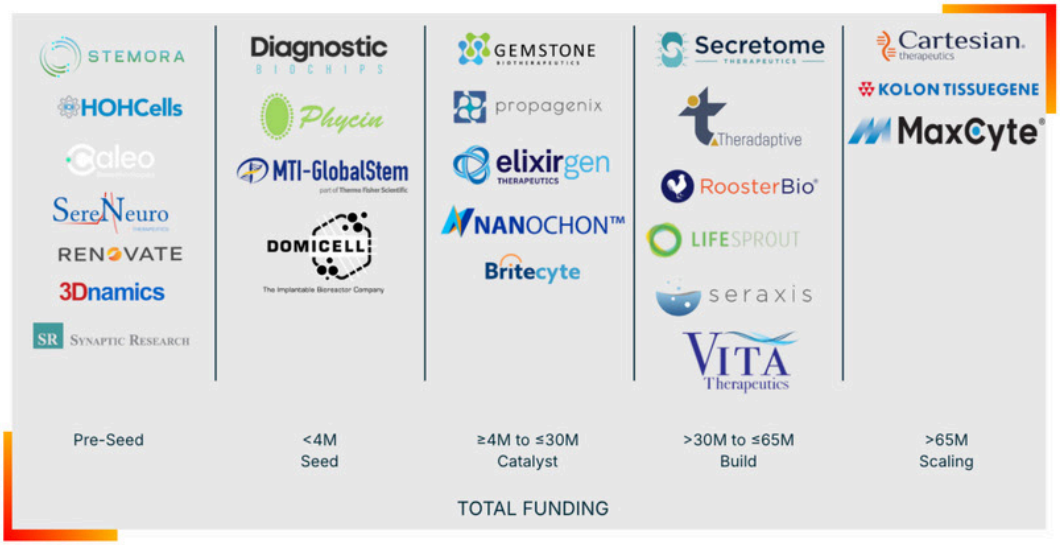
- Completed patient enrollment in October 2025 (spinal fusion implant) for Phase 1/2 clinical trial for Spinal Fusion.
- Initiated Phase I clinical with OsteoAdapt for dental application.
- Therapeutic delivery platform from soft tissue to orthopedics.
- 35 employees, raised $75M to date.

Companies Supported by the MSCRF

To date, MSCRF has supported **36 companies,** deploying more than **$28 million** in grant funding to advance regenerative medicine innovations across Maryland. MSCRF-funded companies often follow a clear and compelling growth trajectory—from early-stage discovery to mature, market-ready organizations—demonstrating the catalytic role of early state investment. Early, non-dilutive state funding enables companies move discoveries into development reduce risk, and attract follow-on private, federal, and strategic investment. As milestones are reached, this layered financing fuels pipeline expansion, job creation, and progress toward commercialization.

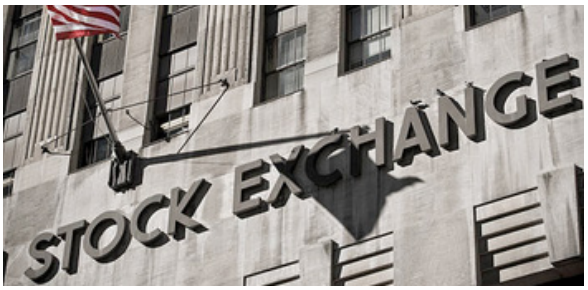
The graphic on the page illustrates the distribution of MSCRF portfolio companies across financing stages, with more than half **raising between $4 million and $65 million in follow-on capital.**

Capital Raised by Some MSCRF Companies

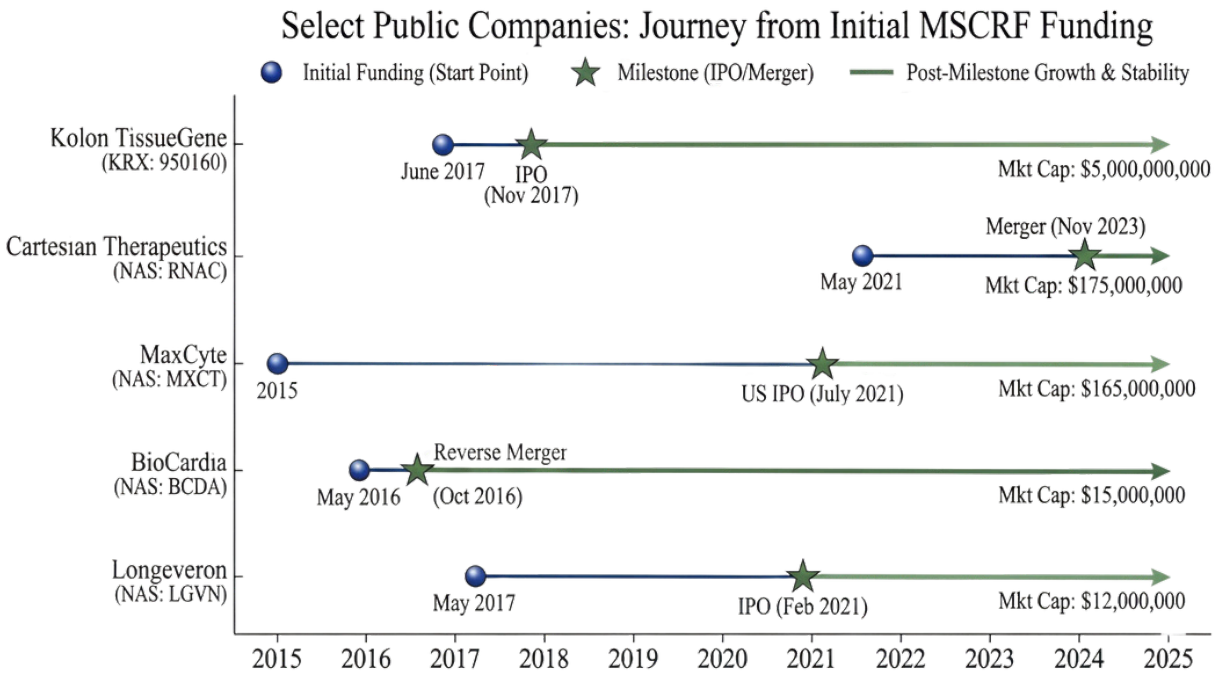


> Funding from MSCRF was instrumental in driving our product manufacturing methods forward toward commercialization. The success of this program allowed us to win critical additional funding.

Dr. Luis Alvarez
Theradaptive Inc.



For a subset of MSCRF-supported companies, sustained progress led to successful initial public offerings (IPOs), generating significant economic value and reinforcing Maryland's position as a leader in life sciences innovation- highlighting MSCRF's role in building a strong and growing life sciences economy in Maryland. The figure below illustrates MSCRF-funded companies that reached IPOs.



- **Kolon TissueGene**, first supported by MSCRF in 2017, grew its Maryland roots to ~$5 billion market cap in 2025, with its $137 million IPO supported by early MSCRF investment.
- **Cartesian Therapeutics**, in Frederick, received MSCRF support in 2021 and expanded to 66 employees as its lead therapy, Descartes-08, advances to late-stage development for generalized myasthenia gravis.
- **MaxCyte**, Rockville-based and first funded by MSCRF in 2015 and has grown into a commercial cell-engineering company, reporting $34M in trailing twelve month revenue and increasing its workforce from 25 to 114 employees.

These outcomes provide significant context for the following pages, which spotlight select MSCRF - funded companies in 2025 poised for similar innovation, growth, and impact. Note that the companies supported through MSCRF manufacturing grants are highlighted separately in the Manufacturing Grants Impact Section.

SereNeuro THERAPEUTICS Advancing Non-Opioid Pain Solutions

It's estimated that one in five Americans, more than 54 million people, have some form of arthritis, with osteoarthritis being the most common type. Symptoms of osteoarthritis, a degenerative joint disease, include pain, stiffness and swelling in the joint. The joint, often the knees, can have limited range of motion and make odd noises when in motion.

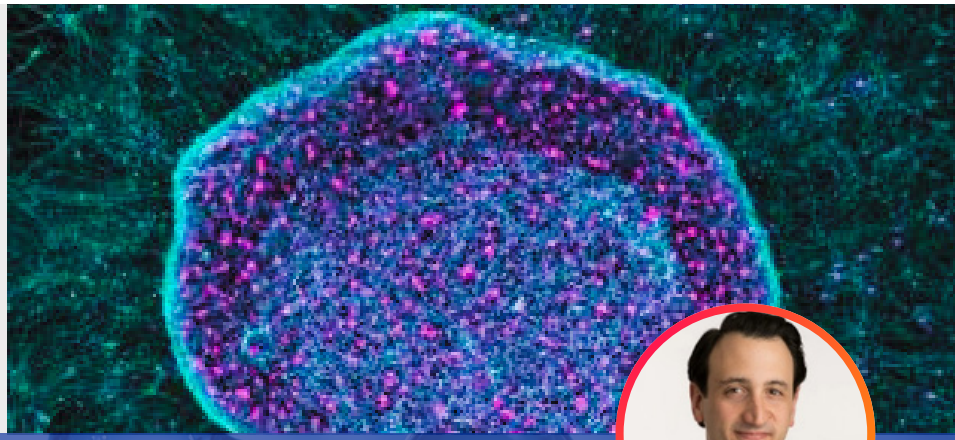
Pain medication is one of the most common forms of treatment for osteoarthritis. But with concerns over prescribing opioid-based medicines, new approaches to treating osteoarthritis pain are necessary.

"**For most patients, today's options are limited choices: addictive opioids or temporary anti-inflammatories that just mask symptoms. Neither stops the disease from getting worse**," explains Daniel Saragnese, CEO and Co-founder of SereNeuro Therapeutics, Inc. Backed by MSCRF's Commercialization Grant in 2025, SereNeuro is developing a stem cell-based approach that will spare patients from both the pain of their disease and the risk of opioid addiction. A spinout of Johns Hopkins University (JHU), **SereNeuro Therapeutics is developing SN101, a first-in-class, non-opioid, non-addictive iPSC-derived cell therapy designed to stop joint pain and inflammation at the source.**

The technology was developed and validated by Dr. Gabsang Lee and his team at JHU with support from MSCRF. The therapy involves injecting purified nociceptive (pain-sensing) neurons derived from human iPSCs (SN101). These cells act as "biological sponges," soaking up pain and inflammatory factors at the source, without sending pain signals to the brain. And more importantly, the therapy is disease-modifying- **it not only stops the pain but also stops the degeneration of the joint.**

Within five years, Saragnese hopes the company will deliver a Phase II data package that fully demonstrates both symptomatic relief and disease modification.

SN101 SEQUESTERS ALL LOCAL PAIN FACTORS



> In today's tight funding environment, which often prioritizes short-term, "safe" projects, MSCRF provided stable, long-term funding for the foundational science. Instead of just pursuing an incremental step, the company's scientific founders were able to build a complex, high-fidelity human platform for pain research massive undertaking. Without MSCRF backing, SereNeuro wouldn't exist.

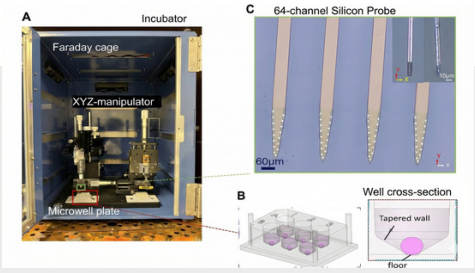
Daniel Saragnese
CEO, Sereneuro Therapeutics

Expanding Product Offerings with AI-Driven Analytics

Brian Jamieson founded Diagnostic Biochips (DBC) in 2013. Based in Glen Burnie, Maryland- half-jokingly described by the DBC team as the emerging neurotech capital of the world- the company delivers advanced neural probes and software, and assays to its customers.

In 2025, with the support of MSCRF's Commercialization grant, **DBC is expanding its product pipeline by combining stem cell–derived brain organoids with machine-learning–driven analytics.** Unlike traditional, low-throughput assays that disrupt the model, DBC preserves biological integrity while capturing meaningful electrophysiological data on how neurons form and communicate within circuits. With more than 10 years of development and over $10 million in non-dilutive funding, the company is creating a powerful discovery engine that strengthens preclinical prediction and creates a durable competitive advantage. **DBC has also received Second-tier MSCRF funding to collaborate with Dr. Brady Maher at the Lieber Institute for Brain Development in Baltimore, highlighting the importance of the industry–academic partnerships in product development.** Merck committed $1 million in the first two years of collaboration to support instrument and software development.

In November 2025, DBC launched SomaFocus, an instrument that delivers high-resolution, high-throughput functional analysis of brain organoids for both R&D and quality control applications. In fact, DBC was selected as a finalist in the BioTools Innovator program, which "**helped put us on the map with investors and strategies in the tools space, and has led to some useful partnerships and mentoring opportunities.** As a result of the new high throughput offerings, the company projects **annual revenues to quadruple by 2028.**



Organoid recording set-up

Dr. Brian Jamieson
CEO, Diagnostic Biochips

> MSCRF funding made a significant difference to our company, allowing us to develop our prototype instrument and to roll out our marketing offering, SomaFocus- a first instrument for brain organoid analysis.

From Startup to Clinical-Stage Company: Britecyte's Path Forward

Founded in 2020 as a one-person startup, Britecyte set out to develop **regenerative therapies derived from allogeneic adipose tissue** for patients with limited treatment options. **A critical inflection point came in 2022, when Britecyte received an MSCRF Commercialization Grant.** This early support validated the company's science, enabled key data generation, and helped refine its development strategy. The results accelerated product development, supported the launch of an adipose tissue allograft, and positioned Britecyte's lead osteoarthritis therapy for clinical advancement.

In early 2025, the team secured FDA authorization to proceed with its first human clinical trial and was subsequently awarded an MSCRF Clinical Grant to accelerate development of its knee osteoarthritis therapy.

Today, Britecyte operates from a **9,400-square-foot laboratory in Frederick, Maryland**, and collaborates with leading clinical and academic partners in Maryland, including Johns Hopkins University, Regenerative Orthopedics and Sports Medicine (ROSM), and Amarex Clinical Research. The company has **raised $11M in capital** and has grown to **a team of six—**laying the foundation to become a clinical-stage regenerative medicine company.

Britecyte®
Brilliant therapies. Brighter lives.

"Collaboration is the heartbeat of innovation. Strong collaboration results in robust innovation. The MSCRF has truly synergized collaboration at Britecyte, and they are without question one of the primary reasons for the positive impact that we have already generated for our patients."

Dr. Samson Tom
CEO, Britecyte

HOHCells Translating Academic Insight into Commercial Impact

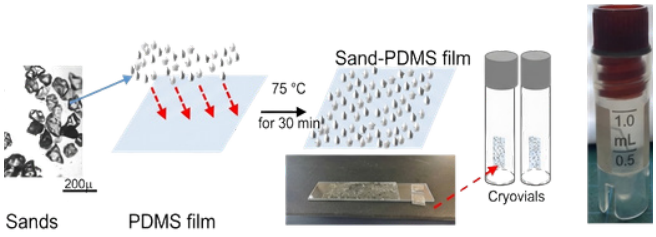
HOHCells illustrates how MSCRF support helps transform academic discovery into commercial innovation in Maryland. **Founded in 2023,** the company emerged directly from MSCRF-supported research led by **Dr. Xiaoming (Shawn) He** at the University of Maryland, where his work explored how physical environments influence stem cell health and survival.

The company's lead technology, FreezOpt™, was inspired by a simple observation from nature—how ice forms earlier and more uniformly over sandy beaches. That insight led to a novel approach for controlling ice formation during cryopreservation, significantly improving post-thaw cell viability without altering existing protocols.

Dr. Xiaoming He

"Nature often reveals elegant solutions—we just have to translate them into tools scientists can use," says Dr. He. MSCRF support at the discovery, validation, and commercialization stages enabled HOHCells to move these innovations from academic prototypes to market-ready technologies. "**MSCRF supported this work long before it was a company," Dr. He notes. "Their early investment in the science made HOHCells possible.**" With MSCRF Commercialization Program funding, HOHCells completed design for manufacturing for FreezOpt™, generated key validation data, and advanced Coldetach™, a chemical- and enzyme-free cell detachment technology, as a pipeline product. In 2025, the company strengthened its commercial leadership with the addition of CEO, Greg Merril and is now **preparing for FreezOpt™'s launch in early 2026.**

HOHCells' trajectory reflects the broader impact of MSCRF—bridging the gap between academic research and real-world application and helping build a pipeline of innovative companies poised for growth in Maryland.

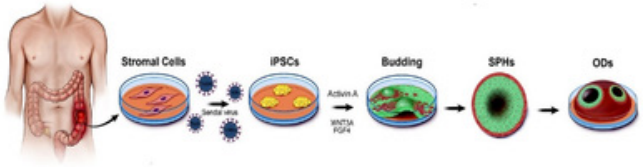


Greg Merrill
CEO, HOH Cells

> We're launching FreezOpt™ in early 2026 -it is the first step, and our pipeline builds from there. Nature gave us the idea; engineering made it a product. MSCRF is making it possible.

Caleo Biotechnologies Anchoring Innovation in Maryland

A spin-off from the **Cleveland Clinic Foundation**, Caleo Biotechnologies found its ideal home in Germantown, Maryland. Founder and CEO Dr. Sam Kamali, the visionary behind the technology, chose Maryland for its robust startup ecosystem and the unique synergy between the MSCRF and a world-class stem cell community.



To address a critical gap in drug development, Caleo Biotechnolgies (Caleo Bio) creates patient-relevant, immune-competent preclinical models for inflammatory and fibrotic diseases. Their Organ-Dish (OD) Platform recreates patient-specific tissue architecture, allowing biopharma teams to accurately compare therapies and identify the most effective treatments for specific populations. By integrating AI-based phenotypic readouts, Caleo Bio brings human biology into the decision-making process earlier, ensuring more reliable data than traditional systems.

MSCRF's Commercialization Program played a pivotal role at the company's earliest stage.

The support enabled Caleo Bio to establish core infrastructure, validate its minimum viable platform for inflammatory bowel disease, and refine workflows based on the customer needs. **"MSCRF's early commercialization support gave us the opportunity to take the first real steps in building CaleoBio," Kamali said. "That foundation helped make this early stage of development possible."**

Enabled by MSCRF's Second-tier Funding. CaleoBio is currently partnering with Dr. David Hackam at Johns Hopkins University, leveraging his deep clinical expertise to further validate the platform's capabilities.

Beyond funding, MSCRF provided credibility and visibility that accelerated connections across Maryland's innovation ecosystem. "The credibility that comes with MSCRF's backing has opened doors and helped us build meaningful partnerships," Kamali noted, underscoring the importance of mentorship and community for young companies.

Today, the company is positioned for rapid growth and deeper collaborations, bringing the next generation of life-saving therapies closer to the patients who need them most.

> "MSCRF is a true partner. Their expert guidance helped us navigate complex technical challenges, while their ecosystem provided the credibility and connections necessary to grow our footprint in Maryland."

Dr. Sam Kamali
CEO,
Caleo Biotechnolgies

MSCRF

Annual Report
-2025-

ACADEMIC AWARDEE
Spotlight

Exosome-Based Therapy for OSTEOPOROSIS

DR. JIABANG FAN

In May 2025, **University of Maryland Eastern Shore (UMES)** researcher Dr. Jiabang Fan, an assistant professor, secured a Discovery Grant from Maryland Stem Cell Research Fund to help advance his studies in stem cell drug delivery and bone loss disease treatment, focused on exosome-based therapies for tissue and bone repair. Specifically, **Fan is focused on developing a stem cell therapy for osteoporosis**, a disease that causes bones to become weaker and more likely to fracture.

It's a disease that has no symptoms, until a bone breaks. Fan notes that osteoporosis is a leading cause of disability in people. There's no effective treatment for this disease. However, stem cells shows promise in some regenerative ability, Fan says. Fan's lab at UMES focuses on exosome-based therapies for tissue and bone repair, working with graduate students and postdocs. he Discovery Grant funds will support Fan's efforts to develop engineered human mesenchymal stem cells for treating osteoporosis.

The Discovery Grant funds will support Fan's efforts to develop engineered human mesenchymal stem cells for treating osteoporosis. The project aims to address how stem cells shift from bone-forming pathways toward fat-forming pathways in the bone marrow, contributing to bone loss. **Research shows that increased bone marrow fat is associated with reduced bone mass, and visceral fat may further accelerate bone loss by driving inflammation. This can address the systemic nature of osteoporosis, Fan says.**

He explains that exosomes offer advantages such as less immune rejection, high biocompatibility and fewer side effects compared to traditional stem cell therapies. Fan says that many research institutions and biotechnology companies are now shifting towards exosome-based therapies due to these benefits, while still considering them part of the broader stem cell therapy field.

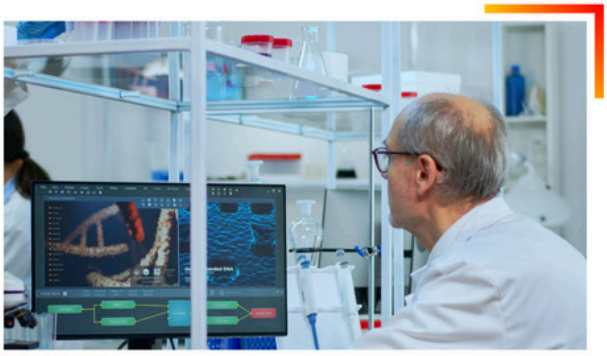
> We are proud to contribute to a growing ecosystem of innovation in the state. We will use this grant to continue our good work and contribute to the Maryland stem cell regenerative medicine ecosystem. It helps our lab and our team to develop our therapy for clinical application. It allows us to attack critical applications in regenerative medicine .
> - Dr. Jiabang Fan

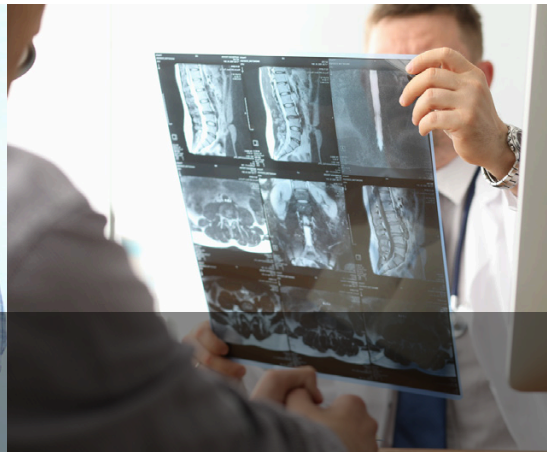
Dr. Jiabang Fan - *Cont'd*

MSCRF Funding

Fan is the first research from UMES to receive funding from MSCRF. He says there is limited funding available through the university and the MSCRF money is beneficial. **He calls it as an honor to be the first and says the grant will not only support his research, but also provide new opportunities for students to gain a greater understanding of regenerative medicine.**

MSCRF support is critical for the stem cell community, Fan says. It keeps the state competitive in stem cell research and regenerative medicine, especially at a time when reduced federal funding is negatively impacting academic institutions and early career investigators. Fan stressed the need for continued state-supported investment to maintain Maryland's competitiveness in stem cell and regenerative medicine.





Revolutionizing STEM CELL Radiolabeling Through 3D-Printed Automation

DR. RYAN SOCHOL

Stem cell therapy holds distinctive promises for treating a wide range of conditions. At present, stem cells are primarily administered without monitoring. This 'black box' approach is inefficient and results in variable outcomes. In vivo tracking of radiolabeled stem cells via positron emission tomography (PET) could overcome these challenges; however, current radiolabeling techniques require highly trained personnel, involve radiation exposure, and entail manual techniques that are time- and labor-intensive.

In this project, Dr. Ryan D. Sochol from the University of Maryland, College Park proposes to leverage recent advancements in 3D-printed microfluidic technologies to address these challenges and enable near autonomous, enhanced radiolabeling of human stem cells. Their overarching goal is to improve the efficacy of stem cell radiolabeling while limiting exposure to radioactivity.

The innovation of automating and enhancing the processes for radiopharmaceutical synthesis and stem cell radiolabeling via microfluidics and 3D printing can enhance the efficacy of not only stem cells treatments but other regenerative medicine therapies, including radiolabeling of biologics, drugs, macromolecules, and other novel nanomedicines

Next-Gen Human STEM CELLS

DR. LUDOVIC ZIMMERLIN

Dr. Ludovic Zimmerlin from the Johns Hopkins School of Medicine, Institute for Cell Engineering developed a chemical method in the laboratory of Dr. Elias Zambidis to rejuvenate human pluripotent stem cells to an even earlier embryo-like state termed TIRN stem cells. This unique stem cell state addresses many limitations of conventional pluripotent stem cells, offering improved reproducibility, greater efficiency to produce many cell types, but also better quality and survival of the tissues that are grown from them in the dish or in animal models.

The method was originally developed during Ludovic's MSCRF-sponsored post-doctoral fellowship and the latest findings on TIRN stem cells were published in Cell Reports in May 2025. In the article titled "Proteogenomic reprogramming to a functional human blastomere-like stem cell state via a PARP1-DUX4 regulatory axis", Zimmerlin provide a compre-hensive characterization of TIRN stem cells using sophisticated bioinformatics and embryo models. These MSCRF-funded studies revealed that these cells express a non-natural mix of embryo-like programs and can form many tissues. Ongoing works from Dr. Zimmerlin exploits the singular capacity of TIRN stem cells to produce cell lines of more advanced lineage-specific stem cells. In recent MSCRF-sponsored studies, Dr. Zimmerlin and his team validated the improved capacity of TIRN stem cells to form whole human retina in a dish through an organoid approach. TIRN stem cell-derived retinal organoids produce self-renewing retinal stem cell lines that can be cryopreserved and expanded for unlimited passages. These retinal stem cell lines can be directed - on demand - to recapitulate the entire three-dimensional developmental process of forming a whole eye organ in a dish. These novel TIRN stem cell-derived retinal stem cell lines promise breakthrough translational applications for treating degenerative blinding disorders.

Understanding DNA Packaging Defects in DEVELOPING BRAIN

DR. ERIN GREEN

Growing evidence indicates that various neurodevelopmental disorders, such as autism spectrum disorders and intellectual disability, result from disruptions in proteins that regulate gene expression through modifications to chromatin, the structure in cells that packages DNA and controls access to genetic information. Dr. Erin Green's laboratory at the University of Maryland, Baltimore County investigates a family of enzymes known as the SET domain family, which helps control DNA packaging by adding chemical tags to proteins called histones. Mutations or loss of these proteins are thought to disturb gene expression during brain development.

In this project, Dr. Green will generate induced pluripotent stem cell (iPSC) models that contain these genetic mutations. These iPSC models will then be differentiated into neurons (brain cells) to examine how the mutation affects chromatin structure and neural gene expression during development**. Findings from this work will advance understanding of the mechanisms underlying this disorder, identify potential therapeutic targets, and establish a framework for extending this approach to other rare neurodevelopmental diseases** caused by disrupted SET domain family of enzymes.

> The Launch award from MSCRF has been instrumental in supporting our efforts to develop iPSC models of a rare neurodevelopmental disorder characterized by improper epigenetic regulation. This award provides the foundational support for developing a robust set of experimental tools and expertise in testing the role for mis-regulation of epigenetic processes in neurodevelopmental disorders and identifying new therapeutic avenues that will be evaluated using stem cells. We are excited to have the opportunity to develop and test these models at UMBC and to support the training of a talented workforce in stem cell research. - Dr. Erin Green

Uncovering the Link Between Mitochondria & Immune Cell Problems in BARTH SYNDROME

DR. HILARY VERNON

Barth Syndrome (BTHS) is caused by mutations in the TAZ gene, resulting in cardiomyopathy, skeletal myopathy, and low levels of specialized immune cells that fight infections, known as neutrophils (i.e., neutropenia). Neutropenia leads to serious infections in BTHS and despite existing therapies, one third of treated patients endure hospitalizations for infections and are at risk of cancer.

Although researchers know that Barth Syndrome involves defective mitochondria, the cell's energy factories, the reason for low neutrophil levels is still unknown. Dr. Hilary Vernon's team from Johns Hopkins University hypothesizes that neutropenia in BTHS results from: 1) defects in the capacity for mitochondria to shift from glycolysis to oxidative metabolism (required for neutrophil development) and 2) impaired mitochondrial function results from disrupted clearance of defective mitochondria. To study this, Dr. Vernon will develop two complementary stem cell models. One model will grow hematopoietic (blood-forming) stem cells from Barth Syndrome patients in special laboratory mice, allowing the team to observe how neutrophils develop in a living system. The other will use genetically engineered human stem cells to create neutrophils carrying the same TAZ gene defect linked to Barth Syndrome.

By uncovering how mitochondrial problems disrupt neutrophil development, this research may lead to new treatments for Barth Syndrome and other conditions where immune cell production fails. Ultimately, Dr. Vernon's work will shed light on neutropenia in related disorders of neutrophil developmental failure, driving the impact of her research beyond BTHS.

As a result of this early work in stem cell models, Dr. Vernon has published a paper this year in a well-regarded journal, entitled: Stem cell models of TAFAZZIN deficiency reveal novel tissue-specific pathologies in Barth syndrome as well as awarded an NIH (R01) grant, entitled: 'Understanding Cardiac Mitochondrial Quality Control Through The Lens Of Barth Syndrome'. Finally, and most importantly, her lab's pivotal work has led FDA approval of a first-of-its-kind therapy in patients suffering from BTHS.

> Our work in stem cell models of Barth Syndrome are an example of how this technology can be used to understand molecular targets and develop new therapeutics for ultra rare diseases.
> - Dr. Hilary Vernon

Defining the Epigenetic Mechanisms of BECK-FAHRNER Syndrome

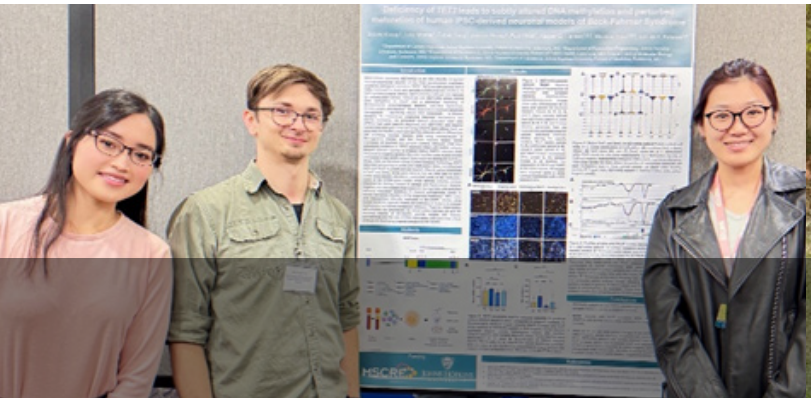
DR. JILL FAHRNER

Beck-Fahrner syndrome (BEFAHRS) is a newly identified rare genetic disorder that affects brain development. People with BEFAHRS often experience developmental delays, intellectual disability, low muscle tone, anxiety, ADHD, autistic traits, and sometimes seizures. The condition is caused by inherited changes in a gene called TET3, which converts 5-methylcytosine (5mC) to 5-hydroxymethylcytosine (5hmC), the first step in active demethylation. When TET3 doesn't function properly, these chemical marks become unbalanced, and this can affect how genes function, especially in the brain.

Researchers have found that people with BEFAHRS show higher levels of 5mC in their blood, but it's still unclear how these DNA changes relate to the symptoms seen in patients. This is partly because measuring these chemical markers in brain cells has been extremely difficult — until now.

Dr. Jill Fahrner from Johns Hopkins University will use a novel, cutting-edge tool called nanopore sequencing to accurately measure both DNA marks (5mC and 5hmC) in lab-grown human neurons that model BEFAHRS as well as evaluate experimental treatments to see if these chemical imbalances can be corrected.

This study is groundbreaking because it uses advanced technology to explore how subtle DNA changes affect brain development. The insights gained could lead to new treatments not only for BEFAHRS, which currently has no cure, but also for more common conditions linked to similar DNA regulation patterns.



Shedding Light on a CURE for Age-Related VISION LOSS

DR. ZUBAIR AHMED

Age-related macular degeneration (AMD) is a common eye disease that damages the macula, the small area in the back of the eye that lets us see fine details clearly. Over time, this damage can cause blurred or lost central vision, making it difficult to read, drive, or recognize faces. The most common form, called dry AMD, happens when the macula becomes thin and part of it wears away, leading to areas of vision loss known as geographic atrophy. Unfortunately, there are currently no effective treatments that can stop or slow this type of vision loss. AMD is a major public health concern, estimated to affect more than 10% of Americans over 40 and projected to affect 288 million people globally by 2040.

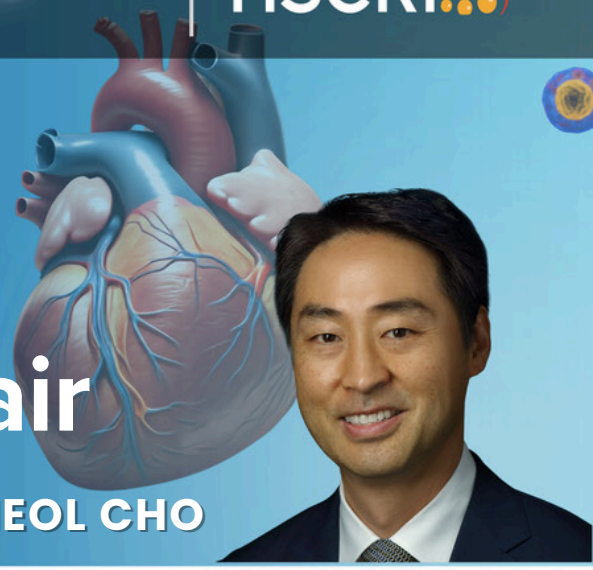
Dr. Zubair Ahmed from the University of Maryland School of Medicine focuses on finding new ways to protect vision by studying a protein called CIB2, which may help prevent damage in dry AMD. Early findings suggest that people with the disease have lower levels of CIB2 in their retinal cells, along with overactive cellular pathways and buildup of damaged cell components that can worsen the condition.

This points to CIB2 as a possible protective factor that helps cells clean up waste and stay healthy.

To understand how this works, Dr. Ahmed will grow in the lab retinal pigment epithelium (RPE) cells, the type of cells affected in AMD, from induced pluripotent stem cells (iPSCs). These lab-grown cells mimic many features of the human disease, allowing Dr. Ahmed's team to closely investigate how CIB2 functions and to test compounds that might enhance its activity. By uncovering how CIB2 helps maintain healthy RPE cells, his work could lead to new treatment strategies for dry AMD and potentially preserve sight for millions of people at risk of vision loss.

> Dr. Ahmed's Lab of Neurogenetics and Translational Research has long been working toward the development of rational therapeutic strategies for neurosensory diseases, and we welcome the opportunity to expand this work using stem-cell based model systems, thanks to Launch support from the MSCRF. - Dr. Zubair Ahmed

Replacing Wires with CELLS
A New Approach to
Heart Rhythm Repair



DR. HEE CHEOL CHO

Congenital heart disease (CHD) affects 1 in 100 newborns, with heart rhythm issues linked to the worst outcomes. Current treatments involve pacemaker implantation, leading to complications and repeated surgeries, especially in children.

In this project, Dr. Hee Cheol Cho from Johns Hopkins University aims to develop a new kind of biological heart pacemaker using human stem cells. In a healthy heart, the rhythm is controlled by a small cluster of specialized cells known as the sinoatrial node (SAN), which acts as the heart's natural pacemaker. Rather than focusing only on the pacemaker cells themselves, Dr. Cho takes a broader approach by including other types of cells found within the SAN, particularly non-muscle cells that help support and regulate heart rhythm. By capturing this cellular diversity, his goal is to create more stable and functional biological pacemakers.

This project challenges traditional approaches in stem cell research by incorporating multiple cell types to work synergistically and maintain healthy heart pacing. It also explores how stem cell-derived tissues and advanced technologies can improve treatments for heart rhythm disorders, especially in children, who often face complications with traditional electronic pacemakers. By creating miniature heart pacemaker models (organoids) that closely mimic the structure and behavior of the natural SAN, this research could pave the way for personalized, regenerative therapies for patients with slow or irregular heartbeats.

> The MSCRF funding helped us win an American Heart Association postdoc fellowship award to Dr. Misato Nakanishi-Koakutsu. We also submitted a provisional patent application this summer and just started a venture biotech company based partly on this intellectual property. We are excited to take the technology toward eventual commercialization! - Dr. Hee Cheol Cho

Charting the Brain's Blueprint to Unlock New Treatments for MENTAL HEALTH Disorders

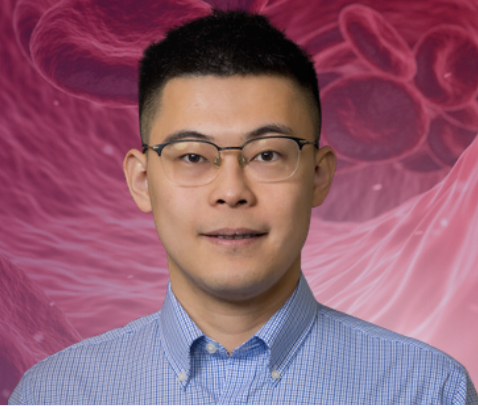
DR. SETH AMENT

Understanding the biological causes of brain and mental health disorders, such as autism spectrum disorder (ASD) and schizophrenia, remains a major scientific challenge. Combining advanced genetic tools with human stem cell models has become a powerful way to study how the brain develops and to identify potential treatment strategies. Dr. Seth Ament from the University of Maryland School of Medicine is building a suite of stem cell–based models representing different brain regions to explore how genetic and environmental risk factors disrupt neuronal development and function. His work has been supported by three Discovery Awards from MSCRF.

With his first MSCRF award, Dr. Ament created an induced pluripotent stem cell (iPSC) model of human cortical development, which his lab used to investigate psychiatric risk variants enriched in the Old Order Amish founder population. This work led to an NIH R01 grant to expand studies of how inherited risk influences early brain development. MSCRF funded a second project focused on the striatum, a brain region critical for movement and reward processing. Dr. Ament's team developed a stem cell–derived model to study epigenomic mechanisms in Huntington's disease and later extended this research to examine how opioids like fentanyl alter striatal neurons. Their findings support the NIH SCORCH consortium, which investigates biological links between addiction & HIV. In 2025, MSCRF funded Dr. Ament to develop cerebellar organoid models to study how genetic and immune-related risk factors for autism affect cerebellar neuron development. This project builds on his contributions to the NIH BRAIN Initiative Cell Census Network, where his team used single-cell genomic technologies to map human cerebellar development and identify vulnerable windows impacted by early-life inflammation. These discoveries now guide new stem cell–based models to test disease mechanisms in a human-relevant system. Dr. Ament's long-term goal is to uncover the root causes of brain disorders and translate those insights into novel strategies for treatment.

> We are deeply grateful for MSCRF's early and sustained support. MSCRF funding allowed us to take risks and build new human stem cell models that would not have been possible otherwise. Those early investments were essential for generating the preliminary data that ultimately led to larger NIH awards, including support from the NIH, as well as open opportunities for commercialization, and they continue to shape the direction of our research . - Dr. Seth Ament

In Vivo Gene Therapy for SICKLE CELL Disease



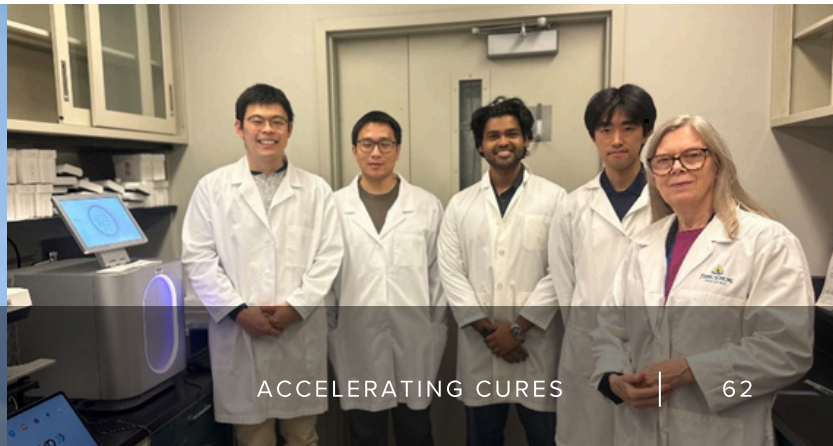
DR. XIZHEN LIAN

Sickle cell disease (SCD) is a serious inherited blood disorder caused by a single tiny change in a person's DNA. This mutation in the β-globin gene changes how red blood cells are formed, making them stiff and sickle-shaped instead of round and flexible. These misshapen cells can block blood flow, causing pain, organ damage, and other serious health problems.

For many years, treatments for SCD could only manage symptoms and prevent complications, but they couldn't cure the disease. In 2023, the FDA approved the first two gene therapies for SCD and a related condition, β-thalassemia. While these new treatments constitute a major breakthrough, they require complex procedures that involve removing a patient's stem cells, editing them in a lab, and then transplanting them back into the body. Because this process is complex, it can lead to side effects, such as inflammation, infertility, and tissue damage, and it isn't suitable for all patients, especially children.

The project by Dr. Xizhen Lian from Johns Hopkins University takes a new approach to tackle these issues. Instead of editing stem cells outside the body, Dr. Lian aims to deliver the treatment directly inside the body (in vivo) to correct the DNA change that causes SCD. Dr. Lian's team is using lipid nanoparticles (LNPs), tiny, fat-based particles similar to those used in some vaccines, to carry the gene-editing tools straight to blood stem cells.

By improving how these nanoparticles target cells and making sure the treatment is safe, they hope to create a safer, simpler, and more affordable therapy that could transform care for people with sickle cell disease. This work has the potential to make gene therapy safer and more effective as well as accessible to more patients worldwide, bringing us closer to a lasting cure for SCD.



STEM CELL Based Organoids for Neurological Disorders

DR. ANNIE KATHURIA

Traumatic brain injuries can be devastating. Memories, skills, and even communication capabilities can be lost. The brain is one of the few organs in the body that does not regenerate. But stem cell therapies can play a potential role in addressing these medical tragedies.

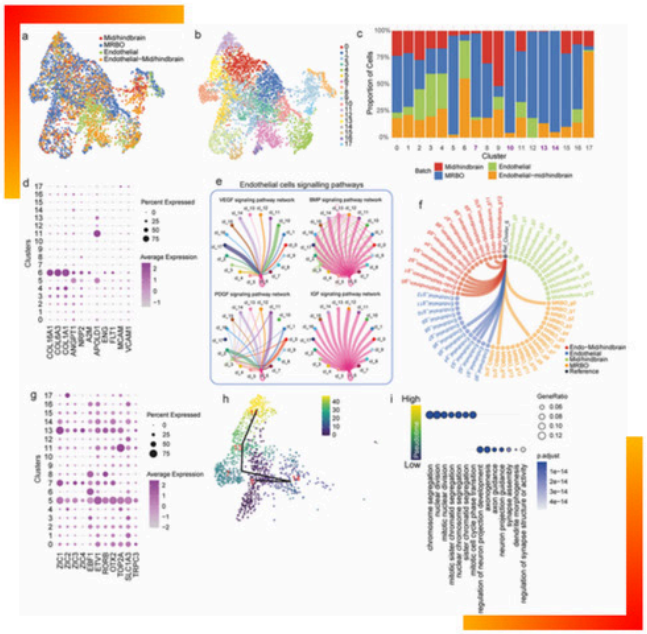
At Johns Hopkins University, researchers are exploring the potential of organoids, which are lab-grown versions of organs made from induced pluripotent stem cells. These organoids mimic the structure and function of real organs, including the brain. They can be potentially used for transplanting it into patients and potentially heal some traumatic brain injuries.

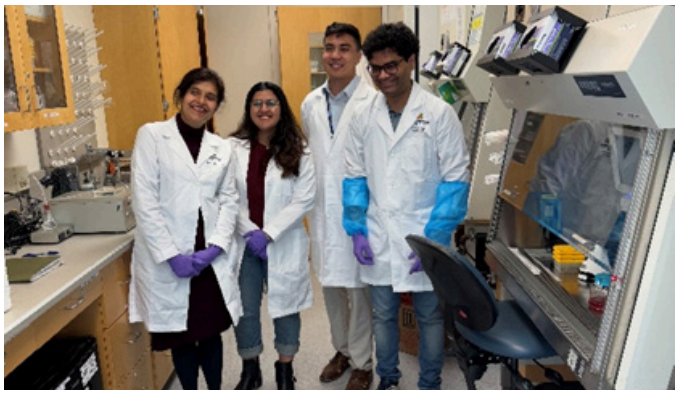
Johns Hopkins scientist, Dr. Annie Kathuria, supported by a MSCRF Discovery Grant, is focused on the promise of organoids in treating neurological conditions. Kathuria's lab at JHU is leveraging the regenerative capacities of pluripotent stem cells to develop highly-detailed 3D tissue models, or organoids. Organoids mirror the complexities of natural organs within the body, including the brain. They allow researchers to more deeply explore neurological disorders, such as schizophrenia, autism and Alzheimer's disease. Kathuria explained that organoids, are derived from a patient's cell samples, can be used to gain greater insights into the developmental trajectory of diseases and provide opportunities to assess potential therapeutic approaches, including drugs or medical devices.

Dr. Kathuria's TEDx talk on her transplantable brain organoids is included here.

> With MSCRF's support, we are recreating coordinated brain networks from patient derived cells to map how circuits malfunction and test interventions in a controlled environment. This brings us closer to personalized, predictive, and ultimately regenerative care for neurological injuries.
> - Dr. Annie Kathuria

An assistant professor in the university's Department of Biomedical Engineering, Kathuria believes these brain organoids can be used in early-stage clinical trials within the next five-year horizon and significantly move the field of transplants forward. But that's not all that's happening with stem cell organoids. Kathuria and her colleagues are also growing complex, whole-brain organoids called multi-region brain organoids (MRBO). Engineered with tissues from each region of the brain, the MRBOs act in concert like the human fetal brain. Each section of the brain is grown separately and then connected by sticky proteins. Once connected, the organoids begin to communicate with electrical currents and form a network.





In July, Kathuria and other JHU scientists published a paper in Advance Science demonstrating the potential of the MRBOs in multiple neurological indications that impact the whole brain, such as schizophrenia and autism. In fact, the MRBOs have been used to determine the differences in brain signaling patterns between patients with schizophrenia and bipolar disorder. Machine learning algorithms classified the electric activity in the brain organoids and identified the neural patterns in both healthy and unhealthy conditions – including distinguishing electrophysiological spikes in the two disorders. The MRBOs can be used to assess experimental therapeutics and possibly speed up pre-clinical drug discovery.

The findings from this are significant for mental health disorder diagnoses and treatments. Kathuria predicts the MRBOs can be used to help treat physicians discover which medicines will be the most effective in their patients, rather than relying on trial and error, which can take months to determine.

OPTRACE: Precision Imaging to Transform Brain STEM CELLS

DR. YAIJIE LIANG

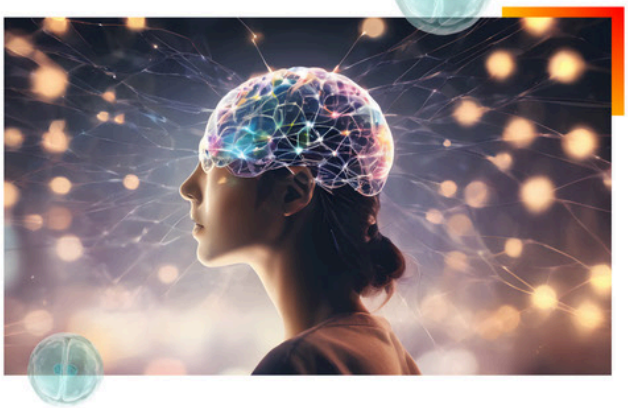
Finding an effective way to treat the brain has become a holy grail in medicine. The brain is a highly complex organ and is fiercely protected by the body. The blood-brain barrier regulates substances that can enter the brain through the bloodstream, including preventing drugs from reaching targets in the brain.

Cell therapy may prove to be the best approach to treating neurological-related issues, but so far, efforts have come up short. Only about 3% of transplanted cells survive in the brain. But, a new approach developed by Dr. Yajie (Kevin) Liang, an assistant professor in the Department of Diagnostic Radiology and Nuclear Medicine; Center for Stem Cell Biology & Regenerative Medicine at the University of Maryland School of Medicine, could be the key to overcoming these difficulties.

One of the issues with injecting cells into the brain is current technology prevents researchers from effectively tracking the transplanted material. When it's difficult to see what's going on, it's difficult to determine how to address those issues. That's where Liang's research is making a breakthrough. At University of Maryland, Liang and his team have developed OPTRACE (optical imaging-guided transplantation and tracking of cells), a new blueprint to illuminate the brain. OPTRACE precisely guides and tracks cells during transplantation and combines real-time imaging with advanced delivery techniques for better outcomes in regenerative medicine. The OPTRACE platform allows scientists to see exactly where the cells go in

> With OPTRACE, a scalable imaging-guided platform, we hope to accelerate the development of regenerative therapies by improving the precision of brain delivery and providing a practical way to track transplanted stem cells over time in real-time. OPTRACE was made possible by the Maryland Stem Cell Research Fund's generous support. - Dr. Yaijie Liang

the brain, and how they behave at the single-cell level following transplantation. OPTRACE bridges the precision of microscopy with transplant research. OPTRACE removes the guess work scientists have tried to overcome in the past. OPTRACE uses a glass pipet to see where the cells are being injected, and light and imaging technology allows those cells to be tracked over the long term.



OPTRACE removes the guess work scientists have tried to overcome in the past. OPTRACE uses a glass pipet to see where the cells are being injected, and light and imaging technology allows those cells to be tracked over the long term.

Liang's team has also developed a way to overcome cell leakage, the loss of cellular integrity. OPTRACE is combined with pulse elevation technique, repeated tiny pulses that create pockets in the brain tissue where the cells can settle. Smaller, more targeted injections offer better chances for cellular survival. The approach unlocks a way to do positively address the 3% survival rate, and figure out why things work, and ultimately speed up development for real cures for some of the most devastating diseases.

Liang's research was published in the prestigious online journal, Advanced Science. Liang said the project was directly supported by the MSCRF Discovery award, and it would not have been possible without that support.

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Community ENGAGEMENT

2025 MSCRF Felicitation Ceremony

MSCRF's 3rd **Annual Felicitation Ceremony**, held in June, recognized 2025 grant awardees and convened researchers, entrepreneurs, legislators, and leaders from across Maryland's innovation ecosystem. The program opened with a powerful patient perspective from Shauna Whisenton highlighting the importance of research and public–private partnerships in delivering real benefits to patients, honored 2025 awardees, and concluded with poster presentations that brought MSCRF-funded companies and academic teams together to spark dialogue and collaboration around advances in stem cell research.

Maryland Stem Cell & Regenerative Medicine Tech Showcase (2025)

In 2025, MSCRF strengthened Maryland's regenerative medicine ecosystem by convening stakeholders across, industry, government, academia and investment to spark new connections and accelerate translation. Key highlights included the 2nd **Annual Stem Cell and Regenerative Medicine Tech Showcase**, co-hosted with the Maryland Department of Commerce (in April), which brought together more than 200 companies, entrepreneurs, and scientists to spotlight cutting-edge innovations and foster public–private partnerships.

2nd Annual Stem Cell Symposium & Workshop (2025)

The 2nd **Annual Stem Cell Symposium and Workshop** held in October, co-hosted with JHU and the UM School of Medicine, marked a major milestone in community building by convening scientists, early-career investigators, and state legislators. The event highlighted the impact of MSCRF supported research, promoted new collaborations, and showcased how scientific discovery is translating into patient-focused outcomes. This momentum continued at **TEDCO's Entrepreneur Expo**, where MSCRF hosted panels on AI in regenerative medicine and the path to clinical trials by bringing experts together to ultimately foster public–private partnerships.

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GRANT AWARDS
Funded

2025 AWARDS

CLINICAL:

Alla Danilkovitch | Britecyte, Inc.
Heather Symons | Johns Hopkins University

COMMERCIALIZATION:

Brian Jamieson | Diagnostic Biochips Inc.
Daniel Saragnese | SereNeuro Therapeutics
Srujana Cherukuri | Stemora Inc.
Luis Alvarez | Theradaptive, Inc.
Gregory Merril | HOHCells
Jonathan Rowley | RoosterBio Inc

MANUFACTURING ASSISTANCE:

William Rust | Seraxis Inc
Nathan Castro | Nanochon, Inc.
Rama Modali | Reprocell USA

VALIDATION:

Elias Zambidis | Johns Hopkins University

LAUNCH:

Erin Green | University of Maryland, Baltimore County
Mahaa Umapathi | Johns Hopkins University
Marjan Gharagozloo | Johns Hopkins University
Qun Li | Johns Hopkins University School of Medicine
Ryan Sochol | University of Maryland, College Park
Sui Seng Tee | University of Maryland School of Medicine
Vivek Garg | University of Maryland Baltimore
Whitney Parker | University of Maryland School of Medicine
Xiao Yang | Johns Hopkins University
Zubair Ahmed | University of Maryland School of Medicine
Herana Kamal Seneviratne | University of Maryland - Baltimore County
Soojung Hur | Johns Hopkins University
Steven Hsu | Johns Hopkins University
Seunghyun Lee | Johns Hopkins University
Yuchuan Miao | Johns Hopkins University

DISCOVERY:

Kathleen Pratt | Uniformed Services University of the Health Sciences
Tae-In Kam | Johns Hopkins University School of Medicine
Linda Resar | Johns Hopkins University School of Medicine
Jiabing Fan | University of Maryland Eastern Shore
William Dalton | Johns Hopkins University
Daniel Lobo | University of Maryland, Baltimore County
Lena Smirnova | Johns Hopkins University
Brian O'Rourke | Johns Hopkins University School of Medicine
Ricardo Feldman | University of Maryland, Baltimore
Curt Civin | University of Maryland
Alan Friedman | Johns Hopkins University
Younggeon Jin | University of Maryland College Park
Alyssa Coyne | Johns Hopkins University School of Medicine
Nicholas Maragakis | Johns Hopkins University
Gabsang Lee | Johns Hopkins University
Xizhen Lian | Johns Hopkins University
Pan Li | Johns Hopkins University School of Medicine
Arens Taga | Johns Hopkins Hospital
Jeff Bulte | Johns Hopkins University School of Medicine
Mohamed Farah | Johns Hopkins University School of Medicine
Seth Ament | University of Maryland School of Medicine
Ludovic Zimmerlin | Johns Hopkins School of Medicine
Hee Cheol Cho | Johns Hopkins University, School of Medicine
Jill A Fahrner | Johns Hopkins University School of Medicine
Rajini Rao | Johns Hopkins University
Shaun M Kunisaki | Johns Hopkins University
Jiou Wang | Johns Hopkins University
Hilary Vernon | Johns Hopkins University School of Medicine
Xitiz Chamling | Johns Hopkins University School of Medicine

POST-DOCTORAL FELLOWSHIP:

Longfei Li | Johns Hopkins University School of Medicine
Luis Carlos Pinzon Herrera | University of Maryland, Baltimore County
Hira Butt | Johns Hopkins University School of Medicine
Siddharth Shah | University of Maryland, Baltimore
Willem Buys | Johns Hopkins University School of Medicine
Niannian Xu | Johns Hopkins University School of Medicine
Sterling Arjona | University of Maryland School of Medicine

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Clinical Program

Alla Danilkovitch, PhD

Britecyte, Inc.
Awardee Amount: $1,000,000
Disease Target: Osteoarthritis

Heather Symons, MD

Johns Hopkins University
Awardee Amount: $499,145
Disease Target: Bone Marrow Failure, Primary Immunodeficiencies, Dyskeratosis Congenita, Bone Marrow Transplants, Other

A Phase 1/2a, Multicenter, Randomized, Controlled, Single-Blind, Dose-Finding Study to Evaluate the Safety and Efficacy of BRC-OA, a Human Adipose Allograft, for Treatment of Knee Osteoarthritis

Osteoarthritis (OA) is the most prevalent chronic joint disease, contributing significantly to disability among adults. Chronic pain due to cartilage damage, one of the key manifestations of OA, is the greatest burden driving patients to seek medical treatment. Current therapies provide only short relief in addition to having side effects. At the present time, there are no approved therapies targeting OA pathophysiology that can slow or reverse the progression of OA. Recently, autologous adipose intra-articular injections have emerged as a new therapeutic modality for the treatment of OA. This therapy is based on the regenerative properties of adipose tissue, which contains mesenchymal stem cells, growth factors, and other bioactive components. Although promising, clinical outcomes are highly variable due to differences in tissue processing techniques and variations in tissue quality among patients. Recognizing the therapeutic potential of adipose, Britecyte has developed an "off-the-shelf" allogeneic adipose technology that retains the inherent properties of tissue with simultaneous elimination of immunogenic components, allowing allogeneic use of the tissue without rejection. Anti-inflammatory and stem cell recruiting activities make Britecyte's technology a drug candidate that can target OA pathology and delay OA progression. This prompted Britecyte to start the development of BRC-OA, an adipose therapy, for OA. The hypothesis is that an intra-articular injection of BRC-OA will block inflammation in the joint, leading to pain reduction, improved functionality, and stimulation of stem cells in the joint to repair damaged cartilage. This project is focused on testing this hypothesis in the First in Human (FIH) Phase 1/2a clinical study for the treatment of knee OA.

Regenerative Medicine to Restore Hematopoiesis and Immune Function in Immunodeficiencies and Inherited Bone Marrow Failures in Short Telomere Syndromes

Despite an increasing understanding of the role of stem cell failure in the pathophysiology of the short telomere syndromes (STS), there has been limited progress in modifying the natural history of these disorders with premature death due to failure of the bone marrow, immune system, liver and/or lungs. Ultra-short telomere length manifests as bone marrow failure and/or severe T cell immunodeficiency in children and young adults and unfortunately is followed by inevitable progression to end-stage liver and lung disease. Reduced intensity conditioning (RIC) hematopoietic stem cell transplant (HSCT) has offered new opportunities for STS, but there remain outstanding questions as to the optimal regimen, feasibility of expanding the donor pool to haploidentical donors and adequacy of long-term T cell reconstitution and function. This application will address these questions by taking advantage of the unique resources and expertise at our institution to expand access to HSCT and improve survival for STS patients. Establishing an intact hematopoietic and immune system will allow patients to later be candidates for liver and/or lung transplants. The central goal of this project is to harness the regenerative capacity of adult HSCs to cure STS. We will conduct a Phase II clinical trial using our novel RIC HSCT with post-transplant cyclophosphamide (PTCy) platform with haploidentical donors to prospectively evaluate outcomes, identify the optimal dose of PTCy, and determine quantitative and functional T cell immune reconstitution post HSCT. The RIC and lower dose PTCy is novel -- combining only the necessary chemo and immunotherapy to promote engraftment and low rates of GVHD while preventing the short and long-term toxicities unique to this patient population.

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Commercialization Program

Daniel Saragnese

SereNeuro Therapeutics
Awardee Amount: $492,786
Disease Target: Osteoarthritis

Brian Jamieson, B.Sc., MS, PhD

Diagnostic Biochips Inc.
Awardee Amount: $499,924
Disease Target: Schizophrenia

Commercialization of In Vivo Pain-Relieving Human Pain-Sensing Neurons

Over one-third of the world's population suffers from pain caused by neurological disorders, car accidents, war injuries, chemotherapy, etc. Most drugs on the market for pain treatment have undesired side effects because their targets exist both inside and outside the pain pathways. Recent research has shown that nociceptive (pain-sensing) and are highly diverse, with varied expressions of ion channels and receptors. This complexity has hindered a deeper understanding of human pain mechanisms and slowed the development of effective pain-relief drugs. Human pluripotent stem cells (hPSCs) show promise for creating targeted therapies by generating nociceptive neurons, but challenges remain in defining and purifying specific subtypes. To harness the promise of hPSCs and address such issues, we generated multiple genetic reporter hPSCs by knocking in GFP-tagged constructs into receptor and ion channel loci, characteristic of nociceptors. Pure subtypes of nociceptive neurons can be efficiently generated and isolated from hPSCs, exhibiting selective responses to noxious stimuli. These purified nociceptors closely resemble human DRG neurons and show heightened sensitivity to synovial fluid harvested from patients with osteoarthritis (OA). Furthermore, we discovered that injecting these hPSC-derived nociceptive neurons into knee joints provides dual benefits: alleviating pain and promoting bone regeneration in a mouse model of OA. In this commercialization proposal, we will move into our first commercial laboratory and optimize a cGMP alternative to the GFP-tagged purification approach and test if these hPSC-derived sensory neurons can provide long-term pain relief in a non-human primate (NHP) model of OA.

A High-throughput Instrument for Neurological and Psychiatric Drug Screening Using iPSC- Derived 3D Cultures

This Commercialization proposal aims to revolutionize the preclinical drug screening process by developing a high-throughput, electrophysiology-based model using human brain organoids derived from induced pluripotent stem cells (iPSCs). Our approach integrates advanced in vivo electrophysiology techniques with machine learning algorithms to evaluate the predictive power of organoids as models for psychiatric diseases. Unlike traditional animal models, which are labor-intensive, time-consuming, and often poorly translatable to human conditions, brain organoids offer a scalable and human-relevant platform. By recording from within the intact 3D structure of organoids, we can capture complex circuit- level phenomena that mirror the functional connectivity of the human brain, a critical factor often missed by surface readout methods. Our innovative technology allows for the precise and rapid assessment of spiking and field activities within organoids, ensuring that the full utility of these models is harnessed. We have already demonstrated the capability of our system to record single-unit activity across large numbers of neurons within organoids and to detect disease-relevant network events. Additionally, our machine learning framework, which integrates organoid-specific electrophysiological features, has shown strong potential in identifying biomarkers that distinguish between healthy and diseased states. This project aims to further refine these tools and validate their use in a specific Schizophrenia disease model, while ultimately preparing for commercialization of the high-throughput instrument that will be widely used for preclinical drug safety and efficacy screening.

Srujana Cherukuri, PhD

Stemora, Inc.
Awardee Amount: $400,000
Disease Target: Musculoskeletal System Disease

(2026 1st Funding Cycle)

Harnessing Endogenous Skeletal Stem Cells for Hyaline Cartilage Regeneration

Osteoarthritis (OA) is a widespread and often debilitating joint condition that affects millions of people around the world. It occurs when cartilagethe smooth, protective tissue that cushions the ends of bonesgradually breaks down due to wear, injury, or aging. This loss of cartilage leads to joint stiffness, pain, inflammation, and a significant reduction in mobility, often impacting quality of life. Unfortunately, cartilage has limited regenerative capacity and efforts to generate de novo cartilage remain unsuccessful. Consequently, current treatment options do not restore healthy cartilage. Instead, they focus on symptom relief through medications or rely on surgical interventions such as joint replacement, which may be invasive, costly, and not suitable or accessible for many patients. The proposed research project introduces an innovative regenerative therapy using the bodys own skeletal stem cells (SSCs) to regenerate durable, hyaline cartilagethe type naturally found in healthy joints. It builds upon the common microfracture technique but enhances it by delivering FDA-approved agents encapsulated in an alginate-based gel that ensures controlled, site-specific release. Preclinical studies in mice and human xenograft tissue have already shown the ability of this approach to generate full-thickness, structurally robust cartilage. This proposal aims to validate the feasibility of this new approach to generate hyaline cartilage in a full-thickness cartilage defect in mouse xenograft and large animal model and to establish an OA large animal model to test its efficacy in a clinically relevant setting. By leveraging FDA-approved components, our stem cell therapy offers a fast-track, minimally invasive solution to cartilage losspotentially transforming joint care.

Luis Alvarez, PhD

Theradaptive, Inc.
Awardee Amount: $400,000
Disease Target: Musculoskeletal System Disease

(2026 1st Funding Cycle)

Bioactive Titanium for Improved Osseointegration and Stability of Orthopedic Hardware

Theradaptive has developed a novel protein engineering technology that has transformed bone regeneration by enabling precision, potency, and persistence of bioactivity that gives rise to anatomically precise regeneration. We engineered a protein a variant of bone morphogenetic protein 2 (BMP2) called AMP2, which induces local stem cells to produce new bone, thus accelerating bone healing. AMP2 specifically binds to ceramic surfaces, yielding implants with improved bone healing and reduced unwanted off-target effects. In this project we expand the use of the AMP2 protein to titanium implants used to stabilize and repair injured bones. Titanium (Ti) is the most widely used implant material in all orthopedics and is commonly used in surgeries throughout the skeleton including spine, total joint replacement, trauma, dental and craniomaxillofacial surgery. Current titanium implants, while suitable for certain applications, lack the ability to achieve complete bone integration on their own and require the addition of donated cadaver bone grafts to attempt integration. These implants are insufficient to heal critical sized defects such as interbody spinal fusions, trauma reconstructions of the skeleton, and other applications, highlighting a limit in the state of the art. We propose to integrate AMP2 as a coating on the surface of porous titanium implants. This will be the first bioactive metal implant of its kind. This technology will improve surgical outcomes by enabling complete osseointegration throughout porous titanium implants, leading to faster healing and better mechanical strength than existing implants. This program will advance our mission to transform patient care through development of targeted therapeutics and regenerative stem cell-based technologies.

Gregory Merril

HOHCells
Awardee Amount: $400,000
Disease Target: Stem Cell and Organoid-Based Therapies
(2026 1st Funding Cycle)

Jonathan Rowley, PhD

RoosterBio Inc.
Awardee Amount: $400,000
Disease Target: Tool for Therapeutic Development
(2026 1st Funding Cycle)

FreezOpt Sand-Mediated Cryopreservation System

HOHCells proposes a 12-month commercialization effort for FreezOpt, a novel cryopreservation accessory designed to improve post-thaw viability of human stem cells and organoids by promoting controlled, sand-mediated automatic ice nucleation. Conventional freezing methods often yield low reproducibility and viability due to random, damaging ice formation. FreezOpt induces earlier and more uniform ice nucleation using a polymer rectangle embedded with sterile silicate sand, reducing deep supercooling-induced freezing stress and enhancing cell survival. Building on prior MSCRF-funded work, this project advances FreezOpt into late-stage validation and pilot manufacturing. The team will test FreezOpt with viability-sensitive human cell types including iPSC-derived organoids and finalize the product design. Global CRO Ascend Advanced Therapies through their Rockville, Maryland-based ABL facility will provide third-party performance benchmarking under standardized cryopreservation workflows to enhance credibility FreezOpt will be manufactured in-house using a cost-effective, scalable process. Polymer-silicate sheets will be formed by casting PDMS and silicon dioxide into trays, cured, and cut into 3 mm 5 mm units. This eliminates the need for injection molds or CDMO involvement, allowing agile iteration and efficient scale-up. In-house QC proce-dures will include dimensional checks, particle distribution inspection, and batch testing with cryomicro-scopy or DSC to confirm ice nucleation performance. SOPs for produc-tion, sterilization, and packaging will be established and refined through iterative runs. FreezOpt is well-positioned for RUO deployment in cell therapy, biobanking, and research markets, with future GMP expansion anticipated.

A Complete Bioprocess for the Scalable Production of Extracellular Vesicles from Induced Pluripotent Stem Cells

Induced pluripotent stem cells (iPSCs) offer revolu-tionary opportunities for regenerative medicine due to their capacity for self-renewal and pluripotency. Additionally, recent advances in extracellular vesicle (EV) biology have enabled a shift toward cell-free therapeutic platforms. EVs are nano-sized membrane-bound vesicles secreted by cells that carry or display bioactive cargo, including proteins and RNAs, which influence recipient cell behavior. EVs ability to mediate paracrine effects akin to their cell of origin without the perceived risks associated with cell-based therapy makes them ideal candidates for regenerative interventions. A growing body of evidence suggests that EVs secreted by undifferentiated iPSCs may possess a distinct regenerative signature enabling their pro-angiogenic, anti-inflammatory, and anti-oxidative effects with the potential to cross the blood-brain barrier. A potential iPSC-derived EV therapy would require billions of cells and trillions of EVs to be manufactured at a low cost, something achievable only by culturing cells in bioreactors. Recent studies suggest the processes used to collect iPSC-EVs impact their ultimate yield and function, underscoring the major impact of process parameters on the manufacture of high-quantity and high-quality iPSC-EVs. However, the market currently lacks a scalable, complete, end-to-end system for iPSC expansion and iPSC-EV collection. We aim to address this unmet need by designing bespoke iPSC-EV bioprocess media optimized for cell expansion and EV production. By establishing a scalable, defined bioprocess with custom media for producing iPSC-EVs, this project will significantly advance the clinical readiness of iPSC-EVs and inform their integration into translational pipelines.

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Manufacturing Assistance Program

William Rust, PhD

Seraxis, Inc.
Awardee Amount: $918,534
Disease Target: Diabetes Mellitus

Nathan Castro, PhD

Nanochon, Inc.
Awardee Amount: $999,937
Disease Target: Musculoskeletal System Disease

(2026 1st Funding Cycle)

Design, Build and Qualification of a Stem Cell Manufacturing cGMP Suite

Islet replacement therapy is the best option to improve long-term health outcomes for patients of type 1 diabetes. Patients of diabetes with implanted replacement islets have healthy glucose control, are no longer dependent upon insulin injections, and avoid deteriorating health outcomes associated with diabetes. Seraxis is currently manufacturing and evaluating a stem cell-derived islet replacement therapy in an ongoing clinical study. However, this therapy requires concurrent immune suppression to prevent rejection of the graft. To be practical for most patients of diabetes in need, the use of immune suppression therapy must be eliminated. Seraxis has engineered a version of its cell replacement therapy, called SR-03, that can be implanted to patients without immune suppression therapy. Manufacturing of this second- generation therapy for clinical testing requires a dedicated cGMP manufacturing facility, distinct from the manufacturing suite of the original islet replacement therapy. This grant is intended to support the design, build and validation of this second cGMP manufacturing suite at Seraxis' manufacturing facility in Germantown, Maryland.

Nanochon Chondrograft Manufacturing Buildout for Clinical Production

The current proposal aims to design, develop, and test Nanochon's Chondrograft for the treatment of ankle osteoarthritis (OA). In our previous work, we have validated the efficacy of an implantable cartilage repair device, made from new tissue growth materials and designs manufactured by fused filament fabrication. We have successfully developed a novel 3D printable synthetic bone, vascular, and cartilage structure from these materials and have developed a prototype implant. The current work aims to extend the core Chondrograft technology to acute ankle injury and post-traumatic ankle osteoarthritis.

To this end, the work in this grant will include;

Aim 1. Procurement, buildout, and Verification-validation of 3D printing and purification processes: Aim 1 will focus on capital equipment procurement, buildout of 3D printing and purification processes, and installation, operational, and performance qualification. Key milestones will be the manufacture of equivalent Chondrograft devices under fully validated processes.

Aim 2. Completion of Nanochons filament extrusion process validation per GMP as well as verification and validation of clinical production to include material shelf life. Key milestone will be delivery of the recovered yield of each batch, together with a certificate of conformance.

Aim 3. Verification and Validation of packaging and autoclave sterilization: In Aim 3 Nanochon intends to continue and finalize efforts in developing, verifying and validating finished good packaging, sterilization, and delivery of the Chondrograft. In addition, Nanochon will pursue full validation of the finished good packaging as well as sterilization

Rama Modali

Reprocell, USA
Awardee Amount: $357,881
Disease Target: N/A
(2026 1st Funding Cycle)

Development of a Centralized (GMP) Contract Development and Manufacturing Organization (CDMO) and iGRP Manufacturing

hiPSC are used in cell therapy, drug discovery and drug development. REPROCELL USA (REPROCELL) supports the entire workflow of stem cell research and pre-clinical drug development. Our unique portfolio includes proprietary RNA reprogramming technology, commercial biorepository of ethically sourced human tissues and hiPSC line generation and development. Our additional services include multilineage differentiation of iPSCs, stem cell culture media and reagents. With our deep knowledge of stem cell biology, REPROCELL is a recognized leader in cutting-edge tools and services to accelerate regenerative medicine and drug development. To further speed up clinical and translational research we have recently installed the Cytocentic, Xvivo system model X2 Closed GMP System (Xvivo System) manufactured by BioSpherix Medical, Ltd. (Parish, NY). We are currently using this system to manufacture GMP grade iPSC and mesenchymal stem cells (MSC) master cell banks (MCB). This system provides an ISO 5 quality GMP working environment approved by FDA. As we are using and promoting this system, we were approached by multiple customers requesting large-scale production of billions of hiPS cells and iMSC that exceed Xvivo system capabilities. To address this, we are proposing to upgrade the existing semi-clean room into a full clean room environment that can accommodate bioreactors, additional laminar-flow hoods and more incubators. This improvement will allow us to generate cell numbers at the scale needed by therapeutic, pharmaceutical, and biotech clients, all at competitive prices. With over 15 years of expertise, and an extraordinary team of qualified stem cell scientists, the Xvivo system and support already in place, REPROCELL is well positioned to deliver on these requirements.

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Validation Program

Elias Zambidis, MD, PhD

The Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Blindness; Eye & Vascular Diseases

Functional Validation of MoroPLUR Human Stem Cells in Clinical-Grade Conditions

We have derived a new class of human stem cell termed Tankyrase/PARP (poly (ADP-ribose) polymerase) Inhibitor-Regulated Naïve Stem Cells ('TIRN-SC'). TIRN-SC are derived with a PARP-mediated chemical method that reprograms conventional hiPSC to a more primitive 'totipotent' state enriched in expression of 4- to-8-cell embryonic factors. We have optimized the TIRN reprogramming system into a chemically-defined formulation termed 'MoroPLUR'. MoroPLUR TIRN-SC possess significantly higher differentiation performance than conventional hiPSC; including efficient capacity to contribute human tissues into developing animal embryos. Generation of Universal TIRN-SC (UTIRN-SC) banks from HLA-defined blood and fibroblast donors may make cell therapies more accessible to wider patient populations. In this project, we will partner with REPROCELL USA, a Maryland biotechnology company with expertise in GMP hiPSC, to commercialize a small bank of GMP-compliant HLA-defined MoroPLUR TIRN-SC. The pre-clinical safety of chemically-reprogrammed MoroPLUR TIRN-SC and their derivative retinal progenitors will be validated for normal epigenomes. We will similarly employ MoroPLUR technology to directly derive low- passage TIRN-hESC from IVF-derived human embryos. These Aims will be coordinated with our commercial partner to optimize MoroPLUR into cGMP-compliant cellular and media products for future Phase I/II clinical trials. Clinical-grade MoroPLUR UTIRN-hiPSC and TIRN-hESC lines will expand the potential of current stem cell technologies and their applications to tissue engineering. Moreover, these commercially-available banks of human totipotent stem cell lines will greatly expand opportunities for studying the earliest molecular and epigenetic events of human embryonic development.

MSCRF

Annual Report

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Launch Program

Erin Green, PhD
University of Maryland Baltimore County
Awardee Amount: $349,907
Disease Target: Neurodevelopmental Disorders

Mahaa Umapathi, MD
The Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Cardiac Arrhythmia, Cardiomyopathy

Leveraging Human iPSC Models for Mechanistic Investigation of Chromatin Regulators Linked to Rare Neurodevelopmental Disorders

The genetic characterization of autism spectrum disorders, intellectual disability, and rare, monogenic neurodevelopmental disorders has revealed that proteins required for the proper regulation of gene expression through chromatin modification are frequently disrupted in individuals with these disorders. Research in my lab has focused on investigating the molecular mechanisms of a family of enzymes that predominantly catalyze methylation on histones, known as the SET domain family. A substantial proportion of proteins within this family have been genetically-linked to rare neurodevelopmental disorders, likely due to the dysregulation of chromatin and gene expression that occurs during development when they are absent or mutated. The primary goal of this proposal is to develop induced pluripotent stem cell lines which carry loss of function and patient derived mutations of a gene encoding one of the poorly-characterized SET domain proteins linked to a rare neurodevelopmental disorder. Using these cell lines, we will test the role for this factor in neural developmental gene expression programs and regulation of the chromatin landscape in stem cells differentiated into neurons. This will provide new insights into the molecular causes associated with this rare neurodevelopmental disorder, reveal potential strategies for therapeutic intervention, and provide a foundation for expansion of this approach to investigating the etiology of other rare neurodevelopment disorders caused by loss of function of SET domain chromatin regulatory proteins.

Clinical Trial in a Dish: Identifying Novel Molecular Mechanisms and Translating Therapies for Lamin Cardiomyopathy

Mutation in the Lamin A/C (LMNA) gene is one of the most common causes of life-threatening electrical disturbances (arrhythmia) in the heart and a major cause of heart failure in young people. There is no current cure or medication for the disease. Many patients require heart transplant as their only therapeutic option. Why the LMNA mutation causes problems with arrhythmia and/or contractility is not well understood. There is a critical, unmet clinical need for molecular mechanistic understanding of LMNA heart disease in order to develop new therapies. This project proposes creating a translational, platform using human induced pluripotent stem cell derived cardiomyocytes obtained from patients with prevalent and clinically relevant LMNA gene mutations.

The aims of the proposal are two-fold:
1) Identify salient molecular mechanisms in LMNA cardiac disease and
2) Test novel drug and gene based therapeutic strategies in LMNA heart disease.

The platform will test and identify molecular pathways significant to LMNA disease pathology. Potential candidate mechanisms to be tested as mediators of arrhythmia and contractile dysfunction in LMNA disease include the role of calcium, the regulatory enzyme, CaMKII, and cardiac energetics. The proposal will additionally test novel therapeutic approaches to mitigate LMNA heart disease based on molecular pathways identified in this proposal. Two orthogonal strategies, one drug-based and an additional gene editing approach, will be tested utilizing the LMNA iPSC derived cardiomyocyte platform for therapeutic efficacy.

Marjan Gharagozloo, PhD
The Johns Hopkins University
Awardee Amount: $349,478
Disease Target: Nervous System Disease

Qun Li, PhD
The Johns Hopkins University
Awardee Amount: $296,449
Disease Target: Anesthesia Neurotoxicity

Investigating the Regulatory Role of NLRX1 in Inflammatory Reactive Astrocytes Derived from Human Stem Cells

Emerging evidence reveals that chronic glial activation, mitochondrial dysfunction, and neuronal cell death contribute to neurodegeneration in multiple sclerosis (MS). NLRX1 is an innate immune sensor in mitochondria that inhibits major pro-inflammatory pathways including NF-kB and regulates mitochondrial function, preventing cell death and tissue injury. However, its role in the chronic inflammatory response of astrocytes and neurodegeneration in MS is not fully understood. We hypothesize that NLRX1 controls the astrocyte-specific immunometabolic pathways that lead to chronic inflammation and neurodegeneration. We will address this hypothesis with the following aims: (i) To generate NLRX1-/- human induced pluripotent stem cell (hiPSC) lines using CRISPR/CAS9 genome editing and differentiating them to astrocytes; (ii) To investigate the role of NLRX1 in the functional, proteomic, and metabolic profiles of reactive astrocytes; (iii) To assess the therapeutic effect of NLRX1 agonists on human astrocytes. We will test whether activating NLRX1 with small molecule agonists could modify the reactive/neurotoxic profile of astrocytes and restore their neuroprotective phenotype. The findings from this study will support the translation of CNS penetrant NLRX1 agonists for neuroinflammatory diseases like MS.

Effects of Early General Anesthetic Exposure on Neural Development: An In Vitro Study Using Human Induced Pluripotent Stem Cell Derived Brain Microphysiological System

Clinical studies have raised a concern that childhood exposure to general anesthetics (GAs) for surgery and diagnostic procedures may increase the risk of cognitive and behavioral impairments later in life. Animal studies have shown that early life exposure to GAs profoundly impairs neuronal development and disrupts myelin formation in CNS. However, the implications of this phenomenon in human patients remain unclear. At present there is very limited mechanistic understanding of processes related to developmental neurotoxicity and neurological disorders in patients given the challenges of basic science studies in human tissue. Animal studies do not faithfully reflect key elements of human physiology and mimic human pathology. In this proposal, we will employ an in vitro human induced pluripotent stem cells (iPSCs) derived brain microphysiological system (bMPS) to investigate the toxic effects of GAs on the developing brain in human. bMPS is a versatile 3D culture system that replicates key structure of human brain and facilitates the highest degree of applicability to patients. This model comprises a variety of neurons and glial cells, and consists of connections between cells, such as synapse and myelin. After bMPS are exposed in GAs, we will examine the alteration of neuronal and glial proliferation/differentiation, myelination, and synaptogenesis). Our previous studies have shown that early GA exposure disrupts neural development via aberrant upregulation of mammalian target of rapamycin (mTOR), a signaling pathway involved in normal brain development. In this study, we will also examine the role of mTOR in human anesthesia neurotoxicity. We will apply mTOR inhibitors to test whether mTOR inhibition rescues the human brain from GA induced developmental disruptions.

Ryan Sochol, PhD
University of Maryland, College Park
Awardee Amount: $350,000
Disease Target: Stroke

Sui Seng Tee, PhD
University of Maryland School of Medicine
Awardee Amount: $345,000
Disease Target: Nervous System Disease

Automated Stem Cell Radiolabeling via 3D Microprinting-Enabled Microfluidics

Regenerative medicine—namely, stem cell therapy—holds distinctive promise for treating wide-ranging conditions, including neurodegenerative diseases, spinal cord injuries, heart disease, and, in particular, stroke. At present, stem cells are primarily administered without monitoring, which can contribute to therapeutic inefficiencies, outcome variability, and adverse effects. In vivo tracking of radiolabeled stem cells via positron emission tomography (PET) could overcome these challenges and, in turn, improve the efficacy of stem cell therapies; however, pervasive issues stemming from radiolabeling protocols remain a critical barrier. For example, conventional stem cell radiolabeling requires highly trained personnel for whom there are risks of high radiation exposure, while the underlying time- and labor-intensive manual ("by hand") protocols are susceptible to human error that can lead to undesired variability in outcomes. We propose to leverage recent advancements in 3D-printed microfluidic technologies to address these challenges and enable near-autonomous and enhanced radiolabeling of human mesenchymal stem cells (MSCs). Our goal—improving the efficacy of stem cell radiolabeling while limiting exposure to radioactivity scientists' and laboratory staff's—bridges an important need in both preclinical and clinical settings for stem cell therapies. The innovation of automating and enhancing the processes for radiopharmaceutical synthesis and stem cell radiolabeling (and resuspension) via microfluidics and 3D printing holds promise not only for regenerative medicine ($35B market), but also for broad cell therapeutics as well as for radiolabeling additional biological drugs, such as viruses, macromolecules, and nanomedicines.

Peripheral Lipid Metabolism as a Modulator of Synucleinopathies

Aggregation of proteins is a central feature of neurodegenerative diseases such as Parkinson's disease. As such, many researchers have focused on clearing these aggregates in the brain. This proposal uniquely focuses on the liver and the brain, predicting that diets high in fat impact both tissues, to promote Parkinson's, by limiting the ability of these tissues to break down protein aggregates.

Vivek Garg, PhD
University of Maryland Baltimore
Awardee Amount: $350,000
Disease Target: Metabolic Disease

Whitney Parker, MD, PhD
University of Maryland School of Medicine
Awardee Amount: $350,000
Disease Target: Polyhydramnios, Megalencephaly, & Symptomatic Epilepsy

Biophysics of Mitochondrial Membranes in Cardiolipin-Deficient iPSCs: Pathophysiology and Treatment of Barth Syndrome (BTHS)

Barth Syndrome (BTHS) is a severe genetic disorder caused by mutations in the TAFAZZIN gene, leading to loss of cardiolipin (CL), a key phospholipid in the inner mitochondrial membrane (IMM). This defect disrupts mitochondrial function, causing muscle weakness and cardiomyopathy. Using induced pluripotent stem cells (iPSCs) and innovative mitochondrial patch clamp technique, our research proposal focuses on understanding BTHS pathophysiology and refining treatments for this mitochondrial disease. Utilizing WT-iPSCs and TAFAZZIN knockout iPSCs, we plan to investigate how CL deficiency affects ion transport across mitochondrial inner membrane. We employ mitochondrial patch clamp technique, which allows high-resolution measurement of calcium and proton currents in mitochondria stripped of their outer membrane. This method will provide unprecedented precision in quantifying ion transport alterations due to CL deficiency. Additionally, we will investigate the mechanism of action of SS31 (aka elamipretide), how it affects membrane biophysics and mitochondrial bioenergetics. Besides BTHS, this research has broader implications for developing mitochondrial therapies for various metabolic and cardiovascular diseases. iPSCs offer a robust in vitro model, replicating BTHS phenotypes and enabling high-throughput screening of potential treatments. By elucidating the regulatory role of CL and impact of SS31 on IMM ion transport, our study aims to advance mitochondrial biology and therapeutic strategies for conditions like BTHS. Integrating findings across multiple models will enhance our understanding of mitochondrial dysfunction and aid in designing targeted interventions for mitochondrial-related disorders.

A Human Neurodevelopmental Model for Investigating the Role of STRADA in Inhibitory Neuron Cortical Lamination and Epilepsy

Pediatric epilepsies resulting from malformations of cortical development (MCDs) are notoriously difficult to treat. Research models of MCDs have previously been limited to animal models, non-neuronal human cells, and operative or post-mortem tissue specimens, each of which are limited in their ability to recapitulate the human neurodevelopmental condition and assess disease mechanisms. Induced pluripotent stem cell (iPSC) models uniquely solve this problem. Differentiated into neural progenitor cells and neurons, iPSCs can provide a human model of early brain development critical for solving the mechanisms underlying key aspects of MCDs and testing therapeutic strategies that can be used for early intervention in patients. Polyhydramnios, Megalencephaly, and Symptomatic Epilepsy (PMSE) is a severe MCD predominantly diagnosed in the medically-underserved Old Order Mennonite population, characterized by intractable epilepsy, neurocognitive impairment, and a high early mortality rate. PMSE is caused by a loss of the protein STRADA, and has no effective treatment options. We observe that both PMSE patient brain and Strada knockout (KO) mouse brain exhibit a notable lack of inhibitory neurons (INs) in cortex, though the mechanism for this remains unknown. INs are critical for the modulation of excitatory:inhibitory tone, and their dysfunction can yield hyperexcitable neural networks, promoting epilepsy. In this project, we will use an iPSC model to study STRADA-dependent IN development mechanisms which are disrupted in PMSE, as well as test treatment strategies that can be used for patients with this and other similar MCDs. This will establish a platform for modeling key features of MCDs including cell migration, neuronal differentiation, and neuronal function, using iPSCs.

Xiao Yang, PhD

Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Developmental Disorder and Nervous System Disease

Vascular-Mimetic Devices for Vascularization and Monitoring of Human Neural Organoids

Organoids represent an advanced stem cell-based in vitro model for studying human neural development, diseases, and drug discovery. However, a significant challenge in organoid culture is the lack of a vascular system, which limits the size and longevity of these models. Integrating vascular-mimetic networks into organoids is critical for creating more complex, functional models that better represent in vivo physiology.

We aim to address this challenge by designing and implementing multifunctional vascular- mimetic devices to integrate vascular functionality into human neural organoids. These devices will serve as both perfusion systems and bioelectronic probes for vascularization and real-time monitoring of organoid health, growth, and differentiation. Central to this project is an innovative design that allows oxygen and nutrient penetration while monitoring neural activity via integrated electronic sensors. This platform will seamlessly integrate neural, vascular, and electronic networks.

The successful development and integration of vascular-mimetic devices with organoids will have a transformative impact on stem cell biology, neuroscience, and biomedical engineering. By vascularizing human neural organoids with our devices, we will create more complex, mature, and robust models for studying neural development, diseases, and drug screening. Additionally, the ability to simultaneously monitor the electrophysiological states of organoids during neural development will provide valuable insights into stem cell-based organoid research. This research aligns with the Maryland Stem Cell Research Fund goals by advancing innovative stem cell-based models that address critical challenges in disease modeling and therapeutic development.

Zubair Ahmed, PhD

University of Maryland School of Medicine
Awardee Amount: $349,600
Disease Target: Age-Related Macular Degeneration

Molecular Modulators of Autophagy

Age-related macular degeneration (AMD) is a common condition characterized by progressive damage to the macula, the area of the retina that controls sharp central vision. Dry-AMD, the subtype that is associated with macular thinning and geographic atrophy, is the most common form and can cause permanent vision loss. Although it has been estimated that over 10% of the US population over the age of 40 has some form of AMD, there are no effective treatments currently available to preserve vision. We have identified a promising new therapeutic target for dry-AMD: calcium and integral binding family member 2 (CIB2). However, we need a cellular model that mimics the salient features of the disease. Recent studies reported induced pluripotent stem cells (iPSCs) based AMD models, which recapitulated drusen and retinal pigment epithelium (RPE) atrophy. Through proposed studies, we will established several iPSCs-derived RPE lines in the lab for translational research. Several studies have implicated phagocytosis and autophagy pathways within the RPE as a key mechanism of dry-AMD pathogenesis, which is an appealing node of potential therapeutic intervention. We have previously identified a role for CIB2 in modulating mTORC1 signaling and autophagy within the RPE. Surveyed RPE/choroid tissue from dry AMD patients demonstrated accumulation of autophagy proteins, over-active mTORC1 signaling, and decreased CIB2 expression. These recent studies lead us to hypothesize that CIB2 may offer a protective role in the context of dry AMD within the RPE, by enhancing phagosomal and autophagic clearance of cellular components that drive disease progression. Thus, current studies are geared to identify modulators of CIB2 expression in iPSCs-derived RPE models.

Herana Kamal Seneviratne, PhD
University of Maryland - Baltimore County
Awardee Amount: $349,335
Disease Target: Neurodegenerative & Nervous System Diseases
(2026 1st Funding Cycle)

Soojung Hur, PhD
Johns Hopkins University
Awardee Amount: $349,990
Disease Target: Glaucoma - Visual system disease
(2026 1st Funding Cycle)

Understanding Drug-Induced Neurotoxicity Using Stem Cells

The overall goal of this project is to understand how widely used clinically important antiretroviral and anticancer drugs such as dolutegravir and oxaliplatin contribute to the neurotoxicity that leads to neurodegeneration. Neurodegeneration is a worldwide public health problem affecting millions of people. Of note, drug-induced neurotoxicity is considered a major cause of neurodegeneration. It is known that certain classes of well-established, clinically important antiretrovirals that are used to treat HIV infection and anticancer agents used in chemotherapy can significantly contribute to neurotoxicity that leads to neurodegeneration. For example, dolutegravir, a crucial antiretroviral, and oxaliplatin, a first-line anti-cancer drug, are known to exert neurotoxicity, manifesting in increased rates of adverse drug events. However, the molecular mechanisms of the above drug-induced neurotoxicity leading to neurodegeneration remain unexplored. Traditionally, neurotoxicity investigations have relied on mouse models and cells because of limited availability and challenges associated with obtaining human primary neural cells. However, studies in animal models are time-consuming and have major limitations due to physiological differences from humans. To address this issue, we propose the use of neural cells derived from human induced pluripotent stem cells as a novel and physiologically relevant model to investigate drug-induced neurotoxicity. Our long-term goals are to elucidate molecular mechanisms underlying drug-induced toxicities and to develop therapeutic interventions to minimize these adverse effects. In this MSCRF Launch project, we will determine how select antiretrovirals and anticancer agents affect endogenous lipid metabolism dysregulation during neurotoxicity.

Label-Free Microfluidic Sorting of Stem-Cell-Derived Retinal Ganglion Cells for Glaucoma Research

This study focuses on developing a new method to purify specialized nerve cells called retinal ganglion cells (RGCs), which play a key role in transmitting visual information from the eye to the brain. Damage to these cells is a major cause of vision loss in glaucoma, a leading cause of irreversible blindness worldwide. Recent advances in stem cell research have made it possible to create RGCs in the lab from human stem cells. However, separating these lab-grown RGCs from other unwanted cells in the mixture is a significant challenge. Current purification methods often use chemicals or genetic modifications that may not meet safety standards for use in patients. Our research aims to solve this problem by developing a safe and efficient way to isolate RGCs without altering or damaging the cells. We are creating a microfluidic system that sorts cells based on their natural physical properties. By adjusting the devices dimensions and operation conditions during the sorting process, we can optimize it to gently and effectively separate RGCs from other cell types. This method avoids the need for foreign chemicals or genetic changes, making it more likely to meet safety and regulatory standards for future clinical use. This breakthrough technology has the potential to enable the transplantation of healthy RGCs into patients with advanced glaucoma, offering hope for restoring vision to those who have lost their sight to this debilitating disease. Beyond RGCs, the system could be adapted to purify other types of stem-cell-derived cells, opening new possibilities in regenerative medicine. By addressing a key obstacle in developing cell-based therapies, this work offers hope for those affected by vision loss and may improve the lives of countless individuals in the future.

Steven Hsu, PhD

Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Heart Failure - Circulatory System Disease
(2026 1st Funding Cycle)

Mechanism and Treatment of Ventricular Contractile Reserve Dysfunction in Human Heart Failure

Heart failure with reduced ejection fraction (HFrEF) is a leading cause of morbidity, mortality, and hospitalization in the U.S. HFrEF is difficult to treat in its later stages, as poor cardiac contractile reserve makes the heart progressively intolerant of stress and volume. Teasing out the underlying mechanism of contractile reserve failure would help us better understand and treat human HFrEF. Our recent work in human HFrEF reveals a novel deficit in thick filament-mediated cardiac contractile reserve, unique to humans and large mammals and absent in rodents. New preliminary phosphoproteomic data from these same patients reveal hypophosphorylation of regulatory sites on myosin binding protein-C (MYBPC). Phosphorylating these sites helps to restore contractile reserve in ex vivo human tissue. We hypothesize that human myocyte contractile reserve is diminished in HFrEF, owing to MYBPC hypophosphorylation that depresses myosin recruitment. In this proposal, we leverage human induced pluripotent stem cell (hiPSC) models to study this mechanism, since it cannot be studied in pre-clinical models. We test our hypothesis via two aims. In Aim 1, we determine the effect of hypophosphorylated MYBPC sites on myocyte thick filament-mediated length-dependent reserve. Candidate MYBPC sites in hiPSC lines are mutated via CRISPR-Cas9; their impact on contractile reserve in engineered heart tissue is then assessed. In Aim 2, we determine whether novel sarcomere-activating drugs can restore thick filament contractile reserve in an established hiPSC-based model of human heart failure. Our findings will help clarify novel mechanistic insights and help pave the way to novel therapies for heart failure.

Seunghyun Lee, PhD

Johns Hopkins University
Awardee Amount: $349,999
Disease Target: Cardiomyopathy - Circulatory system Disease
(2026 1st Funding Cycle)

Developing a Therapeutic Strategy for Cardiac Laminopathy

This project aims to develop genotype-specific therapies for inherited cardiomyopathies by reprogramming disease-associated phenotypes in fully differentiated human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs). Focusing on LMNA mutations, which are a major cause of dilated cardiomyopathy, we will test whether pharmacologic activation of canonical Wnt/[B]-catenin signaling can reverse structural and functional defects in pathological iPSC-CMs. Unlike prior studies that leverage Wnt signaling to induce cardiomyocyte differentiation during early development, our strategy targets postmitotic, disease modeled cardiomyocytes allowing us to assess the therapeutic potential of Wnt pathway activation after the onset of pathological phenotypes. Using genome-edited iPSC lines carrying defined LMNA mutations, we will apply small-molecule Wnt activators and evaluate functional recovery through electrophysiological and calcium imaging assays. To uncover the molecular basis of genotype-specific responses, we will conduct single-cell RNA sequencing and ATAC-seq, identifying transcriptional and chromatin-level factors that mediate Wnt-driven phenotypic rescue. This approach may reveal biomarkers that predict therapeutic efficacy and support the development of precision medicine strategies for genetic cardiomyopathies, a class of disorders that currently lack effective, mutation-targeted treatments.

Yuchuan Miao, PhD

Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Segmenation Defects of the Vertebrae Developmental Disorder
(2026 1st Funding Cycle)

Illuminating The Etiology of Human Segmentation Disorders Using Stem Cell Derived Embryo Models

Segmentation disorders of the vertebral column are a series of congenital diseases characterized by malformation of the axial skeleton. These segmentation defects usually result from flawed somitogenesis in the early embryo between 3 to 4 weeks after fertilization, influenced by genetic mutations and environmental insults. Investigating the etiology is challenging due to limited access to human embryos and ethical concerns. Previously we used human induced pluripotent stem cells (iPSC) to establish organoid systems that faithfully recapitulate the spatiotemporal features of human somitogenesis. Here, we leverage on the novel in vitro models to illuminate intrinsic and environmental causes of human segmentation defects. We focus on the key somitogenesis regulator MESP2, whose mutated forms have been identified in causing disorders and whose expression and function are regulated by the environmental factor hypoxia. We will introduce pathogenetic mutations to human iPSCs and combine functional genomics and live imaging to illuminate mechanisms of somitogenesis defects. In parallel, we will control oxygen levels during cell culture to identify effects of hypoxia on somitogenesis and investigate entry mechanisms to the molecular and cellular networks. We will further utilize our in vitro platform to identify environmental substances that potentially cause segmentation defects. Altogether, the proposed work is expected to advance the prevention and treatment of human segmentation disorders by (1) illuminating fundamental details of human development and disorders; (2) gaining understanding of environmental insults during human segmentation; (3) providing a tractable platform to identify teratogens that specifically cause early segmentation defects to guide healthy pregnancy.

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Discovery Program

Ricardo Feldman, PhD
University of Maryland, Baltimore
Awardee Amount: $350,000
Disease Target: Parkinson's Disease

Curt Civin, MD
University of Maryland
Awardee Amount: $350,000
Disease Target: Anemia

Therapeutic Targets in Microglia for Prevention and Treatment of GBA1-Associated Parkinson's Disease

Bi-allelic mutations in GBA1 cause Gaucher disease (GD). Mono-allelic GBA1 mutations do not cause overt neuronopathy, but GD patients and carriers have a 5 to 20-fold increased risk of developing Parkinson's disease (PD); 7% of all PD patients harbor GBA1 mutations, which are the highest risk factor for PD. It is believed that neuroinflammation mediated by microglia contributes to GBA1-associated PD (GBA1/PD), but the mechanisms involved are not understood. To uncover these mechanisms, we generated iPSC-derived microglia from individuals harboring GBA1 mutations with and without PD. We first found that mutant microglia produced elevated levels of inflammatory cytokines and exhibited other parameters of microglia activation. To determine if mutant microglia play a role in the induction of alpha-synuclein aggregation in dopamine (DA) neurons and neuronal loss, we analyzed DA neuron/microglia co-cultures. We found that the GBA1 mutant microglia induced higher levels of aggregated phospho-alpha-synuclein(Ser129) (alpha-SYN-p129) in DA neurons than control microglia. We hypothesize that activated microglia from GD patients and heterozygote carriers of the disease play a key role in inducing pathogenic a-synuclein species in DA neurons, leading to DA neuronal loss. In this application we will use isogenic midbrain/microglia organoids derived from heterozygote GBA1/PD patients covering the most frequent GBA1 mutations, to elucidate the mechanisms by which the pathogenic activation of GBA1 microglia leads to DA neuronal loss. We will then determine if targeting key nodes that we identified in the microglia activation cascade, can prevent alpha-synuclein aggregation and DA neuronal loss. The outcome of these studies has important clinical implications for GBA1- associated PD.

Molecular Regulation of Human Erythropoiesis by SIX

Ex vivo generation of mature and maturing erythroid cells from hematopoietic stem-progenitor cells offers a potential alternative to blood and bone marrow donation, yet challenges, such as low erythroid cell yield, limit clinical application. Our long-term goal is to achieve large-scale ex vivo production of mature and maturing erythroid cells for use in clinical transfusion, hematopoietic stem cell transplantation, and gene therapies by manipulations of erythropoiesis-regulatory molecules. Human SIX proteins belong to the PAX-SIX-EYA-DACH Network (PSEDN), which orchestrates development of multiple organs in mammals. We have identified SIX1 and SIX2 as important positive regulators of human erythropoiesis, working in a GATA1-dependent manner. Human SIX proteins include 6 isoforms (SIX1-6), each containing conserved domains important for binding to other proteins and to DNA. Our recent preliminary results indicated that overexpression of each SIX family member increased erythroid differentiation - maturation. However, SIX overexpression also resulted in reduced total cell numbers, which might limit the utility of SIX for massive expansion of ex vivo erythropoiesis. To address this, we propose in Aim 1 to identify discrete regions of SIX proteins that regulate erythroid differentiation, maturation vs proliferation, and thereby to define a small SIX-based construct sufficient to enhance both erythroid differentiation , maturation, and survival, proliferation. In Aim 2, we plan to combine this with manipulation of levels of selected, newly discovered SIX/GATA-interacting proteins, in order to further enhance erythropoiesis generated by primary human hematopoietic stem-progenitor cells.

Alan Friedman, MD

The Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Pancreatic Cancer, Brain Cancer

Human Marrow Stem-Cell Derived Pro-Inflammatory CAR-Myeloid Progenitors as Immunotherapy for Cancer

Pancreatic ductal carcinoma (PDC) has a median survival 10-12 months. Glioblastoma (GBM) is a highly aggressive brain cancer, with less than 5% survival at five years. We seek to optimize proinflammatory immature myeloid cells (IMC), derived from human marrow hematopoietic stem cells, as a component of PDC and GBM treatment to improve outcomes. NF-kB is a key transcription factor favoring proinflammatory, M1 gene expression. Adoptive transfer of murine IMC activated by absence of the repressive NF-kB p50 subunit (p50-IMC) slows the growth of PDC and GBM via activation of anti-tumor T cells. STAT6 is a key transcription factor mediating tumor-suppressive M2 gene expression, while repressing a subset of M1 genes. p50/STAT6-IMC are more effective than p50-IMC at slowing murine tumor growth. Expression of a chimeric antigen receptor (CAR) in p50-IMC increases their ability to localize to tumors and to phagocytose cancer cells, the latter expected to enhance anti-tumor T cell immunity. Our specific aims are to: Aim 1. Develop human p50/STAT6-IMC expressing a PSMA.CAR, EGFR.CAR, or GD2.CAR suitable for clinical translation and determine whether these CARs increase localization to human tumors and phagocytosis of human cancer cells expressing the cognate CAR epitopes. Aim 2. Determine whether addition of EGFR.CAR or GD2.CAR increases anti-tumor efficacy of murine p50/STAT6-IMC against syngeneic pancreatic ductal carcinoma or glioblastoma, alone or with ICI. Proposed studies are intended to demonstrate substantial efficacy of p50/STAT6-IMC combined with tumor-specific CARs against PDC and GBM in immunecompetent hosts and to develop and validate corresponding human marrow hematopoietic stem cell-derived pro-inflammatory immature myeloid cells for rapid clinical evaluation.

Younggeon Jin, PhD

University of Maryland College Park
Awardee Amount: $350,000
Disease Target: Digestive System Disease

Finetuning of MSC Priming for Mucosal Healing in IBD: Dual Targeting Intestinal Stem Cell Regeneration and Immunomodulation

Inflammatory bowel disease (IBD) affects millions of people and costs billions in medical expenses each year. While current treatments focus on controlling inflammation, many patients still struggle with relapses due to incomplete healing of the intestinal lining. Mucosal healing, the regeneration of damaged intestinal tissue, is vital for improving patient outcomes; however, most available therapies primarily target inflammation reduction. A promising potential solution involves mesenchymal stem cells (MSCs), known for their ability to promote tissue repair and reduce inflammation. Nonetheless, current MSC-based treatments demonstrate limited clinical success, partly because they do not specifically concentrate on regenerating intestinal stem cells (ISCs), essential for mucosal healing. Our research seeks to advance MSC therapy by developing innovative techniques to "prime" MSCs that enhance ISC regeneration while also boosting their anti-inflammatory properties. We recently found that human MSCs, when exposed to injured intestinal tissues, release factors that improve ISC regeneration and inflammation control. These findings suggest that damaged intestinal tissue can effectively "teach" MSCs to better support healing. This project aims to pinpoint the specific factors from injured epithelium necessary for priming MSCs, enhancing their therapeutic efficacy. We intend to test these primed MSCs in laboratory models of IBD to evaluate their potential to improve mucosal healing more effectively. If successful, this approach could revolutionize IBD treatment, providing a targeted, regenerative solution that surpasses mere inflammation management. Furthermore, our findings may have implications for other immune-related diseases where MSCs are a potential treatment option.

Alyssa Coyne, PhD

Johns Hopkins University School of Medicine
Awardee Amount: $349,842
Disease Target: Amyotrophic Lateral Sclerosis

Nicholas Maragakis, MD

Johns Hopkins University
Awardee Amount: $349,663
Disease Target: Nervous System Disease

The Role of CHMP2B in NPC Injury and TDP-43 Dysfunction in Sporadic ALS

Maintenance of the protein complexes called nuclear pore complexes (NPCs) that control communication between the nuclear and cytoplasmic compartments of cells is essential for proper neuronal function and survival. Recent work has demonstrated that defects in a nuclear surveillance pathway initiate damage to these cellular communication channels as an early and significant event in sporadic and familial forms of Lou Gehrig's disease or Amyotrophic Lateral Sclerosis (ALS). Critically, this damage cascade contributes to common pathological hallmarks of ALS such as altered function and mislocalization of specific proteins. Cumulatively, this NPC injury cascade can lead to impaired neuronal survival in ALS pathogenesis. This proposal will examine the contribution of and mechanism by which specific proteins that comprise the fundamental nuclear surveillance pathway trigger NPC injury cascades. Ultimately, these studies will evaluate the potential efficacy of novel therapeutic targets for modulating pathophysiologic events related to NPC injury events in ALS.

A Human iPSC Platform for Investigating a Translationally Relevant P2X7R-Mediated ALS Target

Understanding the potential pathways by which both disease onset and progression occur in patients with Amyotrophic Lateral Sclerosis (ALS) is one of the fundamental limitations to designing disease therapies that may be utilized at the onset of disease, and certainly after diagnosis. Our previous MSCRF-supported published studies have demonstrated that the astrocyte Cx43 hemichannel is a novel propagator of disease progression in ALS. Amongst the factors released by these hemichannels into the extracellular milieu is ATP and our current data demonstrate a newly described mechanism of ATP-mediated purinergic receptor (P2X7R) activation directly on human iPSC-derived motor neurons—resulting in motor neuron death. These data suggest that it is a desirable pharmacological target for the interrogation of the dual role of ATP in the development and propagation of disease in ALS. This translationally-relevant proposal builds upon our initial observations by using a fully humanized, spinal cord-specific, ALS iPSC-astrocyte/motor neuron platform to investigate our hypothesis that there are dual effects of ATP-mediated P2X7R activation both directly on motor neurons as well as through purinergic activation of P2X7R on astrocytes as part of the neuroinflammatory cascade in ALS. As we think about translational potential, we will test newly developed and more specific P2X7R blockers, with BBB penetrability, to define cell-specific mechanisms of neuroprotection in this platform. The rationale of the proposal is to understand the dual neuronal and glial contributions of P2X7R to the initiation and propagation of ALS in order to identify appropriate biomarkers for study and inform the timing and duration of administration of P2X7R antagonists as ALS therapeutics.

Gabsang Lee, PhD
Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Nervous System Disease

Xizhen Lian, PhD
Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Sickle Cell Disease

Characterization of New '4-Factor Induced Schwann Cells and Testing its In Vivo Myelination

In the U.S., over 20 million people suffer from peripheral neuropathies, and some peripheral nerve injury (PNI) patients can access proper treatments; however, those with severe nerve disconnections do not have therapeutic options. One potential treatment is to transplant myelination-competent human Schwann cells to promote nerve reconnection, regeneration and functional recovery. To address this issue, we initiated a new approach to enhance the Schwann cell fate determination, led us to identify four core genetic factors sufficient and necessary to confer functional Schwann cell identity in accelerated timeline with significantly high yield. In this proposal, we continue our efforts in detailed cellular and molecular characterization of the novel Schwann cell and testing therapeutic efficacy in a traumatic PNI rat model.

In Vivo Genome Editing in the Hematopoietic Stem Cells to Treat Sickle Cell Disease

Sickle cell disease (SCD) originates from a single base mutation in the β-globin gene, causing a Glu-to-Val single amino acid substitution. The treatment of SCD and other β-hemoglobinopathy has been limited to phenotypic management and complication prevention for decades without a cure. In 2023, two gene therapies for SCD and β-thalassemia received FDA approval, marking a significant milestone for SCD patients. Both of these two approaches employ autologous editing and bone marrow transplantation procedure. Although effective and generally safe, such invasive procedures still cause a number of side effects, including inflammation, infertility, tissue damage, and even blood cancer. In this proposed project, we aim to shift the existing paradigm of ex vivo gene therapy to treat SCD by developing in vivo gene delivery and SCD mutation correction in the human HSCs. Building upon preliminary studies on the successful lipid nanoparticle (LNP) mediated in vivo gene editing in murine HSCs, we will i) engineer the chemical properties of LNPs to maximize therapeutic base editing in the SCD-patient-derived HSCs; ii) modulate the endogenous targeting capability of LNPs for in vivo SCD correction in the NBSGW mice; and iii) evaluate the systemic toxicity and genotoxicity of base editor – LNP administration to facilitate clinical translation. If successful, the results have the potential to revolutionize the current SCD gene therapy and lead to the development of first-ever in vivo SCD gene therapy approach, which will substantially alleviate side effects, be more accessible to different patient groups especially to pediatric and critical patients, lower the cost, and improve patient outcomes compared with the current ex vivo gene therapy approaches.

Pan Li, PhD

Johns Hopkins University School of Medicine
Awardee Amount: $350,000
Disease Target: Psychiatric Disorders

Arens Taga, MD

Johns Hopkins Hospital
Awardee Amount: $348,781
Disease Target: Amyotrophic Lateral Sclerosis (ALS)

Investigating the Role of PKA Activation in Bipolar Disorder: Functional Characterization of AKAP11 Protein Truncating Variants in Genetically Engineered Human iPSCs.

This research project aims to investigate the molecular mechanisms underlying bipolar disorder (BD) by using genetically engineered human isogenic control and AKAP11 mutant induced pluripotent stem cells (iPSCs). The AKAP11 mutations are associated with BD, and the project seeks to understand how these mutations impacts neuronal function, particularly through the modulation of the cAMP-PKA signaling pathway. Using these iPSC-derived neurons, the project will examine cellular processes that are disrupted by the AKAP11 mutations, focusing on neuronal phenotypes and PKA signaling. This approach offers a unique advantage over traditional animal models, as it provides a more accurate representation of human neuronal behavior. Additionally, the study will explore the potential of these models to screen for therapeutic compounds that could correct cellular abnormalities linked to BD.

Exploring the Role and the Therapeutic Potential of β1-Importin in Axonal Regeneration in ALS

This project investigates the role of β1-importin (β1imp) in axonal regeneration in C9orf72 ALS, the most common genetic form of the disease. Using human induced pluripotent stem cell-derived motor neurons (hiPSC-MN) and a microfluidic-based platform, we aim to establish a direct link between dipeptide repeat proteins (DPRs) translated from the C9orf72 gene, β1imp subcellular mislocalization, and impaired axonal regeneration. Our central hypothesis is that in C9orf72 ALS, DPRs cause axonal β1-importin mislocalization within cytoplasmic inclusions, leading to reduced axonal regeneration. In proof-of-concept experiments, we seek to demonstrate that β1imp is a targetable therapeutic mechanism. Specifically, we hypothesize that overexpression of axonal β1-importin, combined with preventing its accumulation in the cell body, enhances axonal regeneration following axotomy.

Jeff Bulte, PhD
Johns Hopkins University School of Medicine
Awardee Amount: $349,857
Disease Target: Glioblastoma

Mohamed Farah, PhD
Johns Hopkins University School of Medicine
Awardee Amount: $350,000
Disease Target: Amyotrophic Lateral Sclerosis

Mannose Overexpression by Mesenchymal Cancer Stem Cells as Imaging Biomarker for Tumor Aggressiveness

Glioblastoma multiforme (GBM) is one of the deadliest forms of cancer in man. Its growth is driven by cancer stem cells that share some similarities with bone-marrow derived mesenchymal stem cells. One particular feature is their high mannose expression on the cell membrane, with mannose being a molecule containing two glucose molecules. We have discovered that this different sugar expression can be visualized with a special magnetic resonance imaging (MRI) technique that is fine-tuned to imaging sugars. We aim to follow the growth patterns of implanted GBM in mice and study the role of blocking the expression of mannose. This will help us to better understand some of the biology of mesenchymal cancer stem cells and we hope that our MRI technique can be used to predict how aggressive the tumor will become. Since MRI is already widely used for diagnosis of GBM in patients, we believe that it can be used fairly quickly in a hospital setting at JHU and elsewhere.

Reversibility & Prevention of Axonal Dysfunction in Mutant hiPSC-Derived Neurons

Long axons of motor neurons rely on both proteins transported from cell bodies and those locally translated from axonal mRNA repertories to maintain their health and functionality. Given the early axonal damage seen in ALS and widely accepted notion that axonally translated proteins are critical for maintaining axon health and proper neuronal signal transmission, we hypothesize that altered levels of a subset of locally translated proteins contribute to early axonal deterioration and dysfunction in ALS. We recently analyzed RNA profiles of axons and somas from ALS patient iPSC-derived motor spinal motor neurons. We identified differentially expressed genes in ALS-linked mutant axons as compared to controls, but whether altered levels of these genes are required or sufficient to cause axonal pathogenesis and dysfunction is not known. Among the differentially expressed mRNAs, we selected eight candidates for further analysis (for SOD1+/A4V axons: SMAD2, EEF1D, SNAP29, and DNM2; for C9orf72 repeat expansion axons: ASRGL1, MORN2, ARFGEF3, and SYTL2). We will use mutants and isogenic controls iPSC-derived spinal motor neurons cultured in modified microfluidic devices with chambers separating axons from cell bodies that are compatible with multielectrode array electrophysiological techniques. Mutant and control neurons will also be cultured in a three-dimensional platform where prevention/reversibility of axonal pathologies can be reliably and reproducibly investigated over time. We plan to examine whether: 1) treating ALS iPSC-derived motor neurons with siRNAs targeting newly identified upregulated mRNAs can reduce axonal pathology; and 2) increasing via AAV vectors the expression of mRNAs downregulated in ALS patient iPSC-derived neurons can prevent axonal pathogenesis.

Seth Ament, PhD

University of Maryland School of Medicine
Awardee Amount: $345,000
Disease Target: Autism Spectrum Disorder

Convergent Effects of Genetic and Inflammatory Risk Factors for Autism Spectrum Disorders on the Development of Human Purkinje cells

We will use patient-derived and genome-edited human pluripotent stem cells to study the effects of genetic and inflammation- related risk factors for autism spectrum disorders on the maturation of neurons in the cerebellum. We will compare phenotypes in cerebellar organoids to post-mortem brain tissue from the cerebellum of human children with autism spectrum disorders.

Ludovic Zimmerlin, PhD

Johns Hopkins University School of Medicine
Awardee Amount: $349,512
Disease Target: Visual system disease

Improved Engraftable Retinal Organoid Progenitors from TIRN Totipotent Stem Cells

The neuroregenerative capacity of the human retina is poor. Retinal disorders that cause the definitive loss of neuro-retinal cells or its supportive choroidal and vascular tissues typically result in permanent visual impairment and blindness and there is currently no therapy to reverse retinal cell death. Stem cell-based therapies show promise in preventing and rescuing the degenerated retina but remain challenging. Retinal tissues or cells have been successfully derived from human induced pluripotent stem cell (iPSC) using many methods. However, there are still limitations for the generation and isolation of fully differentiated, transplantable, adult-stage ocular tissues that can integrate properly with a host retina. The use of multipotent retinal progenitor cells has been proposed, but current iPSC methods may limit their proliferation and reproducibility for efficient clinical applications. We have derived a new class of human stem cells termed Tankyrase/PARP (poly (ADP-ribose) polymerase) inhibitor-regulated naïve (TIRN) stem cells. TIRN stem cells (TIRN-SC) demonstrated increased multilineage differentiation performance in vitro and in transplantation studies, including their differentiation to retinal lineages using retinal organoid methods. This proposal aims to perform basic molecular studies of TIRN-SC-derived retinal progenitors (RP) and evaluate their capacity to engraft into the retina in a xenotransplantation mouse model. It will provide the basis for a future translational evaluation of TIRN-RP in retinal cellular therapy. TIRN-RP could ultimately procure a new reliable and easily scalable source of progenitors for disease modeling and for future clinical transplantation to treat blinding eye diseases.

Hee Cheol Cho, PhD

Johns Hopkins University School of Medicine
Awardee Amount: $350,000
Disease Target: Cardiac Arrhythmias

Autonomous Electrical Organoids for Treating Heart Rhythm Disorders

This project aims to create a new type of heart pacemaker using human stem cells. The heart's natural pacemaker, called the sinoatrial node (SAN), is the driver of the heart rhythm. Instead of focusing only on pacemaker cells, this research takes a novel approach by considering the diverse types of cells in the SAN, including non-muscle cells. These non-muscle cells play an important role in the heart's pacing function, and by including them in the model, we seek to create functional and stable biological pacemakers. The project challenges traditional thinking in stem cell science by highlighting the importance of this cellular diversity in creating effective cell therapy. The research also explores the potential of stem cell-derived cells and technologies that could improve treatments for heart rhythm disorders, particularly for pediatric patients who struggle with traditional pacemaker devices. By developing pacemaker organoids that replicate the structure and function of the natural SAN, this work could lead to personalized and regenerative treatments for patients with slow heart rhythms, offering a potential alternative to implantable devices. The explicit goal of the project is to support efforts to advance the field of regenerative medicine and improve patient care.

Jill Fahrner, MD, PhD

Johns Hopkins University School of Medicine
Awardee Amount: $349,999
Disease Target: Beck-Fahrner Syndrome/TET3 Deficiency

Nanopore sequencing of TET3-Deficient Neurons: a Path to Understanding DNA Methylation and Correcting it in Disease

Beck-Fahrner syndrome (BEFAHRS) is the first monogenic neurodevelopmental disorder of DNA demethylation and thus represents a new biochemical category of disease. Affected individuals exhibit global developmental delay, intellectual disability, hypotonia, anxiety, ADHD, autistic features, and in some cases seizures. It results from germ-line hypomorphic mutations in the gene encoding TET3, which converts 5- methylcytosine (5mC) to 5-hydroxymethylcytosine (5hmC), the first step in active demethylation. Not surprisingly, functional studies overexpressing TET3 patient variants led to reduced 5hmC, and patients with the disorder have a characteristic DNA methylation profile in whole blood consisting of increased 5mC. It is unknown if the DNA methylation changes are biologically relevant. 5hmC is notoriously difficult to measure in most cell types but is abundant in brain, a cell type relevant to the BEFAHRS phenotype. Moreover, 5mC and 5hmC cannot be distinguished with existing methods. Here, we propose to use a new technology - nanopore sequencing - to elucidate changes in 5mC and 5hmC in BEFAHRS and to attempt to ameliorate them with targeted therapies. This work is innovative because it takes advantage of a cutting-edge technology (nanopore sequencing) to measure both 5mC and 5hmC in a phenotype-relevant human neuronal model of BEFAHRS. This work is significant because it has the potential to improve understanding of the fundamental roles of DNA methylation in normal neurodevelopment and disease and to identify targeted therapies for a currently untreatable rare disorder. Importantly, therapies may also be effective in treating more common related disorders with disrupted DNA methylation.

Rajini Rao, PhD

Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Lactation Failure, Drug Safety

Shaun Kunisaki, MD

Johns Hopkins University
Awardee Amount: $344,814
Disease Target: Myelomeningocele (LA02.Y)- Structural Anatomic Anomalies of the Central Nervous System

A Lactating Mammary Organoid Model from Human iPS Cells

Breast milk is critical for the health and development of newborns, providing essential nutrients and immune protection. However, many mothers experience challenges related to the quantity and quality of milk production or the transfer of harmful substances, like medications and environmental pollutants into milk. These challenges impact both maternal and infant health, yet our understanding of the underlying biological processes is limited. This project aims to address these knowledge gaps by creating a cutting-edge laboratory model of the human lactating mammary gland using stem cell-derived organoids. Organoids are 3D mini-organs grown from human induced pluripotent stem cells that mimic the structure and function of the mammary gland during lactation. Using this model, we will study how key transporters—specialized proteins that move nutrients, ions, and drugs—regulate milk composition. Specifically, we will focus on three types of transporters: lipid transporters (for energy production), calcium transporters (for mineral content), and drug transporters (for medication safety).To achieve this, we will generate organoids under lactation- like conditions, validate their functionality and generate a comprehensive catalog of genes, proteins and metals expressed during lactation. This research will advance our understanding of lactation biology, improve the diagnosis and treatment of milk production disorders, and establish guidelines for medication use in breastfeeding mothers. By developing a human-relevant and ethical model, this project has the potential to significantly impact maternal and infant health while advancing the field of regenerative medicine.

Human iPSC Derived Spinal Organoids in a Preclinical Model of Fetal Myelomeningocele Repair

Myelomeningocele (MMC) is a severe form of spina bifida resulting from failed fusion of the caudal region of the neural tube during embryonic development. The diagnosis of MMC is synonymous with substantial and permanent disabilities secondary to leg weakness and paralysis, hydrocephalus, cognitive impairment, bladder and bowel dysfunction, and orthopedic abnormalities. Given this high morbidity, there remains a critical need to better understand the mechanisms and extent of neural regeneration within the MMC spinal cord at the time of surgical repair. Using our unique biorepository of amniotic fluid samples from MMC fetuses, our laboratory has recently established a reliable protocol to generate human spinal cord organoids (SCOs) for disease modeling and cell therapy applications. In this MSCRF proposal, our central hypothesis is that the integration of microglial cells into early human induced pluripotent stem cells (iPSC)-derived SCOs improves spinal cord development, engraftment, and regeneration. In Aim 1, we seek to determine whether microglia enhance the neuronal differentiation and functionality of human iPSC-derived SCOs in vitro. In Aim 2, we evaluate whether human spinal cord organoids and microglia can engraft and improve neuroregeneration in a preclinical, large animal model of fetal MMC spinal cord repair. Completion of this work will have elucidated our understanding of the critical role of microglia in spinal cord development and will enable us to transition this platform organoid technology for clinical translation in affected fetuses and newborns with MMC.

Jiou Wang, PhD

Johns Hopkins University
Awardee Amount: $345,000
Disease Target: Amyotrophic Lateral Sclerosis (ALS)

Deciphering the Link Between Epigenetic Regulation and Lipid Metabolism in C9orf72-ALS/FTD Using iPSC and Organoid Models

Amyotrophic lateral sclerosis (ALS) is a devastating disease that attacks nerve cells controlling muscles, leading to loss of mobility and independence. ALS is associated with frontotemporal dementia in some cases, adding cognitive decline to physical challenges. In this study we will focus on a common genetic cause for ALS, which is thought to disrupt normal cell functions either by reducing the gene's normal activity or by triggering harmful processes. Our research sheds light on a novel aspect of this genetic puzzle: a novel factor regulating the ALS gene expression levels, potentially influencing the disease's onset and progression. By focusing on this novel factor, we're exploring how the ALS gene's mis-regulation affects cell metabolism—essentially, how cells process nutrients and energy. This insight could pave the way for innovative treatments, aiming not just to slow the disease but to address its root causes by stabilizing the gene's function and correcting metabolic imbalances. Our work is a step toward unraveling ALS's complexities, offering hope for therapies that could one day significantly extend quality of life or even cure this relentless condition.

Hilary Vernon, MD, PhD

Johns Hopkins University School of Medicine
Awardee Amount: $349,184
Disease Target: Other

Harnessing Stem Cell Technology to Understand Mitochondrial Neutropenia Through the Lens of Barth Syndrome

The goal of this project is to define the role of mitochondrial dysfunction in neutrophil development through the lens of Barth Syndrome (BTHS). BTHS is caused by mutations in the TAZ gene, resulting in cardiomyopathy, skeletal myopathy, and neutropenia. Neutropenia leads to serious infections in BTHS and despite therapies such as G-CSF, 1/3 of treated patients endure hospitalizations for infections and are at risk of cancer due to long-term GCSF use. While prior studies identified underlying mitochondrial dysfunction in BTHS, the cause for neutropenia remains elusive. Based on our prior work in cellular models of TAZ-deficiency, we hypothesize that neutropenia in BTHS results from: 1) defects in the capacity for mitochondria to shift from glycolysis to oxidative metabolism (required for neutrophil development) and 2) impaired mitochondrial function that results from disrupted clearance of defective mitochondria. Given the lack of adequate experimental models for neutropenia in BTHS, we will develop two complementary cell models: 1) an in vivo hematopoiesis system by engrafting human CD34+ hematopoietic stem cells from BTHS patients in NBSGW mice to assess myeloid development and 2) CRISPR-edited TAZ- deficient iPSC-derived neutrophils to dissect mitophagy, mitochondrial morphology, and bioenergetics during differentiation. Pinpointing the mechanisms of neutropenia in BTHS will potentially lead to new targets for therapeutic intervention. We will also contribute foundational knowledge about how mitochondrial quality control and bioenergetics participate in neutrophil maturation. We anticipate that this will be impactful in understanding neutropenia in related disorders of neutrophil developmental failure, driving the implications of our research beyond BTHS.

Xitiz Chamling, PhD

Johns Hopkins University School of Medicine
Awardee Amount: $349,619
Disease Target: Multiple Sclerosis

Brian O'Rourke, PhD

Johns Hopkins University School of Medicine
Awardee Amount: $350,000
Disease Target: Heart Failure

Advancing Remyelination Drug Discovery Using Human OPCs and Inhibitory Microenvironment Model

Multiple Sclerosis (MS) is a leading cause of neurological disability in young adults. In MS, the immune system mistakenly attacks the protective myelin sheath around nerve fibers in the brain and spinal cord, leading to damage that disrupts normal nerve function. This damage can also result in the loss of nerve cells themselves. While current disease-modifying treatments mainly target the immune system to slow disease progression, they do not effectively reduce long-term disability. Researchers are increasingly focused on promoting remyelination, the process of repairing or replacing damaged myelin, as a potential way to restore nerve function and reverse some of the disability caused by MS. However, most drug discovery efforts to promote remyelination have not yet led to successful treatments, partly because existing studies often use animal models or systems that do not fully replicate the harmful environment of MS lesions. In this project, we aim to improve drug discovery for MS by using two advanced human cell models. One model uses CRISPR-edited human stem cells to generate and study the myelin-forming oligodendrocyte (OLs) cells, enabling high-throughput screening of compounds that promote myelin repair in human cells. The second model uses human stem cell-derived reactive astrocytes to mimic the harmful environment of MS lesions, helping us better understand the obstacles to remyelination. By combing these two models, we are creating an advanced drug screening platform that integrates physiologically relevant human cells and disease-relevant conditions. This approach aims to identify compounds with a higher likelihood of success in clinical settings, ultimately improving treatment options and quality of life for people with MS.

Discovery of Cell Cycle Activators to Promote Myocardial Regeneration and Contractile Function in Human Engineered Heart Muscles

Heart failure incidence is rising in the US, particularly due to an aging population and factors like hypertension, cardiometabolic syndrome, and infarction. Despite advancements in symptom management, 5-year mortality rates remain above 50%. Adult mammalian hearts have limited regenerative capacity, necessitating breakthrough treatments to regrow cardiac tissue and improve contractile function. This research proposes a novel approach to discover cell cycle modulators that enhance both human cardiomyocyte proliferation and cardiac muscle force production. Our first goal is to develop a high-throughput screening platform for cardiac cell cycle activators that improve cardiac function. We will generate cardiac ring muscles from human iPSC-derived cardiomyocytes, screening a library of compounds for those that can induce both cell cycle reentry and increased contractile force. In the engineered cardiac ring muscles, we will also investigate the mechanism of one pharmacological compound that we found increases cardiac cell cycle activity and mitochondrial energy production. We will determine if it is capable of enhancing cardiac function by stimulating growth of the muscle. To identify the key transcription factors and signaling pathways involved in activating the cell cycle, contractility, and metabolism, we will analyze the trajectory of transcriptome changes induced using single-cell mRNA sequencing. This approach will establish the strategy for elucidating the mechanism of additional hits identified in the larger screen. This research aims to advance cardiac regeneration therapies by identifying agents that promote hyperplastic muscle growth in differentiated heart tissue, potentially leading to new treatments for heart failure.

Daniel Lobo, PhD

University of Maryland, Baltimore County
Awardee Amount: $350,000
Disease Target: Clonal Hematopoiesis

Lena Smirnova, PhD

Johns Hopkins University
Awardee Amount: $349,915
Disease Target: Nervous System disease

Revealing the Genetic Drivers and Regulation of Human Hematopoietic Stem-Progenitor Cell Differentiation with a Systems Approach

Human hematopoietic stem progenitor cells (HSPCs) produce and maintain a healthy and balanced range of diverse blood and immune cells. However, we lack a mechanistic understanding of how different lineages differentiate and which genetic drivers control this process. Furthermore, recent single-cell sequencing analyses have shown that this differentiation process is continuous, rather than discrete, which adds complexity to our understanding. Therefore, advanced computational approaches are required to infer mathematical models of HSPC differentiation, ultimately leading to a predictive understanding of lineage dynamics and their genetic drivers. The central hypothesis of this project is that a systems-level mechanistic model can identify the main genetic drivers of HSPC differentiation and their regulatory interactions. For this, we will produce experimental loss-of-function datasets based on in vitro cultures of human HSPC subjected to gene knockout (KO) interventions aimed at targeted lineage commitment manipulations. Through high-resolution flow cytometry combined with RNA-seq assays, we will obtain dynamic population and transcriptomic datasets that will serve as input to our machine learning methodology to train and validate a computational model of HSPC differentiation. The outcomes of this project will significantly advance our understanding of the major molecular regulatory mechanisms governing human HSPC biology. This research is innovative in integrating dynamic, predictive models at the transcriptomic and population levels using data from in vitro HSPC cultures under genetic loss-of-function conditions. This approach provides a comprehensive understanding of HSPC control and could be extended to study stem cell differentiation in other tissues and organs.

Advancing Alzheimer's Disease Research with Organoid Intelligence: A Synaptic Plasticity and Learning-on-a-Dish Approach

Alzheimer's disease (AD) is a leading cause of dementia, with no effective therapies due to limitations in preclinical models that fail to replicate human-specific aspects of AD pathology. This project leverages organoid intelligence (OI) to develop a human-relevant model focusing on early AD events, such as ApoE ε4/ε4-driven neuroinflammation and synaptic dysfunction, which precede formation of beta- amyloid plaques and tau tangles. Using ApoE ε4/ε4 iPSC-derived brain organoids with integrated microglia and isogenic controls (ApoE ε3/ε3), we will investigate synaptic plasticity, network dynamics, and cognitive deficits using advanced electrophysiology (HD-MEAs) and OI-based learning paradigms. Aligned with the FDA Modernization Act 2.0, this work advances New Approach Methodologies (NAMs), offering scalable, human-relevant alternatives to animal models for drug development and precision medicine. The OI platform will provide a high-throughput system and human relevant alternative to animal behavior studies to address cognitive functionality and decline due to AD, with strong potential for commercialization. Expected outcomes include insights into interplay of ApoE ε4/ε4 and neuroinflammation in early AD pathology, functional validation of synaptic disfunction and the development of a learning- on-a-dish system to model learning and memory in vitro. By targeting early potentially reversible disease mechanisms, this project aims to accelerate drug development, which might preserve cognitive function.

William Dalton, MD, PhD

Johns Hopkins University
Awardee Amount: $350,000
Disease Target: Clonal Hematopoiesis

Jiabing Fan, MD, PhD

University of Maryland Eastern Shore
Awardee Amount: $350,000
Disease Target: Osteoporosis

Human Stem Cell Models for Investigating Clonal Hematopoiesis of Indeterminate Potential (CHIP)

Clonal hematopoiesis of indeterminate potential (CHIP) is an age-associated condition where mutations in hematopoietic stem cells (HSCs) drive their expansion in bone marrow and blood. CHIP mutations, particularly in spliceosome genes like SF3B1, are linked to increased risks of myeloid neoplasms (MN) and nonmalignant diseases, but the mechanisms underlying their clonal fitness advantage remain poorly understood. Current animal models and standard assays fail to replicate the biology of spliceosome mutations due to species-specific differences and limited focus on HSCs. This project aims to address these gaps through innovative human-specific in vitro and in vivo systems. Using CRISPR-engineered isogenic human induced pluripotent stem cells (hiPSCs) and advanced culture techniques, we will investigate how SF3B1 mutations confer fitness advantages by promoting quiescence and altering differentiation in HSCs. Long-term culture assays will test various environmental conditions, including oxygen tension, bone marrow organoids, and cytokine-free media. Additionally, refined xenograft methods in NSG/NSGS mice will allow in vivo tracking of mutant and wild-type HSC dynamics. Our approach seeks to establish robust experimental platforms for studying CHIP biology and provide a platform for future mechanistic studies and testing of therapeutic targets to prevent progression to MN and related diseases.

Engineering Human Mesenchymal Stem Cell-Derived Exosome Mimetics for Osteoporosis Treatment

Osteoporosis is a major public health concern that affects millions of individuals, particularly within the aging population, and is a leading cause of disability due to bone fractures. Stem cell therapy offers a promising approach to treating bone loss-related diseases. However, the direct use of stem cells faces challenges in clinical settings. The objective of this research is to develop an alternative stem cell-based therapy by engineering exosome mimetics (EMs) for the treatment of osteoporosis. Age- related osteoporosis stems from imbalanced bone metabolism and remodeling, often attributed to increased marrow fat and reduced bone mass. Mesenchymal stem cells (MSCs) in bone marrow are central to this process. Aberrant MSC lineage allocation, favoring fat formation over bone, exacerbates bone loss in osteoporosis. Modulating MSC lineage commitment is, therefore, a promising therapeutic avenue. MSC-derived exosomes have shown promise in skeletal regeneration but face low production yields and inconsistent outcomes. To address this, we developed an efficient extrusion-based EM production method. Additionally, Trib3, a critical regulator of cellular metabolism and differentiation, promotes osteogenic differentiation at the expense of adipogenesis in MSCs. Here, we hypothesize that Trib3-enriched, bone-targeting EMs will effectively enhance bone regeneration in osteoporosis. The successful completion of this project will establish a novel therapeutic strategy with the potential for clinical translation. The development of Trib3-enriched bone-targeting EMs may also foster collaborations with the biopharmaceutical industry, driving innovation in Maryland's stem cell-based biotechnology.

Linda Resar, MD

Johns Hopkins University School of Medicine
Awardee Amount: $350,000
Disease Target: Blood disease, Circulatory System Disease

Tae-In Kam, PhD

Johns Hopkins University School of Medicine
Awardee Amount: $350,000
Disease Target: Alzheimer's Disease, Parkinson's Disease

Targeting HMGA1 Stem Cell Networks to Prevent Atherosclerosis in TET2 Clonal Hematopoiesis

The goal of this project is to understand why people with clonal hematopoiesis (CH) develop atherosclerosis (AS) and related cardiovascular diseases (CVDs). CH is a common blood disorder that occurs in older people when blood stem cells acquire a mutation that allows this clone to expand and generate abnormal blood cells. Unfortunately, individuals with CH are at risk for AS, an inflammatory disease of blood vessels that leads to diverse CVDs, including stroke, coronary artery disease, and heart attack. While the causes for AS in CH remain poorly understood, recent research suggests that inflammatory signals from mutant blood cells help to fuel the development of AS. We are studying a protein, called HMGA1, which acts as a molecular key that "unlocks" regions of the genome to activate genes that trigger inflammatory signals. In a form of CH caused by a mutation in the JAK2 gene, our research team discovered that HMGA1 is a critical regulator of genes that activate inflammatory signals. We therefore hypothesize that HMGA1 contributes to the development of AS in the setting of CH by activating inflammatory gene networks. To test this, we have developed innovative mouse models and technologies to dissect the underlying gene networks and downstream inflammatory signals. At the completion of this project, we expect to: 1) illuminate the role of HMGA1 in AS that occurs in individuals with CH, and, 2) identify underlying mechanisms mediated by HMGA1 that could be blocked in therapy. Our proposed studies should lay the groundwork necessary to develop novel therapies to intercept the development of AS in the setting of CH.

Glial Mitochondrial Dysfunction Contributes to the Pathogenesis of Neurodegenerative Diseases

Despite their enormous diversity in pathological and clinical phenotypes, a common feature of neurodegenerative diseases, such as Alzheimer's disease (AD) and Parkinson's disease (PD), is the accumulation of pathologic proteins in brains, which leads to neuronal dysfunction and eventually to neuronal death. Oligomeric amyloid-beta (Abeta) and Tau in AD and aggregated alpha-synuclein (a-syn) in PD are the main pathologic proteins that are thought to drive the disease process. Although these pathologic proteins also affect to other type of cells, glial cells including microglia and astrocytes, the majority of neurodegenerative research has been focused on selective loss of specific neuronal populations. Less effort has been spent understanding the contribution of glial cells, the most abundant cell type in the central nervous system (CNS), to neuro-degeneration. Emerging findings have revealed that resting astrocytes become reactive to different subtypes, among them disease-associated reactive astrocytes are observed during aging and in post-mortem tissues of neurodegenerative diseases. However, the mechanisms by which reactive astrocytes contribute to vulnerability of neurode-generative diseases has not been determined. Our preliminary studies from the murine primary cultures revealed that AD- and PD-associated microglial activation commonly induces the formation of neurotoxic reactive astrocyte, which discovers the microglia-astrocyte-neuron axis (M-A-N axis) as a novel and common mechanism of neurodegenerative diseases. These studies will provide a platform for the discovery of new therapeutic approaches to limit the contribution of the glial cell-derived novel targets in human disease.

Kathleen Pratt, PhD
Uniformed Services University of the Health Sciences
Awardee Amount: $167,431
Disease Target: Hematologic Disorders

Engineered iPSC-Derived Platelets as Clotting Factor Delivery Vehicles for Trauma Resuscitation

The central goal of this project is to generate a hemostatic therapeutic that incorporates engineered platelets derived from induced pluripotent stem cells (iPSCs) for trauma resuscitation, for use in scenarios where matched human blood donors are unavailable. Our approach relies on generating human megakaryocytes (MKs) from iPSCs in vitro and differentiating them to form platelets. The novelty is that we will engineer these MKs, using cutting-edge clustered regularly interspaced palindromic repeats (CRISPR)/Cas9 technology, to express a natural fibrinolysis inhibitor to stabilize clots at wound sites. Factor V (FV) is a coagulation cofactor that enhances the proteolytic conversion of prothrombin to thrombin, which activates platelets and cleaves fibrinogen to create a fibrin mesh. Clots are then broken down by plasmin, which is generated from plasminogen by tissue-type plasminogen activator (tPA) and urokinase-type plasminogen activator (uPA). The primary inhibitor of tPA and uPA is plasminogen activator inhibitor-1 (PAI-1). Impaired coagulation and/or excessive fibrinolysis can exacerbate traumatic bleeds. Thus, both coagulation and fibrinolysis are appropriate targets for modulation to restore hemostasis. In this project, we will differentiate iPSCs into MKs, which will be engineered to express PAI-1. We will differentiate these MKS to produce platelets as efficient delivery vehicles for PAI-1 and/or FV. We will characterize their activation and aggregation kinetics and will further employ a microfluidics system mimicking the vasculature by incorporating plasma, endothelial cell-lined channels and physiological shear forces. We will employ a GMP-compliant iPSC line for proof of concept that will enable future scale-up and translation of the enhanced platelets.

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Annual Report

- 2025 -

Post-Doctoral Fellowship Program

Longfei Li, PhD

Johns Hopkins University School of Medicine
Mentor: Ted Dawson, PhD
Awardee Amount: $130,000
Disease Target: Alzheimer's Disease

Luis Carlos Pinzon Herrera, PhD

University of Maryland, Baltimore County
Mentor: Jorge Almodovar, PhD
Awardee Amount: $130,000
Disease Target: Nerve Injuries, Nervous System Disease

The Roles of MIF Nuclease Activity in Tau-Induced cGAS-STING Activation in hiPSC-Derived Microglia

Neurodegeneration and neuroinflammation are characteristics in Alzheimer's disease (AD). Neuronal loss could be autonomous or non-autonomous mediated by glial cells. Tau-induced innate immunity that includes NLRP-3 and cGAS-STING pathways has been implicated in neurodegeneration in AD mouse models. But the molecular mechanisms of Tau-induced innate immnunity are still unknown. Macrophage migration inhibitor factor (MIF) has nuclease activity and mediates DNA cleavage and fragmentation. As DNA fragments are one of the sources for iniating innate immnuity, we speculate MIF nuclease activity participates in activating innate immunity. We plan to use iPSC-Derived Human Microglia-like Cells (iMGLs) to test our idea.

Innovative Strategies for Schwann Cell Precursor Studies Using hiPSC-Derived Models on ECM Coatings: Advancing Myelination, Morphological Insights, and Neural Regeneration

This research project aims to advance neural regeneration strategies by optimizing the behavior of Schwann cell precursors (RealSCPs) derived from human induced pluripotent stem cells (hiPSCs). The study focuses on enhancing RealSCP adhesion, proliferation, and myelination through interactions with biomimetic extracellular matrix (ECM) coatings composed of heparin and collagen. These ECM coatings are applied using a layer-by-layer deposition technique to mimic the native environment of Schwann cells.

The project is structured around two specific aims. The first aim is to evaluate the effects of heparin-collagen coatings on RealSCP differentiation and protein expression, with a focus on markers critical for myelination and nerve repair. The second aim is to assess the ability of RealSCPs to promote axon alignment and myelination in co-culture systems with hiPSC-derived sensory neurons. Advanced imaging techniques, functional assays, and transcriptomic analyses will be used to quantify outcomes and explore the mechanisms underlying these interactions. Preliminary data demonstrate that heparin-collagen coatings significantly enhance the expression of neurotrophic factors like brain-derived neurotrophic factor (BDNF), which is critical for myelination. Additionally, RealSCPs exhibit scalability, high purity, and functional resemblance to native Schwann cells, making them an ideal platform for studying nerve repair and developing potential therapies.

This study aligns with the goals of advancing stem cell research and regenerative medicine and the findings have the potential to transform the treatment landscape for these conditions by contributing to the development of innovative cell-based therapies.

Hira Butt, PhD
Johns Hopkins University School of Medicine
Mentor: S. Amer Riazuddin, PhD
Awardee Amount: $130,000
Disease Target: Glaucoma

Siddharth Shah, PhD
University of Maryland, Baltimore
Mentor: Graeme Woodworth, MD, B.S.
Awardee Amount: $130,000
Disease Target: Brain Cancer

Nanoparticle-delivered, CRISPR/Cas9-mediated Gene Editing of Patient-Specific, Induced Pluripotent Stem Cell-Derived Trabecular Meshwork Cells

The front of the eye includes the cornea, iris, ciliary body, and lens. The ciliary body produces aqueous humor (AH), a fluid that nourishes the eye. A balance between AH production and its drainage through the trabecular meshwork (TM) regulates intraocular pressure (IOP). Disruption in AH drainage leads to elevated IOP, a major risk factor for glaucoma, which causes optic nerve damage and progressive vision loss. According to the National Eye Institute, treatment options for glaucoma include topical medications (typically eye drops), laser treatment (to improve fluid drainage), and surgical interventions (such as creating a small opening or implanting a tube for fluid drainage). However, none of these treatments can reverse optic nerve damage or restore vision. Many glaucoma cases have a genetic predisposition, with mutations identified in several genes. Despite identifying the genetic causes, there is currently no treatment to correct these mutations. My long-term research goal is to develop a minimally invasive therapeutic approach to correct the genetic disposition of glaucoma in TM, the tissue responsible for AH drainage. We envision a nanoparticle-delivered, CRISPR/Cas9 gene editing strategy to correct pathogenic mutations in human peripheral blood mononuclear stem cell-originated, induced pluripotent stem cell-derived TM cells. This research represents the first step in a long-term endeavor, followed by further validation studies in pre-clinical animal models, including non-human primates. Ultimately, this approach aims to shift from current treatments, focused on lowering IOP, to a long-term solution that corrects mutations in dysfunctional TM, potentially offering a more effective treatment for glaucoma.

Innovative Strategies for Schwann Cell Precursor Studies Using hiPSC-Derived Models on ECM Coatings: Advancing Myelination, Morphological Insights, and Neural Regeneration

Neural stem cells (NSCs) are influenced by mechanical interactions within the brain microenvironment, impacting their behavior, migration potential, and tumorigenicity. One such process, confined migration (CM), involves cells moving through spaces smaller than their nucleus, creating mechanical challenges that affect DNA repair, genomic stability, and cell fate. Despite its importance, the effects of CM on NSC behavior are not fully understood. This research aims to investigate the role of CM on NSC behavior using Brillouin microscopy, a non-invasive imaging technique that measures the mechanical properties of cells. We will extend previous in vitro findings to in vivo models that mimic the human brain, focusing on how CM influences NSC migration and the mechanical stress involved.

Specific Aims:

Demonstrate the effects of CM on NSC behavior in vivo, focusing on changes in nuclear envelope integrity and cell mechanics using two-photon microscopy. Investigate phenotypic and mechanical changes during NSC migration using Brillouin microscopy, assessing stemness, chromosomal stability, and potential tumorigenic alterations. This study will provide insights into the mechanical stress induced by CM and its impact on NSC function, which could have significant implications for cancer research and regenerative medicine. The findings will improve our understanding of how mechanical forces affect cellular behavior in the brain, potentially informing therapeutic strategies

Willem Buys, PhD

Johns Hopkins University School of Medicine
Mentor: Elias Zambidis, MD, PhD
Awardee Amount: $130,000
Disease Target: Cancer

Design and Validation of iPSC-based uniCAR Myeloid Progenitors as Versatile Tumor Immune Therapy

Many cancers evolve strategies to escape the patient's immune response. To counter this, scientists have developed structures called "chimeric antigen receptors (CAR)" that help immune cells recognize cancer cells. I plan to add such a chimeric antigen receptor to immune modulatory "myeloid" cells. While myeloid cells can also directly attack the tumor, they particularly excel at attracting and activating other host immune cells to enter and attack the tumor; which may enable a lasting immune response by the patient's own immune system. And make it harder for the tumor to evolve escape mechanisms.

In my previous project, I have developed a technology to produce myeloid cells at a 5-50-fold greater efficiency than previous methods, using a type of stem cells that is very amenable to stable gene editing. In this project, I will add a CAR to these cells and test their potential to kill tumor cells and activate other immune cells. I will analyze for how long they remain inside a living organism using mice, to gage a possible duration of effect for future animal and ultimately clinical studies. Instead of a CAR that binds to the tumor directly, I will use an adaptor-based design, which relies on a co-administered linker-protein. Due to the linker's short half-life, this design greatly increases therapy safety and may facilitate the re-targeting of existing immune cell lines against new cancer types. To quickly progress towards clinical phases, I have chosen two adaptor proteins based on FDA-approved anti-cancer antibodies against adenocarcinoma: the most common and deadly class of cancers in the US and worldwide. In addition, I am collaborating with an industry partner experienced in CAR design, who will provide the CAR construct and adaptor proteins.

Niannian Xu, PhD

Johns Hopkins University School of Medicine
Mentor: Shuying Sun, PhD
Awardee Amount: $130,000
Disease Target: Amyotrophic Lateral Sclerosis (ALS), Alzheimer's Disease

The Role of TDP-43 Dysfunction in Neuroinflammation

Dysfunction of RNA metabolism has emerged to play a crucial role in multiple neurodegeneration diseases, including frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS). The key pathologic hallmark of both diseases is the nuclear clearance and cytosolic aggregation of the RNA binding protein (RBP) TAR DNA binding protein-43 (TDP-43). In addition, TDP-43 proteinopathy also occurs in about half of Alzheimer's Disease (AD) cases. TDP-43 has multiple functions in RNA processing and cellular homeostasis. While its dysfunction is well-studied in neurons, its role in microglia remains poorly understood. This project investigates the dysfunction of TDP-43 in microglia and its contribution to neurodegeneration. Using human-induced pluripotent stem cells (iPSCs)-derived microglia and microglia-neuron co-culture systems, we aim to uncover how TDP-43 loss-of-function impacts RNA metabolism and inflammatory signaling pathways in microglia and whether this disrupts neuronal health. This study will provide novel insights into the unique role of TDP-43 in microglia, advancing our understanding of non-cell autonomous toxicity to neurons from microglia and identifying potential therapeutic targets to mitigate microglia-driven neurotoxicity.

Sterling Arjona, PhD

University of Maryland School of Medicine
Mentor: Seth Ament, PhD
Awardee Amount: $130,000
Disease Target: Schizophrenia

Implication of SETD1A Loss-of-Function in DNA Replication Stress During Neural Induction

Histone modifications are emerging as key factors in the risk for developing schizophrenia and other neuropsychiatric disorders. Similarly, alternative mechanisms of histone modifiers, such as DNA damage repair, are also being implicated in these disorders. SETD1A, a methyltransferase responsible for H3K4 methylation, has been identified as a top risk gene for schizophrenia, with rare loss-of-function (LoF) variants conferring ten-fold increased risk. SETD1A has been shown to play a protective role during DNA damage by stabilizing stalled replication forks and facilitating DNA repair. However, most evidence of SETD1A mechanisms and pathways comes from cancer research and the impact of SETD1A LoF on DNA damage repair in neurons has not been fully elucidated. Furthermore, since schizophrenia has long been considered a neurodevelopmental disorder, the role of SETD1A LoF in early stages of neuron development, neural induction, is also important to consider. Therefore, this proposal aims to bridge the gap between increased susceptibility to DNA damage during neural induction and SETD1A LoF. iPSCs deficient in SETD1A and controls will be assessed for DNA damage, DNA replication fork stalling, and cell cycle arrest. Next, rescue experiments aimed at restoring SETD1A function will be performed to better associated H3K4 methylation with the previously observed effects. The composition of known replication fork machinery in these iPSCs will be assessed using iPOND and mass spectrometry technology. Finally, further H3K4 methylation rescue will be performed to assess the specific changes in replication fork machinery that was just elucidated.

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