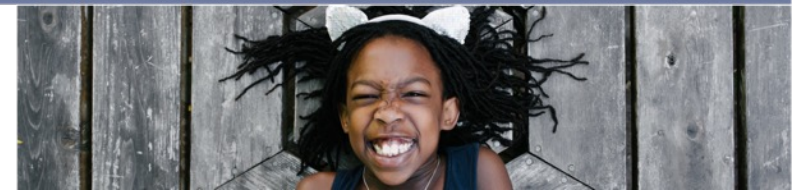


# Translational Research Program annual report

December 2023



# Introduction: A message from Director Mustafa Sahin, MD, PhD



## Meeting tomorrow's challenges: The future of the Translational Research Program

Five years ago, I wrote here about the **Translational Research Program (TRP)** developing its first-ever strategic plan for the future, an effort that would help us break down research silos, make greater connections with industry and, perhaps most importantly, invest in the next generation of translational scientists.

We could never have known then what the future had in store for us, but as I take a moment to reflect on how far we've come, I'm proud of everything the TRP has accomplished in the last few years.

## Revisiting our strategy for the opportunities ahead

I think it is important for the TRP to continually reassess its strengths and look to build on its legacy of bringing cutting-edge science into the clinic. For that reason, we will once again be launching a strategic planning process to look for opportunities to grow our mission in the next five years. As we do, I'll be looking to connect with members of the **Venture Philanthropy Network (VPN)**, who have long been financial supporters of the program, to help us think through the possibilities and plan for the challenges.

One area of focus for us, and for all of Boston Children's Hospital, is the pediatric mental health crisis. It's undeniable that this challenge will shape the future of the TRP just as it will the rest of the institution. We are actively exploring how the TRP can help play a role in addressing the mental and behavioral health challenges facing children today, and I look forward to sharing more news of our efforts in the year ahead.



## Finding the next generation of translational scientists

We are also navigating what I would call a crisis in the postdoctoral fellowship landscape. As we look ahead, it becomes increasingly clear that we must innovate to spark interest in translational research among young scientists. The reality is that many potential researchers do not follow through on an academic path because they are often disconnected from the tangible impact of their work.

At Boston Children's, we've bridged this gap by immersing researchers in an environment where the outcomes of their efforts are vividly displayed in the lives of the patients we serve. To replicate this inspiration, we recognize the need for initiatives that expose postdoctoral fellows to the rewarding journey of translational research—where they can see, feel and experience the direct influence of their work. We were ahead of the curve in seeking to address this challenge with the establishment of our mentored Translational Investigator Service (mTIS) award, but there is still much more to do.



## The power of you: Fueling the science that answers tomorrow's questions

Thankfully, the foundation provided by the VPN's support means we are well poised to face these challenges. We have another pair of brilliant young researchers joining the ranks of our junior and mentored TIS awardees. We're excited to reveal the latest recipients of the **Mooney Family Initiative for Translational and Clinical Studies in Rare Diseases**, which will help more families access our landmark clinical trials. And a TRP stalwart, associate director **Suneet Agarwal, MD, PhD**, received this year's Boston Investment Conference funding.

As we embark on our new strategic vision for the future, we do so with sure footing because of the steadfast commitment of the VPN families. I'd like to end by thanking them for all they do for the TRP and the patients and families who benefit.



**Mustafa Sahin, MD, PhD,**  
Director, Translational Research Program  
Rosamund Stone Zander Chair, Boston Children's  
Professor of Neurology, Harvard Medical School

# 2023 Impact



## Making a difference: Results from the 2023 TIS survey

Each year, we survey **Translational Investigator Service (TIS)** awardees about their research milestones, gathering essential metrics such as their scientific publications, external grants, patents and other indicators of success in translational science.

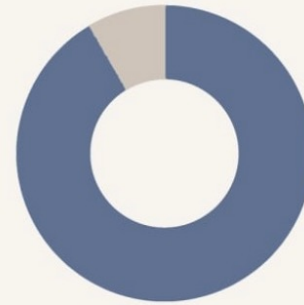
While these survey results capture only a snapshot in time of the work happening within the TRP, they are clear indicators that we are delivering on the promise of our mission—ensuring bench science has a clinical benefit for patients.



## Young faculty carry clinical science forward

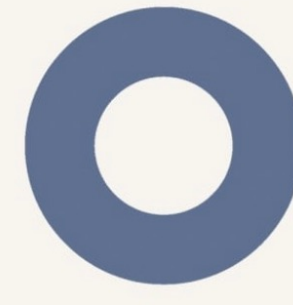
Survey results from 12 of our recent TIS awardees show a strong commitment to translational science, with half filing patents for their work and more than two thirds reporting a positive change in the mortality or morbidity of a serious childhood illness.

Our strategic investment in early career faculty means that this year's survey represents our youngest ever class of researchers, and excludes our Pappendick awardees, which explains why none have yet launched clinical trials. It's also the first time that all those surveyed reported leveraging TRP funding into additional grant support, however, showing the power of our investment.



92%

of awardees used data from TRP-funded research in published manuscripts or professional presentations



100%

of awardees used data from TRP-funded research to successfully submit for and receive external grant funding



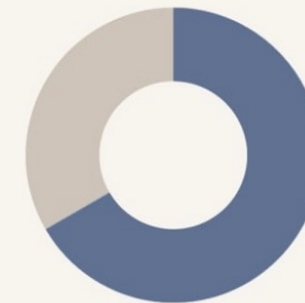
0%

of awardees launched a clinical trial that enrolled patients based on TRP-supported research



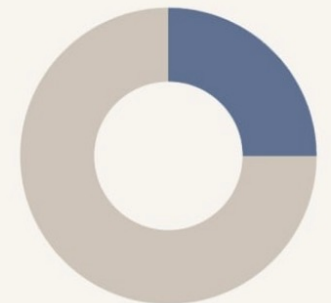
50%

of awardees filed patents based on TRP-supported research



67%

of awardees reported a subsequent change in the morbidity or mortality of a serious childhood illness due to TRP-funded work



25%

of awardees said their TRP-supported work resulted in an enhancement of patient or family satisfaction

## A formula for success in translational research

While the yearly survey offers an essential temperature check on the state of translational research at Boston Children's, we've also been tracking results since the TRP was founded in 2008. We continue to be a model for transforming clinical science with a dramatic return on donor investment and robust track record of launching clinical trials.

# 150 Total TRP Awards over 15 Years

The Results:



TRP investment of \$30M has resulted in more than \$360M in outside funding.



of TIS awardees have filed patents.



trials have been launched from TRP Awardees.

# 2023 Awardees

## Announcing the 2023 TIS and Mooney Family awardees

The TIS awards serve as the bedrock of the TRP, giving our best scientific minds the ability to pursue breakthrough research driven by clear clinical need and a desire to bring transformative treatments to patients.

Meanwhile, the **Mooney Family Initiative for Translational and Clinical Studies in Rare Diseases** (Mooney Family awards) helps patients and families access the cutting-edge clinical trials of some of our most promising researchers.

Read on for profiles of this year's awardees.



## Turning cutting-edge research into new hope for treating neurodegenerative diseases in children

Junior TIS awardee Darius Ebrahimi-Fakhari, MD, PhD, is a pediatric neurologist and neuroscientist and director of the Movement Disorders Program at Boston Children's. An expert in the study of neurogenetic and neurodegenerative disorders of childhood, particularly hereditary spastic paraplegia (HSP), Dr. Ebrahimi-Fakhari's goal is to facilitate clinical trial readiness and to develop molecular therapies for a variety of genetic movement disorders. He is leading the first natural history study for childhood-onset HSP and a comprehensive genomics platform for unsolved cases.

By developing platforms for high-throughput small molecule and genetic screening, the Ebrahimi-Fakhari lab is paving the way for novel therapies for rare neurodegenerative diseases. With more than 100 peer-reviewed publications and early NIH/NINDS funding, Dr. Ebrahimi-Fakhari is fast becoming a leader in pediatric neurology research aimed at translating research findings into clinical applications.



## Understanding how DNA damage helps to promote a rare bone cancer

Mentored TIS awardee Riaz Gillani, MD, is a pediatric oncology physician-scientist committed to combating Ewing sarcoma. His translational research, from nanomedicine to computational genomics, has been published in several prominent journals. At Boston Children's, he focuses on the intersection of germline and somatic genetics in pediatric solid tumors. Dr. Gillani's work has already earned him multiple career development awards, including from the National Cancer Institute. His career goal is to pioneer an independent research lab, advancing the understanding of germline and cancer genomics in pediatric solid tumors for better patient outcomes.

With support from his mTIS award, Dr. Gillani will investigate the role of DNA damage repair deficiency in Ewing sarcoma further. His proposed research has the potential to significantly advance the field of Ewing sarcoma and how we think about DNA damage in pediatric cancer more broadly.



## Leveraging EEG technology to better understand language development in kids with neurodevelopmental disorders

The innovative research of **Carol Wilkinson, MD, PhD**, uses electroencephalogram (EEG) technology to explore the complex neural pathways of language development in children with Fragile X Syndrome, Down syndrome, and autism. This pivotal study aims to identify specific neural markers to assess and predict language abilities, providing a beacon of hope for enhancing therapeutic strategies.

By integrating insights across different neurodevelopmental disorders, Dr. Wilkinson strives to revolutionize the approach to language impairment interventions. Anchored by her extensive background in developmental behavioral pediatrics and neuroscience, Dr. Wilkinson's team is on a quest to transform the landscape of pediatric care, ensuring a future where every child has the opportunity to reach their full communicative potential.



Support from the Mooney Family award will allow more children to enroll in Dr. Wilkinson's research study, particularly from families living outside of New England.



In early testing, Dr. Yu's newest ASO therapy suppressed expression of the gene, resulting in a dramatic decrease in seizures. Support from the Mooney Family award will allow more children to access this trial.

## Expanding access to custom-tailored drug trials for rare disease

Timothy Yu, MD, PhD, stands at the forefront of pediatric genomics, crafting unique genetic therapies for rare diseases. His work has revolutionized the treatment of conditions once deemed untreatable, providing hope to families worldwide. By targeting errant RNA splicing via antisense oligonucleotide (ASO) technology, Dr. Yu has pioneered patient-specific drugs, demonstrating remarkable success.

Despite the challenges of high costs and regulatory barriers, Dr. Yu has been relentless in his drive to expand access to this innovative care. His latest ASO therapy targets a rare form of early onset epileptic encephalopathy characterized by genetic mutations in a gene called KCNT1. Children with the illness suffer from dozens of daily seizures beginning in their first few weeks of life, which greatly damages brain development and leads to early death—making new treatments critical.



# 2023 Grants

## 2023 Pilot Awards: Powering clinical translation

Our project-based pilot awards are an essential component of the translational research enterprise at Boston Children's. These one-time awards give researchers the timely support they need to complete essential proof-of-principle studies that unlock outside grant funding.

This year, the TRP selected three exciting research projects all focused on different elements of improving cardiovascular care for patients—from the development of a novel diagnostic device to innovative genetic approaches to treating rare



## Reshaping care for children with a dangerous heart condition

Coarctation of the aorta (CoA) is a serious heart condition in which part of the main blood vessel narrows, restricting blood flow to the body. It often goes unnoticed in newborns when detection is critical.

A team led by **John Kheir, MD**, has developed a noninvasive diagnostic tool using resonance Raman spectroscopy (RRS) to assess oxygen delivery in at-risk newborns. RRS is highly sensitive and precise in detecting compromised blood flow.

Success with this tool could revolutionize CoA detection, leading to its use in hospitals and doctors' offices. Early diagnosis can prevent severe complications, saving lives and improving the health of newborns. This research has the potential to reduce the health care burden associated with late CoA diagnosis and treatment. Ultimately, Dr. Kheir's goal is to ensure more newborns grow up healthy and thrive.



RRS uses refracted light waves to determine the molecular composition of matter. Dr. Kheir's breakthrough was to configure an RRS device to assess the health of mitochondria, a proxy for cell health overall.

## Promising treatment of rare heart arrhythmias

The lab of **William Pu, MD**, is hoping to develop a groundbreaking therapy for calmodulinopathies, which are rare and life-threatening genetic arrhythmias caused by mutations in the CALM1, CALM2, and CALM3 genes. These genes produce calmodulin, a vital protein for heart function. By using ASO therapy, Dr. Pu's team has been able to target these genes to correct the abnormal heart rhythms seen with the disorder.

The team's early studies have shown promise, demonstrating the effectiveness and safety of ASOs in both *in vitro* and *in vivo* models. In the year ahead, Dr. Pu and his colleagues will continue to validate the therapy's efficacy and expand its application to different calmodulinopathy types. This work has the potential to transform the management of these life-threatening conditions and open the door for ASO therapies in other cardiovascular conditions.



This is Dr. Pu's second pilot award to study ASO therapy for calmodulinopathies, which underscores the potential of the research. This award will help his team draw closer to a potential clinical trial.

## Zeroing in on better diagnostic tools and treatments for Kawasaki disease

Kawasaki disease (KD) is a serious inflammatory condition affecting young children with a risk of coronary artery damage if left untreated—making early detection critical. Unfortunately, current diagnostic methods for KD are often inconclusive. The lab of Pui Y. Lee, MD, PhD, discovered that the interleukin-17 (IL-17) family of cytokines (proteins that regulate blood cells) are highly elevated in KD patients, particularly those with coronary artery issues. These cytokines could serve as diagnostic markers and predictors of coronary aneurysms.

Dr. Lee seeks to validate the presence of IL-17 cytokines in a multicenter cohort of KD patients and determine the effects of each IL-17 cytokine within the cells that line the coronary artery. His team aims to establish the role of IL-17 cytokines in the origins of KD and set the stage for future investigations of IL-17 as a target for treatment.



While interest in KD rose during the pandemic because it shares symptoms with a rare Covid complication called multisystem inflammatory syndrome in children (MIS-C), KD research remains woefully underfunded.

Thank You



**Boston Children's**

Where the world comes for answers

