THE MEDULLOBLASTOMA INITIATIVE

A blueprint for hope

The Medulloblastoma Initiative Report

April 2024

Are you still using these technologies?

The 1980s: This is when the medulloblastoma treatment protocol was established. And it is still being used. In addition to not curing a high proportion of children affected by medulloblastoma, the kids who survive face severe side effects for the rest of their lives.

The MBI knows that research can change this scenario. And this is why we work to link private donors to leading scientists. Join us now — spread the word and make a donation for research that will find a cure for this brain cancer.

Help now!

THE MEDULLOBLASTOMA INITIATIVE

www.mbinitiative.org

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We are back! Please join us in celebrating many achievements since August 2023, as reported by the MBI and Children's National Hospital Foundation. Thank you for your continued support throughout this journey!

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Motivation, persistence — and hope

In a few months, MBI will be turning three years old. As I look back, I can hardly believe the progress we have been able to make. Despite all the obstacles, our group of scientists is advancing steadily towards the cure. We were able to submit two clinical trial protocols to the US Food and Drug Administration (FDA) in a remarkably short time and have two more in our pipeline.

In the present report, we provide an update on the recent progress made by the researchers in the Cure Group 4 Consortium, founded and led by Dr. Roger J. Packer from Children's National Hospital — a team working in 13 labs in the USA, Canada and Germany and including the most renowned medulloblastoma specialists on the planet.

In addition, we report on the many networking and advocacy actions that the MBI has been doing to break paradigms, achieve solutions, and save lives. Thanks to the support provided by many people, the work of MBI has been recognized across borders. We were invited to tell the MBI story in different and important arenas — such as the Permanent Council of the Organization of the American States (OAS), in Washington, DC, where we recently represented the millions of people with a rare disease and their families; and the largest Neuro-Oncology Congress in Latin America, SNOLA 2024, in São Paulo.

It takes desire to change, it takes persistence, and more than anything, it takes hope. We believe in the power of the MBI story to inspire families to seek more cures for rare diseases. We also hope we can influence governments to invest in more research to treat and cure rare diseases. And finally, we hope that our story can persuade donors to keep funding this important research.

We have no time to lose!

Fernando Goldsztein

Founder of The Medulloblastoma Initiative
Children's National Foundation Board Member

Global Innovation Born in Brazil

Watch a 3-minute video in which Dr. Roger J. Packer, Principal Investigator of the Cure Group 4 Consortium, and William Ling, Brazilian philanthropist and MBI supporter, talk about what makes the MBI special.

Watch it here

Inspiration for change

Philanthropy has the power to change the world. Witnessing this power inspires my work to advance children's health. Sick children cannot wait for science and medicine to take their own course. That's why I love to partner with philanthropists. It takes teamwork, vision, dedication and inspiration to push for better results that save lives and lifetimes.

The Medulloblastoma Initiative (MBI) donor community led by Fernando Goldsztein demonstrates all of these qualities — and more. I believe that MBI is showing the world what's possible in the fight against rare pediatric brain tumors. The MBI's partnership with Dr. Roger J. Packer at Children's National and investigators at more than a dozen laboratories in three countries is yielding results that no one in the field predicted would come so quickly. The Cure Group 4 Consortium is on the cusp of clinical trials of new therapies for relapsed Group 4 medulloblastoma.

This is a monumental feat, but two additional factors astonish me:

The MBI achieved these promising results less than 30 months after its launch. Additional accomplishments came even quicker, including the first replicable human cell line of Group 4 tumors. This comes on the heels of decades in which the field progressed incrementally over decades, but children with relapsed tumors continued to die. Rather than tiny steps taken slowly, The MBI is fueling giant leaps forward in our quest for cures.

Most of MBI's supporters to date come from Brazil, a country with relatively small philanthropic and medical sectors compared to Europe, Canada and the United States. This shows me that anyone around the world can make a global difference by coming together for children. Each MBI supporter inspires me. Led by an amazing man and father, thank you for joining Fernando Goldsztein in choosing to change the world.

I join each of you in eagerly awaiting approval of clinical trials from the US Food & Drug Administration (FDA). Until then, please know how grateful I am to you for joining Fernando, Dr. Packer and the MBI's global scientific team.

DeAnn Marshall, MHA
President of the Children's National Foundation
Washington, DC

Children's National
Hospital Foundation

Our Journey: Highlights

Based on Dr. Roger J. Packer's vision, The Medulloblastoma Initiative (MBI), is created with support from a founding donation of USD 3 million.

"Our work will culminate in novel therapeutic approach, not in 3-5 years, but in 18-24 months."

The Cure Group 4 Consortium is established with Dr. Roger J. Packer as principal investigator. Three institutions in the US and one in Canada constituted the initial Consortium group.

Children's National · SickKids · Sanford Burnham Prebys · UFHealth University of Florida Health

JUNE JULY AUG SEPT DEC JAN MAR APR MAY JULY SEPT OCT

2021

By August 2021, MBI's consistent fundraising efforts had secured the first million USD from non-founder donations.

Dr. Sheila Singh

McMaster University

Dr. Javad Nazarian joins the Consortium to develop a platform for liquid biopsy - a simple blood draw that among others may enable doctors to monitor how a child's tumor is responding to the treatment.

Children's National

Dr. Tobey McDonald joins the Consortium to work with molecularly targeted therapies.

Emory University School of Medicine

Work on PARP protein inhibitors — potent but non-toxic drugs that have shown promise in the treatment of brain tumors — starts as Drs. Lena M. Kutscher and Carl Koschmann join the Consortium.

KiTZ Hopp-Kindertumorzentrum Heidelberg · Michigan Medicine University of Michigan

The year 2021 ends with USD 5 million raised.

USD 5 mi

A **major breakthrough** is achieved: Dr. Sheila Singh establishes the first line of human stem cells capable of generating Group 4 medulloblastoma in a laboratory model — a critical basis for multiple investigations aimed at discovering new drug candidates for clinical trials.

"If the problem is going to be solved, it's going to be solved by this group."

2022

The first face to face Consortium workshop is was held at the Children's National Research & Innovation Campus, in Washington DC.

The MBI is featured in the MIT Sloan alumni website. The story told by Fernando Goldsztein was chosen one of the top 10 MIT Sloan alumni stories in 2022.

MIT Management Sloan School

Three Consortium members co-author an article published in the prestigious journal Nature, describing a groundbreaking discovery that traces the origins of medulloblastoma. The MBI support is acknowledged in the article.

nature

Dr. Dalia Haydar

Children's National

"Bringing all of the investigators together - people who see things from different angles enchances our focus on how we make a therapy work."

THE MEDULLOBLASTOMA INITIATIVE

DEC

The year 2022 ends with USD 8 million raised.

USD 8 mi

JAN

MAR

The MBI is presented at MIT to a packed Wong Auditorium as part of the Ideas Made to Matter Talks in 2023 MIT Sloan Alumni Reunion.

MIT MANAGEMENT SLOAN SCHOOL

Dr. Michael Taylor

Texas Children's Hospital®

2023

Dr. Wechsler-Reya's lab moves to Columbia University, where the team will continue the Consortium's essential work.

COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK

JUNE

The most important highlight of the Cure Group 4 Consortium Workshop was the announcement that the Consortium's advances **have enabled the planning of two clinical trials to be launched over the next 6 to 12 months.**

AUG

MBI launches an effort to engaje scientific partners in Brazil for the planning of clinical trials.

SEPT

International Symposium on Pediatric Neuro-Oncology

Drs. Michael Taylor and Vijay Ramaswamy participed in Brazil of the 1st International Symposium of Pediatric Neuro-Oncology. MBI founder Ferndando Goldsztein and Daniel Scola, medulloblastoma survivor and MBI supporter, also presented at the conference.

NOV

The Brazilian-American Chamber of Commerce (BACC) hosts a webinar to explore the MBI experience in "Brazil-US Partnerships in Health Science and Human Medicine."

BRAZILIAN AMERICAN CHAMBER OF COMMERCE, INC.

DEC

The year 2023 ends with USD 10 mi raised.

USD 10 mi

2024

PUCRS | ALUMNI

In Brazil, the MBI takes part in Valued Connections, a program aimed at raising awareness about the power of local initiatives to impact global causes and generate change.

FDA U.S. FOOD & DRUG ADMINISTRATION

Two trial protocols submitted to the FDA

- Adoptive Cell Therapy with Checkpoint Blockade
- RNA Nanoparticle Vaccine optive Cell Therapy with Checkpoint Blockade

FEB

MAR

OAS More rights for more people

The MBI joined the OAS Permanent Council in Washington, DC, for a session dedicated to World Rare Disease Day.

APR

SNOLA·2024 STATE OF ART IN NEURO-ONCOLOGY São Paulo 2024

The MBI participates in the Present-Future session of Snola 2024, the largest scientific event in neuro-oncology in Latin America, held in the city of São Paulo.

EMBASSY OF BRAZIL WASHINGTON

The work done by the MBI and Children's National is recognized in a special event at the Brazilian embassy in Washington, DC.

International Symposium on Pediatric Neuro-Oncology

United Voices

This past September the Federal University of Rio Grande do Sul, Brazil, hosted the 1st International Symposium on Pediatric Neuro-Oncology — featuring Drs. Michael Taylor and Vijay Ramaswamy, scientists from the MBI-supported Cure Group 4 Consortium — along with MBI founder Fernando Goldsztein and journalist Daniel Scola, a medulloblastoma survivor who has been an important partner in spreading the word about the MBI mission.

"In many places around the world, medulloblastoma is still being diagnosed as it was nearly 100 years ago," said Dr. Michael Taylor, who opened the event. "We have to develop better treatments for medulloblastoma," added Dr. Vijay Ramaswamy — a fact well documented by journalist Daniel Scola, who survived medulloblastoma but still faces the side effects.

MBI founder Fernando Goldsztein recalled the question he asked Dr. Roger J. Packer of Children's National Hospital in 2021: What can we do to advance research? The answer came through philanthropy, which enabled the creation of the Cure Group 4 Consortium. Since then, the MBI has built a supportive community that brings together everyone who understands that philanthropy can change the landscape of science.

"It is time for us to stop using just a microscope."

- Dr. Michael Taylor

"We need more than survival: we need more precise and less toxic treatments."

- Dr. Vijay Ramaswamy

"Surgery, radiotherapy, and six cycles of chemotherapy. Then I felt really sick."

- Daniel Scola, MBI partner

A Novel Approach: Brazil-US Partnerships in Health Science and Human Medicine

In October the MBI was featured in a live webinar organized and hosted by the Brazil-American Chamber of Commerce (BACC). Entrepreneur and MBI donor William Ling, Brazilian Ambassador Otávio Brandelli, and Dr. Roger J. Packer, head of the Cure Group 4 Consortium, contributed their perspectives on the many strengths of the MBI. They were joined by MBI founder Fernando Goldsztein, who shared the story that originated the Initiative.

As put by Mr. Ling: "The MBI is a rare case of cross border cooperation led by a Brazilian citizen to find a solution that will impact the lives of uncountable children and families, and we are proud to be a part of it."

"We knew we were getting a group of people who could work together, who would focus on the problem and would use the best science to give us our best option [...] the best option in two years to try to save more children," explained Dr. Packer. "I've been doing this for 40 years, taking care of children with brain tumors. This is an unparalleled opportunity. I wanna take it."

Thank you BACC for the opportunity to showcase our work with the presence of invaluable partners!

Valued Connections

In November, the MBI took the stage in its home town of Porto Alegre, in the South of Brazil, to tell its story of innovation, courage, and creativity. As alumnus of the Catholic University of Rio Grande do Sul (PUCRS), Brazil, MBI founder Fernando Goldsztein joined Dr. Maira Caleffi (IMAMA Breast Cancer Institute) and Dr. Jorge Audy (Tecnopuc Technology Innovation Center) to brilliantly kick off the first edition of Valued Connections, a program aimed at raising awareness among scientists, academics, entrepreneurs, and society at large about the power of local initiatives to impact global causes and create real change.

A Huge Step for MBI

OAS More rights for more people

On March 6th, The Medulloblastoma Initiative (MBI) joined the Permanent Council of the Organization of American States (OAS) in Washington, DC, for a session dedicated to World Rare Disease Day.

The event featured three main speakers, including MBI founder, Fernando Goldsztein.

The MBI was born from the realization that research in pediatric brain cancer was not working well enough to improve the life of children, who are still being left behind. With Dr. Roger J. Packer, one of world's foremost clinical experts and applied science researchers of pediatric brain tumors, and Children's National Hospital, we were able to engage scientists to work synergistically with a laser focus on finding the cure. Now, supported by donors, the MBI provides the hope that a cure can be found to save thousands of children.

Today, MBI is a philanthropic initiative that finances a consortium with 13 research laboratories, bringing together renowned scientists from the US, Germany, and Canada.

The MBI's compelling story led to an invitation by the OAS to represent the fight of the 300 million people affected by rare diseases around the world.

During his speech, Fernando Goldsztein presented MBI's unique approach to philanthropic engagement and shed light on urgent topics, such as the toxicity of available treatments for the most common type of pediatric brain tumor and the need for funding for scientific research. It also invited governments, the scientific community, and civil society to reflect on the relevance of these themes in the context of rare diseases.

The MBI was honored to share its history — and its message of hope — on this important occasion.

Permanent Council meeting at OAS in Washington, DC

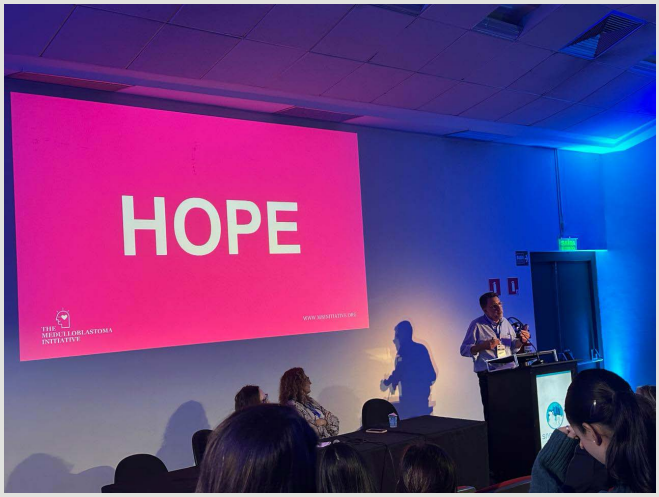
SNOLA·2024
STATE OF ART IN NEURO-ONCOLOGY
São Paulo 2024

Science with a Heart

On March 23rd, the MBI took part in the Present-Future session of Snola 2024, the largest scientific event in neuro-oncology in Latin America, held in the city of São Paulo.

In the session, an update was provided on the advances of MBI-supported Cure Group 4 Consortium — a research collaboration among top experts and laboratories from the US, Canada, and Germany. An exciting achievement addressed was the submission to the Food and Drug Administration (FDA) of two trial protocols for innovative treatments — in less than three years. Additional topics included the urgent need of resources for research in this area, in addition to the limitations of current treatments.

MBI's participation in this major scientific event attests to the power of the innovative research support model that the MBI has been developing — to advance science and provide hope!



EVERY CHILD DESERVES A FUTURE

THE MEDULLOBLASTOMA INITIATIVE

Give Now!

A blueprint for hope

What makes the MBI and the Cure Group 4 Consortium different? Four points to consider

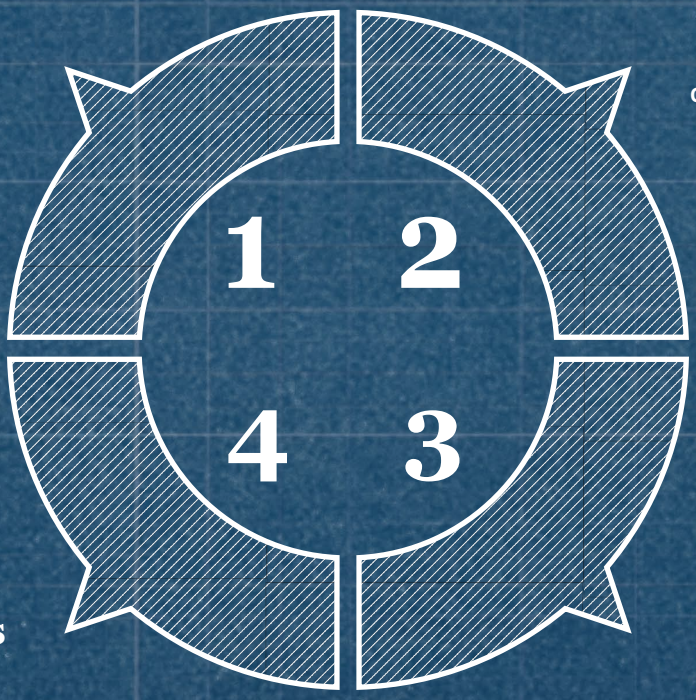
The MBI was born from the realization that research in pediatric brain cancer was not working to improve the life of children. With Dr. Roger J. Packer and Children's National Hospital, the MBI discovered the power of philanthropy. By aligning with Dr. Packer, the MBI found focus and was able to leverage scientific collaboration. Then, the MBI built a community of donors and supporters that provides passion and the hope that a cure can be found to save thousands of children — our greatest value.

1 The right science partner

Finding a partner with expertise in the scientific field of interest is essential — this partner can help establish the main focus of research, engage the necessary supporters, and liaison for resource allocation.

2 Focused research & investment

Once you define your focus, you can concentrate your investment, measured in both money and time, on this objective. The seed money needs to go to one comprehensive project that will cover all the way from development to preclinical steps to clinical trials.



4 Passion & public awareness

The mission to find the cure for any disease cannot be confined to the scientific community. Donors and supporters play a vital role in sharing stories, using the power of example to show why pediatric cancer research deserves funding and investment.

3 Infrastructure for synergy

In research, funding organizations usually divide resources among projects — this dynamic may not be the best for diseases which lack funding such as pediatric cancer. You need to secure a structure that will allow scientists to work synergistically toward a common goal, and not in competition.

*We thank FGS Global for support with text development.

Stepping stones *noun*

/ˈste-piŋ-ˌstōns/

• A means of progress or advancement.

In the MBI ecosystem, donors and supporters — individuals who contribute through networking and awareness building — fuel the progress towards the cure. We are deeply grateful for all their support, and proud to share their message of hope.

Nelson Sirotsky
MBI Great Donor

"A gesture of solidarity and love for others has the power to rekindle hope, illuminating a world full of possibilities.

Rare diseases are moving and deserve every gesture of solidarity, especially when, with no possibility of cure, they affect children and young people, lives that are still blossoming. This is the case with medulloblastoma, a pediatric brain tumor. Thanks to Fernando Goldsztein's true devotion, MBI has been developing efforts together with advanced research centers to achieve a cure for this devastating disease."

"MBI has shown that it is possible to advance the cure for this childhood brain tumor by mobilizing society, researchers and laboratories. Thanks to MBI, huge advances have been achieved in the short term, providing perspective for families affected by the disease. This is an inspiring example of how to overcome obstacles in the market structure in the healthcare sector, using empathy and solidarity. MBI shows a path not only for this disease, but also for other so-called rare diseases that affect millions of people. At the OAS, we have given visibility to this effort so that governments in our region can join the cause and so that the hope of a cure becomes reality."

Benoni Belli
Permanent Representative of Brazil to the OAS

Elena Proakis Ellis
MBI Great Donor

"Throughout Leah's cancer journey, I have not done any sort of fundraising. We have been helped by so many organizations, and they are all worthy of our donations. I've decided now, however, to focus on requesting donations for one particular organization: The Medulloblastoma Initiative. They are the only organization I am aware of that is funding research specific to Leah's exact cancer diagnosis (...). This organization is partnering with Children's National Hospital in DC, in collaboration with institutions that are part of the Cure Group 4 Consortium. I am asking anyone who can to contribute and to pass this request along to others."

Luiz Seabra
MBI Great Donor

It is heartbreaking to know that there are rare diseases, with no cure, that affect children. This is the case with Medullobastoma, a pediatric brain tumor. I came to deeply admire the example of humanity set by Fernando Goldsztein who, faced with this fatality that struck his son, did not let himself be discouraged and, with true devotion, arranged and sought resources to establish the MBI, bringing together specialized doctors and advanced research centers, today, very close to new protocols for treating and curing this disease, which devastates lives while it is still in its infancy. It is an initiative that deserves not only solidarity but all possible support.

Fernando has done what I wished I could have done for my brother who died from a rare cancer caused by the mono virus. He has not only funded almost a dozen labs globally. These labs are working together collaboratively, sharing data. We will get better treatments for brain cancers that affect children and adults.

Importantly, please take a look at the work and consider donating. Fernando was a trained in business and is truly thoughtful. He is truly a game changer approaching treatment of cancer. It's hard and has shared a better approach. Working together as researchers and leveraging capital.

Please consider giving.

Debra Coleman
Children's National
Foundation Board Member

Amy Baier
Children's National
Foundation Board Member

Fernando Goldsztein, a cancer survivor himself, is pioneering the future treatment for medulloblastoma, the cancer his young son is battling. The funds raised through MBI are sent to the Cure Group 4 Consortium, a multi-institutional research initiative led by Dr. Packer. Fernando's passion to create change will impact his son and other kids battling medulloblastoma.

MBI's tireless dedication and hard work are trully remarkable. Your contributions not only advance the understanding of pediatric brain tumors but also offer hope & support to countless families facing these difficult circumstances.

Please know that your unwavering commitment serves as a source of inspiration, motivating us to continue striving for excellence in our work for CNH.

Kathie Williams
Children's National
Foundation Board Chair

Children's National Impact Report

See the next pages for the report produced by MBI's strategic partner.

The Medulloblastoma Initiative

Impact Report | March 2024

SOLVING THE PUZZLE

Each year, we lose thousands of children worldwide when brain tumors relapse. Recurrent medulloblastomas are among the most aggressive and difficult to treat. Surgery, radiation and chemotherapy — care protocols developed decades ago — often fail or lead to devastating side effects.

We know we can do more. Recent innovations offer the potential for a treatment revolution. Yet newer approaches — from cell therapies to genomic medicine — still resemble scattered pieces of a puzzle. The Medulloblastoma Initiative (MBI) brings the puzzle pieces together.

The MBI fuels the work of 13 laboratories in Canada, Germany and the U.S. — each laser-focused on our initial goal: to unleash the full potential of science and cure relapsed Group 4 medulloblastoma. Together, our community has raised more than $10 million to fuel the Cure Group 4 Consortium.

We present this report on the MBI's impact with deep gratitude for your support of our movement to save lives.

Children's National

CLINICAL TRIALS: A BIG LEAP FORWARD

"Today, thanks to the MBI, we have the chance of a lifetime to transform care," says Roger J. Packer, MD, who leads the Children's National Brain Tumor Institute. Dr. Packer convened the Consortium in partnership with philanthropist Fernando Goldsztein.

As we shared in our last community report, the Consortium is ready to launch clinical trials of two novel cell therapies. Duane Mitchell, MD, PhD, and Elias Sayour, MD, PhD — investigators at the University of Florida — submitted applications to the U.S. Food and Drug Administration and their institutional review board (IRB) at the end of February. The team anticipates initial feedback in early April and hopes for approval within three months.

> **"Getting a new immunotherapy approach to the FDA in a two-and-a-half-year period from idea to conception to delivery is essentially unheard of. Are these therapies going to be successful? We hope so, and we have to try. That is the vision that Fernando gave to me, and that is what we are delivering on."**
>
> —Roger J. Packer, M.D.

TWO REVOLUTIONARY APPROACHES

We spoke with Drs. Mitchell and Sayour about the first two MBI-sponsored trials we anticipate launching this year.

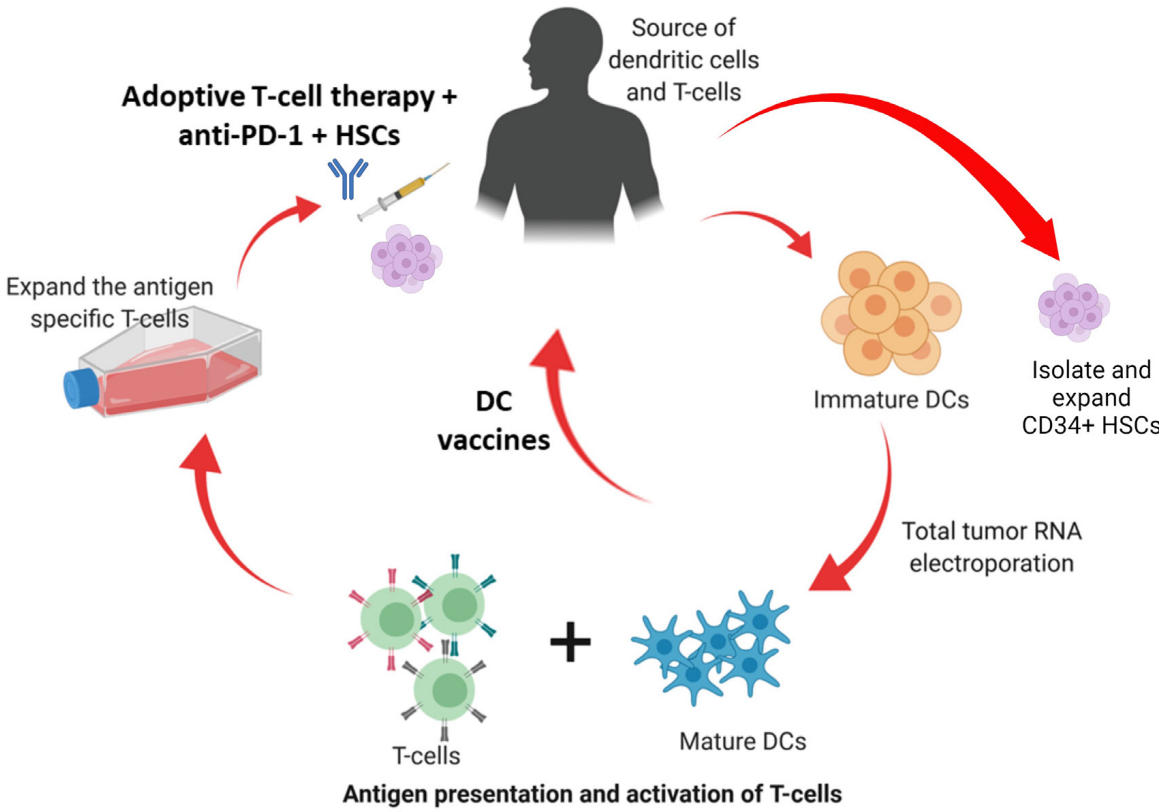
Trial 1: Adoptive Cell Therapy with Checkpoint Blockade

Dr. Mitchell will lead the first of the two trials, which seeks to enroll six patients with relapsed Group 4 medulloblastoma. The trial will harness the power of adoptive cell therapy (ACT), which programs a patient's T cells (white blood cells that drive immune responses) to seek and destroy cancer cells. In his recent ReMATCH trial, Dr. Mitchell's lab demonstrated ACT's significant promise as a safe and effective treatment for relapsed medulloblastoma. One patient saw a nearly total elimination of widespread metastatic disease.

Dr. Mitchell's new trial will test this technique for Group 4 tumors in combination with a drug called an immune checkpoint blockade. This drug prevents the tumor from protecting itself with immune checkpoints. In a checkpoint, the tumor cell binds with an immune cell and sends a stop signal to the attacking T cell. The blockade drug eliminates this line of defense, which increases the immunotherapy's effectiveness.

Years of groundwork in Dr. Mitchell's lab have set the stage for rapid approval of the MBI's new trial. "For our ACT approach, this protocol will be filed under an existing Investigational New Drug (IND) application. This means that the FDA has already reviewed and approved the process by which we generate T cells and vaccines," says Dr. Mitchell. "We have safety and outcomes data, and we already have several patients who have undergone treatment for medulloblastoma with T cell therapy alone. The checkpoint blockade is also a drug that the FDA is very familiar with. Based on these factors, we don't anticipate there being significant delays in terms of FDA approval."

This trial also got a boost from collaboration across the Consortium. Brian Rood, MD, at Children's National, and Michael Taylor, MD, PhD, FRCS(C), at Texas Children's Hospital, are collaborating with Dr. Mitchell to refine tumor-related antigen targets.



The MBI's first proposed clinical trial combines adoptive cell therapy with checkpoint blockade.

Trial 2: RNA Nanoparticle Vaccine

Dr. Sayour, a pediatric oncologist, will lead the second trial. This pioneering treatment employs nanotechnology to build an mRNA vaccine — an innovation the world learned about during the COVID-19 pandemic.

"We all are somewhat familiar with lipid nanoparticles, because they're the delivery systems for the COVID-19 mRNA vaccines — spheres injected in the muscle," says Dr. Sayour. "This [potential Group 4 medulloblastoma] vaccine delivery system is more like an onion cluster. It's given intravenously — injected into the blood stream."

Recently, Dr. Sayour's team became the first in the world to test this new vaccine approach with a clinical trial on four adults with glioblastoma — another brain cancer. "In effect, the vaccine makes your own tumor RNA look like a really dangerous virus. In the patients we treated for glioblastoma, they all had very rapid immune responses within hours. So, we're basically simulating flu-like illness very rapidly in these patients. We believe this will trigger an intense immune response against medulloblastoma."

Dr. Sayour predicts that the vaccine trial may proceed more slowly than the first trial due to its novelty and lack of prior testing in children. Success would fulfill a lifelong ambition for him. "Vaccines and preventive care are the hallmarks of healthcare," he says. "As a pediatrician, I have often wondered why in oncology we couldn't prevent disease better. The idea of a cancer vaccine always appealed to me. It wasn't until I met my mentor, Dr. Mitchell, that I could imagine that becoming a reality."

Dr. Elias Sayour plans to lead a pioneering clinical trial of an mRNA vaccine to treat relapsed medulloblastoma. Photo: Jesse S. Jones/ University of Florida

A FAMILY COMMITMENT

William Ling is a Brazilian businessman and philanthropist who supports the MBI through Instituto Ling, his family's charitable organization. Mr. Ling explained his family's commitment during a webinar hosted in October by the Brazilian-American Chamber of Commerce:

My parents immigrated to Brazil from China in the early 1950s, fleeing from the communist revolution, and settled in the southernmost state of Brazil, Rio Grande do Sul, where Fernando and I live. They had little money, no family, no relatives, no friends in Brazil to support them. They couldn't speak Portuguese and they had to rely on the hospitality and generosity of people. My father became a serial entrepreneur and was one of the pioneers in the soya bean industry in Brazil. Over seven decades, we were able to build a solid family enterprise with global reach.

My parents always recognized that they wouldn't be able to prosper without the support of fellow Brazilians, and they always had the desire to give back. In 1995, we established our family philanthropy, Instituto Ling. Its original purpose was to grant scholarships to promising Brazilian students. In 2014, we opened a Cultural Center in our hometown, Porto Alegre.

Over the years, we had many cancer incidents within our family. So, when Fernando presented The Medulloblastoma Initiative, it wasn't difficult for me and my family to make the decision to join his efforts. I've known Fernando and his family for decades. His leadership of the MBI is a guarantee that the funds raised will be well invested. I was very impressed since the beginning by the credentials of the many talented people that he was able to attract and support. He was able to harness top research officials in Canada, U.S. and Germany. Fernando's passionate determination to find the cure for this disease is contagious and worthy of our support.

Another aspect worth mentioning is that, in Brazil, there are no incentives for such initiatives at all. It's extremely difficult to raise funds for research. I do hope that my family's gesture resonates, and other supporters will follow our lead. MBI is a rare case of cross-border cooperation led by a Brazilian citizen to find a solution that will impact the lives of countless children and families.

OTHER HIGHLIGHTS FROM THE CURE GROUP 4 CONSORTIUM

Cell distribution

The laboratory of Sheila Singh, MD, PhD, FRCS(C), at McMaster University in Ontario, Canada, continues to supply the Consortium with an essential resource for drug discovery efforts – human cells capable of generating Group 4 medulloblastoma tumors in pre-clinical studies. In July 2023, her lab sent each Consortium laboratory vials containing the cells.

Drug development

The Group 4 cells enable ongoing drug discovery work in the Singh, Kutscher, MacDonald, Rood, Wechsler-Reya and Ramaswamy laboratories. The teams are taking a synergistic approach to screening multiple agents, but a breakthrough remains elusive.

Genetic discoveries

Dr. Taylor continues to refine therapeutic targets for medulloblastoma based on genetic discoveries in his lab. Results from his latest experiments are anticipated this spring. Dr. Rood's laboratory continues to make progress in proteomics studies that shed new light on the proteins that Group 4 tumors rely on to survive.

A NEW IMMUNOTHERAPY LAB AT CHILDREN'S NATIONAL

In late 2022, the Consortium helped bring Dalia Haydar, PharmD, PhD, to Children's National. Since then, Dr. Haydar has worked tirelessly to establish one of the world's leading laboratories for testing immunotherapies for rare brain tumors. "Work in Dr. Haydar's laboratory is ahead of schedule," says Dr. Packer. "Her lab is fully staffed, and multiple experiments are underway developing an augmented CAR-T cell approach." This approach equips T cells with chimeric antigen receptors (CARs) that enable the T cell to recognize, target and destroy tumor cells.

In 2023, Dr. Haydar's team launched the following groundbreaking experiments:

Enhancing the tumor-fighting power of CAR-T cells through gene editing

Investigating whether manipulating tumor-associated macrophages (immune cells abundant in solid tumors) can improve immunotherapy results

Exploring the use of focused ultrasound in combination with CAR-T cell therapies

"Preliminary results of the focused ultrasound experiments indicate improved penetration of CAR-T cells into tumors," says Dr. Haydar. "Looking ahead, we anticipate generating data that will support the development of future clinical trials. This marks a pivotal step forward in our quest to revolutionize treatment approaches for brain tumors and underscores the transformative impact of the Cure Group 4 Consortium."

DETECTION IN A DROP: THE POWER OF LIQUID BIOPSY TO TRANSFORM CARE

The MBI's impact goes beyond the quest for cures. Its investment in liquid biopsy promises to transform care for children with relapsed medulloblastoma worldwide.

Early and accurate diagnosis of relapsed brain tumors saves lives. Yet our current protocol – MRI scanning and biopsy of tumor samples – is costly, intensive and disruptive for families. It also comes with risks. An MRI can miss small tumors or produce unclear images. Decisions based on imperfect information can mean the difference between life and death for a child.

Liquid biopsy is emerging as a platform to detect the molecular signature of tumor cells with potentially greater accuracy through easy-to-collect samples. These can include blood,

serum, plasma, cerebrospinal fluid or urine. The MBI investments are fueling crucial research into discovering biomarkers that enable doctors to detect disease and monitor treatment inexpensively and easily – in real time.

In 2023, the MBI's support helped Dr. Nazarian collect vital tumor samples and assemble a team to conduct biomarker discovery. New members of his laboratory focused on this work include a postdoctoral researcher, Shefali Singh, PhD, and a staff scientist, Soniya Chatterjee, PhD.

"Liquid biopsy expands our ability to observe tumors. I believe it will one day eliminate invasive and expensive procedures for patients."

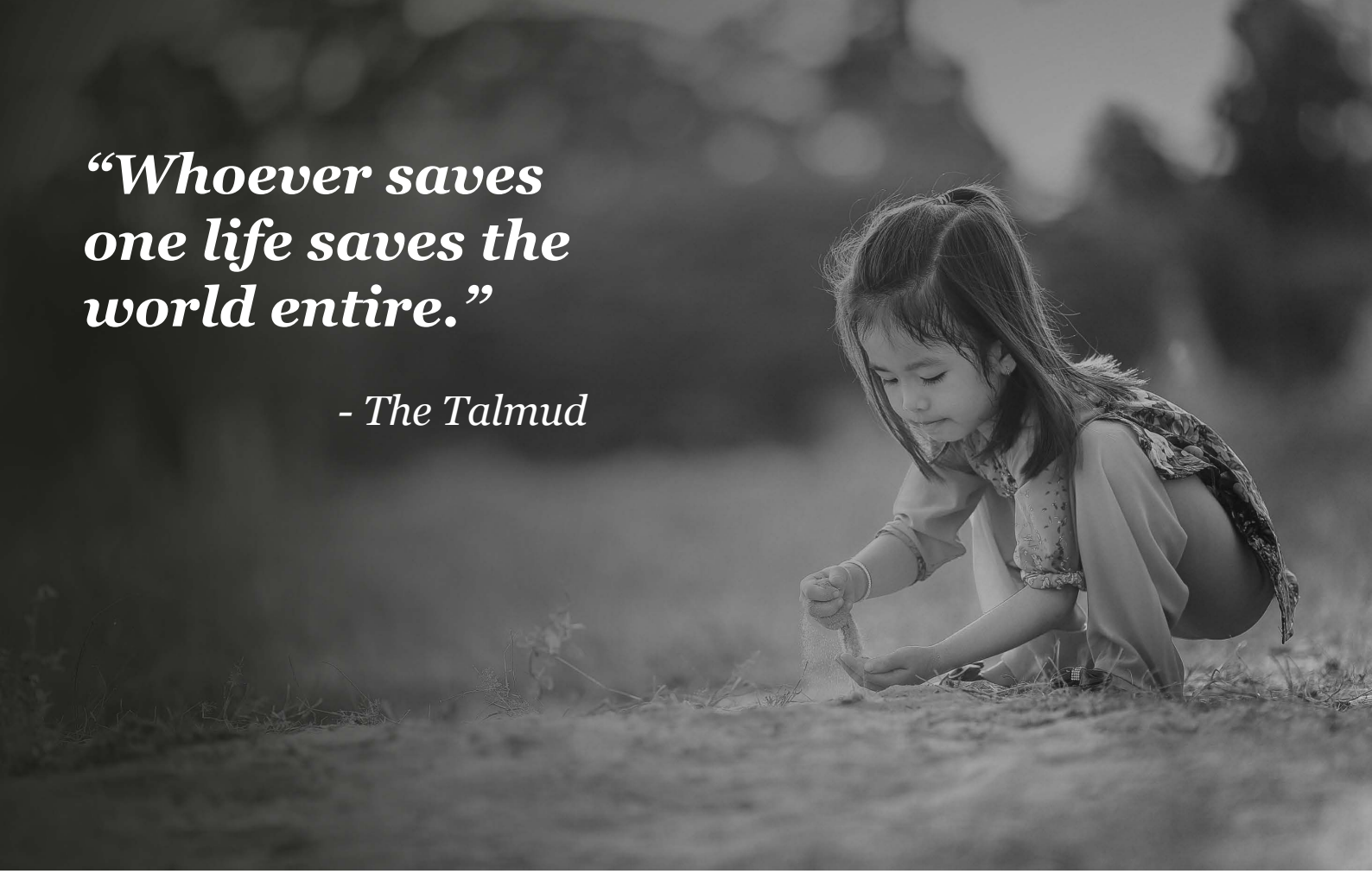
–Javad Nazarian, PhD

This year, the team is pursuing the following priorities to establish liquid biopsy:

- Conducting biomarker discovery experiments using the collected tumor samples
- Optimizing a platform to understand the immune signature of disease, which will help advance immunotherapy trials
- Mapping the tumor genome, helping researchers predict whether patients will respond to treatment

YOU ARE MAKING A WORLDWIDE DIFFERENCE

Each member of the MBI community is making a difference for children with medulloblastoma. From the clinical trials on our doorstep to the liquid biopsy poised to transform care, your generosity is increasing hope for families worldwide. On behalf of the MBI and the entire Consortium, we thank you for your interest and support.



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Kids with brain tumors were left behind.

The treatment, from the 1980s, is highly toxic and ineffective.

It's time for change!

~ The MBI

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