2025 CANADA GAIRDNER AWARD WINNERS

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ABOUT GAIRDNER

The mission of the Gairdner Foundation is to celebrate, inform and inspire scientific excellence around the globe.

Established in 1957, the Gairdner Foundation is dedicated to fulfilling James A. Gairdner's vision to recognize major research contributions to the treatment of disease and alleviation of human suffering. Through the prestigious annual Canada Gairdner Awards, the Foundation celebrates the world's most creative and accomplished researchers whose work is improving the health and wellbeing of people around the world. The Canada Gairdner Awards are recognized internationally as being among the most prestigious in the world, based on our reputation for rigorous review and early recognition of breakthroughs in science.

The Gairdner Foundation brings people together to openly discuss science in order to better engage the public, understand the problems we face, and work together to find solutions. Through Gairdner Connects, our national outreach program, we bring science to communities across Canada to inspire future innovators and spark public dialogue about the role of research in addressing the world's most pressing health challenges.

BY THE NUMBERS

5 CANADA GAIRDNER **International Awards**
For excellence in biomedical research

2 PETER GILGAN CANADA GAIRDNER **Momentum Awards**
For mid-career investigators with exceptional research

1 JOHN DIRKS CANADA GAIRDNER **Global Health Award**
For outstanding achievements in global health research

434 AWARDS
to laureates from over **40** countries

103
laureates have gone on to win the **Nobel Prize**

20
CANADIAN UNIVERSITIES

ENGAGING
6000+
students and researchers annually
through outreach programs that give Canadians access to world-renowned scientists

MEET THE 2025 LAUREATES

Canada Gairdner International Award

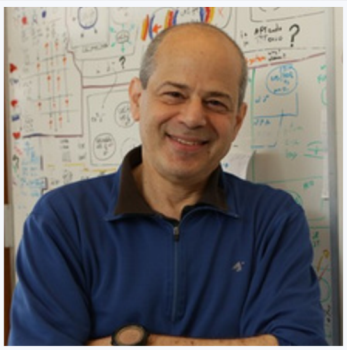
For pioneering work on the Notch signalling pathway, which has significantly contributed to our understanding of how cells communicate with each other during development, how these signals regulate cell fate determination and how disruption can lead to developmental defects and cancer.

Spyros Artavanis-Tsakonas

Professor Emeritus, Cell Biology, Harvard Medical School; Professor Emeritus, Collège de France

Iva Greenwald

Da Costa Professor of Biology, Dept of Biological Sciences, Columbia University; Professor of Biochemistry & Molecular Biophysics, Columbia University's Vagelos College of Physicians and Surgeons



Gary Struhl

Herbert and Florence Irving Professor at the Zuckerman Institute; Professor of Genetics and Development, Columbia University's Vagelos College of Physicians and Surgeons

Canada Gairdner International Award

For pioneering research into the cellular and molecular mechanisms underlying the genetic disease cystic fibrosis, leading to the development of transformative drug therapies based on these mechanisms, thereby improving and saving countless lives.

Paul Negulescu

Senior Vice President, Vertex Pharmaceuticals

Michael J. Welsh

Roy J. Carver Professor of Internal Medicine and Molecular Physiology and Biophysics; Director, Pappajohn Biomedical Institute; Roy J. and Lucille A. Carver College of Medicine, University of Iowa

John Dirks Canada Gairdner Global Health Award

For the invention of a ready-to-use therapeutic food, which has revolutionized management of severe acute malnutrition in children, allowing treatment to shift from inpatient care to community-based management and saving countless lives.

André Briend

Former Senior Scientist, Institut de Recherche pour le Développement; Adjunct Professor, Tampere Center for Child, Adolescent and Maternal Health Research, University of Tampere, Tampere, Finland; Affiliated Professor, Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Demark

Peter Gilgan Canada Gairdner Momentum Award

For the ground-breaking discovery of the role of transposable elements in regulating anti-tumour immunity through viral mimicry, which holds transformative potential for cancer therapy, and for pioneering the development of a novel blood-based test for early cancer detection, classification, and therapy monitoring.

Daniel De Carvalho

Senior Scientist, Princess Margaret Cancer Centre, University Health Network; Professor, Department of Medical Biophysics, University of Toronto; Allan Slaight Scientist and Senior Scientist, Princess Margaret Cancer Centre.

For international leadership in digital therapeutics and training initiatives focused on childhood illness-related pain assessment and self-management for conditions such as juvenile idiopathic arthritis, sickle cell disease, chronic pain and cancer.

Jennifer Stinson

Senior Scientist, SickKids Research Institute; Nurse Practitioner, The Hospital for Sick Children (SickKids); Co-Director, SickKids Centre for Pain Management, Research and Education; Professor, Lawrence S. Bloomberg Faculty of Nursing and Institute of Health Policy, Management and Evaluation, University of Toronto

Keep reading to learn more about their award-winning research in this collection with Frontiers for Young Minds.

GAIRDNER CONNECTS

Gairdner Connects brings award-winning scientists to communities across Canada to engage, inspire, and spark dialogue. In doing so, it fosters meaningful connections between Gairdner Award-winning scientists and the next generation of researchers. Through interactive events, classroom visits, community discussions, and digital resources, we inspire future innovators and spark dialogue about the role of science in addressing global health challenges.

This booklet, developed in partnership with Frontiers for Young Minds, is part of the Gairdner Foundation's national outreach program to bring science to communities across Canada.

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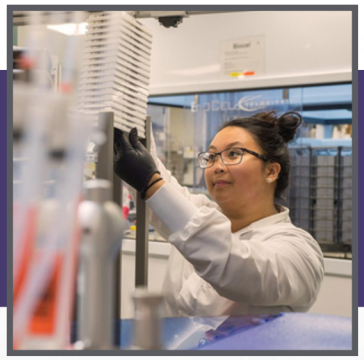
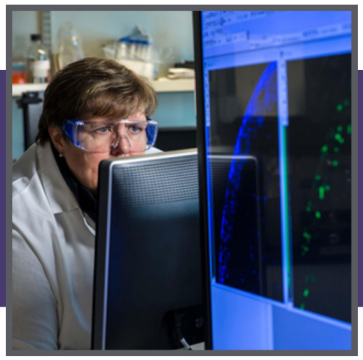
As a valued partner of Gairdner Connects, Vertex Pharmaceuticals plays a key role in inspiring the next generation of scientists. With support from Vertex, thousands of students across Canada will gain access to transformative science experiences — connecting directly with world-renowned researchers, engaging in mentorship opportunities, and discovering what is possible in their own futures. Vertex is a leader in scientific innovation, talent development, and investing in our collective scientific future.



Vertex invests in diseases where there is a significant unmet need and it can have a transformative impact for patients.

Vertex's research and development strategy is unique and includes a portfolio approach to development. When Vertex decides to work on a disease, it investigates the disease from multiple angles.



Vertex invests the majority of its resources and 3 out of 5 employees to research and development.

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The Canada Gairdner Awards Collection: Celebrating Outstanding Health Researchers

Edited by
Fulvio D'Acquisto and Pasquale Maffia

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LES PRIX CANADA GAIRDNER AWARDS

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About Frontiers for Young Minds

Frontiers for Young Minds believes that the best way to make cutting-edge science discoveries available to younger audiences is to enable young people and scientists to work together to create articles that are both accurate and exciting. That is why distinguished scientists are invited to write about their cutting-edge discoveries in a language that is accessible for young readers, and it is then up to the kids themselves – with the help of a science mentor – to provide feedback and explain to the authors how to best improve the articles before publication. As a result, Frontiers for Young Minds provides a collection of freely available scientific articles by distinguished scientists that are shaped for younger audiences by the input of their own young peers.

What are Frontiers for Young Minds Collections?

A Collection is a series of articles published on a single theme of research and curated by experts in the field. By offering a more comprehensive coverage of perspectives and results around an important subject of research, we hope to provide materials that lead to a higher level of understanding of fundamental science. Alternatively, a collection could feature articles by scientists who received special recognition, such as a Nobel Prize. Frontiers for Young Minds Collections offer our international community of Young Minds access to the latest and most fundamental research; and, most importantly, empowering kids to have their say in how it reaches their peers and the wider public. Every article is peer reviewed according to the Frontiers for Young Minds principles. Find out more on how to host your own Frontiers for Young Minds Collection or contribute to one as an author by contacting the Frontiers Editorial Office: kids@frontiersin.org

The Canada Gairdner Awards Collection: Celebrating Outstanding Health Researchers

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Human Health

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About this collection

As we face increasing global challenges, and are living longer, we all have a strong common need for good lifelong health, and access to effective medical care for sickness and injuries. Scientists studying health-related questions are leading our journey towards improved human wellbeing. To succeed, they must understand very complex body processes, and not just one, but also how the processes relate to each other, and how they all affect human health. Through ongoing research, our understanding of the human body deepens, enabling us to solve issues which could not be managed before, and improving human health with each breakthrough.

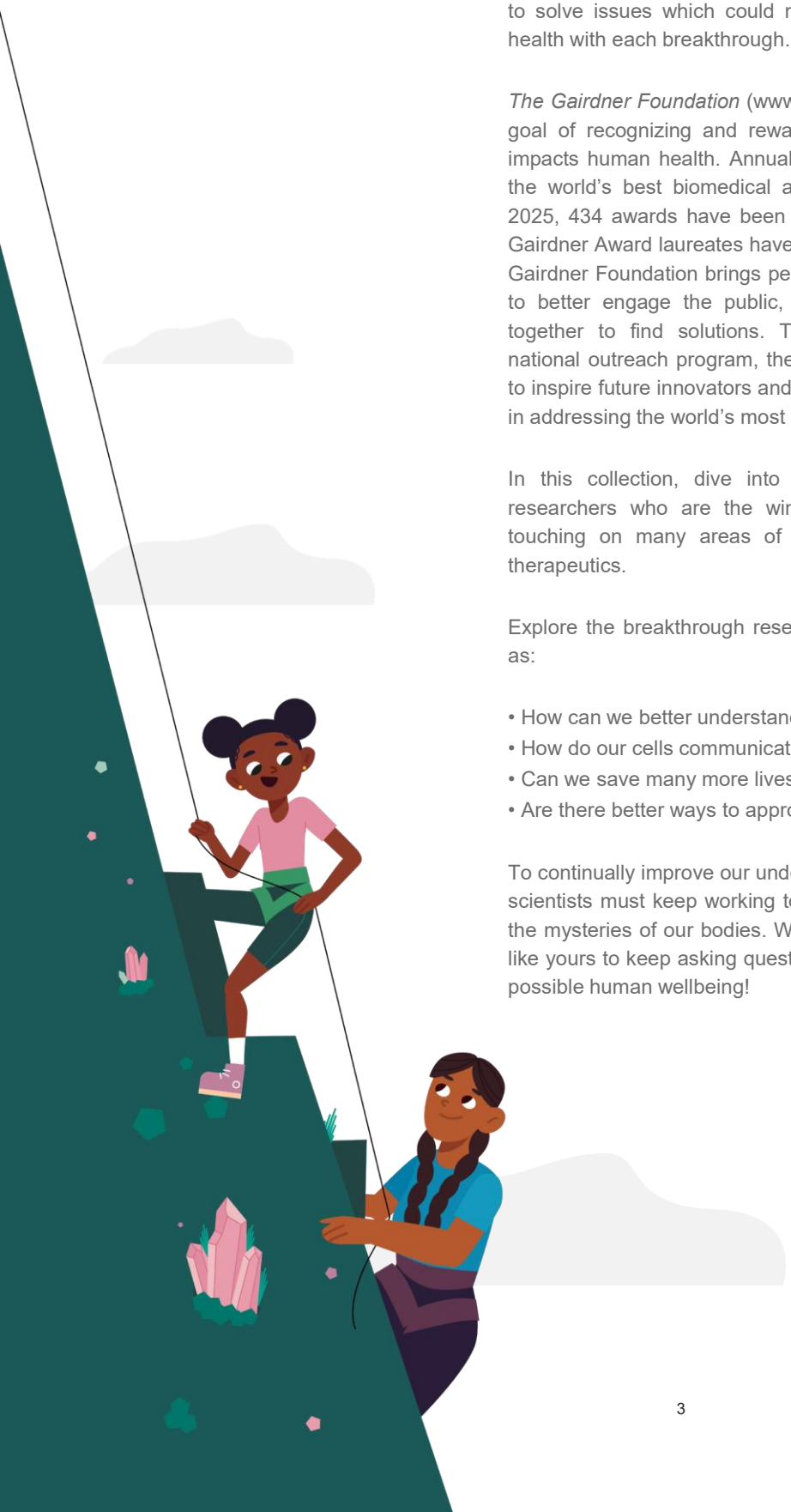
The Gairdner Foundation (www.gairdner.org) was established in 1957, with the goal of recognizing and rewarding international excellence in research that impacts human health. Annually, eight Canada Gairdner Awards are given to the world's best biomedical and global health researchers. Between 1957–2025, 434 awards have been given to scientists from over 40 countries. 102 Gairdner Award laureates have gone on to win the prestigious Nobel Prize. The Gairdner Foundation brings people together to openly discuss science in order to better engage the public, understand the problems we face, and work together to find solutions. Through Gairdner Connects, the Foundation's national outreach program, they bring science to communities across Canada to inspire future innovators and spark public dialogue about the role of research in addressing the world's most pressing health challenges.

In this collection, dive into the latest discoveries made by the leading researchers who are the winners of the 2025 Canada Gairdner Awards, touching on many areas of research, from cell-level processes to digital therapeutics.

Explore the breakthrough research which answers fascinating questions such as:

- How can we better understand and treat cystic fibrosis?
- How do our cells communicate, and how can this help us understand cancer?
- Can we save many more lives from malnutrition?
- Are there better ways to approach and treat childhood illnesses-related pain?

To continually improve our understanding and our approaches to human health, scientists must keep working to deepen our collective knowledge, and explore the mysteries of our bodies. We hope this Collection will inspire curious minds like yours to keep asking questions, and join the future efforts towards the best possible human wellbeing!



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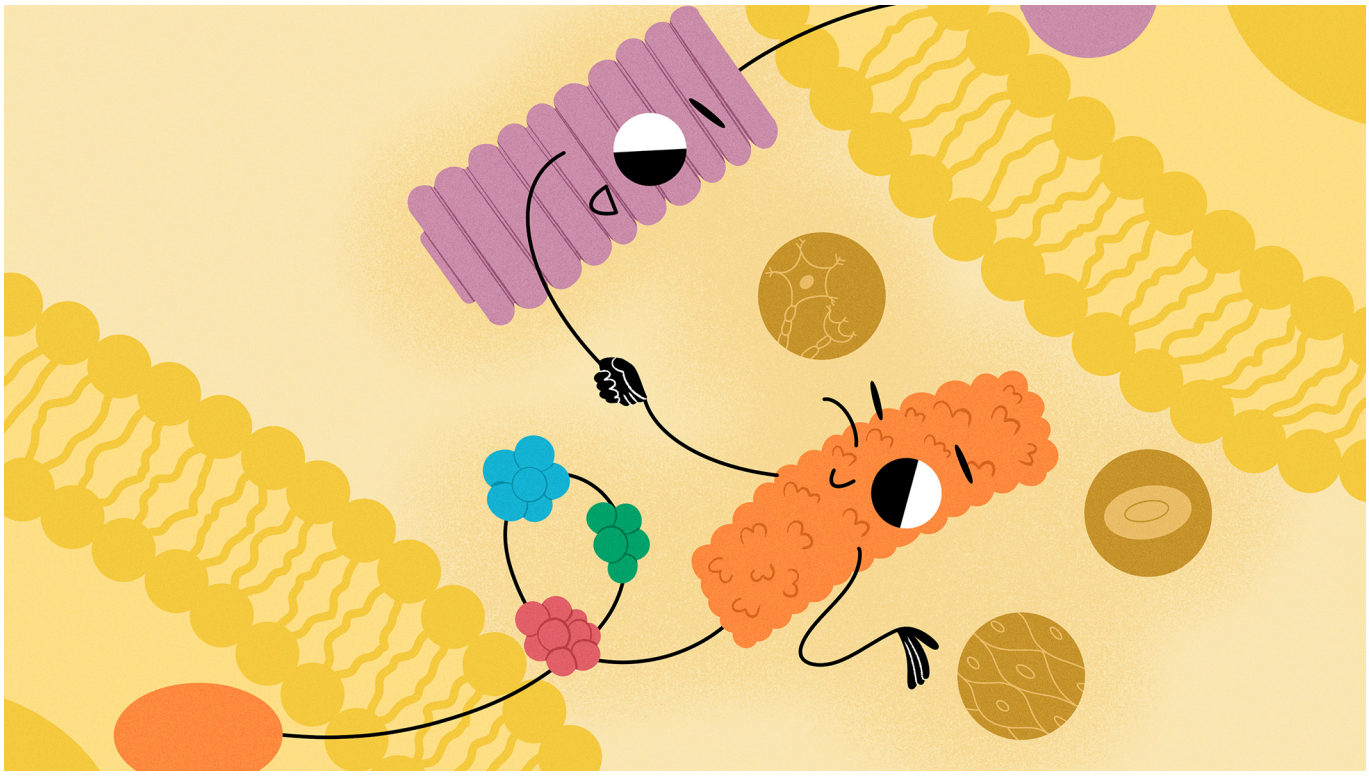

NOTCH: A SIGNALING PROTEIN THAT HELPS CELLS MAKE BIG DECISIONS

Spyros Artavanis-Tsakonas [1,2]***, Iva Greenwald*** [3,4*] ***and Gary Struhl*** [5,6]

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YOUNG REVIEWERS:

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As an organism develops from a single fertilized egg cell, how do all the different organs and tissues of its body come to be? How do some cells know to become nerves, others skin, and others bone or blood? We have spent decades studying a protein called Notch that plays a role in these kinds of decisions. Notch sits on the cell surface and helps cells communicate with each other to decide whether to grow, divide, specialize, or stay quiet. This communication, called signaling, guides how cells organize themselves during development. In this article, we describe how Notch carries messages from the outside of a cell all the way to the nucleus, where genes are turned on or off. Our

work in flies and worms helped show that this system is important in many animals, including humans. Understanding how Notch works has revealed fascinating connections between development, normal tissue upkeep, and even diseases like cancer and Alzheimer's.

Drs. Artavanis-Tsakonas, Greenwald, and Struhl were awarded the 2025 Canada Gairdner International Award "For pioneering work on the Notch signalling pathway, which has significantly contributed to our understanding of how cells communicate with each other during development, how these signals regulate cell fate determination and how disruption can lead to developmental defect and cancer".

DECISIONS, DECISIONS

All animals are made of millions (or even billions) of cells, arranged in astonishingly complex and carefully repeated patterns. Have you ever looked closely at a butterfly wing? Butterflies of the same species have wings that are nearly identical, with the same shapes, sizes, and colorful patterns of stripes and spots. To build such precise and beautiful patterns, cells need to know where they are, decide what to do, and coordinate their choices with their neighbors.

But how do cells know what to become? In the earliest stages of life, the first few cells that make up an embryo are almost the same. But as the body takes shape, those cells start to make decisions. One might become part of the nervous system. Another might help form an eye, or a digestive organ, or a limb. These decisions depend on conversations between cells—signals that say things like, "You become a nerve cell—I will become a skin cell" or "You stay quiet while I divide". These cell-to-cell conversations happen constantly as the body takes shape, ensuring that every part develops at the right time and in exactly the right way. One of the most important ways this happens is through a communication system called **Notch signaling**.

The three of us have spent many years uncovering how Notch signaling works, from identifying the gene, to the first "handshake" between two cells, all the way to the changes inside the cell's control center, the nucleus. We each focused on different aspects of the process, often using different organisms. Our discoveries, along with those of many other researchers, have helped explain one of the most important communication systems in biology. Iva was fascinated by this problem from a young age. "As a child, I had a book on the human body and was amazed that it all starts with one cell", she said. "So, I was curious about 'developmental biology' even before I knew there was such a field".

NOTCH

A protein found on many cells that helps them "talk" to their neighbors and decide what to do during development, repair, and other important processes.

SIGNALING

The way cells send and receive messages, often using special proteins, to help them make decisions, work together, or respond to changes in the body.

MEET NOTCH: A PROTEIN THAT HELPS CELLS COMMUNICATE

The gene that encodes the Notch protein was first identified more than 100 years ago, when scientists studying fruit flies found a mutant fly with notched wings (Figure 1). But it was not until the 1980s that the gene (DNA instructions) that caused the wing defect when mutated was identified [1]. Around the same time, a similar gene called **LIN-12** was discovered in *C. elegans*, a microscopic roundworm, and shown to code for a protein that is the worm version of fly Notch [2]. Finding that Notch-related proteins help cells communicate in both flies and worms—two very different species—suggested that this signaling system is likely to work in a similar way across many species—even humans. In addition, the ability to study these proteins in both systems allowed researchers to take advantage of the distinct experimental strengths of each organism.

LIN-12

A gene in roundworms that encodes a protein closely related to Notch that helps cells decide what to become during development.

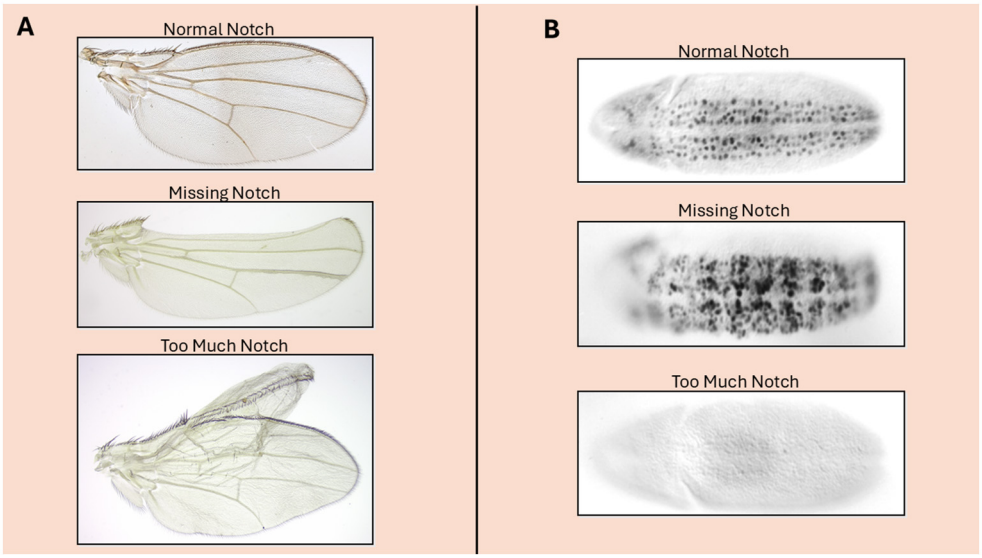

Figure 1

(A) A fruit fly wing. When Notch is "missing" from part of the wing, some wing tissue is lost (creating a "notch"). Conversely, cells with "too much" Notch can induce an extra wing. **(B)** When Notch is functioning normally in a fruit fly embryo, cells called neuroblasts (which will develop into nerve cells, stained black) develop in an organized pattern because cells communicate via Notch so that some cells become skin cells while others become neuroblasts. When Notch is missing, no cells get the message, and all become neuroblasts. When there is "too much" Notch, all cells become skin cells, and none become neuroblasts.

Notch sits on the surface of many cells, with one part outside the cell and another part inside (Figure 2A). You can think of it like a sensor: it helps a cell respond to signals from its neighbors and decide what to do next. The signal comes from a partner protein, called a **ligand**, on the surface of a neighboring cell. For the signal to work, the two cells must touch to bring Notch and its ligand together, like a handshake (Figure 2B). These signals happen again and again during development to help cells decide whether to divide, specialize, or just chill out. One special feature about how Notch works is that it is often involved in communication that goes both ways, from one cell to its neighbors and then back again, allowing cells to coordinate their choices about what to do.

LIGAND

A molecule on the surface of one cell that binds to a receptor on another cell—like Notch—to start a signal between the two.

Figure 2

Events in Notch signaling. **(A)** Notch and its ligand on neighboring cells. **(B)** Notch and its ligand bind, as if the molecules are "shaking hands". **(C)** The signal-sending cell pulls the ligand back into itself, through a process called endocytosis. This stretches out a special part of Notch that sits just outside the cell, exposing a site that is cut by a first "molecular scissors" called Kuzbanian. **(D)** This cut allows the rest of the protein to be cut by a second molecular scissors called Presenilin. The second cut releases the intracellular domain so it can travel to the nucleus to control the activity of development-related genes (Figure credit: Somersault18:24).

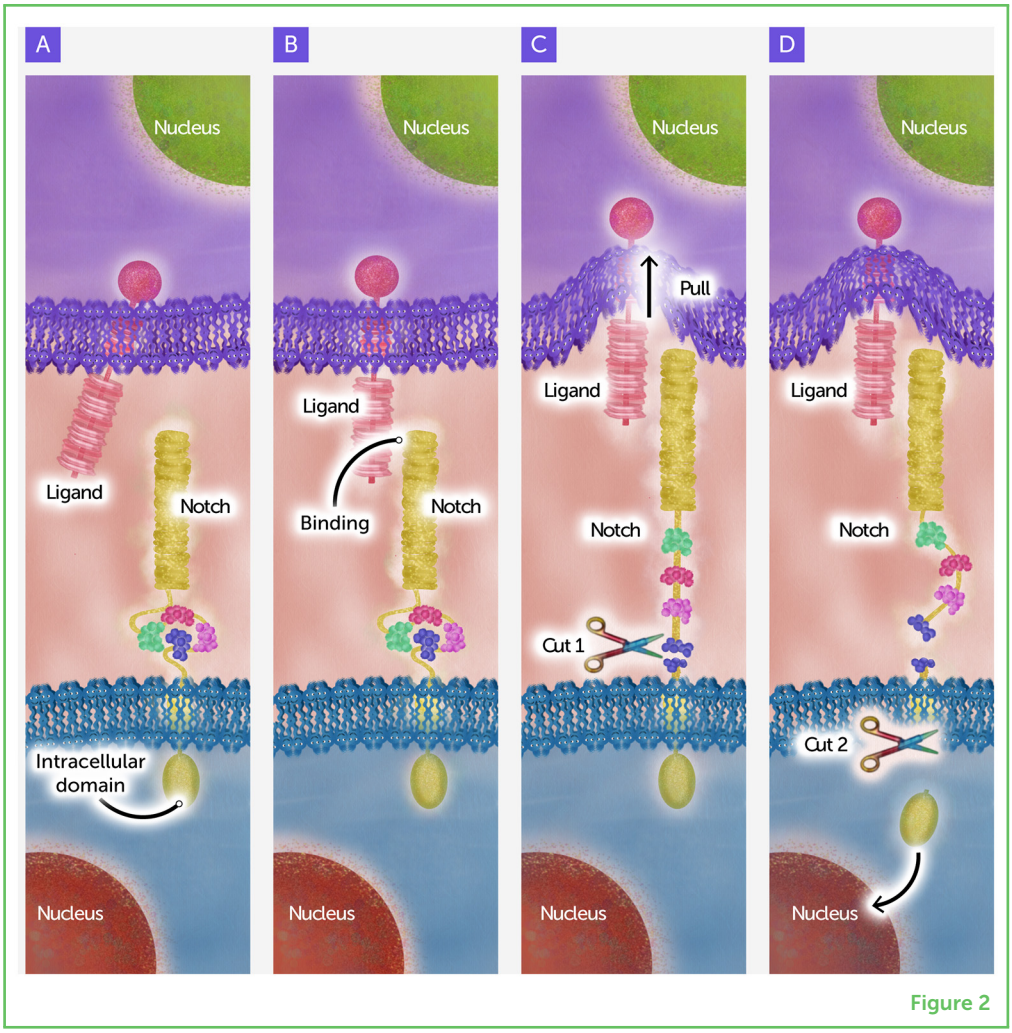

Figure 2

CUTTING THE SIGNAL LOOSE

Once researchers realized that Notch helps cells make decisions, the next big question was: how does a signal on the outside of a cell control how decisions are made by turning genes on or off inside the nucleus? The answer turned out to be both surprising and elegant.

When Notch "shakes hands" with its ligand, special molecular "scissors" cut the protein in two places—first outside the cell membrane and then inside (Figures 2C, D). These cuts release a portion of Notch within the cell, called the **intracellular domain**, which can then enter the nucleus. This finding raised the possibility that the intracellular domain might travel to the nucleus to control the activity of development-related genes—but this "cleavage and nuclear import" hypothesis needed proof.

To get this proof, new molecular tools were developed in fruit flies to track whether the intracellular domain of Notch could get to the nucleus and, once there, turn genes on and off (Figure 2D)

INTRACELLULAR DOMAIN

The part of a protein, like Notch, that is inside the cell. When released, it can travel to the nucleus and help control which genes are active.

[3]. Further studies in worms and flies confirmed the hypothesis by identifying proteins called **Kuzbanian** and **Presenilin** as the molecular scissors that make the first and second cuts, respectively, releasing the intracellular domain for its trip to the nucleus [2, 4]. Overall, this work helped explain how a signal that begins at the surface of a cell can change what happens deep inside.

KUZBANIAN

The first "molecular scissors" that helps cut Notch after it receives a signal. This first cut prepares Notch for the second cut by Presenilin.

PRESENILIN

The second "molecular scissors" that helps cut Notch after it receives a signal. This cut releases a piece that goes to the nucleus and turns genes on or off.

ENDOCYTOSIS

A process where a cell pulls molecules on its surface back inside by wrapping them up in membrane—a key event in activating Notch signaling.

PULL TO ACTIVATE

At first, many scientists thought that the ligand handshake was enough to activate Notch—but there was another surprise in store. Instead of just touching, the signal needs to tug on Notch (Figure 2C) [5]. After the ligand binds to Notch, the signal-sending cell pulls the ligand back into itself, through a process called **endocytosis**. Imagine it like the signaling cell yanking its hand back during the handshake. This yank unfolds a portion of Notch on the outside of the cell, causing it to be cut by Kuzbanian, the first molecular scissors. It is only after this first cut happens that Presenilin, the second molecular scissors, can do the final cut that releases the intracellular domain. So, without the tug, neither of the cuts happen.

One of the first clues about the tug came from studies showing that special "adapter" proteins are needed in the sending cell to bind the ligand and mark it for endocytosis [5]. The process of endocytosis then stretches the Notch molecule and exposes the right part of Notch to the Kuzbanian scissors. "The idea that Notch needs to be yanked open to be activated was a big advance", Gary explained. "What brought it to our attention was finding the specific adapter proteins necessary for the pull".

NOTCH IN HEALTH AND DISEASE

Notch is not just important for helping embryos develop correctly. Even in adult organisms, Notch allows cells to make choices based on signals from their neighbors. This process helps regulate cell division and repairs normal wear-and-tear on tissues, especially tissues that are constantly growing or changing like the skin or intestines. It even helps brain cells communicate with each other and form memories of past experiences.

When the Notch pathway is too active or not active enough, it can garble the communication between cells and cause them to make the wrong decisions [6]. This can cause problems in development; for example, some heart defects that babies are born with are associated with mutations in Notch. Many other molecules also help control the activity of Notch. They make sure the signal is not too strong or too weak, which is important for healthy development and for preventing disease. For example, a gene Iva found in *C. elegans* that

prevents "too much" Notch signaling can help stop certain blood cells from growing out of control in a type of cancer called leukemia [6]. Spyros has discovered how these additional layers of control add complexity to the basic Notch signaling system [7], findings that he says "make us realize how closely connected different biological systems can be".

LOOKING BACK, THINKING AHEAD

Together, our work has helped uncover how Notch signaling allows cells to communicate in precise, coordinated ways—from the moment cells begin "shaking hands" to the changes in gene activity deep inside the nucleus. Notch is essential during development and continues to shape the body throughout life. Although this research began with simple organisms like fruit flies and worms, the discoveries turned out to be important for many animals, including humans. These discoveries helped reveal how changes in a single pathway can affect everything from development to disease.

Famous scientists are often asked what they would say to young people who are curious about science or want to help others. For Spyros, it starts with persistence and a sense of wonder. "I never had a moment when I considered quitting", he said. "When you analyze biological phenomena, there is always a next step and a next question. Have I been disappointed by some experiments? Certainly. But in doing science, this is part—a big part—of our existence". Iva reminds young scientists that progress is rarely neat—there are always confusing results, failed experiments, and dead ends. But if you stay with it, the moment something finally works can be unforgettable. Gary emphasizes that science is not just about collecting facts—it is about thinking clearly, building strong arguments, and having the courage to question what others take for granted. In a time when scientific evidence is sometimes dismissed, misunderstood, or bent to fit someone's opinion, we find hope in your generation. Young people who are curious, think critically, follow the evidence, and keep asking bold questions even in the face of challenges are the ones who will carry science—and society—forward.

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YOUNG REVIEWERS

AANJANEYA, AGE: 11
I like painting, reading books and making crafts. I love playing chess and badminton.

KATYAYANI, AGE: 9
My favorite subject is science. I like to read and learn about different science topics. I also like to write short fiction stories for fun and hope to have them published into a book one day.

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Dr. Spyros Artavanis-Tsakonas is a professor of cell biology who has spent his career studying how living things grow and develop. He has worked at some of the world's top universities, including Yale and Harvard in the United States and the Collège de France in Paris. His research helped scientists understand how cells communicate with each other and make decisions—e.g., when to become a nerve cell or a skin cell. This kind of work is very important for learning how the body forms and how diseases like cancer can happen when cell signals go wrong. Dr. Artavanis-Tsakonas has also helped lead big science teams, taught students, and started new research programs and companies to turn discoveries into real-world tools and medicines. He believes in supporting young scientists and has helped fund science projects in Greece and Cyprus through a non-profit foundation he co-founded. He still runs a lab and keeps asking new questions about how life works.

IVA GREENWALD
Dr. Iva Greenwald is a professor of biology at Columbia University who studies how cells make decisions during development—like whether to become part of the brain, skin, or other tissues in the body. She has been studying Notch signaling for many years. This system helps cells talk to each other and make choices at just the right time during growth. Her research helped scientists understand how this system works, including how signals get from the outside of a cell to the inside and how there are many regulatory mechanisms that help resolve the conversations between cells so that the right number and kinds are made. Dr. Greenwald also discovered

some parts of this system that are involved in diseases like cancer. Her work has helped uncover how tiny changes in cell signals can have big effects on health. Through her discoveries, she has helped scientists all over the world understand how life develops, step by step. *isg4@columbia.edu

GARY STRUHL

Dr. Gary Struhl is a professor of genetics and development at Columbia University who studies how animals grow and develop from just a few cells into complex creatures with organs, limbs, and body parts in exactly the right places. He is especially interested in how cells talk to each other during this process to make sure everything forms correctly. His work has helped explain how signals called morphogens guide growth and how a system called Notch signaling helps cells make decisions and take on the right jobs. Dr. Struhl discovered how part of the Notch protein sends messages from outside a cell into the cell's nucleus—the control center—so the cell knows what to do. He found that a special kind of protein cutting, triggered by signals from neighboring cells, is what gets the message from the cell surface to the nucleus. His discoveries changed how scientists understand the ways cells communicate and cooperate to build a working body.

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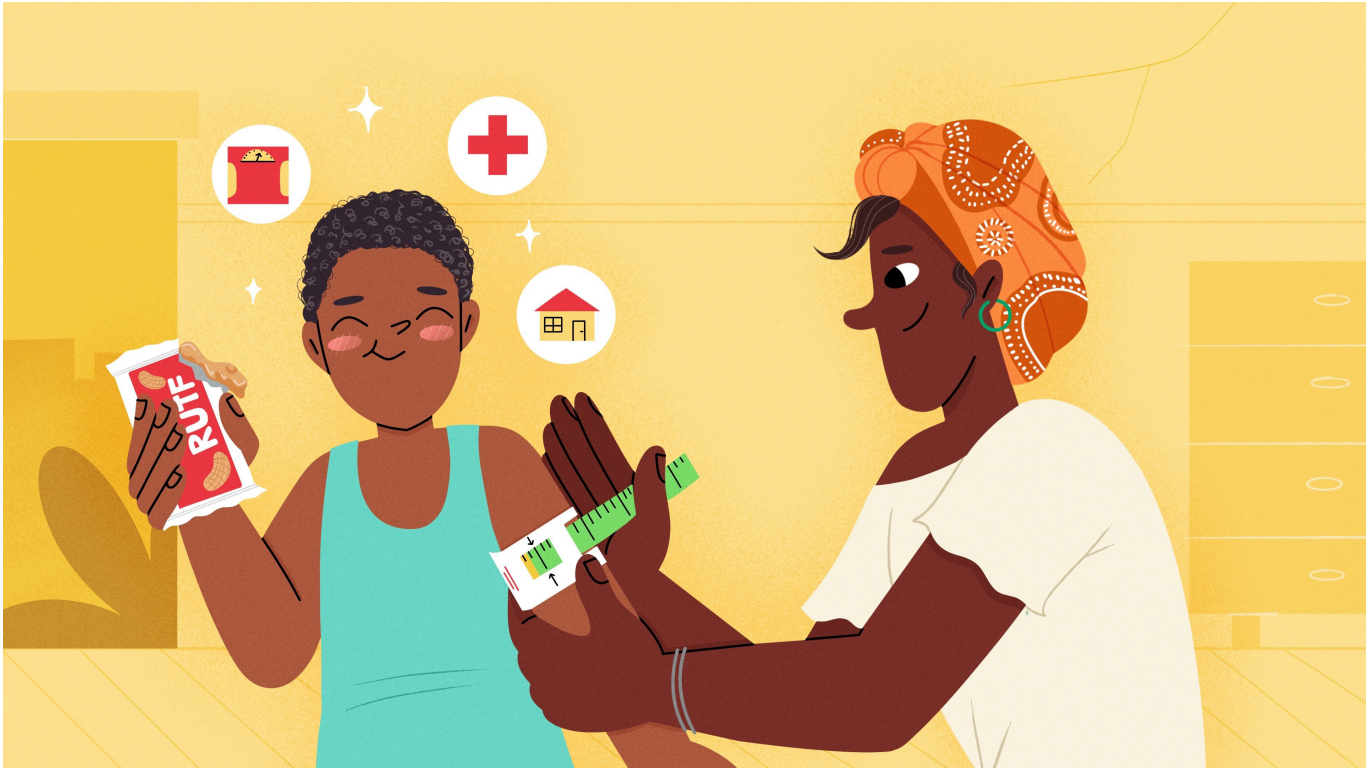

A PACKET OF HOPE: CHANGING HOW THE WORLD TREATS CHILDHOOD MALNUTRITION

André Briend [1,2,3*]

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YOUNG REVIEWERS:


ARISHA
AGE: 12


NANA YAW
AGE: 14


NANAABENA
AGE: 13


NANAYAA
AGE: 11

Severe acute malnutrition is a life-threatening condition that affects millions of children worldwide. For many years, treatment was only available in hospitals, requiring special feeding routines, clean water, refrigeration, and trained medical staff. Dr. André Briend helped change that by developing a new kind of treatment called ready-to-use therapeutic food—a safe, nutritious paste that children can eat at home without needing special preparation. He also helped promote a simple measuring tool called mid-upper arm circumference, which makes it easier to find children who are most at risk of dying from malnutrition. These two simple tools made it possible for families to get life-saving care at home, without the need for long hospital stays—even in remote areas. Thanks to Dr. Briend's work, millions of children have received faster treatment,

improved nutrition, and a better chance to survive, recover, and grow up healthy.

Dr. André Briend was awarded the 2025 John Dirks Canada Gairdner Global Health Award "For the invention of a ready-to-use therapeutic food, which has revolutionized management of severe acute malnutrition in children, allowing treatment to shift from inpatient care to community-based management and saving countless lives".

A DIFFERENT KIND OF HUNGER

Most people have felt hungry at some point—maybe you skipped breakfast because you were late for school or had to miss lunch to make up a missed assignment. You might have felt your stomach growl or found it hard to concentrate in class. That kind of hunger is uncomfortable, but it usually goes away once you eat.

In some cases, hunger becomes something much more dangerous and does not go away after a meal. **Severe acute malnutrition** is a medical emergency. It happens when a child's body does not get enough of the energy and **nutrients** it needs, not just for days, but for weeks or months. When this happens, the body begins to break down. Muscles shrink, energy disappears, and the immune system becomes too weak to fight off infections. Severe acute malnutrition affects about 19 million children, especially in low-income countries. Worldwide, it is one of the leading causes of death in children under five—and yet it is often preventable and treatable.

For many years, the main way to treat severe acute malnutrition was in a hospital. Children were given special milk-based diets through careful feeding routines several times a day. This kind of care was not easy to provide, however. The milk had to be mixed with clean water, used quickly, and kept cold in between feedings to keep it from spoiling. That means hospitals needed safe water, refrigeration, trained staff, and close monitoring to keep the treatment safe—things that were often in short supply.

In many places, hospitals were overcrowded, did not have enough staff, and were too far from children's homes. Families had to travel long distances and sometimes wait for days to get a bed. Once treatment began, it could take weeks—and many parents could not afford to stay at the hospital that long, especially if they had other children at home or jobs to go to. Some children never reached a hospital at all, and others left before they fully recovered.

When I worked as a young doctor in Africa and Asia, I saw this problem firsthand. Too many children were dying because the right

SEVERE ACUTE MALNUTRITION

A serious condition where the body does not get enough nutrients over time, causing weight loss, weakness, and a higher risk of infection and death.

NUTRIENTS

The parts of food that the body needs to grow, stay healthy, and have energy. These include proteins, fats, vitamins, and minerals.

care was out of reach for them and their families. I wanted to find a better way.

A PASTE THAT CHANGED EVERYTHING

In the late 1990s, I began thinking about a new kind of food to treat severe acute malnutrition—one that could be just as effective as hospital diets, but easier to use and safer in places without clean water or electricity. Instead of starting from scratch, I tried to connect simple facts we already understood to find a better solution.

To recover from malnutrition, children need food that is dense in energy, especially from fat. I already knew that the liquid, milk-based hospital diets were dangerous outside the hospital because bacteria grows quickly in foods that have water in them. Bacteria need both food and water to grow, so I had an idea: if we could make a high-fat food that did not contain water, it might be much safer to use in the community. And if it tasted good, children would eat it on their own.

I worked with a food technologist named Michel Lescanne and, together, we explored several options: biscuits, bars, pancakes, and even doughnuts. But these were either too fragile, too hard to store, or the cooking or baking process needed to make them destroyed some of the vitamins children required. Then we realized that a spread—like a nut butter—might work. It could hold all the nutrients of the hospital milk formula, but without the water. We replaced some of the dried milk in the original hospital recipe with peanut butter and created a paste that has the same nutritional value, lasts for months without the need for refrigeration, and tastes good. We tested it for safety by contaminating a sample on purpose—and found that bacteria could not grow in it. That meant it could be stored without refrigeration and safely eaten straight from the packet. The end product was what we now call **ready-to-use therapeutic food** (RUTF; Figures 1A, B).

READY-TO-USE THERAPEUTIC FOOD (RUTF)

A special kind of food paste used to treat children with severe malnutrition. It does not need to be cooked or mixed with water.

At first, we tested RUTF in hospitals to make sure there were no adverse effects and to check how it compared to the standard treatment. The results were better than expected. Children liked RUTF and ate it easily, gained weight faster, spent less time in treatment, and recovered just as well—or even better [1, 2]. Even though the idea of treating malnutrition with a sweet, peanut-based spread seemed strange to many experts at the time, we began to wonder: if this paste worked in the hospital, could it also work in the home?

FROM HOSPITALS TO FAMILY HOMES

Once RUTF had been shown to work in hospitals, the next step was to see whether it could help children recover at home. Home-based

Figure 1

(A) RUTF is an energy-dense paste that comes in easy-to-use packets and lasts for months without the need for refrigeration (Wikimedia Commons, CC BY 2.0). **(B)** Children can eat RUTF right from the packet at home, reducing the need for hospital stays to treat their malnutrition (Flickr, CC BY-NC 2.0). **(C)** A MUAC tape being used to measure a child's upper arm circumference. If the reading is in the red range, the child is in danger of dying from severe acute malnutrition. Yellow indicates they are at risk, and green means they are likely to be okay (Wikimedia Commons, CC BY-SA 2.0).

treatment was a major shift in thinking that many experts did not agree with. But I knew that if a safe, nutritious food could be used outside the hospital, we would be able to reach many more malnourished children—especially in areas where hospitals were overcrowded or far away.

Although I did not lead the first community trials myself, several researchers were willing to test this new approach. In Malawi, a team of researchers began giving RUTF to children in their own homes [3]. Around the same time, another researcher worked with community health programs in Ethiopia and other countries [4]. Their early results were clear: children treated at home with RUTF gained weight, recovered well, and were more likely to finish treatment.

These studies helped change the way people thought about treating malnutrition. When families could give the treatment themselves, care started earlier, reached more children, and fit better with real life (Figure 2). That made recovery faster, safer, and more successful.

FINDING THE KIDS WHO NEED HELP MOST

MID-UPPER ARM CIRCUMFERENCE (MUAC)

A quick way to check for malnutrition by measuring around a child's upper arm. A small measurement can be a warning sign.

Even the best treatment cannot help if we do not know which children need it. For many years, the main way to identify severe malnutrition was by comparing a child's weight to their height. This required careful measurements, special equipment, and complicated charts—things that were difficult to use in crowded clinics or rural villages.

A simpler option is to take a measurement called **mid-upper arm circumference** (MUAC) (Figure 1C). This method uses a small, color-coded measuring tape that wraps around the middle of a child's

Figure 2

Figure 2

RUTF changed treatment of severe acute malnutrition. **(A)** Before RUTF, treatment involved long hospital stays during which children received a milk-based formula on a regular schedule. The formula required refrigeration so it would not spoil. Hospitals were often crowded and sometimes families lived far away and could not stay for the whole treatment. **(B)** RUTF has many advantages over the traditional milk-based therapy. Studies showed that malnourished children who ate RUTF at home gained weight, recovered well, and were more likely to finish treatment (Figure credit: somersault18:24 Studio BV).

upper arm. Children with severe malnutrition often have very thin arms, so a small measurement can be a warning sign. If the tape shows red, the child is in danger. Yellow means they are at risk. Green means they are likely to be okay. It only takes a few seconds, and even parents or community volunteers can learn to do it.

I was not the first person to suggest using MUAC—that idea had been around for years. But during my research in Senegal and Bangladesh, I helped show something crucial: that MUAC could accurately identify the children who were most at risk of dying from severe acute malnutrition [5]. In other words, it was not just easy to use—it was effective. Today, MUAC is used around the world to spot malnutrition sooner, so that children can get help before it is too late.

FROM DOUBT TO A WORLDWIDE SHIFT

When we first introduced the idea of using a spread to treat severely malnourished children, many experts did not believe it would work. They were convinced that children who were this sick could only recover by drinking liquid formulas in a hospital, where they could be taken care of by trained staff. A peanut-based paste seemed too simple...and too risky. Some even told us the idea would never succeed.

As more researchers studied the use of RUTF in the community, the results became hard to ignore. Children liked the paste, ate it easily, gained weight, and got better. Families liked being able to treat their children at home. Even for those with complicated cases who still needed hospital care, the time spent in the hospital was considerably shorter and, after the complications were treated, malnutrition treatment could be continued safely at home. The evidence changed opinions—and policies. Today, more than 70 countries use RUTF to treat severe acute malnutrition. UNICEF now

calls it a "wonder food", and the World Health Organization includes it on its list of essential medicines. In 2022 alone, UNICEF obtained enough RUTF to treat an estimated eight million children.

When others doubted the idea, I kept going—because I believed it could help. Now when people who use RUTF tell me that it saves many lives, that is very rewarding for me. However, thinking about past successes should not cause us to forget that many children are still suffering from malnutrition—so, trying to improve their situation should still be a major focus. Many scientists from all over the world are working to improve the effectiveness of the current RUTF recipe or trying to make it less expensive. Others are developing products that are better suited for children with health complications, while still others focus on preventing malnutrition in the first place. I try to follow all this research the best I can, offering advice whenever I have the opportunity to help.

A MESSAGE FROM THE SCIENTIST WHO HELPED CHANGE THE SYSTEM

My goal has always been to make sure that children with severe malnutrition can get the care they need, no matter where they live. That meant finding practical solutions, testing them carefully, and working with others to make them available around the world. What inspired me the most was simple: watching a child who had been too weak to smile recover and smile again. That moment reminds me why the work matters.

This kind of progress—turning a scientific idea into a simple tool that helps millions of people—requires teamwork. My role was to connect commonly known facts from different fields and work with others to turn those ideas into something useful. Some of the most important breakthroughs happen when people from different backgrounds—medicine, nutrition, and food science, for example—listen to one another and build on each other's work.

If you are curious about food, health, or fairness, there are many ways to make a difference. You might become a scientist, a doctor, an engineer, or something else entirely, but the important thing is to stay open-minded, keep asking questions, and look for new ways to use what you already know—especially by working with others. Even problems that seem too big to fix can be solved through small, practical ideas and teamwork.

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created by Somersault18:24. Written informed consent was obtained from the individual(s) for the publication of any identifiable images or data included in this article.

AI TOOL STATEMENT

The author(s) declare that no Gen AI was used in the creation of this manuscript.

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CONFLICT OF INTEREST: AB was a consultant for Nutriset, the company that industrially produced the earliest RUTF, during the development and testing phases, from 1996 to 2003.

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YOUNG REVIEWERS

ARISHA, AGE: 12

I am in 8th grade and enjoy reading, listening to music, and spending time with my family and friends. I have been playing the violin for 4 years and recently started playing tennis. My favorite subject in school is math and my favorite colors are light pink and purple. I act in musicals during the summer and attend the student council and orchestra club at my school.

NANA YAW, AGE: 14

I enjoy playing sports mainly basketball and football. I support Liverpool Football Club and I hope to play in the NBA in the future. I am a very competitive and passionate person. I also love to eat a lot to gain energy.

NANAABENA, AGE: 13

Hello my name is Nanaabena. I enjoy reading books and chatting in my free time, expecially with my friends. I also enjoy cooking, it brings out my inner happiness. I am a curious person and look forward to learning new stuff everyday.

NANAYAA, AGE: 11

Hi, my name is Nanayaa and I mainly love to sing and do all kinds of sports. I also like to read interesting books, paint and draw.

AUTHORS

ANDRÉ BRIEND

André Briend is a doctor and nutrition scientist who has spent his career working to improve the health of children around the world. He grew up in France and began his research in the 1970s, studying how to help children who were sick because they did not have enough to eat. He worked in countries like Senegal and Bangladesh, where he helped show that a simple tape measure around a child's arm could help find children most at risk. Later, he helped develop ready-to-use therapeutic food (RUTF)—a peanut-based paste that has saved the lives of millions of children with severe malnutrition. Dr. Briend has worked with many global health organizations, including the World Health Organization, and still works with teams around the world to find better ways to care for malnourished children. *andre.briend@gmail.com

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EPIGENETICS IN ACTION: FINDING AND FIGHTING CANCER IN NEW WAYS

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YOUNG REVIEWERS:

EUGENE
AGE: 15

Dr. Daniel De Carvalho studies how to fight cancer in new ways. He works in a field called epigenetics, which looks at how cells turn genes on or off. He discovered that cancer cells can be made to look like they are infected with a virus, by turning on old virus-like parts of DNA that are usually kept silent. This process, called viral mimicry, helps the body's defense system notice the cancer and fight it. Dr. De Carvalho also helped create a blood test that uses epigenetics to find cancer early—even before symptoms appear. This test, which looks at patterns of epigenetic "switches" found on tiny bits of DNA floating in the blood, can sometimes even tell what kind of cancer is growing. His discoveries could help doctors find and treat cancer more effectively, using just a blood sample.

Dr. Daniel De Carvalho was awarded the 2025 Peter Gilgan Canada Gairdner Momentum Award "For the ground-breaking discovery of

the role of transposable elements in regulating anti-tumour immunity through viral mimicry, which holds transformative potential for cancer therapy, and for pioneering the development of a novel blood-based test for early cancer detection, classification, and therapy monitoring".

CANCER: A HIDDEN ENEMY

When you hear the word cancer, you might feel scared or worried. Maybe you know someone who has had it, or you have heard adults talk about how serious it can be. Cancer affects millions of people every year and causes more deaths than almost any other disease. But what exactly *is* cancer, and why is it so dangerous? And most importantly, how can science help us fight back?

Normally, the cells in our bodies grow and divide in a controlled way, but sometimes, something goes wrong. Cells start growing out of control, ignoring the usual signals to stop. When this happens, a mass of abnormal cells can form, called a tumor. Tumors can start in almost any organ (e.g., lungs, brain, skin, blood) and some can spread throughout the body, taking over organs and blocking the critical functions that keep us alive and healthy.

One thing that makes cancer so dangerous is that the immune system—the body's natural defense force—does not always catch it. The immune system is great at spotting threats like bacteria and viruses, helping us to recover from common infections. Cancer is more challenging because cancer cells come from our own cells, which means they do not look as "threatening" and can more easily hide from the immune system. Tumors can grow quietly, without being attacked or eliminated, until they become large enough to cause damage or spread.

WHEN GENE CONTROL GOES WRONG

As you probably already know, DNA contains the genetic instructions that tell cells how to build the proteins that help them do their jobs. Some instructions also help control when cells divide or stop dividing. For many years, scientists thought that cancer was entirely caused by changes in the genetic code, called mutations. While mutations that damage the genetic instructions *can* cause cells to start behaving abnormally and turn into cancer, this is not the whole story. Even when the instructions look normal, problems can still happen—because there is another layer of control involved.

Roughly every cell in the body has the same full set of genetic instructions. For example, skin cells and brain cells contain the same

code, but they activate different parts of the code to make only the proteins they need. This system of gene control, called **epigenetics**, involves chemical tags that attach to DNA and instruct the cell to turn specific genes on or off—like a set of switches. These switches can change over time in response to the environment, diet, stress, or even infection. That flexibility is generally a good thing.

EPIGENETICS

A system that helps cells control which genes are turned on or off, using chemical tags. Epigenetics does not change the DNA itself, but it changes how the DNA is used.

Sometimes, the switches get stuck in the wrong position. Genes that normally protect us from cancer can be turned off, while harmful ones that help cancer to grow stay active. The instructions are undamaged, but the cell no longer reads them correctly. When I learned how epigenetic changes might help explain how cancer works, I became interested in whether we could use epigenetics to *fight* cancer. But how?

SECRETS HIDDEN IN THE DARK GENOME

As I mentioned, many cancer researchers originally focused on the role of mutations that changed the genetic instructions coding for important proteins. But most of our DNA—an amazing 98%—*does not* code for proteins. For a long time, this "non-coding" DNA was dismissed as unimportant "junk", but that view has changed. Scientists now believe that many non-coding regions have important functions. This vast, complex region is often called the **dark genome** because much of it is still poorly understood.

DARK GENOME

The parts of our DNA that do not code for proteins. Once thought to be "junk", this region includes many elements that help control gene activity or affect how cells behave.

One specific part of the dark genome particularly caught my attention—stretches of DNA left behind, sometimes by viruses that infected our ancestors thousands or even millions of years ago. These ancient sequences, including a type called **transposable elements**, are usually silent, kept turned off by epigenetic signals. Transposable elements can copy themselves or move to new spots in the genome, which can sometimes change how nearby genes behave. As I learned more about these transposable elements, I began to wonder: what if we could use epigenetics to turn them back on in cancer cells, to make those cells look like they were infected by a virus? Could that "wake up" the immune system and help it recognize cancer as a threat?

TRANSPOSABLE ELEMENTS

Pieces of DNA that can copy or move to new spots in the genome. Some came from viruses that infected our ancestors. They are usually kept turned off by the cell.

THE VIRUS ALARM INSIDE OUR CELLS

In healthy cells, the ancient viral sequences are usually kept silent through a common epigenetic "switch" called **DNA methylation**. This is a normal process in which cells attach small chemical tags called methyl groups to parts of the DNA, to block the activity of instructions that are not needed. My team and I wanted to know what would happen if we turned the quiet transposable elements back on in cancer cells. Might doing so make cancer cells look like more of a threat to the immune system?

DNA METHYLATION

A chemical tag made of a methyl group that attaches to DNA. It helps turn genes off when they are not needed and plays an important role in epigenetic control.

When we treated cancer cells in the lab with drugs that remove methylation marks, we saw something exciting: the cells began making a kind of molecule that is usually only produced when cells are infected by a real virus. This warning molecule alerts the immune system that something is wrong. By "waking up" the ancient viral sequences hidden in the dark genome, the drugs caused the cancer cells to act like they were full of viruses. The immune system, which had been ignoring the cancer, started to respond. It was like pulling a fire alarm inside the cell—the warning went out, and the immune system rushed in to fight the cancer cells [1, 2]. We called this effect **viral mimicry** because it tricks the immune system into seeing cancer cells as if they are infected with a real virus, giving the body a new chance to fight back (Figure 1A).

VIRAL MIMICRY

A process where silent virus-like DNA is turned on in cancer cells, causing them to release signals that alert the immune system, making cancer easier for the body to detect.

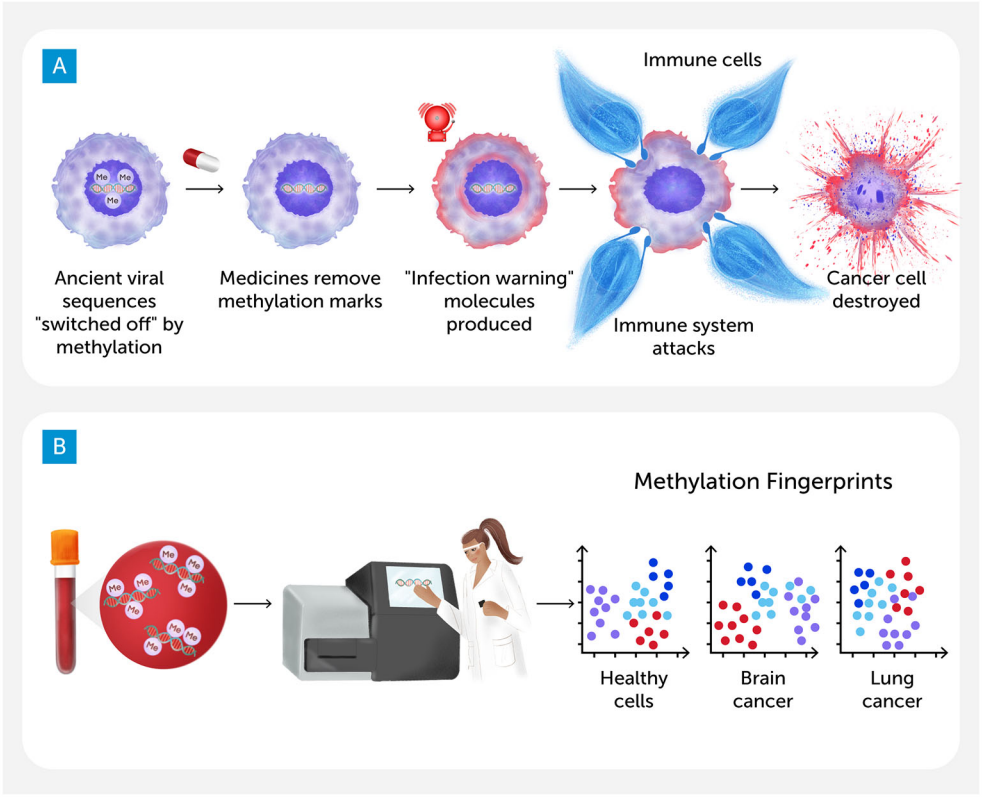

Figure 1

(A) We treated cancer cells with drugs that remove methylation marks. This "woke up" ancient viral sequences, and the cells produced a warning molecule usually only made when a real virus infects them. The immune system rushed in to fight the cancer cells. This effect is called viral mimicry. **(B)** Starting with a simple blood sample, scientists can use lab equipment to determine the methylation "fingerprint" on cell-free DNA floating in the blood. These fingerprints are unique enough that we can tell if the cell-free DNA came from healthy cells or cancer cells—and sometimes we can even identify the kind of cancer cells (Figure credit: Somersault18:24).

FINDING BETTER WAYS TO SPOT CANCER

The sooner doctors can detect cancer, the better the chances of treating it successfully. Unfortunately, many people do not know they have cancer until they start to feel sick—by then, it may have already spread, making treatment more difficult. The scans that doctors typically use to try to find cancer can sometimes miss small tumors. If doctors *do* see something suspicious on a scan, they usually take a small piece of tissue—called a biopsy—to examine further. However, biopsies can be painful or risky, depending on where the tumor is.

BIOMARKERS

Measurable signs in the body—like proteins or DNA changes—that show if a person has a disease, how it is progressing, or how they might respond to treatment.

What if there was a better way to detect cancer? One promising idea is to use **biomarkers**—clues in the body that suggest a disease is present. Biomarkers can be proteins or chemicals in the blood, or a pattern in a person's DNA. My team asked whether epigenetic changes—especially differences in methylation—could work as biomarkers for cancer. Every cell has its own methylation pattern that helps it function normally. In cancer cells, those patterns often change in predictable ways. Some genes are mistakenly turned off, while others are switched on. These changes can be so consistent that they form a kind of fingerprint—a signal that cancer is present, even when we cannot yet see it.

A DROP OF BLOOD—AND LOTS OF DATA

The next question was: how can we find each cancer's unique fingerprint?

As cells get old or damaged, they release tiny pieces of DNA into the bloodstream. These fragments, called cell-free DNA, come from all over the body. In healthy people, most come from normal cells; but in someone with cancer, some come from the tumor. The tricky part is telling the difference.

CFMEDIP-SEQ

A lab method that uses a blood sample to find cancer by detecting DNA methylation patterns in cell-free DNA, with help from machine learning.

My team developed an epigenetic method to help solve this problem, called **cfMeDIP-seq**. It starts with a simple blood test (Figure 1B). We collect cell-free DNA and use advanced tools to scan millions of sites across the DNA, looking for methylation patterns. These patterns help us figure out whether that DNA came from healthy cells or from a tumor. Recognizing the patterns requires powerful computers, which we train to tell the difference between healthy and cancerous DNA. The more examples we give the computer, the better it gets.

cfMeDIP-seq worked better than we expected. In our first studies, we tested blood samples from people already diagnosed with cancer. We could detect cancer-specific methylation patterns even when only a small amount of tumor DNA was present. Eventually, we could even identify what kind of cancer the cell-free DNA came from—such as lung, pancreas, or colon [3]. In another study, we analyzed blood samples from people who were healthy at the time but later developed cancer. In some cases, the test picked up signs of cancer months or even years before symptoms appeared. That means the methylation patterns were already changing long before cancer was diagnosed, giving doctors a chance to act earlier, when treatment is more likely to work. We also used cfMeDIP-seq for brain tumors and found that we could tell the difference between several types of brain tumors without the need for dangerous biopsies [4].

We are still improving this technology, but the goal is clear: to give doctors a faster, easier, and safer way to detect cancer—even before

symptoms appear—and to learn important details about each case. This information could one day help guide **personalized medicine**, allowing doctors to tailor treatments based on the unique features of each person's cancer—all with just a blood sample.

PERSONALIZED MEDICINE

An approach to healthcare where treatments are chosen based on a person's unique features, such as their specific cancer type or genetic patterns, to improve results and reduce side effects.

CURIOSITY, CHALLENGE, AND A BETTER WAY FORWARD

Our work has shown how cancer cells can be unmasked by turning on hidden virus-like parts of the DNA that are usually kept silent. We also found that changes in DNA methylation patterns can help with early detection, using a simple blood test. But I did not start with a grand plan to solve these problems—I followed my curiosity and studied questions that interested me. Over time, those questions led to exciting discoveries, but I did not do it alone. Teams of researchers, doctors, and students worked together across multiple fields, sharing ideas and building tools as a group, and that made all the difference.

When we first started working on viral mimicry, the idea was not widely accepted. It took time—and a lot of evidence—for other scientists to take it seriously. That is starting to change, and the Gairdner award feels like a turning point. At a major genetics conference I recently attended, an entire session was dedicated to viral mimicry—something that would have been unthinkable just a few years ago!

There is still a lot we do not know, but the closer our work gets to real patients—to helping doctors improve peoples' chances of surviving cancer—the more motivated I become to find the answers. If you are curious about science, my advice is simple: learn to enjoy the journey. The questions you ask, the answers you find—and even the ones you cannot—are all part of what makes science rewarding. What stays with you in the end are the people you help, the people who help you, and the joy of discovery along the way.

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The author(s) declare that no Gen AI was used in the creation of this manuscript.

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YOUNG REVIEWERS

EUGENE, AGE: 15

Our young reviewer is a vibrant 15-year-old with a passion for music and games. At nearly 3 years old, he was already exploring toy stores and gravitating toward musical instruments. Today, he plays nicely the violin, somehow of flute, zampoña, and piano. He is also an avid video gamer, especially enjoying Blox Fruits on Roblox. His curiosity and energy extend to sports as well; he practices boxing in the afternoons when his homework load allows.

AUTHORS

DANIEL D. DE CARVALHO

Dr. Daniel De Carvalho is a scientist who studies cancer and works to find better ways to detect it early and treat it more effectively. He leads a research team at the Princess Margaret Cancer Centre in Toronto and teaches at the University of Toronto. His work focuses on a part of science called epigenetics, which looks at how cells turn different genes on or off. He discovered that changing these gene signals in cancer cells can help the immune system recognize and fight the disease. Dr. De Carvalho also helped develop a special blood test that looks for tiny clues from cancer cells in the blood—even before a person feels sick. This test could help doctors find cancer earlier and choose the best treatment. He founded a biotech company, called Adela, to make this test available to patients worldwide. His discoveries are already helping other scientists and doctors around the world, and he has won many awards for his work. His goal is to make cancer easier to find, treat, and cure.
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HUMAN HEALTH
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KIDS AND RESEARCHERS TEAM UP TO TACKLE PAIN

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YOUNG REVIEWERS:

MANUEL
AGE: 11

PHILIPP
AGE: 11

Pain usually goes away after an injury, but for some children and teens, it lasts much longer. This kind of ongoing pain, called chronic pain, can make everyday life difficult. For many years, doctors did not have good ways to recognize or treat chronic pain in young people. Dr. Jennifer Stinson has worked to change that by listening carefully to what young people say about their pain and partnering with them to design better tools and treatments. She helped create tools like *PainSCAN*, *Teens Taking Charge*, and *iCanCope*, to make it easier for kids and teens to get the care they need. Her work has also helped train healthcare providers across Canada and beyond. Today, young people with chronic pain are not just patients—they are shaping the future of healthcare, thanks to leaders like Dr. Stinson who recognized that their voices matter.

Dr. Jennifer Stinson was awarded the 2025 Peter Gilgan Canada Gairdner Momentum Award "For international leadership in digital

therapeutics and training initiatives focused on childhood illness-related pain assessment and self-management for conditions such as juvenile idiopathic arthritis, sickle cell disease, chronic pain and cancer."

WHEN PAIN DOES NOT GO AWAY

Can you remember a time when some part of your body hurt? Maybe you scraped your knee, bumped your elbow, or had a bad headache or toothache. Usually, these types of pain go away in a few hours or days. For some kids, though, pain does not just disappear—it sticks around for weeks, months, or even years. This kind of ongoing pain is called **chronic pain**, and it can make everyday life hard for kids and their families.

CHRONIC PAIN

Pain that lasts for weeks, months, or longer. It can keep going even after an injury heals, and it can make everyday life very hard.

Chronic pain in kids can have many causes. Some kids have medical conditions that cause ongoing pain by affecting their joints, blood, or other body parts over time. Others might have pain after an injury or surgery that does not heal the way it should. And sometimes, the pain does not seem to have a clear cause at all. Whatever the underlying cause, chronic pain has a huge impact on kids' lives.

Kids with chronic pain often miss school, have trouble sleeping, or stop doing the things they love, like playing sports or hanging out with friends. For a long time, doctors and nurses did not have good ways to understand or treat chronic pain in children. That meant children's pain was sometimes ignored or misunderstood—not because people did not care, but because they did not have the right tools to measure and manage it. When I became a nurse, I quickly saw that children's pain was often not recognized or treated properly. There was a big gap between what I had learned in school and what was happening in real hospitals and clinics. That experience made me realize that better tools—and better research—were urgently needed to help kids with pain.

LISTENING TO KIDS—AND LETTING THEM LEAD

Doctors, nurses, and researchers often use special tools to measure pain, including number scales ("How much does it hurt from 0 to 10?"), checklists of symptoms, or diagrams that let a patient mark where their pain is. These tools help healthcare providers understand what a patient is feeling, especially when we cannot see the cause of the pain from the outside, like we can with a cut or a bruise. For a long time, most of these tools were made for adults, not kids. They were not always the right fit for children or teenagers, who might describe their pain differently, experience it in different ways, or need unique kinds of support.

When I first started working with children and teens who live with chronic pain, I did not just want to study them—I wanted to work *with* them to understand their experiences and create better ways to support them. I asked young people to tell me, in their own words, what their pain felt like, what made it harder to deal with, and what helped.

Kids and teens had all kinds of insights I had not seen in the research before. Some told me they wanted to track their symptoms using an app, not on paper forms. Others said that the way pain questions were worded did not match what they were feeling. I realized that if we wanted better tools, we had to build them together—not *for* kids, but *with* them. Over the past 20 years, I have built strong, trusting partnerships with young people and families across Canada to help guide this work. Their voices are at the center of everything I do. I try to follow the principle: "nothing for us, without us", meaning that youth and families are involved at every stage—from designing research studies to testing and improving new tools. Listening to them has taught me more than any textbook ever could.

NEUROPATHIC PAIN

Pain caused by damage or problems in the nerves, often described as burning, tingling, or shooting sensations that can happen after injury, surgery, infection, or medical treatments.

COMPLEX REGIONAL PAIN SYNDROME

A condition where the nervous system becomes overly sensitive after an injury, causing lasting pain, swelling, and changes in skin color, temperature, or touch sensitivity.

DIAGNOSIS

The process of figuring out what health problem a person has by looking at their symptoms, asking questions, and sometimes using tests like blood work, scans, or exams.

SCREENING TOOL

Simple tests or questionnaires that help doctors and nurses quickly find signs of a health problem, even before a full diagnosis is made.

BUILDING BETTER WAYS TO RECOGNIZE KIDS' PAIN

As I worked with families and healthcare providers, I started to notice that some kinds of pain in children and teens were especially difficult to recognize. Pain caused by damage or problems in the nerves, which is called **neuropathic pain**, can happen after surgery, injury, certain infections, or medical treatments like chemotherapy for cancer. Neuropathic pain might feel like burning, tingling, or electric shocks. Another condition, called **complex regional pain syndrome**, sometimes shows up after a minor injury like a sprain or broken bone. For reasons we do not fully understand, the nervous system becomes overly sensitive, and the pain does not go away—it actually gets worse. The affected area might swell, change color or temperature, or become very painful to the touch. These conditions do not always show up clearly on tests or scans, and the symptoms can vary a lot, making it difficult for kids to get an accurate **diagnosis** and the right kind of care.

To help with this, a physical therapist and PhD student in my lab worked with my team to create a **screening tool** called *Pediatric PainSCAN*. This is a questionnaire that asks children and teens about the quality, location, and patterns of their pain, in words that make sense to them [1]. We worked closely with young people to test and improve this questionnaire. Their feedback helped us choose the right questions, get the wording right, and make sure it felt easy to use and matched what kids were feeling. The result is a tool that gives kids a stronger voice in the process—and helps doctors and nurses catch pain problems early and start treatment sooner, which can make a big

difference (to learn more about *Pediatric PainSCAN* and the other tools described in this article, see my lab website).

HELPING TEENS TAKE CHARGE OF THEIR HEALTH

One thing I have learned over the years is that teens want to be involved in their own care—they just need the right tools and support. That is what led to *Teens Taking Charge*, a program I helped create for adolescents living with **juvenile idiopathic arthritis** (JIA) [2]. "Juvenile" means that it starts in children and teens, "idiopathic" means doctors do not know exactly what causes it, and arthritis is a disease that causes joint pain, stiffness, and fatigue. JIA can make everyday life more complicated, especially during a time when teens are trying to gain more independence.

JUVENILE IDIOPATHIC ARTHRITIS

A long-term illness in children that causes pain, swelling, and stiffness in the joints. "Idiopathic" means doctors do not know exactly what causes it.

Teens Taking Charge is a freely available web-based program that helps young people learn how to manage their symptoms, cope with stress, and stay involved in health decisions. It includes interactive lessons, quizzes, and videos. We also created a version for caregivers, so parents and guardians could support their teens without taking over. In a large national study, teens who used the program reported less pain and a better quality of life, and those improvements lasted up to a year later [2].

However, not every project went the way we hoped. A few years ago, we developed a gamified app to help kids with arthritis manage their pain. But just before we were ready to launch it, the company we were working with had to shut down. It was a tough disappointment—but it taught me an important lesson. Even when things do not work out, you can find new paths forward. After that, I built a stronger partnership with a hospital-based digital health team, and together we continue to create even better tools to support young people living with pain. Most importantly, this partnership makes sure that these tools will be supported far into the future.

We have also adapted our digital approach to other conditions, like **sickle cell disease**—a blood disorder people are born with that can cause sudden episodes of severe pain, along with long-term health complications. That program is called *iCanCope with Sickle Cell Disease* (Figure 1) [3]. For both *iCanCope* and *Teens Taking Charge*, the idea is the same: give teens easy-to-understand information, help them track their symptoms, teach them skills for managing stress and pain, and make space for them to set goals that matter to them.

SICKLE CELL DISEASE

An inherited blood disorder where red blood cells are shaped like sickles instead of round, causing pain crises, anemia, and other serious health problems.

CHANGING THE WAY WE CARE FOR KIDS IN PAIN

Creating new tools for kids and teens is one part of the work—but making sure those tools get used in real clinics, by real healthcare

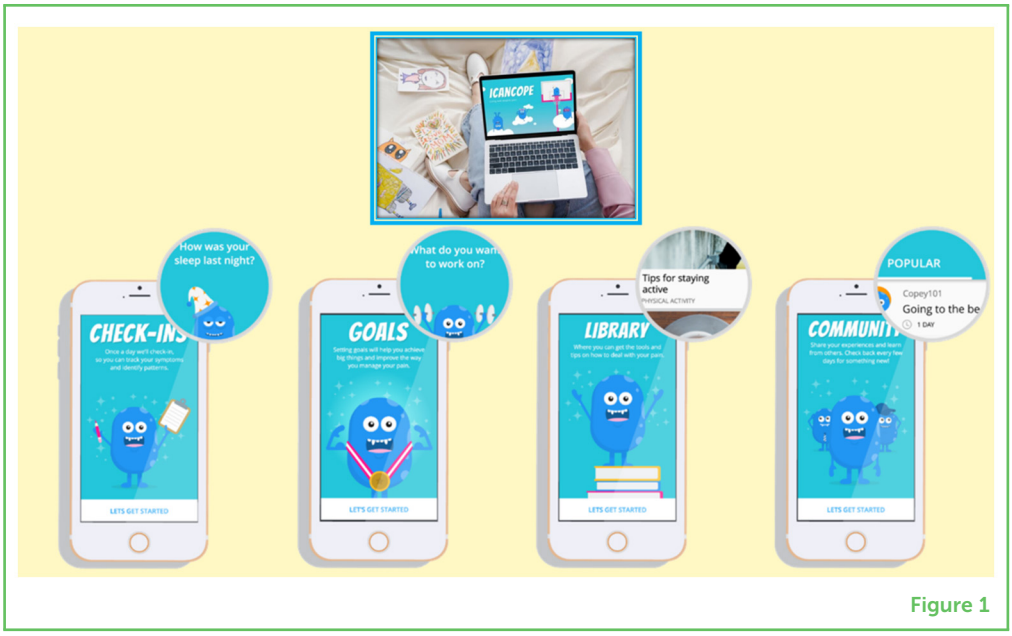

Figure 1

iCanCope with Pain is a digital pain education and self-management platform for kids living with painful conditions including sickle cell disease, chronic pain, arthritis, neurofibromatosis, and post-operative pain. It was built in collaboration with pain management experts from around the world and in partnership with young people living with pain. It allows users to track their symptoms, set goals, learn pain management skills, and get community support.

providers, is just as important. That is why I have also focused on changing the way we train doctors, nurses, therapists, and other professionals who care for children in pain. Many of them received only minimal training in how to assess or manage chronic pain in young people, especially the more complex cases. I wanted to help fill that gap in knowledge and improve their confidence to manage chronic pain in kids.

One way I have done this is through a program called *Pediatric Project ECHO for Pain* [4]. It is a virtual education series that connects doctors, nurses, therapists, and other community medical professionals so they can learn together, share knowledge, and get support as they apply new skills. We cover topics like how to assess pain in kids, how to use different treatment strategies—including physical, **psychological**, and medication-based approaches—and how to work with families as part of the care team. Thousands of professionals have participated, including providers in rural and remote areas who might not otherwise have access to this kind of training.

PSYCHOLOGICAL

Related to the mind, thoughts, emotions, and behavior. Psychological treatments often focus on how people feel, think, and cope with challenges.

At the SickKids Pain Center, which I co-lead, we have a group of more than 60 youth and families who share ideas and give advice to help improve patient care, education, and research. Many of these young people have gone on to become doctors, nurses, psychologists, or researchers themselves. One young person who especially stands out developed chronic nerve pain after a minor sports injury. She was determined to overcome her pain and make a difference. She volunteered in my lab, mentored other young people through our iPeer2Peer mentoring support program, and later became a research coordinator. Today, she is a PhD student in my lab, working to create new ways to help young people with sickle cell disease feel more understood and supported. Watching young people take their

experiences and turn them into ways to help others has been one of the most rewarding parts of my career.

CURIOSITY, COURAGE, AND COLLABORATION

Over the years, I have worked with so many incredible young people who live with pain. They have taught me just as much as I have tried to teach them. They have helped shape better tools, better research, and better care (Figure 2). What is exciting is that these methods work! When teens have access to tools that are made for them—and when they are treated as *partners* in their care—they can learn to manage their health in ways that are both effective and empowering.

Figure 2

To create our tools, we work directly with a team of young people who live with chronic pain, so we can understand their needs and design the tools that will support them as best as possible. After the tools are designed and kids start to use them, the feedback those kids provide helps us to improve the tools, making them even better (figure credit: Somersault18:24).

If you are currently living with chronic pain, I hope this article reminds you that your voice matters. And if you are curious about science, healthcare, or helping others, you can be part of this kind of work, too. Whether you are drawn to technology, nursing, medicine, allied health, psychology, research, or education, there are so many ways to make a difference in the lives of children and teens.

If I could share a few pieces of advice, they would be these: first, *stay curious and passionate*. Some of the best ideas come from asking simple questions and not being afraid to think differently. *Work hard*

and work together—collaboration and communication are just as important as individual effort. And *never stop learning*. Being open to feedback and keeping up with new tools, like the latest advances in technology and AI, will help you tackle challenges in ways we cannot even imagine yet. There are so many important problems waiting for new and fresh ideas. The next great idea could come from someone just like you!

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YOUNG REVIEWERS

MANUEL, AGE: 11
Both of Manuel's parents are academic scientists. Therefore, science is a frequent topic during dinner time. Manuel is a bright, curious young boy, an avid reader of fantasy novels, who enjoys video games as much as fantasy tabletop role-playing games. He loves solving puzzles and riddles, and that is the reason why he fell in love with science; it allows him to logically explain the life around him.

PHILIPP, AGE: 11
I am getting ready to start 7th grade in a new city. My dad is a doctor, so I learn a lot from him. My favorite activities are playing soccer (goalie) and chess. I won a chess tournament at my Scouts summer camp this year. It was fun. My grandmother lives in Germany. We also travel to Canada to see family.

AUTHORS

JENNIFER STINSON
Dr. Jennifer Stinson is a nurse practitioner and scientist at The Hospital for Sick Children in Toronto, Canada, where she helps children and teens who live with pain. She works with a special team of doctors, nurses, and therapists to find better ways to understand and treat pain that lasts a long time. Dr. Stinson also designs new

digital tools—like apps, online programs, virtual reality, and even robots—to help kids manage their pain and feel more in control of their health. She listens closely to what young people say about their pain and uses their ideas to make better treatments. Dr. Stinson also teaches other health-care workers how to support children in pain, including those who live in places far from big hospitals. Her goal is to make sure every child and teen gets the care and support they need, no matter where they live.
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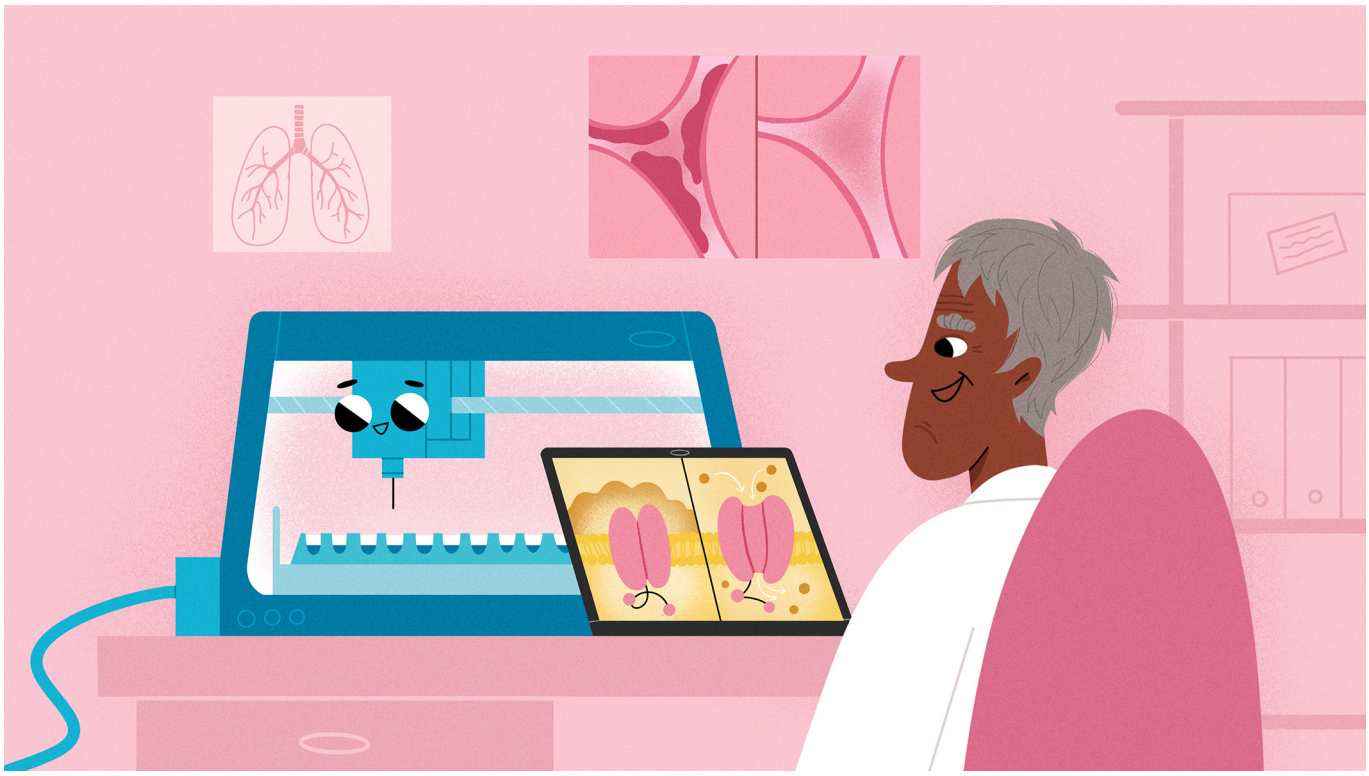

SOLVING CYSTIC FIBROSIS: FROM LAB BENCH TO BEDSIDE

Michael J. Welsh [1*] ***and Paul Negulescu*** [2]

[1] *Department of Internal Medicine and Molecular Physiology and Biophysics, Pappajohn Biomedical Institute, Roy J. and Lucille A. Carver College of Medicine, University of Iowa, Iowa City, IA, United States*

[2] *Vertex Pharmaceuticals, Boston, MA, United States*

YOUNG REVIEWERS:

ADNA
AGE: 12

RISHAB
AGE: 15

Cystic fibrosis (CF) is a serious genetic disease that causes thick, sticky mucus to build up in the lungs and digestive system. For many years, treatments could only manage the symptoms. That began to change with the discovery that CF is caused by problems with a protein called CFTR, which normally helps keep mucus thin and slippery. When CFTR is missing or does not work properly, mucus becomes too thick, leading to serious health problems. After scientists discovered how CFTR works and what goes wrong in CF, another team began developing medicines that help the faulty protein fold correctly, reach the cell surface, and open to let chloride pass through. Today, powerful triple therapies that combine these drugs work for about 90% of people with CF. This work has changed what it means to live with the disease—and has shown how understanding the root of a problem can lead to real solutions.

Drs. Welsh and Negulescu were awarded the 2025 Gairdner International Award "For pioneering research into the cellular and molecular mechanisms underlying the genetic disease cystic fibrosis, leading to the development of transformative drug therapies based on these mechanisms, thereby improving and saving countless lives".

WHAT IS CYSTIC FIBROSIS?

Your body makes mucus every day. Sometimes this is obvious—like when you have a runny nose or a wet cough. But even when you feel fine, mucus is constantly produced in places like your lungs, nose, and digestive system. This thin, slippery mucus does some important jobs: it keeps your airways moist, traps dust and germs, and helps move food through the intestines. However, in people with a condition called **cystic fibrosis** (CF), the mucus becomes thick and sticky. Instead of flowing smoothly, it clogs the lungs and digestive system, making it harder to breathe, harder to digest food, and easier for infections to grow.

CYSTIC FIBROSIS

A genetic disease that causes thick, sticky mucus to build up in the lungs and digestive system, making it harder to breathe, digest food, and fight infections.

CF is a genetic disease, which means people are born with a harmful change in one of their genes. It affects more than 100,000 people worldwide, including over 40,000 in North America. Most people with CF are diagnosed as babies or young children. For many years, doctors could only treat the symptoms of CF: clearing mucus from the lungs, helping with digestion, and treating infections. These treatments helped, but they did not stop the disease from getting worse. Not long ago, many people with CF did not live past their teens or twenties.

My name is Michael Welsh, and I first became interested in cystic fibrosis during medical school. I still remember one of the first young patients I met—a girl around 7 or 8 years old. Even before I opened the exam room door, I could hear her coughing. When I walked in, I saw how hard she had to work just to breathe. I smelled a grape-like smell and later learned that it was due to her lung infection with bacteria called *Pseudomonas aeruginosa*. Talking with her and her parents, I saw how much the disease had taken from her. That moment never left me, and it made me want to understand what was really going wrong in the bodies of people with CF. What exactly was broken—and could it be fixed?

A CLUE HIDDEN IN THE CELLS

Back in 1989, scientists discovered the gene that causes CF. They named it cystic fibrosis transmembrane conductance regulator (CFTR). When the gene was first found, no one knew what the CFTR

protein actually did inside the body, or how a broken version of it could cause such serious symptoms.

My team and I wanted to understand CFTR's job. We discovered that CFTR is a type of protein called an **ion channel**—a tiny tunnel that sits in the membrane that covers the surface of cells where it helps chloride, a type of salt, flow in and out across the cell membrane (Figure 1A) [1]. Where chloride moves, water follows, so chloride movement helps control how much water stays in the thin layer of mucus that coats and protects the lungs and digestive system. When CFTR is working, chloride flows out of cells, and so does water. The water keeps the mucus thin and slippery, so it can do its job. If CFTR is missing or does not work properly—often because of harmful changes called **mutations** in the CFTR gene—chloride cannot flow, and water cannot follow. In people with CF, lack of water makes the mucus thick and sticky.

ION CHANNEL

A tunnel-like protein in the cell membrane that lets charged particles (like chloride and other salts) move in or out of the cell, helping control fluid balance, nerve signals, and more.

MUTATION

A change in a gene's DNA sequence. Some mutations can cause diseases by making a protein that does not work properly or not making the protein at all.

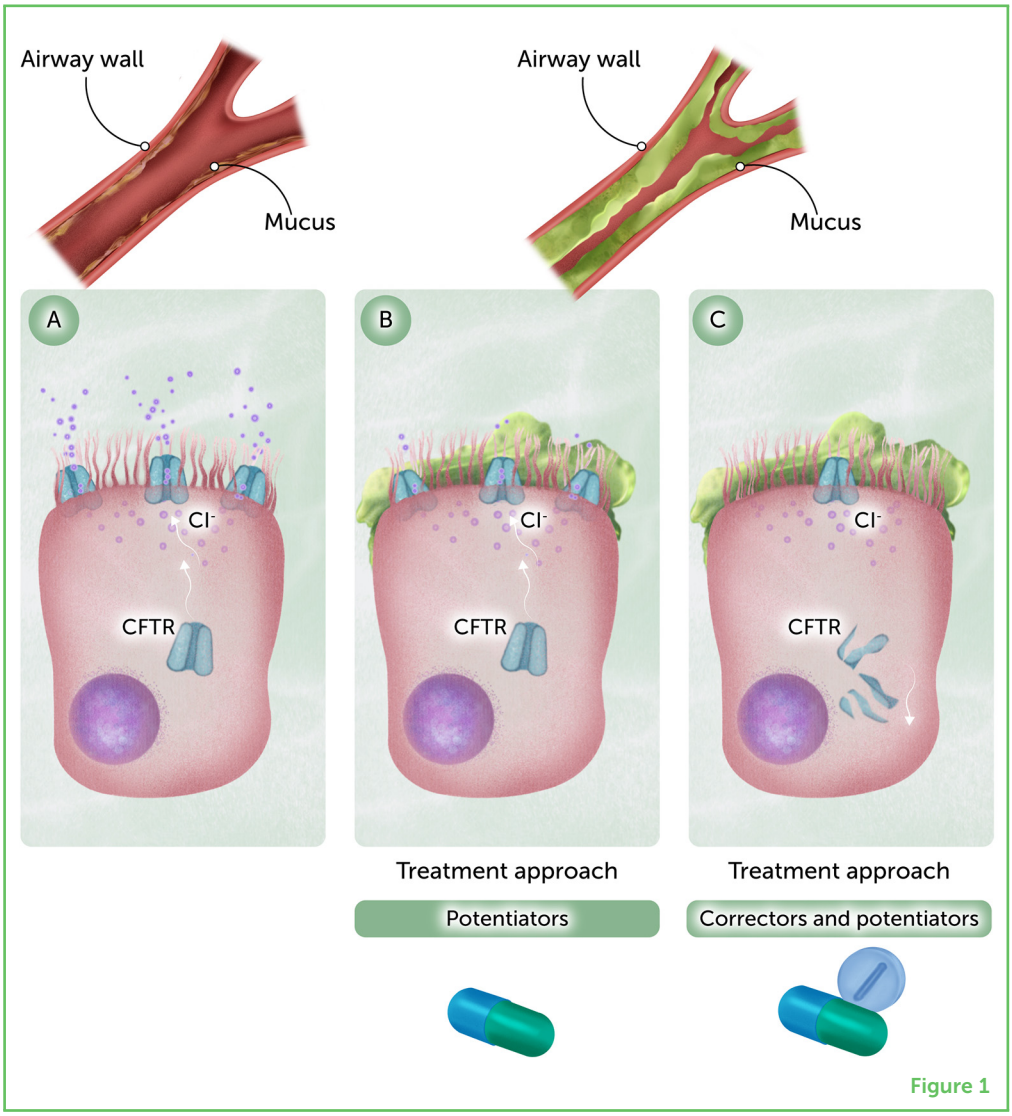

Figure 1

(A) Normal CFTR allows chloride to flow across the cell membrane, keeping mucus thin and slippery. **(B)** With gating mutations, CFTR is present on the cell surface, but it does not let chloride through properly. Drugs called potentiators can improve CFTR function. **(C)** In the most common mutation, ΔF508, a reduced amount of CFTR is found on the cell surface because it does not fold properly and is broken down inside the cell. The CFTR that makes it to the surface does not function properly. A combination of potentiators and correctors (which help CFTR reach the cell surface) can treat this condition (Figure credit: Somersault18:24).

Figuring this out was not easy and it took years. We had to use whatever tools we could find, even ones invented for completely different purposes. One method we used to study chloride flow came from frog skin research. Other techniques were originally developed for studying nerve cells or viruses. We adapted all of them to study CFTR. That kind of flexibility—using the best tools available, no matter where they came from—made a big difference. Understanding how CFTR worked gave us a solid starting point. For the first time, we could begin to look for ways to fix the root of the problem.

WHAT MAKES THE CHANNEL WORK?

After we discovered that CFTR is a chloride channel, we wanted to understand how the tunnel opens and closes. What tells it when to let chloride flow through? We found that CFTR needs a kind of chemical tag called a phosphate group to get ready to open. Only when that tag is in place can the protein respond to signals that tell it to open.

While phosphate tagging gives a CFTR channel "permission" to open, another molecule called **ATP** provides the switch that causes CFTR to open and close. When ATP binds to CFTR the channel changes its shape, allowing chloride to flow through. Understanding what CFTR needs to function gave us another important clue. It helped explain how certain mutations might cause trouble—and pointed to new ways scientists might be able to help the protein work better.

ATP

A molecule that stores and provides energy for many processes inside cells—kind of like a battery that controls cellular machines, including some proteins like CFTR.

NOT ALL MUTATIONS ARE THE SAME

Our discoveries up to this point helped explain what CFTR does and how it works. But how do mutations disrupt its normal function? The answer turned out to be complicated. Scientists found not just one or two mutations in the CFTR genes of people with CF—there are hundreds. Our lab and others discovered that there are several ways mutations can affect the CFTR protein and prevent it from working properly [2].

In some cases, the CFTR channel does not open when it should, or it might not stay open long enough to let enough chloride flow through (Figure 1B). Some mutations prevent CFTR from folding into its normal shape. As a result, after it is made, the cell's quality-control system recognizes CFTR as defective and breaks it down, so it never reaches the cell surface.

One mutation, called ΔF508, is the most common. It causes problems in two ways: it affects how the protein folds *and* how the channel opens (Figure 1C). At first, many people thought this kind of damage would be too hard to fix. But we found early clues that the protein might still work if given the right support. That gave us hope.

As we studied more mutations, we began to sort them into categories based on how they interfered with CFTR. This helped scientists understand that no single treatment would work for everyone. But it also gave us something hopeful: the idea that we might be able to help more people by matching treatments to the specific problems caused by their mutations.

FIXING THE PROTEIN—A NEW KIND OF MEDICINE

My name is Paul Negulescu, and I led a team at Vertex Pharmaceuticals that set out to take what Michael and others had learned about CFTR and turn it into medicines. Our goal was not just to treat the symptoms of CF, but to help the faulty protein itself work better.

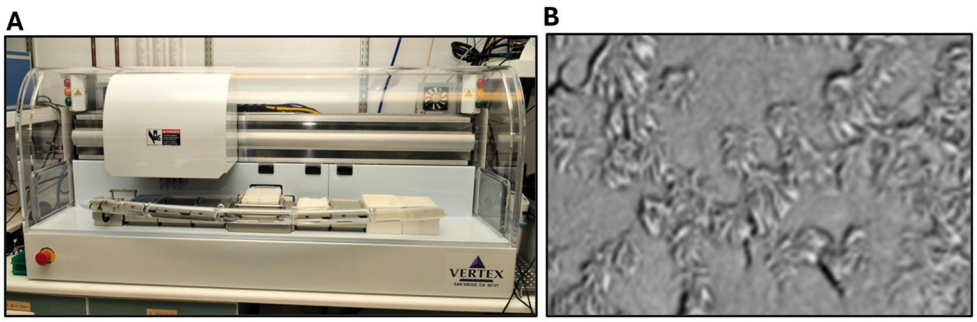

Figure 2

Figure 2

(A) The robotic platform that we used to test thousands of compounds in human airway cells, to see if they could improve the way faulty CFTR proteins worked. **(B)** A microscope view of human airway cells used to test the activity of potentiators and correctors. We tested the compounds on human cells since CF is a human disease. The hair-like structures on the outside of the cells are cilia, which act like little brushes to clear mucus and debris from the lungs.

POTENTIATORS

Medicines that help a protein channel open more easily or stay open longer, allowing it to work better. Used to treat some forms of cystic fibrosis.

GATING MUTATION

A type of mutation that affects how a protein channel opens and closes. In cystic fibrosis, gating mutations can keep CFTR from opening properly to let chloride through.

We started by searching for small drug-like compounds that could help fix the ΔF508-CFTR protein. To do that, we developed specialized lab tests that could measure how well CFTR was working in cells [3]. Then we tested hundreds of thousands of compounds, one by one, using robotic systems. Most did not show improvements, but a few did. Over time, we made better versions of the ones that seemed to help, and we tested thousands of the best ones in human CF airway cells in the lab (Figure 2) [4]. At the time, most research groups tested the effectiveness of new drugs in animals like mice. But we believed that testing compounds on human cells would give us a better chance to select compounds that would work well in people. Michael's team showed us how they grew the airway cells and measured CFTR in those cells, and then we built a system to test compounds.

Over time, we identified two types of compounds that made CFTR work better. The first type we called **potentiators**. These compounds helped the CFTR protein open more easily. After several years of work, we developed one potentiator, called Ivacaftor, that worked well. By itself, it improved the function of CFTR with specific **gating mutations**—mutations that affect how CFTR opens and closes. Ivacaftor was the first drug to treat the underlying *cause* of cystic

CORRECTORS

Medicines that help a faulty protein fold the right way so it can reach the surface of the cell and do its job—used to treat cystic fibrosis.

fibrosis, not just the symptoms. Finding **correctors**, which help correct CFTR processing and allow it to reach the cell surface, took almost a decade longer! But eventually we were able to develop both potentiators and correctors—each solving a different part of the problem.

A TRIPLE THERAPY THAT CHANGED EVERYTHING

Ivacaftor was a big step forward, but it only worked for a small group of people with certain gating mutations. Most people with CF, including those with the most common ΔF508 mutation, still needed a corrector. That is because ΔF508 causes two kinds of trouble: the CFTR protein folds incorrectly *and* does not open properly, even if it gets to the cell surface.

To solve that, we worked on combining drugs [4]. Eventually, we developed a three-drug combination that contained two correctors (to help CFTR reach the cell surface) and one potentiator (to help it work once it got there). This triple therapy is now known as Trikafta, and it works for about 90% of people with CF! In studies with CF patients, Trikafta improved lung function, reduced hospital visits, and helped people gain weight and feel stronger. A new triple therapy, called Alyftrek, works similarly and may further improve CFTR function.

Seeing how much better people felt on Trikafta was incredibly rewarding. For many patients, it changed CF from a life-shortening disease into a condition they can manage—something they live with, not die from. But the work of both my team and Michael's was also a reminder of how much science had to happen first, and how long it took. Our work to discover and develop the medicines was based on efforts by a much larger "team": the doctors who first noticed patterns in patients decades ago, researchers who spent years studying chloride and cell biology, and people with cystic fibrosis who volunteered for studies. I am also very grateful for the inspiration and support of the Cystic Fibrosis Foundation to begin this project. Everyone played a part in making these breakthroughs possible. It was a true bench-to-bedside effort—from basic science in the lab to medical treatments that changed people's lives.

CHANGING WHAT IS POSSIBLE

Because of our work, many people with CF are now living longer, healthier lives. Treatments that target the root cause of the disease have changed what is possible—for patients, families, and doctors. But the impact goes even further. Our discoveries helped show that it *is* possible to repair a faulty protein, even when the problem appears complicated. That idea is now inspiring new research into other diseases caused by gene mutations.

This journey also reminded us that scientific progress takes time, teamwork, and determination. It means using every tool you can, learning from setbacks, and believing that even the hardest problems might have a solution. And it means listening to the people you are trying to help. One patient once told me she joined a research study even though it would not help her, because it might help someone else. This made me feel like failure was not an option—not when people were counting on us. Stories like this help us remember that our work is not finished, because about 10% of people with CF still do not respond to the current therapies.

To anyone interested in science or medicine, our advice is simple: be curious. Ask questions. Try new things. Do not worry about what others expect—focus on what matters to you. If you throw yourself into something fully, you will figure out whether it is the right path. And when you work as part of a team, remember that your effort can help someone else do their best work, too. That is what makes breakthroughs possible.

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AI TOOL STATEMENT

The author(s) declare that no Gen AI was used in the creation of this manuscript.

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YOUNG REVIEWERS

ADNA, AGE: 12
I am an aspiring doctor and my favorite subjects in school are design and science. My dream places to visit are Spain, Egypt, the Bahamas and South Africa. I love to listen to music, hang out with my friends and watch movies. I also dabble in a bit of Chinese painting, piano, ice skating and basketball.

RISHAB, AGE: 15
Rishab is a 15-year-old rising 10th-grader and STEM enthusiast. He is into robotics, car mechanics, and automobile engineering, always asking how things work—from gears and circuits to the mechanisms behind medicines. As a young reviewer, he has edited school research papers, STEM-club newsletters, and draft articles, sharpening clarity, logic, and accuracy. He enjoys turning complex ideas into friendly, precise writing—armed with curiosity, a pencil, and an unreasonable number of sticky notes.

AUTHORS

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Dr. Michael Welsh is a physician and scientist who has spent many years trying to understand and treat lung diseases, especially cystic fibrosis. He worked as a lung doctor and took care of people with cystic fibrosis in the hospital and clinic. Seeing how hard life could be for patients—and how few treatments were available—inspired him to look for the root causes of the disease hoping to find better ways to help. Dr. Welsh leads a research center at the University of Iowa, where he and his team study how lungs work and what goes wrong in diseases like cystic fibrosis. His discoveries helped other scientists create new medicines that treat the disease more effectively. He has taught many young doctors and scientists, and his work has been recognized with some of the highest science and medicine awards in the world. His goal has always been to help people with serious lung problems live longer, healthier lives. *susan.debad@frontiersin.org

PAUL NEGULESCU

Dr. Paul Negulescu is a scientist who helped create some of the first medicines that treat the root cause of cystic fibrosis, a serious disease that affects the lungs and other parts of the body. He started studying how cells work at the University of California, Berkeley. When he began working at a company called Aurora Biosciences, he focused on finding new ways to discover drugs for diseases like cystic fibrosis and pain. Later, when Aurora became part of a company called Vertex, Dr. Negulescu continued to lead the research team in San Diego. Under his leadership, the team discovered several medicines that help fix the broken protein in people with cystic fibrosis. Thanks to their work, many people with this disease now have better treatments that help them breathe more easily and live longer, healthier lives. His team's discoveries have won major science awards and changed the lives of thousands of patients around the world.

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