



PULMONARY HYPERTENSION
ASSOCIATION OF CANADA
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L'ASSOCIATION D'HYPERTENSION
PULMONAIRE DU CANADA

CONNECTIONS

The Official Magazine of the Canadian PH Community



Special Feature:

15 Years of Inspiration

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**PULMONARY HYPERTENSION
ASSOCIATION OF CANADA**
L'ASSOCIATION D'HYPERTENSION
PULMONAIRE DU CANADA

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Message from the Chair & Executive Director

15 Years of Inspiration: A Movement on the Rise



Nicole Dempsey



Jamie Myrab

Dear PHriends,

It usually begins with a small group of people—facing some common struggle—who aren't content to wait for the world around them to change. Instead, they commit themselves to creating their own solutions and finding ways to get what they need. When they find themselves alone and needing support, they seek out others who are also alone and build community. When they have questions and need credible information, they convene experts and create resources to share the answers with everyone. When they need decision-makers to think about their needs, they stand together and ensure that their voices are heard. These inspired—sometimes impatient—but always impassioned people, are the makers of movements.

15 years ago, a small group of pulmonary hypertension patients, care-givers, and medical professionals came together over their collective vision of a better life for Canadians affected by PH. They wanted to fill the gap in support and information, raise awareness, get patients diagnosed sooner, and make sure treatments were available to everyone. And—inspired by the earlier fundraising efforts of their co-Founder, Leon Paroian—they wanted to contribute to excellence in PH research right here in Canada. And so, the Pulmonary Hypertension Association of Canada was born.

A small office was opened in Vancouver, BC, home to the first Board Chair, Darren Bell, and PHA Canada's first part time employee, National Manager, Angie Knott. A website was launched, the first national conference was held in Montreal, and Committees were formed to help develop resources and awareness campaigns. Founding Director, Dr. Sanjay Mehta in London, Ontario acted as the first Chair of the Medical Advisory Committee. Ottawa's PH Nurse, Carolyn Doyle-Cox became the Founding Chair of the Canadian PH Professionals. And in Toronto, pediatric PH specialists, Dr. Ian Adata and Nurse Practitioner, Janette Reyes, were creating the Pediatrics Committee along with Founding Director, Jennifer Gendron and other parents of children living with PH. Patient leaders such as Founding Director, Lynda Beriault and Rita Hebert in Québec, Founding Director, Sharon Proudfoot and Lynn-Marie Cox in Alberta, and Founding Director, Liz McCall and Jasreet James in BC were providing support to peers in their own clinics and beyond. Throughout the country, the network of support for people affected by PH was growing.

Immediately upon being founded, PHA Canada began advocating on behalf of PH patients and in 2009 had an early success helping to stop a “stepped approach” policy to PAH therapy in Ontario. Advocates, such as former Board member, Ruth Dolan, and PHA Canada’s new Ambassador team, met with their elected representatives and spread awareness of the results of PHA Canada’s first Burden of Illness Report in 2014. In 2015/16, when new PAH therapies became available, PHA Canada led the community in a multiyear campaign to ensure that patients in need would have access to optimal treatment options regardless of where they lived or the type of insurance they had. Today, we see new treatment pathways on the horizon for PAH patients (and others with PH) at a time when public drug plans are actively looking for ways to save money on drug expenditures. The PH community will need to band together once again to ensure that no one is left behind.

Research is also necessary for making sure that no patient gets left behind. The research and development of new therapies has dramatically changed the landscape for pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH), but there is much important work to be done. In 2016, PHA Canada launched a Research Scholarship Program to invest in Canadian PH research and the training of the next generation of PH researchers. We have since funded 15 \$10,000 scholarships, supporting projects in everything from nutrition to epigenetics to the breathing mechanisms of newborns. Last year, we embarked on a new initiative aimed at building the capacity of Canada’s PH research sector, with an emphasis on patient-centred practices based on the values and priorities of PH patients and caregivers.

Patients and their caregivers/families have always been at the centre of PHA Canada’s efforts. Throughout the organization—in our programs, campaigns, and materials, at events, in the media, and through the Ambassador Program—we seek to elevate the voices of those living with PH: the voices of those most able to fully express the hopes, dreams, and needs of people with PH. Over the past eight years, one of the most prolific voices in the PH community has been Nicole Dempsey’s. Nicole was diagnosed with idiopathic PAH in 2013. Forced into early retirement from her career as an elementary school teacher, Nicole became a passionate advocate for equal access to PH treatments. In 2014, she became a PHA Canada Ambassador and in 2017 she was elected to the Board of Directors. In 2020, Nicole made history when she became the first PH patient to Chair PHA Canada’s Board of Directors.

This June, as we gather in Ottawa for PHA Canada’s first national conference since 2015, we will be celebrating many things: the many inspiring achievements of the past 15 years, the return to being together in person—the first time since 2019’s Atlantic Forum in Halifax, Nova Scotia—and our hopes and dreams for the years to come, including what priorities should be included in PHA Canada’s new strategic plan. We will also be celebrating Nicole’s retirement from the Board of Directors. PHA Canada’s Annual General Meeting on June 9 will officially mark the end of Nicole’s time on the Board, as she rotates off to make way for new voices and new perspectives.

Nicole has been a steadfast leader through an extraordinary time, helping to guide the organization through both a pandemic and a time of significant organizational change and growth. She has embodied our values of respect and commitment, always encouraging and recognizing the contributions of those around her, while pushing the organization to achieve new and ambitious goals on behalf of the PH community. During her time as Chair, Nicole has helped the organization achieve reaccreditation by the Imagine Canada Standards Program, been the face of the Board during three years of virtual conferences and events, and championed the transition of the Board of Directors to a governance model of leadership.

When Jamie Myrah became PHA Canada’s first Executive Director in 2016, we had only two other part-time employees, and the Board of Directors—especially the Executive members—were integrally involved in the daily administration of the organization. As our resources have grown, so has our team (right across the country!), freeing our directors to focus on matters other than daily operations—strategic planning and evaluation, stakeholder engagement, financial oversight, and supporting the Executive Director to make decisions that have the greatest impact on people affected by PH. Nicole’s leadership—as an advocate, Ambassador, Director, and Board Chair—is a testament to PHA Canada delivering on its mission to empower the PH community, and a perfect illustration of what can be achieved when we work together to uplift patient voices. Nicole, with the support of her family, her PH specialist, Dr. Mehta, and her peers has been empowered to stand up not only for herself, but for the entire PH community.

We hope that Nicole’s experience inspires you to stand up too. For 15 years, we have succeeded because of the passion and dedication of leaders like Nicole—leaders like Loretta Chu, Roberta Massender, and Joan Paulin—who have been willing to work to make things better not only for themselves or their personal family or friends, but for all the people like them, now and into the future. They are people willing to study and share their own difficult experiences to help imagine and create a better way forward; people willing to do the hard incremental work of building a movement and fighting for changes that can take years to realize; people with an eternal hope that change is coming in their lifetime and the drive to turn that hope into a reality.

Have you been inspired? Are you ready to pay it forward? Are you interested in contributing your time, energy, and lived experience to governing PHA Canada and setting us up for another 15 years of success? The Board of Directors is looking for patients and caregivers committed to a brighter future for all Canadians affected by PH. Without access to direct knowledge of what it’s like to live with PH, the Board of Directors cannot succeed in its duty to serve the best interests of those living with PH. If you’re interested in joining us, we hope you’ll reach out to us at Governance@phacanada.ca.

Sincerely,

Nicole Dempsey

Living with IPAH since 2013
Board Chair, PHA Canada

Jamie Myrah

Executive Director, PHA Canada

MEMO: Inside PHA Canada At a Glance

Welcome to *Connections*' message board. This is your peak into things happening inside PHA Canada, from changes in leadership to new resources, special events, and more.



Retirement

**Janette Reyes, NP,
Retiring member of the Board of Directors**

In September 2022, Nurse Practitioner Janette Reyes retired from the Board of Directors after serving since 2018. Janette graduated with a Bachelor of Science in Nursing and a Master's in Nursing (Acute Care Nurse Practitioner NP Program) at the University of Toronto. In July 2000, she joined the PH clinic at SickKids (The Hospital for Sick Children), where she developed the first pediatric PH Nurse Practitioner role in Canada. In 2007, Janette liaised with the Transition Team at SickKids and developed a PH-specific Transition to Adult Care Workshop and Guidelines. Janette continues volunteering her time and expertise to support the PH community as a part of PHA Canada's Pediatrics Committee and the Canadian PH Professionals Network. Thank you for your dedication, Janette!

Welcome

**Michael Pohanka, CPA, CA,
Member of the Board of Directors**

Michael Pohanka joined the Board of Directors in December 2022. Mike gained experience in lung health through a lengthy career as a Vice President of the Trudell Medical Group of companies, where he was responsible for the operations of Pro Resp Inc. Pro Resp provides respiratory home health care to thousands of Ontario lung disease clients each day, including those with PH. Mike saw first-hand the devastating effects of PH when it claimed the life of a friend with a young family.

Mike is a Certified Professional Accountant and Chartered Accountant. For over 20 years, he was

an Ontario Respiratory Care Society member and a Director of the Ontario Home Respiratory Services Association.

In 2017, he and his wife relocated from Ontario to Kelowna, BC to be closer to children, grandchildren, and Okanagan wineries. Mike retired in 2020 and transitioned to volunteer work as a director for several nonprofit charitable organizations. He hopes to apply his knowledge and experience to assist PHA Canada in developing its next strategic plan and raising funds for PH education and research.



**Pat Kelly,
Manager, Research Capacity Building Project**

Pat has been one of Canada's leading advocates for people with cancer and for advancing person-centred healthcare reform. As well as developing provincial and national networks of self-help groups, Pat wrote and published four editions of the book «What You Need to Know About Breast Cancer», along with manuals for policy advocates and self-help group facilitators. Pat has provided training workshops and presented at conferences in Canada, the U.S., and Europe. She received

the Governor General of Canada's Award for her efforts on behalf of people with cancer. Currently, she is a member of the Integrated People-Centred Health and Social Services technical review committee at the Health Standards Organization (HSO). Pat joined PHA Canada in October 2022 to oversee a multi-year project to enhance the capacity for patient-oriented PH research in Canada. Learn more about the Research Capacity Building Project on page 28.



**Jeremy Durand,
Digital Marketing Specialist**

Originally from France, Jeremy moved to Vancouver in May 2017 with two goals, becoming fluent in English and starting a new career based on a simple approach, making a difference. During the COVID-19 pandemic, Jeremy created his own online business. Focusing on marketing trends and digital tools, he successfully grew his audience and opened a second online store. Social media platforms, marketing strategies, design, and video editing software became his areas of expertise.

Finding meaning in his work has always been a significant factor for him, which is why Jeremy is thrilled to start a new chapter of his life in the position of Digital Marketing Specialist at PHA Canada. Jeremy started in January and is excited to contribute his competence in marketing and design to help his new team achieve our mission to raise awareness of pulmonary hypertension, support Canada’s PH community, and make a difference by educating the public.

**James McCallum,
Knowledge Philanthropist**

James comes to PHA Canada’s Knowledge Philanthropist team with an extensive history of volunteerism. He is now bringing his skills and enthusiasm to PHA Canada to honour the memory of a childhood friend whose life was taken by pulmonary hypertension. James attended university in Montreal, earning his Bachelor’s in Mechanical Engineering. His

time spent in Québec and France allowed him to learn the French language. In addition to his bilingual skills, James brings experience in project management, logistics, and proficiency in office software programs. James will work with the team to support our communications and program activities. He resides in Vancouver, BC.



World PH Day, May 5, 2023

Held annually on May 5, World Pulmonary Hypertension Day raises awareness of PH and celebrates the strength and resilience of the PH community worldwide. It is also an opportunity to highlight new developments in PH research and treatment.

Each year, members of the PH community encourage their local community leaders to recognize World PH Day by lighting up local monuments in purple. Thanks to these efforts, monuments have been illuminated in periwinkle purple on May 5 from coast to coast since 2014.

You can help ensure Canada shines brightly in periwinkle purple by requesting that monuments in your area be illuminated on May 5. The earlier you send your request, the better!

—
To find out more, visit
phacanada.ca/worldphday
—

2023 National PH Community Conference

June 9 - 10, 2023

Ottawa, Ontario

Registration now open!
phacanada.ca/conference



Join us in Ottawa, ON for the 2023 National PH Community Conference! Together, we will celebrate 15 years of inspiring achievements in advocacy, research, community support, and more! From our keynote speakers to interactive workshops and engaging panel discussions, be inspired by your peers in the PH community. Please celebrate with us and see how far we've come in 15 years!



“

The great thing about conference is that wherever you are on your PH journey, conference provides an opportunity for you to get whatever you need from it.

– Brooke Paulin, Living with PAH since 2014, Mississauga, ON

Your Community

We have worked to build and inspire our community through social media and video technology these past few years. We have also learned the value of meeting in person and finding ways to have the best of both. In this section, we bring highlights from November's PH Awareness Month, including media interviews from across Canada, your Life in Purple on social media, and community events held in Vancouver, London, and Ottawa. We are also celebrating the return of in-person fundraising and expressing gratitude for your support.

PH Awareness Month: Life in Purple

This past November, the PH community came together again to raise awareness of pulmonary hypertension and what it means to live a Life in Purple. Thank you to everyone who posted your photos wearing purple and shared your stories on social media, in media interviews, and through PHA Canada’s blog! Local communities also issued proclamations and lit up monuments to show their support for PH awareness.



Former PHA Canada Ambassador Jas James and her family raising PH awareness in Cobble Hill, BC by showing off matching purple t-shirts for PH Awareness Month.



Vanda McLean and her husband Gord celebrating their Life in Purple in Orillia, ON.

CANADIAN CARDIOVASCULAR CONGRESS
CONGRÈS CANADIEN SUR LA SANTÉ CARDIOVASCULAIRE
October 27-30, 2022 | 27-30 Octobre 2022

12 minutes
Room: Canada Hall 1

Session: DIAGNOSIS AND MANAGEMENT OF THE PH PATIENT: PATHWAY TO COLLABORATIVE CARE (227)

SUPPORTING PATIENTS (AND THEIR FAMILIES) WITH PH

Presenter:
Lindsay Forsyth Brochu
PHA Canada

Presenter:
Carolyn Doyle-Cox
UOHI

PHA Canada Ambassador Lindsay Brochu, from Almonte, ON, and Ottawa’s PH Clinical Nurse Coordinator, Carolyn Doyle-Cox, present at the Canadian Cardiovascular Congress in Ottawa.

Denise Rumbolt and her family participate in the 6-Minute Walk for Breath in Happy Valley-Goose Bay, NL in memory of her daughter, Candice Cooper. Candice passed away in 2015, at age 21, after being diagnosed with idiopathic PAH in 2014.



“Today, November 13, Government House is glowing purple in recognition of Pulmonary Hypertension Awareness Month” – Judy M. Foote, Lieutenant Governor of Newfoundland and Labrador (Twitter)

Community Events

A highlight of PH Awareness Month 2022 were the community gatherings held in Vancouver, London, and Ottawa. The events, along with PHA Canada's 10th Annual 6-Minute Walk for Breath (see page 10), brought the country together to raise awareness and celebrate the strength of Canada's PH community. A big thank you to all the event organizers for safely bringing their local communities together to reunite with existing friends and make new ones!



Vancouver's PH community endured frosty temperatures as they gathered at Trout Lake Park to celebrate PH Awareness Month and cheer on the 6-Minute Walk for Breath participants.



With support from the PH Clinic, the Ottawa PH Support Group returned to hosting the PH community in-person at The Ottawa Heart Institute for their 10th 6-Minute Walk for Breath event.



Community members gathered in London, ON to watch the virtual 6-Minute Walk for Breath event before participating in the walk together.

PH in the News

Media interviews are a powerful way to build awareness and reach a large audience. This past November, PH stories were featured on radio, television, and online media outlets in communities across Canada. A big thank you to Allison Wells, Andrew Gregg, Beth Slaunwhite, Brinley Marks, Réjean Dupont, Stéphanie Theoret, Dr. Steeve Provencher, and Dr. Sanjay Mehta for volunteering their time and sharing their Life in Purple. Together you reached over 4.5 million people!

Below are some of the volunteers interviewed. You can find all of the interviews and more at phacanada.ca/lifeinpurple.



Dr. Mehta, CTV News



Brinley Marks, Global News



Andrew Gregg, CTV News



Stephanie Theoret, Le Reflet



Rejean Dupont, Le Soleil



Beth Slaunwhite, CBC Radio



Dr. Provencher, Le Soleil



Allison Wells, Best Health Magazine

Raising Awareness, Giving Hope: 2022's Fundraising Heroes

In the PH world, heroes come in all forms, sometimes operating quietly behind the scenes, volunteering their time and unique talents. With sincere appreciation, we recognize the efforts of a special group of heroes who worked tirelessly in 2022 to raise funds for PHA Canada. Their efforts to plan events, bring people together, and ask others to give have helped fund new research scholarships, raise awareness, and provide support and education to those affected by PH. PHA Canada would not be able to do what we do without their help, and we thank them for their selfless support.

6-Minute Walk for Breath

2022 marked the 10th year of PHA Canada's signature fundraising event: the 6-Minute Walk for Breath. Launched in 2012 and championed for years by Ottawa's PH Support Group, the event went national (and virtual) in 2020 and has become bigger than ever. This year, participants from coast to coast raised over \$43,000, smashing the original goal of raising \$30,000. On November 19, families and friends throughout the country gathered online and in-person to connect, share stories, celebrate, and walk to raise PH awareness. See more photos from the community events in Vancouver, London, and Ottawa on the previous page.

Every donation made to PHA Canada makes a difference. These fundraising champions know how to make the most of every opportunity to show support for the PH community. A very special thank you to this year's top fundraisers!

Top Fundraising Teams



1st Place: Team Ottawa - \$10,085



2nd Place: Mayville Movers - \$9,514



3rd Place: Vancouver PH Clinic - \$6,272

Top Individual Fundraisers



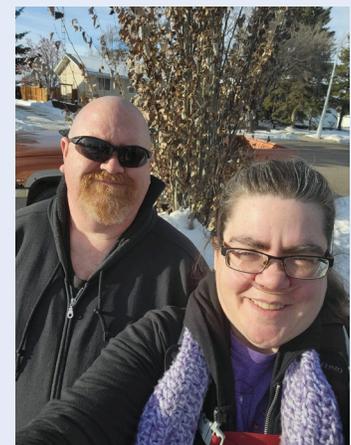
1st Place:
Jessica Marks
- \$4,505



2nd Place:
Donna Downes
- \$4,379



3rd Place:
Michael Pobanka
- \$3,066



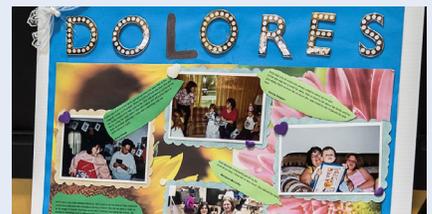
GolPH for PH

On a warm summer day last July, the Paulin Family welcomed guests to their first in-person GolPH for PH event since 2019. Held at Piper's Health Golf Club in Milton, Ontario, participants enjoyed a morning of golf followed by a bar-b-que lunch, raffle, and silent auction. Thank you to the Paulins and all the participants for raising an impressive \$21,500! 50% of the funds raised by GolPH for PH help fund the Paroian Family PH Research Scholarship Fund. Learn more about the 2022 scholarship recipients on page 25.



Dolores' Heavenly Heart

Each year, Corrise Proulx and her family host events in Winnipeg, MB to raise awareness and funds for PHA Canada in memory of their mother, Dolores Rapinchuk, who passed away from PH. Dolores' Heavenly Heart events are family-friendly affairs featuring food, entertainment, laughter, and stories from families impacted by PH. Thank you to all the volunteers at Dolores' Heavenly Heart for another year of great memories.





We are there for you!

The HTAPQ Foundation is there to support you through your illness. We organize events to raise funds to help people in Québec with pulmonary arterial hypertension. A book collection is underway for our big spring event: a book sale under the marquee.

We offer Essentrics exercise classes once a week, and all are welcome to participate and feel a great sense of well-being. Classes are offered on Zoom so that you can enjoy them from the comfort of your home. For more information, contact us at info@htapquebec.ca.

The Foundation also offers periodic meetings so that we can get together to share our personal experiences.

Applications for financial assistance are in progress for 2023. This illness often leads to financial restrictions, which is why the Foundation offers financial assistance to people in Québec with low income. Upon presentation of supporting documents, the Foundation can grant its members aid for certain expenses caused by the illness. To make a request, visit the Foundation's website: htapquebec.ca

Published four times a year, "Virevent d'Isabelle" is a great tool to inform members of our activities and fundraising campaigns. It is also an opportunity to present testimonials from patients or caregivers, conference summaries, and other relevant information. The next issue should be out shortly. The Foundation would like to thank Denis Cormier and Dolores Carrier for their involvement and dedication in writing "Virevent d'Isabelle."

We invite you to consult our Facebook page to keep up to date with the various events and activities offered by the Foundation.

To become a member of the HTAPQ Foundation, visit our website: htapquebec.ca.

We are looking for new dedicated volunteers to join the Board of Directors. We are a warm and welcoming team. You are all welcome, and we look forward to meeting you.



Contributed by: Carine St-Marseille,
Director, HTAPQ Foundation

Special Feature

15 Years of Inspiration

For 15 years, PHA Canada has been empowering the Canadian pulmonary hypertension community through support, education, advocacy, awareness, and research. In this special feature celebrating our 15th anniversary, we will reflect on some of PHA Canada's most inspiring achievements and look forward to the hopes we share for the future. Founding Director, Dr. Sanjay Mehta takes us back to the beginning of PHA Canada's journey to becoming the voice of the PH community, while Joan Paulin shares some of the important ways patient perspectives are shaping the future of PH in Canada.

15 Years of Inspiration: Building a Strong Voice for Canada's PH Community

Sanjay Mehta, MD, FRCPC, FCCP, is a Founding Member of PHA Canada, serving on the Board of Directors since 2008, including as Chair from 2014-19. Dr. Mehta is a Professor of Medicine at the University of Western Ontario and Director of the Southwest Ontario Pulmonary Hypertension Clinic at the London Health Sciences Center in London, Ontario. Dr. Mehta has been caring for patients with PH and doing research in PH since 1989. His current PH activities include the direct clinical care of PH patients, research on new medications and methods to assess PH patients, and the development of the first PH clinical practice guidelines for Canada.



It is my pleasure and indeed an honour to kick off the celebration of the 15th Anniversary of PHA Canada, starting with this Spring 2023 issue of Connections!

Before the founding of PHA Canada in 2008, PH patients and their caregivers already had excellent medical care from a Canadian network of expert PH clinics scattered across the country from Vancouver, BC to St. Johns, NL. Still, there were concerns—not all Canadians affected by PH lived well with PH. At the time, PH patients had variable and typically limited access to only four Health Canada-approved PH-targeted therapies. Moreover, all Canadians affected by PH did not have what they needed: namely, access to a community of other PH patients and caregivers—those who might best understand them because they, too, were dealing with the same illness in themselves or a loved one. Those affected by PH also needed better and ongoing education about their illness and its optimal management, including self-care—what they could do to best look after themselves physically and emotionally. Finally, PH patients and their caregivers needed support through their illness journey, especially in dealing with the resulting physical and emotional tolls of coping with their physical, occupational, and social obligations. As a result, living with PH is often characterized by psychological burdens related to these challenges in fulfilling personal, family, and social roles, as well as the

existential distress of living with a “fatal” illness and eventually having to deal with their mortality, often prematurely.

In 2008, several local and provincial support associations were scattered across Canada, including the BC PH Society out of Victoria, BC, the PH Society of Ontario based in Windsor, ON, the PAH Association of Québec from Plessisville, QC, and the New Brunswick PH Society out of St John, NB. Many special people affected by PH in themselves or their loved ones had recognized the needs outlined above and—amazingly—stepped up to build local support groups for others! These included Liz McCall and Darren Bell from BC, Leon Parioian from Ontario, Linda Beriault from Québec, and Jen Gendron from New Brunswick, some key Founding Board Members of PHA Canada. However, many others affected by PH across Canada did not have easy access to the support and resources of these local organizations. Moreover, increasing challenges in consistent provincial funding of PH-targeted medications and other areas of much-needed advocacy required a national voice to speak on behalf of the Canadian PH community. This was the impetus for the founding of PHA Canada by representatives of all four of the above organizations and two other Founding Board Members, Sharon Proudfoot from Alberta, and me from Ontario.

There is an increasing focus on patient values in medical care, recognizing the patient's critical role in deciding treatment options based on their consideration of potential benefits and risks, especially the effects on their quality of life. This patient perspective is critical to PHA Canada.

PHA Canada's vision has consistently recognized the central value of a better life for all affected by and living with an illness as devastating as PH. A fundamental principle of medicine is that all patients with a specific illness are not homogeneous but very distinct and need to be recognized and cared for as individuals. Patients with any illness follow individual journeys initially guided by their personal and social backgrounds and their families and friends. Landmark events punctuate an individual's PH journey: suffering early symptoms, seeking medical help, eventually being accurately diagnosed, then dealing with initial and often escalating therapies, hoping for improvement in response to treatment, and tolerating worrisome and sometimes scary side effects. Through this entire process, individuals must emotionally deal with their illness and these discrete events, and of course, always reconcile in the back of their minds the idea that "PH is a fatal disease". When patients and their caregivers come for medical attention, they want to be cared for, heard, understood, and respected.

There is an increasing focus on patient values in medical care, recognizing the patient's critical role in deciding treatment options based on their consideration of potential benefits and risks, especially the effects on their quality of life. This patient perspective is critical to PHA Canada. We have always focused on what PH patients and their caregivers have asked for, including assistance with learning about PH and treatment options, being supported in accepting their diagnosis, and facing the challenges of living well with their illness. Specific community surveys, including the 2013 Burden of Illness Survey and the most recent 2021 Community Survey, have captured the perspectives of the Canadian PH community. We also welcome feedback on our goals, programs, activities, and resources. This guidance from PH patients and their caregivers is paramount to all that we do at PHA Canada, which we've captured in our strategic plan and will continue to influence all our programs directly. Indeed, over the past few years, PH patients and their caregivers have pushed PHA Canada to a greater commitment to PH research to improve diagnosis and treatment, further improve their quality of life, and possibly one day find a cure for PH.

As many of you know and face regularly, the Canadian healthcare system is under stress, contributed to by years of underfunding and the lack of a national health vision, and now more severely challenged over the past three years by the global COVID-19 pandemic. Such threats to the excellence and responsiveness of our healthcare system will continue, likely worsen, and will further challenge our ability to care for each patient optimally. At PHA Canada, we are honoured to celebrate 15 years of commitment and success in the critical role and work we took on for ourselves at our founding in 2008. This work will become even more important in the future, as the PH community will require more connection with us and each other, as well as more support around their illness journeys and individual challenges around access to care.

I invite you to celebrate our history and success and to participate with us during the many events happening over the coming months! Moreover, the Board and staff of PHA Canada welcome you to challenge us and to be a part of growing your organization to do more for all Canadians affected by PH. We are honoured to serve all of you and cherish our role as the strong voice of the Canadian PH community.

Contributed by: Sanjay Mehta, MDCM FRCP(C)
Eternal PHriend / Past-Chair / Founding Board Member, PHA Canada
Medical Director, Southwest Ontario Pulmonary Hypertension Clinic,
London Health Sciences Centre
Professor of Medicine, Schulich School of Medicine & Dentistry,
Western University, London, Ontario

15 Years of Achievements

Support

2008

Leaders of Canada's PH community come together to form PHA Canada, a national organization that would unite the thousands of Canadians affected by PH, and help empower and improve their lives through support, education, advocacy, awareness, and research.



2010

Connections Magazine is launched to bring together the Canadian PH community to inform, support, and celebrate one another. Published twice a year, over 800 copies of each special issue are now distributed to households and clinics across the country.

Education

2013

Launch of the Sometimes It's PH campaign aimed at building awareness of the risks and symptoms of PH and reducing the time to an accurate PH diagnosis. In 2016 and 2019, new campaign materials are that create new opportunities for educating health care professionals and patients potentially at risk of developing PH.

2016

PHA Canada shifts from hosting biannual national conferences to holding annual educational events in regions throughout the country, making it easier for patients and their families to attend. 2020 then marks the introduction of online events, including virtual conferences in 2021 and 2022.

Advocacy

2009

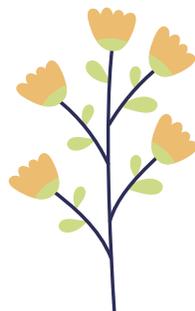
The PH community successfully advocates against the implementation of a 'stepped approach' to PAH therapy in Ontario.



2015

PHA Canada and partners launch the Take Action PAH campaign to advocate for access to all Health Canada-approved PAH therapies through public funding. In the years to come, thousands of advocates are successful in helping to ensure public funding for new PAH therapies throughout the country.

Awareness



2016

Stories of PH patients are featured in a new awareness video and in public service announcements that air across the country on both TV and radio.



Research



2018

PHA Canada hosts its inaugural National PH Medical Think Tank, bringing together PH medical experts and researchers together for two days of research updates, discussion, and collaboration. In 2022, the event is co-presented by the Canadian Thoracic Society and becomes an accredited continuing medical education event for physicians.

2015

PHA Canada's Pediatrics Committee introduces the Back-to-School Package for families of children with PH, adding to the growing list of resources available to provide support and information relevant to a diverse range of PH journeys and experiences.



2020

PHA Canada launches the Monthly Meet-Ups and PH Buddy programs as a response to pandemic lockdowns in order to strengthen peer networks and help reduce isolation.

2020

PHA Canada launches a new website integrating disease and treatment information for patients, caregivers, and health care providers, resources for living with PH, and research and community news.

2021

PHA Canada releases a four-part video series about PH featuring plain language and graphic imagery to help make disease and treatment information more accessible to new audiences.



2020

PHA Canada and its partners at the Respiratory Roundtable, hosted by the Canadian Thoracic Society, call on provincial governments to prioritize patients with lung disease for COVID-19 vaccination.

2021

PHA Canada makes submissions to Health Canada regarding the development of a national Rare Disease Drug Strategy and to the Patented Medicines Pricing Review Board regarding new regulations governing the pricing of patented medicines in Canada.

2019

PHA Canada's Paint Canada Purple lights up 20 monuments across Canada for World PH Day, a record number since the launch of the annual campaign in 2014.

2021

PHA Canada's 6-Minute Walk for Breath event—held annually in Ottawa since 2012 - adapts to become an online event raising awareness and funds in honour of PH Awareness Month. The event expands again in 2022 to include both a virtual event and numerous community events, succeeding in raising an unprecedented \$43,000 in support of the PH community.

2022

Members of the PH community are featured in over a dozen media interviews during PH Awareness Month as part of PHA Canada's annual Life in Purple campaign highlighting the everyday impact of PH on patients and caregivers.

2021

PHA Canada conducts the Canadian PH Community Survey, a follow up to the highly impactful Burden of Illness Survey conducted in 2013. The resulting report – The Impact of Pulmonary Hypertension on Canadians – is released on World PH Day in 2022 and distributed to elected provincial representatives in all 10 provinces.

2022

PHA Canada launches a multi-year initiative aimed at increasing capacity for PH research in Canada. The Research Capacity Building Project will empower patients to be active participants in the entire research process, while also improving coordination and collaboration among PH researchers and increasing access to critical new sources of patient data.

2022

PHA Canada awards its 15th PH Research Scholarship, bringing the total to \$150,000 in scholarships since the first scholarship was awarded in 2016.

Community Quotes

An anniversary is a time to celebrate, reflect on the past, and—importantly—make plans for the future. In 2008 the PH community united, and PHA Canada came into being. Like other PH associations around the world, PHA Canada set a course to work collaboratively with patients, caregivers, families, and medical professionals to create a better life for all those affected by PH. You inspired us each step of the way and showed us what we could accomplish by working together.



Over the past 15 years, the Canadian PH community has benefited from access to new treatments, improved diagnosis and care, and the creation of a hub of support and information for patients and their families. What is your biggest hope for the PH community in the next 15 years?



“My biggest hope, without a doubt, is something resembling a cure. We see hints of this on the horizon—medications currently in trials that don’t just slow progression but could reverse the disease itself. I’d like to see PH patients in Canada thought of in the review process and take success stories from US or international trials as good evidence of a drug working instead of making us wait years for local approval. As an active mother of two, effective oral medication is everything to me. It is the difference between living and just staying alive. Add a medication that offers a potential cure—it’s a dream.”

Robin Latour, Living with PAH since 2017, Hamilton, ON

“I would like to see all patients have easier access to required medications and for PHA Canada to grow, reaching a level where the general public knows exactly what PH is. This will happen with you guys at the helm. You all rock. Thanks for all that the team does.”

Vance Collins, Caregiver since 2003, Paradise, NL



“I hope the PH community will continue to grow, supporting each other and working towards raising awareness and developing new treatments for everyone affected by pulmonary hypertension.”

Isabelle Platnar, Living with PH since 2005, Pickering, ON

“My biggest hope for the PH community over the next 15 years is for increased awareness, compassion, and understanding of what the patients go through daily. Too many people in health care settings do not fully understand what happens to the patient and how this disease affects their quality of life and ability to support their family members.”

Brad Lynch, Living with PAH since 2021, Edmonton, AB



“For me it would be treatment improvement, finding more effective drugs, and stopping this serious illness”

Tania Zhou, Living with PH since 2018, Lachute, Quebec

“In the next 15 years, I would like to see a comprehensive approach to left and right heart failure across Canada. I live in a province that can only deal with the right heart. That leaves me without support. I’m not accepted at the local heart failure clinic. Not being followed will leave me and others with future problems.”

Angela Griffin, Living with PH due to left-sided heart disease since 2021, Dartmouth, NS



“Over the next 15 years, I hope there will be leaps and bounds towards stopping the progression of PH, preferably with oral drugs, thus eliminating intravenous injection. Also, praying for a method of reversing PH progression.”

Jeff Nordlund, Living with PH since 2020, Sherwood Park, AB

“I want to make PH more known. People need more awareness of this disease, as many have never heard of it before! Lots of research has been done, but I’d like more research, better drug options, and possibly a cure. We can all wish just a little.”

Tasha Shuba, Living with PAH since 2018, Regina, SK



“My biggest hope for the PH community in the next 15 years is to have more medication to cure PH illness so they can live the quality of life they deserve. And we are also hoping to have a PH clinic and PH specialist that can provide care anytime. It would be convenient for us parents if we didn’t have to travel to different cities.”

Grace Libuna, Pediatric Caregiver since 2017, Vancouver, BC

15 Years and Counting: Creating Positive Change for the Future

Joan's daughter Brooke was diagnosed with severe PAH in March 2014 at 24. In 2017, Joan became a PHA Canada Ambassador until her election to the Board of Directors in December 2021. As a Director, she strives to use her knowledge to advocate for earlier and more equal access to PH treatments for patients wherever they live in Canada.



In 2018, we celebrated PHA Canada's 10th anniversary and the many achievements that were made possible because of our Founding Members' contributions and the PH community's commitment to unite and create positive change.

Much has changed since 2018, both within our organization and the world around us. Yet, our understanding of the PH community's critical role in achieving our vision has stayed the same. PHA Canada's work continues to be informed and inspired by your needs and expertise. As we celebrate our 15th anniversary, we want to thank you for everything you have contributed so far. You have made a difference with every committee and event you've volunteered for, awareness and advocacy campaign you've shared, survey and form you've completed, act of support and friendship you've provided, and donation you've raised.

In this issue, you will learn about some of the incredible progress we have achieved together in the five years since our 10th anniversary. Here are some of my personal favourite examples of how your voice and lived experience have made a difference:

1. By the end of 2018, Uptravi (selexipag) finally became available through public funding in every province across the country thanks to the efforts of the PH community. Patients and caregivers shared their experiences with provincial decision-makers through PHA Canada's *Take Action PAH* campaign to educate about the importance of the first oral prostacyclin treatment for PAH.
2. In 2020, Nicole Dempsey became the first person living with PH to become Chair of PHA Canada's Board of Directors where she has worked hard on your behalf to ensure the patient perspective is front and centre at Board meetings.
3. PHA Canada was proud to partner with Dr. Jason Weatherald in 2021-22 for the *Canadian Pulmonary Hypertension Priority Setting Partnership*. This innovative research study used a patient-centred approach to identify priorities and questions the community wants answered about pulmonary hypertension. After completing a series of surveys, patients, caregivers, and PH doctors and nurses participated in a two-day workshop to collaboratively identify their 10 most important PH research priorities. Read about the results of this project on page 22.

4. In 2021, over 400 PH patients, caregivers, and healthcare professionals responded to PHA Canada's call and completed the *Canadian PH Community Survey*. The information gathered continues to be analyzed, informing our program planning and strategic decisions, and providing data for future advocacy efforts, including for new drug approvals.
5. After a COVID hiatus, 2021 saw PHA Canada's Ambassador Program rejuvenated. The Ambassador team currently has 10 Ambassadors providing diverse representation of the PH community across the country, including male and female patients/caregivers, parents and youth, patients on oral and infusion-based medications, and those recently diagnosed, living with PH long-term, and post-transplant.
6. Finally, fundraising activities organized by patients and their families and supported by the PH community have funded \$150,000 in PH research scholarships. Learn about our 2022 scholarship recipients on page 25.

Thank you for being part of PHA Canada. We couldn't have done any of this without you. There was—and still is—much work to do but stopping to celebrate what we have achieved allows us to recognize what is possible. With this thought, I want to end by highlighting a new project with incredible possibilities.

PHA Canada recently launched the *Research Capacity Building Project* (learn more on page 28). This exciting project aims to develop education and training initiatives to build patient capacity, establish a Canadian PH Clinical Trials Network, and expand the Canadian PH Registry to include new forms of patient information. These initiatives will require participation and data (including lived experience) from as many patients and caregivers as possible, which means our success depends on you. New therapies that target different pathways are already on their way. Our work together is only beginning. PHA Canada is entering the next phase of our growth full of hope for the future. Can we count you in?

Contributed by: Joan Paulin, Director, PHA Canada Board of Directors

Research Corner

Get ready to feel inspired! In this section, Dr. Jason Weatherald shares the results of the PH Priority Setting Partnership project, where the community helped identify priority areas for future research. You will meet PHA Canada's newest PH research scholarship recipients and get an update from 2021/2022 recipient Yann Grobs about his ongoing research into the role of epigenetic regulation in PAH. Finally, you will hear from Pat Kelly, who will introduce you to PHA Canada's new Research Capacity Building Project.

Research Priorities for Future Pulmonary Hypertension Research: Your Input Leads to Your Impact

Dr. Jason Weatherald is an Assistant Professor at the Department of Medicine, Division Respiriology at Alberta Health Services in Edmonton, Alberta. Dr. Weatherald is also part of the medical team at the University of Alberta Pulmonary Hypertension Program, and led the Pulmonary Hypertension Priority Setting Partnership project.



Although millions of dollars are spent every year on research to develop new ways to diagnose and treat the various causes of PH, progress in medical research is often slow and incremental. More PH research will always be needed, and more funds will be required to conduct it. Because the resources to fund and conduct research are limited, it would be helpful to know which problems are most important to patients. Who better to guide doctors and researchers on where to focus their efforts than those most directly impacted by PH? To understand what questions and problems should be prioritized for future PH research, we decided to ask you!

What is a research Priority Setting Partnership?

There is an established method of setting research priorities. A non-profit organization in the United Kingdom called the James Lind Alliance (JLA) developed an approach to engaging patients, caregivers, and clinicians to determine research priorities. This approach has been applied to over 100 diseases and conditions to date. More information about the JLA is available on their website at www.jla.nihr.ac.uk. With a group of Canadian PH specialists, PH patients, and other experts, we embarked on a PH Priority Setting Partnership project aligned with the JLA guidance. The Canadian PH Priority Setting Partnership was funded by the Canadian Institutes for Health Research and the Libin Cardiovascular Institute at the University of Calgary. Our initial aim was to understand your questions and priorities for future research that the Canadian Pulmonary Hypertension Registry (CPHR) could study. This project's scope quickly expanded, and we decided to do all types of research related to any aspect of PH.

What were the results of the Canadian PH Priority Setting Partnership?

Despite significant challenges related to the COVID-19 pandemic, and thanks to the incredible support of PHA Canada and HTAPQ, we were able to complete the Priority Setting Partnership in 2022. To start, we engaged over 240 individuals across Canada with an online survey. The surveys were distributed by PHA Canada and HTAPQ in both English and French. We asked what questions you had related to the causes and risk factors, diagnosis, treatment and management, and prognosis of PH. We received over 1,800 responses which were grouped into similar ideas. Based on our interpretation, and in consultation with our patient partners, the initial survey responses were rephrased as 187 unique researchable questions that could be addressed by research. We found that good answers already existed for 30 of these questions. So, we next asked the PH community to rank the remaining 157 questions in a second survey. The second survey's top 25 most frequently chosen questions were discussed during a two-day online workshop in February 2022. The workshop included patients, family members and caregivers, and PH specialists from across Canada. At the end of this workshop, we arrived at a top 10 list of questions for future PH research ranked by importance (see Table on page 24).

As you can see, there is a broad range of questions in the Top 10 and Top 25, and the Top 3 questions were unanimous. The number one priority is related to the underlying mechanisms that cause PAH. This is important because the development of new treatments usually depends on a deep understanding of why a disease develops (i.e., the mechanism). The second highest priority question addressed the need for therapies that can reverse PAH. Current treatments stabilize and slow down the disease but do not reverse the abnormal changes in the arteries of the lungs. Therapies that reverse abnormalities in lung arteries may be the next best step to a cure. The third top priority addressed precision medicine. More specifically, precision medicine

The workshop included patients, family members and caregivers, and PH specialists from across Canada. At the end of this workshop, we arrived at a top 10 list of questions for future PH research ranked by importance.

means finding accurate ways of choosing which drug or combinations of drugs will work best for an individual patient. For more details, this priority-setting partnership project has now been published in the *Journal of Heart and Lung Transplantation*, a leading medical journal in the field of PH. The full manuscript is available online at [https://www.jhltonline.org/article/S1053-2498\(22\)02160-X/fulltext](https://www.jhltonline.org/article/S1053-2498(22)02160-X/fulltext). Your Priority Setting Partnership results were also presented to the global PH community at the European Respiratory Society conference in September 2022 to get the word out as broadly as possible.

What does this Priority Setting Partnership mean for future PH research in Canada and worldwide?

Thanks to your input and this Top 10 list, patients and caregivers have an influence on which PH research gets funded in the next few years. Because of the limited dollars available for research, many good ideas and applications do not get funded. For example, only about 15% of health research projects' applications are funded by Canada's main health research funding body, the Canadian Institutes for Health Research. When researchers write grant applications to ask for money to perform their research, they often engage patient partners to provide their perspectives on the importance of the proposed research. Now, researchers can also explain in their grant applications how their research idea directly addresses one or more of the priorities of the entire PH community. These are priorities you helped create and shape. The impact of this is not limited to Canada but can be referred to and cited by researchers all over the world.

Additionally, researchers can still see the long list of 157 unanswered questions you helped create, which may inspire them with new ideas to tackle in their future research. Several pharmaceutical companies are invested in PH, and they may also consider how their research and development align with your priorities. Ultimately, the Canadian PH

Priority Setting Partnership Top 10 list provides a roadmap for future PH research, but off-road travel is always encouraged!

Where do we go from here?

We will periodically evaluate how this list is being used in the coming years. Are projects funded in Canada aligned with these topics? Is the Top 10 list cited by researchers in grants and peer-reviewed research papers? There is also more work to be done as some areas of PH research and types of PH were not addressed in this project. This does not mean such groups are not important or won't be addressed by future research. Rather, other PH groups may require their own dedicated priority-setting partnerships. For example, our team consisted of experts in adult PH, not pediatric PH. We were also concerned that important questions relating to pediatric PH would be diluted by questions from the much larger adult PH community. Therefore, questions about pediatric PH were not included in this project's scope. Given the unique challenges faced by kids with PH and their families, we propose and highly encourage a dedicated priority-setting exercise for future research on pediatric PH.

See next page...

TOP 25 PRIORITIES FOR FUTURE PULMONARY HYPERTENSION RESEARCH

| Rank from Final Workshop | Question |
|--------------------------|--|
| 1 | What are the specific mechanisms that lead to the development of pulmonary arterial hypertension (PAH)? |
| 2 | How can pulmonary hypertension (PH) be reversed or put into remission, and how can we measure disease modification or reversal clinically? |
| 3 | How can we predict which treatment or combination will work best for an individual PH patient (e.g., personalized medicine)? |
| 4 | What are the mechanisms of right heart adaptation to PH and right heart failure? |
| 5 | Which interventions or treatment strategies result in the best outcomes for patients with PH? |
| 6 | What is the role of the immune system and auto-immunity in the development of PAH, and can treatments directed at the immune system help with PAH? |
| 7 | What are the best tools to predict progression of PH and how fast the disease will progress? |
| 8 | What is the most effective and safe amount of exercise training for PH patients? |
| 9 | Are there biomarkers that allow early detection of PH? |
| 10 | Are stem cell therapies effective and safe for treating PH? |
| 11 | What is the underlying cause of idiopathic PAH? |
| 12 | What are the mechanisms by which cardiac function continues to deteriorate despite an improvement in symptoms? |
| 13 | When a PH patient needs surgery, what are the best anesthetic approaches and if general anesthesia is required, which anesthetics are safest? |
| 14 | How can we detect when the disease process (PH) starts, and how long does it take for symptoms to develop after it starts? |
| 15 | What are the long-term consequences and complications in PH patients who are long-term survivors? |
| 16 | How can the delay to diagnosis of PH be reduced? |
| 17 | For how long is PH treatment effective, and will the effect wear off with time? |
| 18 | Is there a relationship between iron deficiency and the development or progression of PAH, and if so, does the treatment of iron deficiency improve outcomes? |
| 19 | Can exercise testing be used to identify early PH and predict the risk of developing PH in the future? |
| 20 | How can the side effects of PH therapies be managed or reduced? |
| 21 | What is the most accurate method to classify the severity or risk of a patient with PH? |
| 22 | Are there any harmful long-term effects of medications used for PH? |
| 23 | How can universal coverage for all PH medications be ensured in Canada? |
| 24 | Can educational interventions targeted at clinicians in training, primary care, and second-line (e.g., specialist) clinicians improve awareness of PH and lead to earlier diagnosis of PH? |
| 25 | How do COVID-19 and COVID-19 vaccinations affect people with PH? |

In conclusion, I extend sincere thanks to all who participated in the project and to all who will use its results.

Contributed by: Dr. Jason Weatherald, MD, MSc, FRCPC
Assistant Professor at the Department of Medicine, Division Respiriology at Alberta Health Services in Edmonton, Alberta.

2022 Research Scholarship Recipients

Research brings hope. It also holds the key to a better understanding of pulmonary hypertension, leading to the development of novel therapies, improved treatments, and more sophisticated tools to care for patients. Research also holds the promise of a healthier and longer life, better management of symptoms, and, ultimately, a cure. PHA Canada is proud to help build capacity within the research community by awarding \$10,000 scholarships to outstanding trainees in support of their research in the field of pulmonary hypertension. We are pleased to introduce PHA Canada's 2022 PH Research Scholarship Recipients Rachel Bentley, Yann Grobs, and Sarah-Eve Lemay.



*Rachel Bentley, Ph.D.
Candidate, Queen's
University, Kingston, ON*

Rachel Bentley

Rachel Bentley is a second year Ph.D. candidate in the Translational Medicine graduate program at Queen's University (Kingston, ON) following her successful promotion from her master's degree in 2021. She obtained a Bachelor of Sciences in Life Sciences at Queen's University in 2019. She is currently studying the oxygen-sensing mechanisms of the ductus arteriosus and pulmonary arteries in a search for novel therapeutic pathways for persistent pulmonary hypertension of the newborn (PPHN).



*Yann Grobs, Ph.D.
Candidate, Laval University,
Québec City, QC*

Yann Grobs

Yann obtained a bachelor's degree in health biology at the University of Montpellier in France in 2011 before specializing in microbiology and immunology during his master's degree at Laval University (QC). During an internship at the Research and Development Institute on the genetic diversity of HIV, he developed a particular interest in translational research, particularly in the physiology of the cardiovascular and respiratory systems. Pulmonary arterial hypertension (PAH) is one of the complications of an HIV infection. In 2020, Yann enthusiastically joined the PAH group of Québec led by Dr. Sébastien Bonnet and Dr. Steeve Provencher. Yann is currently working on his Ph.D. under the supervision of Dr. Bonnet. He received his first PHA Canada research scholarship in 2021.



*Sarah-Eve Lemay, Ph.D.
Candidate, Québec Heart and
Lung Institute, Québec City, QC*

Sarah-Eve Lemay

While completing a bachelor's degree in pharmacology at Sherbrooke University (QC), Sarah-Eve joined Québec's pulmonary hypertension research group for two research internships in the fall of 2019 and summer of 2020. These experiences confirmed her interest in physiology and medical research and motivated her to pursue graduate studies. She enthusiastically began her master's degree in January 2021 in clinical and biomedical Sciences at Laval University (QC) under the supervision of Drs. Bonnet and Boucherat. Since May 2022, she has been pursuing her doctoral studies with the pulmonary hypertension research group, during which she will deepen her knowledge of the molecular mechanisms that lead to pulmonary vascular remodelling and right ventricular failure in pulmonary arterial hypertension (PAH). Her current research work focuses on the implication of hypusine signalling in PAH.

Learn more about their research projects at www.phacanada.ca/researchscholarships.

The Journey from Bench to Bedside: Pre-clinical studies show potential for new PAH therapies

Yann Grobs joined the pulmonary hypertension research group at Laval University (QC) in 2020 and is currently completing his Ph.D. in clinical medicine and biomedical sciences under the supervision of Dr. Sebastian Bonnet. Yann was awarded the Loretta Chu Memorial PH Research Scholarship in 2021 and a Paroian Family PH Research Scholarship in 2022, making him one of only two people to receive two PHA Canada research scholarships. We asked Yann to discuss his 2021 research and explain how his latest project builds upon those results.



Pulmonary arterial hypertension (PAH) is a rare, complex, poorly understood disease affecting the pulmonary arteries, which carry blood from the heart to the lungs for reoxygenation. In PAH, pulmonary circulation pressure increases due to narrowing and, in some cases, complete obliteration of small pulmonary arteries, leading to cardiac dysfunction and premature death. This narrowing is due to abnormal multiplication and growth of the smooth muscle cells (SMC) located in the walls of the pulmonary arteries. These SMC share common characteristics with cancer cells such as hyperproliferation, survival, and inflammation.

It has been proposed that the abnormal behaviour of these cells involves genes regulation, specifically epigenetic regulation. Epigenetic changes are modifications to DNA that regulate whether genes are turned on or off. This includes all reversible, transmissible, and adaptive mechanisms that modify the expression of genes without changing the sequence of DNA building blocks (called nucleotides). Among the various epigenetic mechanisms, several enzymes can modify the DNA structure. These enzymes label the DNA with a tag by adding a chemical group to the nucleotide. According to the tag, the structure of the DNA undergoes modifications. DNA can be lightly packed, allowing gene expression (increasing accessibility) or tightly packed, thus blocking their expression (reducing accessibility).

P300 Protein: A Potential Novel Therapeutic to Treat PAH

In 2021, we studied the role of P300 as a factor in gene expression and its involvement in abnormal cell proliferation in PAH. The P300 protein is an enzyme that labels DNA with a chemical group called acetyl, which makes DNA more accessible (thereby promoting gene expression). Evidence indicates that the P300 protein is a key factor exhibiting pro-oncogenic activity that leads to tumour development in multiple cancers. Indeed, P300 is frequently overexpressed in many types of cancer and stimulates the multiplication and survival of cancer cells. Smooth muscle cells in the walls of the pulmonary arteries share common characteristics with cancer cells. Therefore, we hypothesized that the abnormal expression of genes implicated in cell multiplication and survival of PAH cells is sustained by high levels of the epigenetic regulator P300 protein.

We first compared the level of P300 protein expression in the pulmonary arteries between PAH patients and healthy subjects. We isolated and cultivated both groups' pulmonary artery smooth muscle cells (PASMIC). Compared to healthy subjects, we observed that P300 expression is increased in both the pulmonary arteries and the PASMIC in PAH patients (PAH-PASMIC). To determine the effects of blocking P300 activity on the multiplication and survival of PAH-PASMIC, we treated the cells with the drug CCS1477 for blocking P300 activity. We showed that PAH-PASMIC multiplication and survival is reduced with the drug CCS1477.

This research will provide important knowledge that could lead to new therapeutic strategies.

Animal models are often used in PAH to reproduce human disease. In this study, we used three PAH rat models to develop the obliteration of small pulmonary arteries associated with an increase of pressure in the pulmonary artery and right ventricle and right ventricular dysfunction. We showed that blocking P300 using the drug CCS1477 decreased pressures in the pulmonary artery and the right ventricle, improved cardiac function, and reduced obstruction of the pulmonary arteries.

We then investigated the potential cardioprotective effect of inhibiting the P300 protein. Like for pulmonary arteries, we have demonstrated that the expression of the P300 protein is increased in the right ventricle of PAH patients compared to healthy subjects. In PAH, cells of the heart (called cardiomyocytes) grow abnormally (in response to increased pressure), making the heart less functional (right heart dysfunction). We showed that using the drug CCS1477 to inhibit the P300 protein on PAH cardiomyocytes reduced their hypertrophy (enlargement due to the increased size of the cells), which is beneficial for the heart.

Enzyme ATP Citrate Lyase: Orchestrating Metabolic and Epigenetic Changes in PAH

To tag DNA, the P300 protein needs available chemical molecules containing an acetyl group: acetyl-CoA. In the nucleus of a cell, where most of the DNA is located, acetyl-CoA is mainly produced by another enzyme: ATP citrate lyase (ACLY). Thus, the ACLY enzyme would also have a role in the modification of gene expression and could contribute to the abnormal behaviour of PAH-PASMCs. Indeed, the ACLY enzyme is well known for its role in epigenetic deregulation and the development of many cancers, but its implication in PAH development is still unclear.

In our latest research, we demonstrated that the expression and activity of the ACLY enzyme is increased in both the pulmonary arteries and the PAH-PASMCs compared to healthy subjects. We showed that blocking the activation of the ACLY enzyme using the drug BMS-303141 decreased the growth of PAH-PASMCs and induced their death. We also observed that inhibiting the ACLY enzyme allowed the decrease of P300 protein activity and was associated with a decrease in DNA acetylation (decreasing gene expression). Finally, we demonstrated that the inhibition of the ACLY enzyme in PAH rat models, using the drug ETC1002, reduced pressures in the pulmonary arteries and the right ventricle, improved cardiac function, and reduced pulmonary artery obstruction.

This research will provide important knowledge that could lead to new therapeutic strategies. Our goal now is to identify common genes whose expression is impacted when the P300 protein and ACLY are blocked. We expect that blocking the P300 protein and the ACLY enzyme at the same time will affect the process of cell multiplication and resistance to death. ACLY inhibitors are well tolerated in humans, as evidenced by recent clinical trials in patients with metabolic disorders, which could accelerate the transition of these results from the laboratory bench to the patient's bedside.

Contributed by Yann Grobs

Patients as Partners: Investing in a New Era of Patient-Oriented Research

Introducing the Research Capacity Building Project. In recent years, PHA Canada has deepened our commitment to supporting PH research that advances the care of patients and brings us closer to a cure. We have been proud to invest in the next generation of PH researchers through our PH research scholarship program, partner on innovative research projects like the PH Priority Setting Partnership, and support collaboration among researchers and health care providers. 2022 saw us scale up our efforts with the launch of a new multiyear initiative that aims to enhance Canada's PH research environment and build capacity for patient-oriented research.

Research Capacity Building Project

The Research Capacity Building Project will focus on three main priorities:

1. Establishment of a Canadian PH Clinical Trials Network
2. Expansion of the Canadian PH Registry to include a biobank
3. Development of patient education and training initiatives

These three project areas reflect a broad-based approach that seeks to improve coordination and collaboration among PH researchers, increase access to critical new sources of patient data, and empower patients to be meaningfully engaged in all aspects of the research process.

For 15 years, PHA Canada has thrived as a collaboration between patients, caregivers, and health care providers. Each pillar of the community has drawn strength and inspiration from the other. The Research Capacity Building Project will expand the partnership between patients/caregivers and the PH medical community to ensure that the needs, values, and priorities of patients/caregivers are at the heart of the PH research agenda in Canada.

PHA Canada has always worked closely with the medical community to advance our mission. In addition to the leadership of medical experts on PHA Canada's Board of Directors, the organization is supported by volunteer advisory committees of physicians (the Canadian PH Medical Committee) and nurses (the Canadian PH Professionals Network) who work with staff and the Board to ensure outstanding care and support, through research, advocacy, awareness, and education. The Research Capacity Building Project reflects the strength and solidarity of Canada's PH community and the enduring hope we share that patients and caregivers can live well with PH.

Canadian PH Clinical Trials Network

One example of PHA Canada's leadership in advancing quality care and research is the annual *National PH Medical Think Tank*, which brings together experts for an interactive program aimed at optimizing the diagnosis and management of PH in Canada. At the 2021 Medical Think Tank, participants identified the need for a "Canadian PH Clinical Trials Network."

A clinical trial is a research study that evaluates the safety and effects of one or more treatments on actual patients. Unlike clinical trials for more common diseases such as cancer or arthritis, there are unique challenges associated with rare disease clinical trials. For instance, about 30% of clinical trials fail because they can't recruit enough participants¹. This is especially true in rare disease clinical trials where the patients are fewer and scattered around the globe. Additionally, because patient populations for rare diseases are smaller and often diverse in terms of age, sex, and/or severity of illness, common methods for clinical trial design often fail to demonstrate significant outcomes with certainty. As a result, studies for rare disease research must find ways to adapt their designs without compromising the quality of the research.

Planning rare disease clinical trials can get complicated. To help overcome challenges like these, the emerging Canadian PH Clinical Trials Network will focus on improving information sharing, coordination, and collaboration across research centres and on sharing expertise and resources more efficiently.

Patient Registries and Biobanks

Clinical trials are not the only way for patients to contribute to innovative research. When assisted by new information technologies, the collection of patient data—such as found in patient registries and biobanks—provides researchers with access to information that can reveal previously unknown similarities between patients (i.e., genetic mutations) and potential new treatment pathways.

A disease registry is a unique database that contains information about people diagnosed with a specific type of disease. Human biobanks collect and supply human tissue, blood specimens, and associated data for research. These approaches have the potential to increase scientific efficiency by maximizing the use of valuable and rare data and samples.

The Canadian PH Registry (CPHR) was created in 2017. Since then, approximately half of Canada's established PH expert centres, including two pediatric centres, have joined the registry or taken steps to include their patient population. Adding a biobank to the CPHR—beginning with blood samples that can easily be collected during routine right heart catheterization—has the potential to advance Canada's research capacity significantly. Furthermore, the *Canadian PH Community Survey* firmly established the willingness of patients to provide blood or tissue samples for storage in the Canadian PH Registry, with 78% of patients responding yes to the option.

Patient Education and Training

The third pillar of the Research Capacity Building Project includes a broad range of learning opportunities for patients and caregivers. This includes increasing the availability of research-related blogs, articles, and updates through PHA Canada's regular communication channels, as well as offering research-related workshops via webinars and at the National Community Conference.

This pillar also includes training for community leaders seeking to level up their advocacy skills on behalf of the PH community. Research advocates are patients and caregivers trained to provide patient perspectives for the purpose of advancing science. Most research advocates are not scientists. Training for community leaders—such as PHA Canada's Ambassadors—will help advocates gain skills to collaborate with scientists and clinical researchers.

We also need to increase the PH community's knowledge and understanding of the value of real-world evidence (data generated in settings outside clinical trials) and the role of patient-reported outcomes (an outcome reported directly by patient who experienced it). Both will become increasingly important to the design of future clinical trials and the drug approval and reimbursement process.

Summary

For 15 years, PHA Canada has brought together pulmonary hypertension patients, caregivers, and healthcare professionals to better the lives of all Canadians affected by PH. An underlying principle of the Research Capacity Building Project is that we invest our attention and resources on activities that will be impactful on a national level. We want this initiative to create a foundation of collaboration and cooperation that ushers in a new era in patient-oriented PH research in Canada. Because the only way to achieve better outcomes for patients, is to include patients every step of the way.

We will also be including you every step of the way. Stay tuned for regular updates from the Research Capacity Building Project in future editions of Connections!

Contributed by: Pat Kelly,
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¹ Khaleel, S. L. (n.d.). Rare Disease Patient Recruitment And Retention. Retrieved from <https://www.clinicalleader.com/doc/rare-disease-patient-recruitment-and-retention-0001>.

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Content Disclaimer

The content featured in *Connections* magazine is created by members of our community, and the information is checked for accuracy to the best of our ability. However, each person's PH story is unique, so what works for one individual may not work for everyone. If any information in *Connections* doesn't seem correct to you, please let us know so that we can verify it. Most importantly, always check with your PH team before making any lifestyle or treatment changes.



The Pulse

PHA Canada's monthly newsletter, received a makeover in June 2020!

The Pulse will keep you updated on what's happening in the world of PH in Canada and beyond.

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