



Research Initiative Report 2015-2017

Advancing Towards a Cure



Letter from the Chairman



Since the start of our Research Initiative in 2009, we have worked diligently to build a comprehensive research program. Today, our program spans basic, translational, and clinical research and funds efforts to find a cure and improve the lives of those living with the condition, from the smallest preemies to seniors with Normal Pressure Hydrocephalus.

Over the past three years, excitement in the research community has been building, bringing with it new theories, new discoveries, and a renewed sense of promise. We now have a greater understanding of why hydrocephalus develops.

We are starting to:

- See common links between the different types of hydrocephalus; and
- Test new therapies to prevent the development of hydrocephalus, minimize brain damage, and control hydrocephalus symptoms without a need for shunt surgery.

The Hydrocephalus Association will continue to push promising research forward. Our programs are designed to accelerate the movement of new therapies from bench to bedside – from the lab to you. By continuing to fund innovative projects, leveraging our partnerships with key federal agencies, expanding our network of scientists, and collaborating with patients and industry, I know that we can achieve our vision of a world without hydrocephalus. I hope you will join us as we work toward our vision and advance our research efforts.

A handwritten signature in black ink that reads "Aseem Chandra". The signature is written in a cursive style and is underlined with a single horizontal stroke.

Aseem Chandra
Chairman of the Board
Hydrocephalus Association

Hydrocephalus Association

Today the Hydrocephalus Association is the leading private funder of hydrocephalus research.

Who We Are

The Hydrocephalus Association (HA) is a dedicated team focused on Support, Education, Advocacy, and Research. The mission of the Hydrocephalus Association is to find a cure for hydrocephalus and improve the lives of those affected by the condition. We strive to accomplish these goals by collaborating with patients, caregivers, researchers and industry; raising awareness; and funding innovative, high-impact research to prevent, treat, and ultimately cure hydrocephalus.

Research Initiative

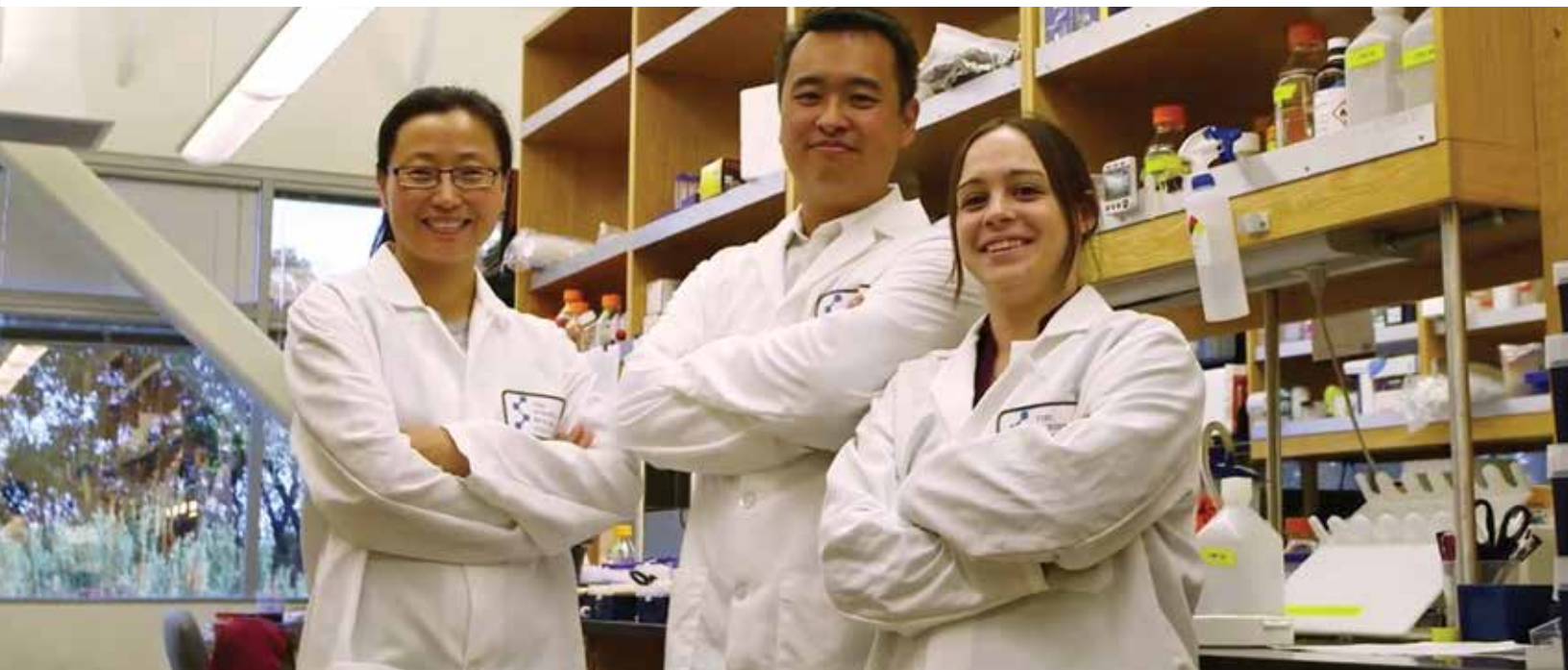
In 2009, the Hydrocephalus Association solidified its commitment to research through the launch of the Research Initiative. The mission of this initiative is to fund research that improves the quality of life for people living with hydrocephalus, and ultimately to find a cure.

To accomplish this mission, the Board of Directors established three priority areas:

1. Stimulate the
Research Ecosystem

2. Improve Clinical Outcomes
and Quality of Life

3. Advance the Study
of Root Causes





“The National Institute of Neurological Disorders and Stroke (NINDS) is committed to basic, translational and clinical research in neuroscience and neurological disorders, including hydrocephalus research.

The Hydrocephalus Association research program has built partnerships with NINDS and across the spectrum of research in a way that supports the development of new ideas, tools and therapies designed to improve patient outcomes.”

Dr. Jill Morris
Program Director
National Institute of Neurological Disorders and Stroke
National Institutes of Health

Our Research Program

Since the start of our Research Initiative in 2009, HA has spent over \$7 million on our Research Programs.

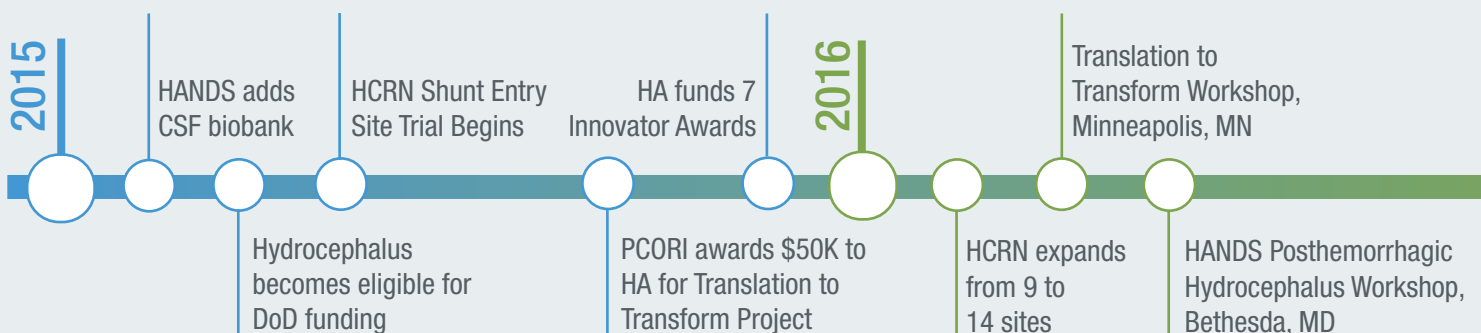
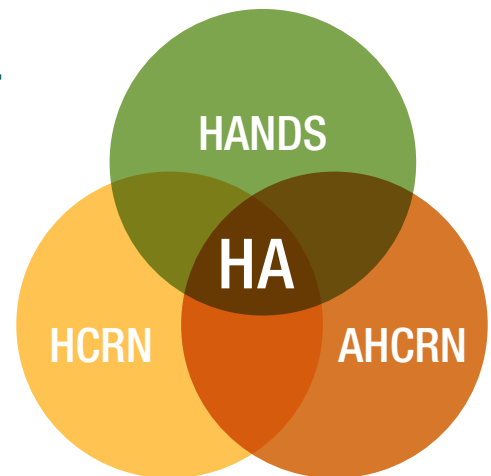
From 2015-2017 we have:

Spent \$3.9 Million on Research Programs

Awarded 18 Grants

Supported 3 Research Networks

Held 2 Research Workshops



What We Do

The Hydrocephalus Association Research Initiative is focused on advancing promising avenues of hydrocephalus research and building a committed and connected hydrocephalus research community.

Research Networks

We support three networks that accelerate high quality, high-impact hydrocephalus research.



Hydrocephalus Clinical Research Network (HCRN)

A network of fourteen children's hospitals that conduct clinical research on hydrocephalus.



Adult Hydrocephalus Clinical Research Network (AHCNRN)

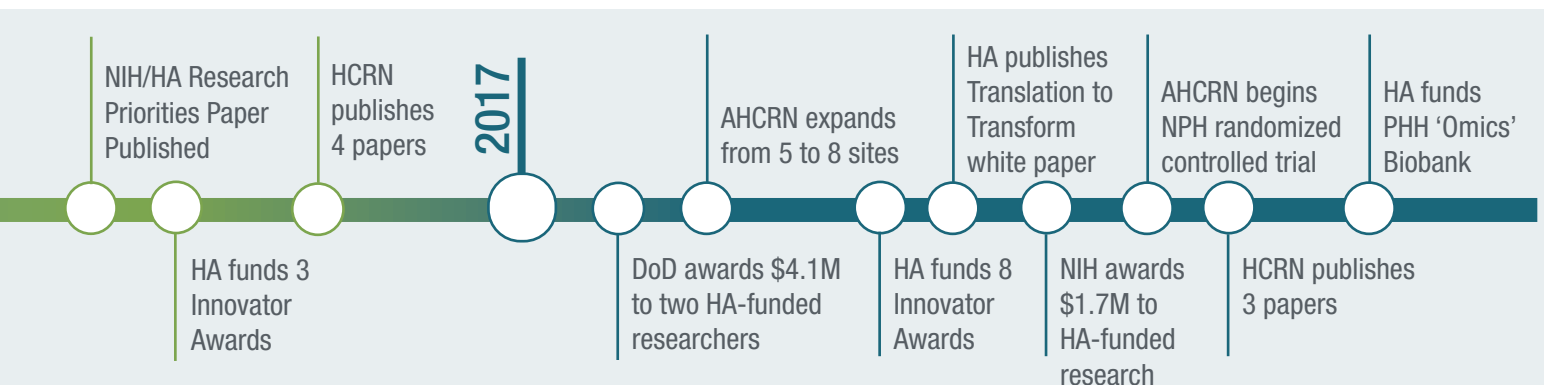
A network of eight hospitals focused on adult hydrocephalus patients.



Hydrocephalus Association Network for Discovery Science (HANDS)

A platform for both communication and collaboration among hydrocephalus basic and translational researchers with a focus on mentorship, innovation, and shared infrastructure.

Through HANDS we award research grants to individual investigators conducting innovative research and also hold research conferences and workshops that are designed to promote collaboration and identify promising new opportunities.

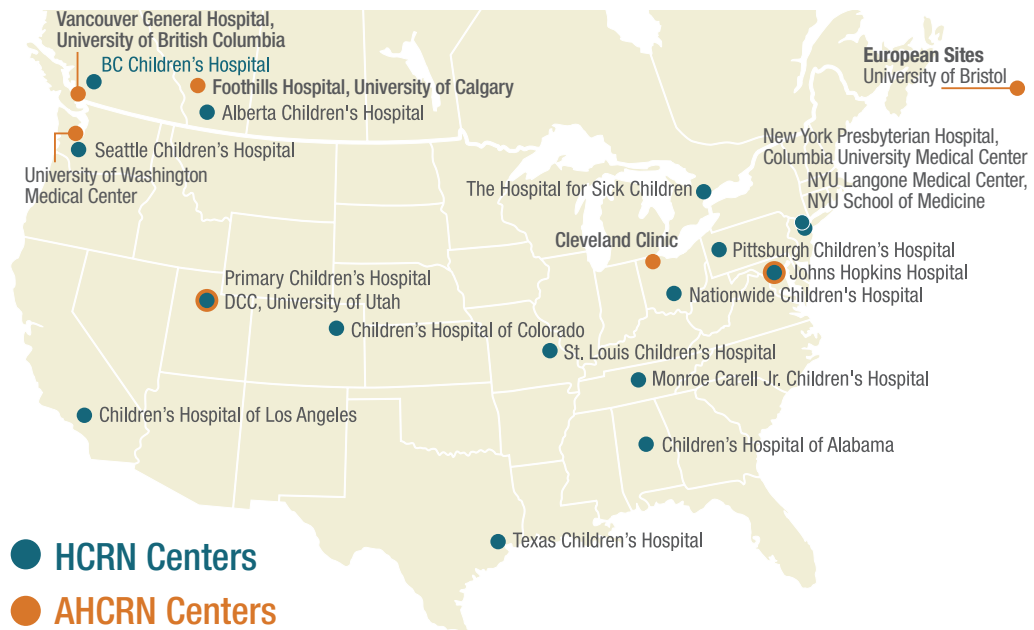


2015-2017 Highlights

Clinical Research Networks

Our Clinical Research Networks have expanded!

The pediatric-focused Hydrocephalus Clinical Research Network (HCRN) added five sites in 2016. The Adult HCRN (AHCRN) added three sites, including our first European site, in 2017.



Meet the Principal Investigators at Our New Sites

HCRN		AHCRN	
	Dr. Jay Riva-Cambrin Alberta Children's Hospital Calgary, AB, Canada		Dr. Edward Ahn Johns Hopkins Hospital Baltimore, MD
	Dr. Mark Krieger Children's Hospital of Los Angeles Los Angeles, CA		Dr. Jonathan Pindrik Nationwide Children's Hospital Columbus, OH
	Dr. Todd Hankinson Children's Hospital Colorado Denver, CO		Dr. Guy McKhann, II Columbia University Medical Center New York, NY
			Dr. Jeffrey Wisoff NYU Langone Medical Center New York, NY
			Dr. Richard Edwards University of Bristol Bristol, UK

Improving Patient Outcomes

Our Clinical Networks are making a difference!

The HCRN and AHCRN are focused on improving the lives of those living with hydrocephalus. Their research programs range from understanding the natural history of the condition, to optimizing surgical procedures and protocols, and finding ways to identify people who are at risk for developing hydrocephalus.

- ▶ **Treatment Options:** The clinical networks are evaluating different treatment options for both our pediatric and adult populations.
- ▶ **Infection Prevention & Treatment:** The clinical networks are working to decrease the impact of shunt infections by developing protocols that reduce the risk of shunt infections and optimizing treatment strategies when shunt infections do develop.
- ▶ **Shunt Longevity:** The clinical networks are finding ways to increase the life of a shunt.
- ▶ **Cognitive Outcomes:** The clinical networks are working to understand how different treatments affect long-term outcomes.
- ▶ **Natural History:** The clinical networks are discovering how hydrocephalus affects people throughout their lives. By understanding the natural history of the condition, the networks will be able to measure changes in outcomes when new therapies are developed.

From 2015-2017 Our Clinical Networks have:

Secured
\$3.1
Million in
New Grants

Added
8
Clinical Sites

Published
7
Studies

HCRN Studies:

Shunt Infection Protocol:

Decrease shunt infections

Shunt Infection Treatment: Optimize treatment protocol for shunt infections

Posthemorrhagic Hydrocephalus Protocol:

Optimize treatment decisions after a brain bleed

Shunt Entry Site Trial: Increase shunt life

Shunt Malfunction Study: Identify risk factors for shunt malfunction

ETV Trial: Decrease shunt dependence

ETV-CPC Trial: Decrease shunt dependence

VINOH Study: Understand relationship between ventricle size and cognitive outcomes

AHCRN Studies:

Shunt Infection Protocol:

Decrease shunt infections

Shunt Malfunction Study: Identify risk factors for shunt malfunction

ETV Study: Decrease shunt dependence

Etiology Study: Understand the natural history of adult hydrocephalus

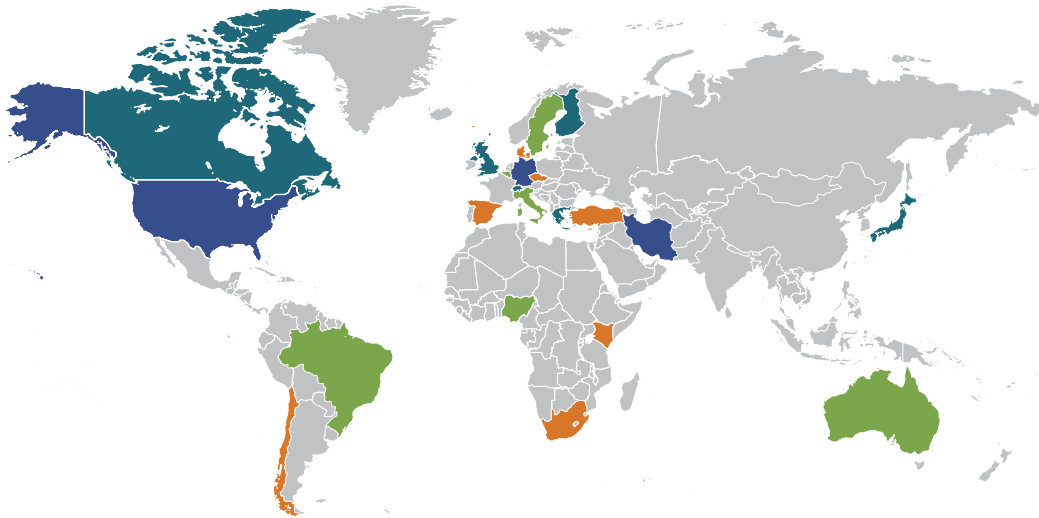
Brain Behavior Study: Understand how brain function changes after CSF removal

PENS Trial: Determine shunting outcomes in the Normal Pressure Hydrocephalus (NPH) population

2015-2017 Updates

HANDS

Hydrocephalus Association Network for Discovery Science



150 Members | 6 Open Source Databases | 2 Biobanks

Researchers in 22 countries are represented through HANDS Membership

Australia | Belgium | Brazil | Canada | Chile | Czech Republic | Denmark
Finland | Germany | Greece | Iran | Italy | Japan | Kenya | Nigeria
South Africa | Spain | Sweden | Switzerland | Turkey
United Kingdom | United States

HANDS launched in 2015 and has been growing quickly since its inception. HANDS is a platform for both communication and collaboration among hydrocephalus basic and translational researchers with a focus on mentorship, innovation, and shared infrastructure to support high quality, high impact research.

By centralizing the hydrocephalus basic and translational research communities, HANDS is becoming the point of contact for researchers, both established and new, in the hydrocephalus field. HANDS is not only a place to meet, debate, and develop collaborations, but also a centralized resource. Databases for research models, therapeutics, biomarkers, and standardized protocols as well as infrastructure that supports the entire research community are being developed.

2015-2017 Innovator Awards

Through HANDS, HA launched the first Innovator Award grant cycle in 2015. The goal of the award was to provide seed funding for bold and innovative research with the potential to transform the field of hydrocephalus through the understanding of disease mechanisms and the development of novel therapies. Seven grants were awarded in 2015. In 2016, HA awarded three grants through our Posthemorrhagic Hydrocephalus (PHH) Initiative. In 2017, HA awarded eight grants, four through the PHH Initiative and four focused on Postinfectious Hydrocephalus (PIH).

Meet our Latest Innovator Award Recipients



Joanne Conover, PhD
Associate Professor
University of Connecticut

GOAL: Investigate the disease progression of PIH



Kristopher Kahle, MD, PhD
Assistant Professor
Yale School of Medicine

GOAL: Understanding the role of the choroid plexus in PIH



Yan Ding, PhD
Research Associate
Loma Linda University

GOAL: Understand how a brain bleed interferes with the CSF reabsorption



David Limbrick, MD, PhD
Chief of Pediatric Neurological Surgery
Washington University

GOAL: Identify the causative organisms of PIH and the patient's immune response to those organisms



Aristotelis Filippidis, MD, PhD
Neurosurgery Resident
Beth Israel Deaconess Medical Center

GOAL: Identify markers of delayed hydrocephalus following subarachnoid hemorrhage



Jennifer Strahle, MD
Assistant Professor
Washington University

GOAL: Understanding how blood is cleared from the ventricles following a brain bleed



June Goto, PhD
Research Instructor
Cincinnati Children's Medical Center

GOAL: Understanding the mechanisms of CSF accumulation in PHH



Hannah Tully, MD, MSc
Assistant Professor
University of Washington

GOAL: Identify how infection and brain structure affect the risk of hydrocephalus after a brain bleed

Focusing Our Research Networks on Posthemorrhagic Hydrocephalus



Posthemorrhagic Hydrocephalus (PHH) is one of the most insidious forms of hydrocephalus. PHH develops after a brain bleed and most often occurs in premature infants, although PHH can also develop in adults.



10% of infants with a brain bleed develop PHH



Nearly **70%** of PHH infants develop epilepsy



25% of all US children with hydrocephalus have PHH

We are Bringing Researchers Together

On July 25-26, 2016, in Bethesda, MD, the HA Network for Discovery Science (HANDS) hosted an international workshop on PHH. The workshop brought together a diverse group of researchers including pediatric neurosurgeons, neurologists, neuropsychologists, and scientists in the fields of brain injury and development, cerebrospinal fluid dynamics, and fluid barriers in the brain.



Dr. Shenandoah Robinson, a pediatric neurosurgeon from Johns Hopkins University, wrote, “By getting such a variety of people together with diverse expertise in a contained environment, this workshop in two days likely advanced the science towards transforming the field more than anything else in the past 20 years.”

We are Funding Critical Research

The PHH Initiative has funded seven Innovator Awards focused on testing new, innovative ways to treat and prevent PHH. Many of the grantees attended the PHH Workshop. The next steps for this initiative are to fund Discovery Science Awards. These awards provide sustained support for the most promising, high quality, cure focused PHH research through a substantial multiyear commitment.

Through these award mechanisms, HA is creating a pathway for new therapies to move from bench to bedside – from our basic science labs, to our clinical networks, and, ultimately, to our community.

Research and Advocacy Working Together

Two hydrocephalus researchers have been awarded funding through the Department of Defense (DoD) Congressionally Directed Medical Research Program (CDMRP).

DoD research dollars became available to our scientific community for the first time on December 19, 2014, when President Obama signed into law H.R. 83, the Omnibus and Continuing Resolution Appropriations Act of 2015. The inclusion of hydrocephalus on the list of eligible conditions under the CDMRP was a direct result of a small dedicated group of HA advocates working with our allies on Capitol Hill. HA's initial funding of these projects supported the collection of critical preliminary data needed to successfully compete and be awarded grants totaling over \$4.1 million through the Fiscal Year 2016 (FY16) Peer Reviewed Medical Research Program (PRMRP) Investigator-Initiated Research Award.

Decreasing CSF Production Through Pharmaceuticals



The lab of Dr. Bonnie Blazer-Yost is testing drug candidates that could improve brain function in hydrocephalus patients. With funding through the 2015 Hydrocephalus Association Innovator Award, Dr. Blazer-Yost has shown that a specific class of drugs can decrease cerebrospinal fluid production (CSF) and reduce the severity of hydrocephalus in an animal model. While initially focused on early interventions in infants, the research could have applications in the treatment of hydrocephalus at all ages. In the future, this line of research could help patients manage CSF production. This could be particularly helpful if a person's shunt is not draining enough CSF. Dr. Blazer-Yost has now established a team of experts to advise on the direct applicability of these drug candidates for hydrocephalus patients.

Preventing the Development of Posthemorrhagic Hydrocephalus



The prevention of posthemorrhagic hydrocephalus (PHH) may be on the horizon. At Sanford Burnham Prebys Medical Discovery Institute, Dr. Jerold Chun and Dr. Yun Yung (Hydrocephalus Association Mentored Young Investigator (MYI) Award, 2010) are now testing drugs that target a molecular pathway involved in the development of PHH. By blocking the activity of a specific compound found in blood,

Dr. Chun and Dr. Yung hope to stop the downstream effects of a brain bleed and prevent PHH. The goal is to develop a drug intervention that can be administered to any patient who has a brain bleed in order to prevent the development of hydrocephalus. The HA MYI Award provided Dr. Yung with the initial funding for this project. Dr. Chun and Dr. Yung's research went on to be funded by a large National Institutes of Health (NIH) grant. This award through the PRMRP will allow the team to continue their groundbreaking work.

Amplifying Patient Involvement

We are constantly working to bring the community, and their voices, together with researchers and doctors.

Translation to Transform Workshop

In June 2016, HA held the Translation to Transform (T2T) workshop. The workshop brought HA's Patient Partner Committees together with translational and clinical researchers with the goal of improving human clinical trial design by incorporating patient-centered outcomes and priorities.

The T2T workshop was the second phase of the T2T project, which was funded by the Patient Centered Outcomes Research Institute. The ultimate goal was the production of a white paper outlining patient and caregiver concerns, insights and recommendations for conducting hydrocephalus clinical research, as well as providing information on how investigators can engage with the HA Patient Partner Committees on future studies. The white paper was published on September 22, 2017 and is available on the Hydrocephalus Association website (<http://www.hydroassoc.org/conferences-and-workshops/>).





Community involvement is key!

Genetics of Congenital Hydrocephalus: In 2016, HA teamed with Dr. Kristopher Kahle, Yale University, to help recruit families to participate in a study to help identify genes that are altered in people who are born with hydrocephalus. By the end of 2017, an incredible 378 families had participated in the study. Outcomes from the study will be released in 2018!

Patient Preferences about Hydrocephalus Treatment: Also in 2016, HA partnered with Dr. Robert Naftel, Vanderbilt University Medical Center, and Dr. Mandeep Tamber, University of Pittsburgh Medical Center, to conduct a risk-benefit trade off analysis for shunt versus endoscopic third ventriculostomy (ETV) treatment. The results were presented at the 2016 fall HCRN meeting and are currently being developed into a paper.

Evaluating the Impact of Socioeconomic Factors on Shunt, ETV, or ETV/CPC Failure

Recognition: A National Caregiver Survey: In 2017, HA collaborated with Dr. Chevis Shannon, Vanderbilt University Medical Center, to conduct a national caregiver survey involving 263 families. The results were presented at the 2017 American Association for Neurological Surgeons (AANS)/ Congress of Neurological Surgeons (CNS) Joint Section on Pediatric Neurosurgery meeting.

Longeviti InvisiShunt Survey: Also in 2017, the company Longeviti NeuroSolutions connected with HA to obtain feedback on a new device for hydrocephalus patients. The resulting survey turned a lot of heads, but the response was amazing. Over 1,300 people completed the survey in only two days. The company is continuing to work with HA to make sure their products are responsive to the needs of our community.



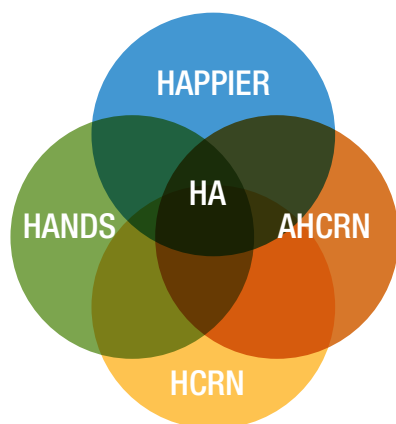
HAPPIER: Prioritizing the Patient Voice

Hydrocephalus Association Patient-Powered Interactive Engagement Registry

HAPPIER, an online database created to bring the patient perspective to hydrocephalus research, is in its final stages of development and will launch in 2018.

HAPPIER will collect information on the treatment and symptoms, health, and quality of life of people living with hydrocephalus. After completion of each survey, HAPPIER participants will be able to see where their responses fall in relation to the rest of the community, helping to address an often heard comment from patients that they feel isolated and alone.

HAPPIER is a part of the larger HA Research Network that is working together to improve outcomes, find new treatments, and develop ways to prevent hydrocephalus all together. With the HA Network for Discovery Science (HANDS), the Hydrocephalus Clinical Research Network (HCRN), and the Adult HCRN (AHCN), HAPPIER will help accelerate hydrocephalus research by providing patient-generated and patient-centered data to the research community.



The data will be used in three ways:

- 1) To help HA improve our research, advocacy, support, and education efforts.
- 2) To provide researchers with data to conduct research projects.
- 3) To identify patients that are eligible to participate in future clinical trials.

We are Building SUCCESS

The Hydrocephalus Association is focused on funding high-quality, high-impact research and building the hydrocephalus research community. Our impact can be seen far and wide throughout the hydrocephalus research field.

6 **NEW DRUG THERAPIES**
HA is supporting the testing of six new drug therapies for hydrocephalus.

13 **NEW COLLABORATIONS**
From 2015-2017, HA helped 26 researchers form collaborations.

17 **NEW RESEARCH ARTICLES**
From 2015-2017, HA's support was acknowledged in 17 peer-reviewed research articles.

84% **OF NIH-FUNDED HYDROCEPHALUS RESEARCHERS**
The majority of NIH-funded hydrocephalus researchers work directly with HA.

Return on Investment

41
FOLD RETURN
One of our Mentored Young Investigators turned an initial investment of \$110K into \$4.5M from the NIH and DoD.

36
FOLD RETURN
One of our Innovator Award Investigators turned an initial investment of \$50K into \$1.8M from the DoD and her home institution.

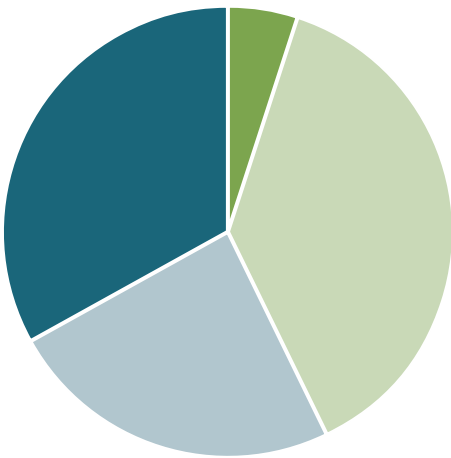
34
FOLD RETURN
One of our Innovator Award Investigators turned an initial investment of \$50K into \$1.7M from the NIH.

3.6
FOLD RETURN
The HCRN Investigators have turned an investment of \$1.5M into \$5.4M from NIH and other sources.

Research Spending

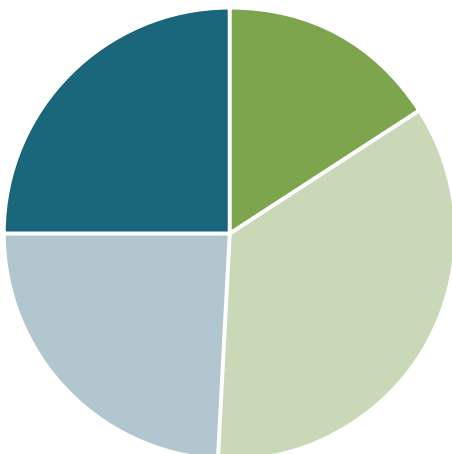
PRIORITY AREA SPENDING (2015-2017)

- Stimulate Research Ecosystem: 5%
- Understand Root Causes: 38%
- Improve Clinical Outcomes-Pediatric: 24%
- Improve Clinical Outcomes-Adult: 33%



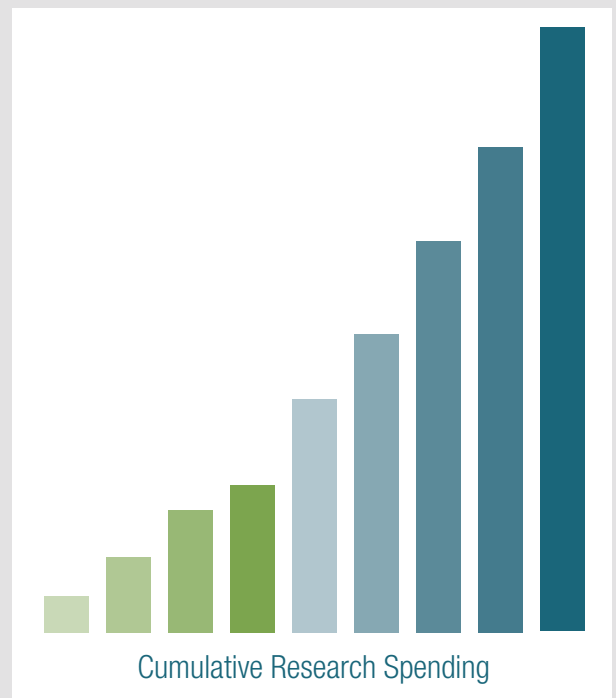
TOTAL PRIORITY AREA SPENDING (2009-2017)

- Stimulate Research Ecosystem: 16%
- Understand Root Causes: 35%
- Improve Clinical Outcomes-Pediatric: 24%
- Improve Clinical Outcomes-Adult: 25%



\$7.8 Million Committed
To Research Since 2009

50% Spent In
The Last 3 Years



2009	\$478,678.00
2010	\$986,510.00
2011	\$1,594,659.00
2012	\$1,925,561.00
2013	\$3,046,459.00
2014	\$3,884,231.00
2015	\$5,097,839.00
2016	\$6,332,351.00
2017	\$7,866,084.37



**“Our Vision is
a world without hydrocephalus.**

By early investment in the most
promising research, we are helping
to make this a reality.”

— Craig Brown, Senior Vice Chair,
Hydrocephalus Association Board of Directors

**ROAD TO A
CURE**



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