

Research

1. Understand BMP signaling and AVM maintenance.
2. Describe cellular and molecular determinants of vascular malformations.
3. Create an HHT-associated biorepository for vascular malformations and other tissues.
4. Harvest endothelial cells from vascular malformations during endovascular therapy.
5. Search for somatic mutations in blood leukocytes and/or circulating cells.
6. Conduct single cell RNA sequencing on human tissue and pre-clinical models to understand the pathway in different endothelial cells.
7. Find long-term strategies for increasing ENG/ALK1/BMP9/10 (RNA-based therapies or exosomes).
8. Increase ENG/ALK1/BMP9/10 as a therapeutic strategy through repurposed drugs and bioactive compounds.
9. Increase ENG/ALK1/BMP9/10 as a therapeutic strategy through engineered ligands and design proteins/specific antibodies to force signaling.
10. Develop high throughput screening tools (cell-based, multiple stable endothelial cell lines, iPSC-ECs, microfluidics, animal models, etc.).
11. Create more infrastructure for patient engagement during drug development.
12. Find promising pathways that can be used for novel drug development.
13. Develop and refine biological outcome measures to facilitate drug development and repurposing, drug discovery, and clinical trials.
14. Identify the determinants of outcomes of PAVMs, including groups where major gaps exist, such as AVM persistence, children, diffuse pulmonary AVMs and PAH.
15. Determine growth rates of PAVMs (untreated and treated, during childhood, pregnancy and adult life), and their determinants, to inform screening protocols, treatment recommendations and outcomes research.
16. Understand more about liver transplant for complicated liver vascular malformations.
17. Find predictors of symptomatic liver vascular malformations.
18. Identify preclinical screening pathway.
19. Develop standardized protocols for screening and rescreening HHT patients for brain AVM.
20. Determine the risk of hemorrhage in brain AVM and other brain VM types in HHT; and what factors influence risk.
21. Develop therapeutic strategies based on patient selection, delivery, and outcome assessment for BAVM.

Treatment

14. Evaluate capillary imaging methodologies in HHT.
15. Develop a multidimensional bleeding severity score.
16. Understand modifiers of bleeding severity (environmental, genetic, and anatomic).
17. Assess the role of antiangiogenic and other pathway-based therapies in the treatment of PAVMs (especially diffuse PAVMs and microscopic PAVMs) and PAH, using animal models and clinical trials.
22. Improve strategies for VUS interpretation in HHT genes.
23. Update clinical diagnostic criteria and guidelines for age in the application of clinical diagnostic criteria and genetic testing.
24. Standardize minimal acceptable components/approach for molecular diagnostic testing of proband.
25. Obtain further data from WGS (short and long reads) and/or RNAseq in patients clinically diagnosed with HHT whose initial genetic test results were negative.
26. Identify and describe patients with positive genetic test results who do not meet Curaçao Criteria & patients clinically diagnosed with HHT whose initial genetic test results were negative.
27. Determine if there are any discrepancies in HHT diagnosis and access to HHT care regarding race, ethnicity, age, gender, socio-economic status, language, geography, or other factors and identify solutions to address barriers and related outcomes

All Roads Lead to a Cure

The Patient Led Roadmap to Cure HHT



The Cornerstone of the HHT Community

Research

1 2

Can we understand how vascular malformations form and function in HHT?

3 4 5

How can we study biospecimens from HHT patients?

6 7 8 9

Can we work toward gene therapy methods to better treat or cure HHT?

10 11 12 13

Can we get a drug approved for HHT patients?

Treatment

14 15 16

How can we better measure and predict bleeding severity?

17 18 19

How can we better understand pulmonary AVMs in how they form, who they form in, how they grow, and how they respond to treatment?

20 21 22

How do we know when liver vascular malformations will be a problem and what do we do about it?

23 24 25

How can we standardize screening for brain AVMs, determine their risk of bleeding, and treat them?

Awareness

26 27 28 29 30

How can we better identify everyone with HHT using genetic testing?

31

How can we improve awareness, access to care, and education surrounding HHT for patients and clinicians?

Each route number on the other side of the roadmap describes the recommendations necessary to answer these key questions.

Recommendations were prioritized and voted on by expert researchers and clinicians in the HHT field alongside HHT patients.

Understanding of HHT Mechanisms

Better Outcomes & Quality of Life

Increased Diagnosis & Access to Care

All Roads Lead to a Cure
The Patient Led Roadmap to Cure HHT

CURE

CURE HHT
RESEARCH NETWORK

