Cure HHT Research Network: Building the Roadmap to Cure HHT

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CURE HHT Introduction

Hereditary Hemorrhagic Telangiectasia (HHT) is a rare, autosomal dominant disorder characterized by vascular malformations. Tangles of blood vessels can form in many locations and be of various size. Malformations in areas such as the nose, mouth, gastrointestinal tract, and brain are prone to rupture and hemorrhage, while malformations in the lungs and liver are prone to shunting. HHT is historically difficult to diagnose, has variable penetrance within families, and is an equal-opportunity disease affecting all ethnicities and nationalities. There are currently no FDA-approved treatments for HHT.

As a grantee of the Chan Zuckerberg Initiative’s Rare as One Project, Cure HHT created a research network (CHRN) to develop a research roadmap for the next 3-5 years. CHRN is led by HHT patients working in collaboration with researchers and clinicians to prioritize research initiatives by order of feasibility, impact, importance, and logical sequence.

Methods

- Form Executive Committee
- Set Goals and Milestones
- Recruit Disease Team of Experts to Draft
- Establish Workstream Topics
- Conference in March 2022
- Final Consensus Topics
- Recruit Disease Team of Experts to Draft
- Establish Workstream Topics
- Patient-Driven Research Roadmap

Survey Results: 1,204 Patients

- 90% of survey respondents experienced epistaxis as a first symptom
- Average onset: 3.4 years old
- Average age: 35 years
- 75% men, 25% women
- 70% African-American
- 35% Hispanic

Building The Network

- To serve on 8 Workstreams
- To meet at least bimonthly for 6+ months
- To complete a comprehensive review of the literature to identify gaps in research
- To propose recommendations to answer the ten proposed questions developed from survey responses and patient priorities

Tools & Resources

- Biobank with HHT Patient Samples
- Longitudinal Patient Outcomes Registry
- Induced Pluripotent Stem Cell Lines
- Capillary Imaging Modalities
- More Animal Models of HHT
- Comprehensive Genetic Sequencing
- High Throughput Drug Screening
- Single Cell RNA Sequencing & Multi Omics
- Researchers co-located with COEs
- Better Patient Surveys & Engagement

Bleeding

- Uncomplicated Telangiectasias in Long AVMs
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- Diversity, Inclusion, & Equity

Symptoms & Mechanism of Disease

- Genetic Considerations in HHT Diagnoses
- BMP Pathways
- Angiogenesis & Blood Vessels

Workstream Recommendations

1. IMPACT
   How likely is the research to improve patient outcomes?
2. IMPORTANCE
   Is this research important to further the understanding of HHT?
3. FEASIBILITY
   Is this research technologically and/or logistically feasible?
4. RATIONAL ORDER
   What is the rational order based on the study topics and questions?

Key Questions & Recommendations

- How do we better understand pulmonary AVMs and how they form, how they grow, and how they respond to treatment?
- How do we better understand multi-organ AVMs and their impact on patient quality?
- How do we better understand liver fibrosis and steatosis?
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