



Cure HHT Research Network Executive Team:

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A Journey to an HHT Research Roadmap

The CHRN Executive Team worked together to develop surveys for the patient, clinical, and basic science communities to understand, from each of their perspectives, what are the gaps in HHT science and knowledge. Based on the responses to these surveys, the Executive Team identified topic areas where further research could result in improved patient outcomes. Then, they invited patients, clinicians, and basic scientists to participate in discussions of these topic areas – these groups are called Workstreams.

The Workstreams will meet twice monthly, with the goal of creating a list of prioritized research within their topic area. There will be “Facilitators” (mostly members of the CHRN Executive Team) who will float between groups and help to facilitate group activities. Collaborations between groups is also encouraged.

In March of 2022, these groups will come together at an in-person meeting in Boston MA to discuss the priorities that they have identified and determine where these priorities fit on an HHT Research Roadmap with consensus from the group as a whole.

The topic areas, problem statements, and subtopics of each of the Workstreams are outlined below, along with the co-leaders and members for each group.

1. BLEEDING

Problem Statement:

- Individual HHT patients have a wide disparity in bleeding severity without obvious explanations.
- Tools are missing to measure severity and response to therapy.

Subtopics:

- Understanding factors that influence epistaxis (frequency, severity, variation between patients; nasal airflow and nasal inflammation)
- Understanding GI bleeding severity amongst patients

Leaders:

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2. AVM PROGRESSION

Problem Statement:

- Natural history and the factors influencing growth and development of AVMs is unknown
- Tools are missing to measure growth and response (routine imaging sensitivity may not be sufficient to measure in real-time)

Subtopics:

- Mechanistic basis of telangiectasia/AVM enlargement over life (disease progression with age)
- Predicting liver VM progression and shunt progression (factors leading to high output heart failure)

Leaders:

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3. DRUG THERAPIES/DISCOVERY – ANTIANGIOGENICS AND NON-BMP PATHWAYS

Problem Statement:

- There are no FDA approved therapies for HHT patients

Subtopics:

- Resistance to anti-angiogenics
- Enhancing ENG/ALK1 signaling
- Drug repurposing and high throughput screening

Leaders:

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4. DRUG THERAPIES/DISCOVERY – BMP PATHWAYS

Problem Statement:

- There are no FDA approved therapies for HHT patients

Subtopics:

- Enhancing BMP signaling
- Drug repurposing and high throughput screening

Leaders:

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5. UNRESOLVED TOPICS IN LUNG AVMS

Problem Statement:

- There is little information on effective treatments to prevent complications of diffuse pulmonary AVMs
- There is a need to understand determinants of PAVM complications
- Pathophysiology and risk factors for embolic complications (migraines with aura; infections; stroke)

Subtopics:

- Diffuse PAVMs
- Mechanisms and research pathway to better understand the embolic potential of PAVMs

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6. GENETIC CONSIDERATIONS IN HHT DIAGNOSIS

Problem Statement:

- There is a significant proportion of HHT patients in whom we cannot confirm genetic diagnosis

Subtopics:

- Noncoding variants in known HHT genes versus new genes
- Updating Curacao diagnostic criteria
- Clinical manifestations of HHT with negative genetic testing and HHT-like syndromes

Leaders:

Name	Role	Specialty	Institution	Country	Email
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7. SOMATIC MUTATIONS AND GENETIC MECHANISMS OF DISEASE

Problem Statement:

- There is a need to understand the balance between primary and any secondary mutations that contribute to the HHT phenotype

Subtopics:

- Role of somatic mutations in visceral organ involvement (how does this role vary between organs?)
- Mosaicism in AVMs

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			Francisco HHT Center		
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8. UNRESOLVED TOPICS IN BRAIN AVMS

Problem Statement:

- There is insufficient knowledge/information available to classify brain VMs as high risk vs low risk, to identify those who need preventive treatment
- Could there be a role for medical therapy for brain VMs

Subtopics:

- Risk factors of intracranial hemorrhage and other brain outcomes
- Outcomes of endovascular, radiotherapy and radiotherapy in HHT
- Determine lifetime protocols

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