Distinguished international researchers gathered for a 1 ½ day workshop at the Lawton Chiles International House on the campus of the National Institutes of Health. The meeting was co-sponsored by the National Human Genome Research Institute, the Office of Rare Disease Research, and the Chediak-Higashi Syndrome Association. Participants included clinical and basic science researchers with expertise in genetics, cell biology, animal models, immunology, hematology/bone marrow transplantation, and neurology. The current state of knowledge was reviewed, accompanied by round table discussions to foster collaborations and determine future objectives.

The workshop was divided into 4 sessions. The first session laid the groundwork for what is known about Chediak-Higashi Disease (CHD) from a clinical, genetic, and cell biological perspective. Emphasis was placed on hematologic, immunologic, and neurologic manifestations of the disease, since these are the principle sources of morbidity and mortality.

The second session focused on the LYST protein and what little is known about its function. Various animal model systems were presented that are phenocopies of the classical and atypical forms of CHD in humans. Also reviewed were ongoing investigations to uncover the role of LYST and other proteins with which LYST may be interacting. Additional proteins were introduced that have domains homologous to those in LYST, such as the BEACH domains, as an alternate route to determine LYST function.

The third session focused on the neurologic manifestations of CHD. The extent and variability of neurologic involvement was reviewed; however, the underlying pathophysiology is poorly understood. Gaucher disease, SPG11 and SPG15 have phenotypic overlap with CHD. The cell biology and clinical parallels of these disorders with CHD were reviewed as paradigms for how to approach the neurologic disease of CHD.

The final session of the workshop was devoted to hemophagocytic lymphohistiocytosis (HLH) and bone marrow transplantation (BMT) in CHD. Genetics, cell biology, and studies of NK cell function all provide insight into the risk and development of HLH. HLH was discussed in detail, including triggers, pathogenesis, treatment, and ultimately a bridge to bone marrow transplantation. Current approaches to BMT including preparatory regimens, timing, risks, and survival were also discussed.

The workshop closed with a round table discussion reviewing what is known and developing a framework to move forward. Since CHD is an extremely rare disease, international collaboration is necessary. There are many unanswered questions. An initial approach to understanding the variability in presentation and response to treatment involves collecting clinical and genotype information on all subjects with CHD. A questionnaire is being developed to reach out to the international community so this information can be collected. Additional bench and clinical collaborations were established. The proceedings of the meeting will be written for publication.