

Human Glycosylation Disorders Network: Future Directions

Meeting analysis and Submitted proposal to Sanford Health/Request for support for Human Glycosylation Disorders Network (HGDN)

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Human Glycosylation Disorders are a group of rare, metabolic diseases resulting from a defect in glycan synthesis and function. The most common, the Congenital Disorders of Glycosylation, may begin in infancy with manifestations ranging from severe developmental delay and hypotonia with multiple organ system involvement to hypoglycemia and protein-losing enteropathy with normal development. The clinical presentations and courses are highly variable, some result in death during infancy others cause mild disabilities in adults. More than thirty new disorders have been defined in the past 10 years with under diagnosis being a consistent hurdle. The past few years have revealed the broadening of phenotypic presentation and the emergence of new therapeutic and management strategies.

The hallmark of this field is the interface between glycobiology and clinical medicine. More than 1% of the human genome is used for glycosylation, the biosynthesis and addition of a nearly infinite variety of sugar chains (glycans) to proteins and lipids. Glycobiology, the study of glycan synthesis and function, is seldom a part of a medical or biomedical education. The diagnosis and approach to the metabolic bases of these disorders is complex both because the metabolic pathways are complicated and because the role of glycans in human physiology remains an advancing field. As more is learned about glycobiology, more children and adults with defective glycobio logic processes, new Glycosylation Disorders, will be identified.

With this growth in the clinical population there has arisen an urgent need for a coordinated network of physicians and scientists to identify, assess, manage and treat these patients. The development of a transdisciplinary consortium with a focus on addressing the immediate and long-term problems of this population would more effectively and efficiently meet the needs of this group and advance research opportunities in the field. This effort will parallel the European development of the group "Euroglycanet" established with a similar direction.

On October 26-28, 2008 in Sioux Fall, South Dakota a successful meeting, funded by Sanford Health and the National Institutes of Health Office of Rare Diseases, began the development of this consortium. The 17 member group included representatives from 11 academic centers, 2 companies, and 4

countries including South America and our European colleagues from Euroglycanet by video remote. This consortium represents a diverse, expert group of physicians and scientists with extensive experience in glycobiology and glycosylation disorders.

The action plan for the group developed by the meeting included:

- Hire a coordinator (genetic counselor or nurse practitioner) to assure the continued growth of the HGDN.
 - Coordinator—The coordinator will work closely with the President of the CDG Family Network and physicians involved in the care of affected individuals to identify families, provide education, triage questions, collect data and improve communication within the HGDN consortium of experts.
 - Key contact with families of affected individuals
 - Clinic coordinator/annual meeting
 - Family network list serve moderator
 - Family network contact person
 - Work on re-vamping web-site—“ask the professional”
- Develop the concept of Expert Clinics both by virtual meetings as well as clinics at Sanford Children’s Hospital that would:
 - Review challenging cases
 - Analyze data to define appropriate management
 - Examine affected individuals to document the clinical features as well as educate other medical personnel
- Advance the consortium by contacting expert physicians in Canada and Asia
- Begin the development of databases which would assist both in supporting the community of affected individuals and their families as well as clinical, basic science and therapeutic research. More specific information about these proposed data bases include:
 - Separate data bases for clinical research data and personal information required to build a family network
 - The Euroglycanet data base, developed 3 years ago may be a model for the global data base envisioned
- Develop a tissue repository
- Support scientific efforts approaching a better understanding of the glycobiologic pathology aiming for better molecular diagnostic techniques and therapeutic options.

- Develop diagnostic algorithms, management ACT sheets for families and physicians

Budget proposal for first year:

Coordinator salary and travel budget:

\$50,000/year

Exploration and development of data bank

\$10,000/year

Exploration and development of tissue bank

\$10,000/year

Cost of maintaining the consortium including video/phone conferencing and travel

\$10,000