“The 2nd World Conference on Congenital Disorders of Glycosylation (WCCDG) for Families and Professionals: a challenging story of sugar trees”, 28 to 30 August 2015, in Lyon (France)

This conference is part of the Educational Program of Excellence on CDG created by the Portuguese Association for CDG (APCDG, www.apcdg.com).

It is organized in partnership with several associations and/or country CDG patient advocates: CDG Australia, CDG Brazil, CDG Czech Republic, CDG Denmark, Foundation of Glycosylation (the FoG) Canada, CDG Denmark, CDG Italy/Ireland, CDG Israel, Les ptits CDG France, CDG Spain, CDG Sweden, CDG USA, CDG UK charity and CDG The Netherlands.

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Out of the NIH Undiagnosed Diseases program: Early Results from the Clinical and Basic Investigations into Known and Unknown CDG’s

Lynne A. Wolfe, MS, CRNP, BC
NIH Undiagnosed Diseases Program
Congenital Disorders of Glycosylation
Clinical and Basic Investigations Into Known and Suspected Congenital Disorders of Glycosylation

This study is currently recruiting participants. (see Contacts and Locations)

Verified November 2014 by National Institutes of Health Clinical Center (CC)

Sponsor:
National Human Genome Research Institute (NHGRI)

Information provided by (Responsible Party):
National Institutes of Health Clinical Center (CC) (National Human Genome Research Institute (NHGRI))

ClinicalTrials.gov Identifier:
NCT02089789

First received: March 14, 2014
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Last verified: November 2014

History of Changes
Congenital Disorders of Glycosylation Pathways

Dolichol Biosynthesis

N-Glycosylation

O-Glycosylation

Glycophosphatidyl-Inositol Biosynthesis

De-glycosylation
Study Objectives

- Delineate the clinical and laboratory findings of CDGs
- Employ medical and family histories, consultations and physical examinations to advise patients and physicians concerning diagnosis, prognosis, and therapy of CDGs
- Perform molecular analysis as indicated
- Obtain fibroblast cultures and lymphoblast lines for RNA and DNA as well as metabolic investigations into the basic defect(s) in CDGs.
- Use this protocol to recruit patients for potential future therapeutic studies.
Clinical Methods (All subjects)

- Baseline Brain MRI/MRS
- Electrocardiogram
- Echocardiogram
- Abdominal Ultrasound
- Bone Age
- DEXA (greater than 3 years of age as tolerated)
- Clinical Photography
- Medical Evaluations: Audiology, Neurology, Neurocognitive testing, Ophthalmology, Nutrition, Immunology, Physiatry, PT/OT
- Urinalysis, Urine Electrolytes Calcium and Creatinine, Urine Amino Acids, Urine Oligosaccharides and Free Glycans, Research
- Skin Biopsy
Clinical Methods (most subjects)

- Schirmer II
- Auditory Evoked Potential
- Lumbar Puncture
- EEG
- Sleep study
- Electromylogram and Nerve Conduction study
- Autonomic testing such as QSWEAT
- Metabolic Cart
- Swallow study
Clinical Methods (some subjects)

- Glycomics &/or Proteomics on CSF & fibroblasts
- Lysotracker on fibroblasts
- Additional Immunologic work on hyper-immune responses
- Sedated ERG (Electroretinogram)
- OCT (Optical Coherence tomography)
- SSEP (Somato-sensory evoked potentials)
- Over-night Video-EEG
<table>
<thead>
<tr>
<th>Time</th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
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<tbody>
<tr>
<td>7:00a</td>
<td>Admission/Voucher Office</td>
<td>Timed Bloodwork</td>
<td>Speech and Swallow Evaluation</td>
<td>Metabolic Cart</td>
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<td>Consent, Admission</td>
<td>Urine Collection</td>
<td>Sedated brain MRI/MRIS, Lumbar Puncture</td>
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<td>Speech and Swallow Evaluation</td>
<td>Auditory Brainstem Response</td>
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<td>Physical Evaluation</td>
<td>Dental and Eye Exam</td>
<td>Nerve Conduction Study</td>
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What we have seen to date

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<tr>
<th>CDG TYPE</th>
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<td>GPI-ANCHOR-RELATED</td>
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<td>DE-GLYCOSYLATION</td>
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<td>SUSPECTED</td>
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*Sterol & Isoprenoid Research Consortium Collaboration
What we have found so far

- Low CSF protein & albumin
- Low CSF IgG
- Neurotransmitter, BH4, or Cerebral Folate abnormalities
- Low tear production
- Dysynchronous and delayed transmission through the brainstem on ABR with normal peripheral hearing in NGLY1
- Hypohydrosis
- Elevated urine glycosaminoglycans
- Hyper-immune response to Rubella and Rubeola vaccines
NHGRI will cover the travel and lodging cost for one parent/legal guardian for each child enrolled on a study. In the event a child requires two adults for travel, the study team may make an exception. An adult guardian must be over the age of 18.

For Families traveling from Outside the United States we can only pay for travel within the United States.
Collaborations

- NGHRI Andrea Gropman MD, Paul Lee MD
- UDP Glyco-core – Glycocomics Mariska Davids PhD, Megan Kane, PhD
- NIAID & CC/DLM Immunology Sergio Rosenzweig, MD & Jon Lyons, MD
- NIH Glycoscience group John Hanover, PhD & Kelly ten Hagan, PhD
- NIDCR Ilias Alevizos, MD & team
- NICHD Constantine Stratakis, MD & team
- NIDDK Marc Ghany, MD & Shilpa Lingula, MD
- NEI Wadih Zein, MD
- NIMH Audrey Thurm, PhD
- NIDCD Carmen Brewer, MD & team
- NINDS Tanya Lehky, MD & team
- CC/RMD Scott Paul, MD, Beth Solomon, SLP & team
- Sanford Burnham Hudson Freeze, PhD, Bobby Ng & team
- Stanford Gregory Enns, MD
- CHOP Miao He, PhD and Marni Falk, MD
Acknowledgements

Our Patients and Families

Christina Lam, MD
Research Fellow
Principle Investigator

Carlos Ferreira, MD
Biochemical Genetics Fellow

Donna Krasnewich, MD, PhD
NIGMS/NHGRI

William A. Gahl, MD, PhD
Clinical Director NHGRI
Director, NIH Undiagnosed Diseases program
Foundation Glycosylation (FoG) is the official sponsor of the videos targeted to the “SSIEM Official Satellite Symposia - Second World Conference on Congenital Disorders of Glycosylation (CDG): a challenging story of sugar trees”:

The Foundation Glycosylation (FoG) founded by Duncan Webster (Canada), is the official sponsor of the videos of all oral session that will be given during the conference. This material will be available in the Youtube channel dedicated to “SSIEM Official Satellite Symposia - Second World Conference on Congenital Disorders of Glycosylation (CDG): a challenging story of sugar trees” at:

For more information about the work of this organization which is focused on research to ALG9 - CDG (CDG -1L), visit the following link: http://www.thefog.ca/main.html

ACKNOWLEDGMENTS

• All speakers
• All participants
• Associations
• Organizations
• Domaine Saint Joseph
• All Volunteers
• Pf Pascale de Lonlay and Nathalie Seta
• Dr Maria A Vilaseca and Pf Jaeken
• Biocommunicat