October 2016
Volume 2

CDG CARE
Where CARE Grows...

CDG CARE Annual Appeal

Open Letter of Appeal to our CDG Community and Supporters,

CDG CARE stands for CDG Community Alliance and Resource Exchange (CARE).

We are a nonprofit organization founded by parents and volunteers seeking to exchange resources and increase education among a group of disorders, known as Congenital Disorders of Glycosylation, or CDG. Our mission is to promote greater awareness and understanding of CDG, to provide information and support to families affected by CDG, and to advocate for scientific research to advance the diagnosis and treatment of CDG.

We are governed by a very passionate and diverse group of volunteer parents, community members and medical professionals. However, even with all of the time and commitment that our leaders are able to give to support our mission, we rely on gifts and donations from you to keep our efforts moving forward.

With your contribution, we can continue to support families, develop programs, promote education and advocate for research, therapies and treatment for CDG. Your gift makes a difference to children who

CDG Tea makes for an excellent holiday gift! Place an order today by e-mailing Christa Thoma.

May 16th - Congenital Disorders of Glycosylation (CDG) Awareness Day!

are still awaiting a rare disease diagnosis and those already affected by CDG. With your gift we are able to personally contact newly diagnosed families, provide them direct resources, and put them in touch with medical experts who can help provide them with encouragement and answers to some of their questions.

With your gift, we will be able to continue our awareness campaign efforts and extend our reach by successfully making May 16, 2017 recognized as CDG Awareness Day in all 50 States. It is only through your support and contribution that we are able to advocate for new treatments and therapies, publish and disseminate our newsletters and educational materials, and develop videos that promote awareness and education to medical professionals and families nationwide.

We ask you to consider making a donation to CDG CARE and greatly appreciate your support to our cause. Please visit our website by clicking on the following link to view the ways in which you can make your tax deductible contribution, www.cdgcare.com.

With Kind Regards,

Andrea Berarducci
President, CDG CARE

Be sure to check out the global updates provided in this newsletter!

Read about Gianna's story in this volume of our newsletter.

Did you miss one of our previous newsletters? Catch up on our web page by clicking here.

Order CDG Tea

By Christa Thoma

CDG is a spicy and tasty, loose leaf, herbal tea; made with berries (**C**hai, **D**yeberry, and **G**ojiberry) cinnamon, cardamom, ginger and hibiscus.

The idea of CDG tea started over a year ago with CDG Mom Anna Lund; her goal of spreading awareness

and raising money to help her son Elmer and so many others soon became a reality. Sales started first in Sweden and then distribution spread across Europe. Money was raised to support CDG awareness and the Rare Commons project (an international database to aid CDG research.)

In February 2016, US CDG tea sales kicked off at the National Family Conference in California. CDG tea was offered for all to try during meeting breaks, given as a “thank you” to conference speakers, and sold to families/ friends. After the conference, we received wonderful feedback from across the country. People loved the tea; giving it as gifts, hosting local tea parties, and sharing the tea to spread awareness in their own communities. It is delicious, healthy, and has turned into more than a fundraiser. The tea is a product that continues to unite the international CDG community with a simple cup of tea and a dream of awareness, research, and a cure.

US CDG tea online sales continue this holiday season, with new inventory available starting mid-November. Bags of loose leaf tea are $10 each plus shipping, contact Christa Doot Thoma to get more information or place an order (christa.doot@gmail.com).

My Beautiful CHILD

By Andrea Berarducci

CDG CARE is honored to announce the recent collaboration with Emory Genetics Laboratory (EGL), specifically as one of the key partners in the new EGL “My Beautiful CHILD” campaign. This social campaign was created to openly communicate and create greater awareness about chromosomal

abnormalities and other genetic disorders seen in children. As a result of the “My Beautiful CHILD” campaign, awareness about genetic disorders throughout the community was increased and families, children, and patients were highlighted to shed light and put a face to what these disorders are and may look like.

Through the campaign, five CDG/NGLY1 families were selected to participate and showcase their photos and stories through social posts, blogs, and the EGL external/internal newsletter. On September 20th, CDG CARE participated in the “My Beautiful CHILD” webinar to Spotlight Sickle Cell Disease and Congenital Disorders of Glycosylation (CDG): Research, Advocacy, and Strong Communities. With over 100 registered webinar participants, CDG research, education and awareness was shared with genetic counselors, geneticists, nurses, primary care physicians and families nationwide.

CDG CARE would like to thank all of the families and medical professionals who participated in the campaign and for supporting CDG CARE’s mission to raise CDG awareness and promote CDG education nationwide!

Click here to view the presentation.

Rare Commons Project Update

By Begonia Nafria

Rare Commons 2.0 is a research platform that is focused on the study of pediatric rare diseases. One of the illnesses that has a project ongoing in the platform is CDG. The study is addressed to all the different types of CDG with the most prevalent being CDG1a (PMM2).

Currently, there are 99 families involved in this project. Most of the participants in the study are from Spanish descent, but the project is also available in English, and all families fluent in these languages are welcome to participate. It is very important to increase the sample of families, as this directly affects the strength of the results. The families that are interested in participating should complete the attached registration form: https://www.rarecommons.org/es/patient/register

How Rare Commons works… The working system is simple. To begin with, a participant is able to access and read a medical chapter about one aspect of the disease (genetics, neurology, cardiology, etc.). Once you have finished reading each chapter, you can access and complete a medical survey regarding the topic of the chapter. This is how Sant Joan de Déu hospital, who leads the project, can describe the natural story of the disease and study the correlation between genotype and fenotype. This information is relevant and necessary to study the effects of potential therapeutic options, as the data is considered a control group and can be compared and analyzed as to whether a drug is effective or not. European Medicines Agency encourages the research team to develop the project and publish the results to help and promote other scientific projects addressing the study of treatments.

With regard to potential therapeutic options, Rare Commons has introduced an improvement within the informed consent that families sign in order to access and participate in the project. This new clause allows the study coordinators to know what the interest is of the family regarding the study of the inclusion and exclusion criteria to access a clinical trial. With the exhaustive clinical data that we collect of one patient, we can analyze whether he or she is a potential candidate for a clinical trial and proceed to inform the family.

For the project to be successful, it is very important to disseminate information and work as a network with other hospitals and doctors, researchers and labs, and of course with a close collaboration with patients associations. This is the reason we are increasing our participation in scientific events. Through the end of the year we have confirmed participation in:

- National Congress of American Academy of Pediatrics (United States) from 21st to the 24th with poster presentation.
- Participation in a round table about the community health in the congress OuiShare Fest on the 26th of October in Barcelona. This is an important event about social innovation.
- Conference in the "Partnerships in Clinical Trials Europe" congress on the 16th of November in Vienna (Austria).

We hope that we can continue to increase the participation of English speaking family involvement through our collaboration with CDG CARE. For more information please contact our project coordination team via email at: rarecommons@sjdhospitalbarcelona.org

Begonya Nafria
Patient Advocacy Manager
www.rarecommons.org

Gianna's Journey to Diagnosis

By Natalie Dragotto

When Gianna was a born, we didn't know she had any problems. Gianna was a normal delivery, attentive to voices and had no feeding problems the day she was born. Before being released from the hospital, a routine Hep B shot was given. (2 days old). The following day, she wouldn't eat/latch on, and would not stop crying. The Doctor told us she had mild jaundice and a colicky baby. The doctors gave us Zantac, and told us she had GERD. Within the next 5 months, we were in/out of the doctor's office due to reflux/gerd, constant crying/colicky and feeding issues.

Gianna's onset of seizures started immediately after her first set of immunizations shots at 2 months old. That was when the eye rolling started. The twitching began after the 2nd set (4 months) and she had her first grand-mal seizure. The ER said it was febrile. The 3rd set (6 months), the grad-mal began to become frequent. Gianna was in/out of the hospital every few weeks from uncontrolled seizures and pneumonia due to aspiration issues. Gianna was diagnosed with epilepsy at 6 months old and was given Phenobarbital. She had difficulty swallowing and couldn't handle her own saliva. We had to suction her constantly to avoid aspiration pneumonia. Gianna lost all head control, didn't reach for toys, hands were always clenched into fist, and stopped rolling on the floor. Gianna's pediatrician was concerned because her arms were continuously in extension and she no longer showed any eye contact.

At 10 months, she was fed only by G-tube, had a variety of seizures lasting 30 seconds to 5 minutes up to 100++ seizures a day and would become lethargic after each seizure. Any body stress such as illness, over-tired and even temperature change would increase her seizure activity. Gianna was shown to have a broad range of seizures all over the brain. The majority of her seizures were a-typical absence associated with Lennox Gastaut Syndrome (LGS). We went to every specialist imaginable with no luck finding an underlining diagnosis. Since Gianna didn't show any characteristics of any known metabolic disorder, they suspected that she created her own disorder unique to her. Gianna had severe developmental delay, could not eat by mouth due to aspiration issues, subject to re-occurring illness, hypotonic, reflux, would not use her hands, did not give you eye contact and had no head control. Doctors told us that Gianna would never be "normal" and most likely would not live past 5. At age 1, we switched pediatricians and discontinued her vaccinations. Although we know today that the vaccination shots were not the cause of her disorder, we feel that it contributed to the severity.

At 1 ½ years old, we were still on a mission to find her diagnosis. We think having this mission helped our healing process of getting through knowing our little girl wasn't getting better and might not make it. Due to Gianna's swallowing issues, we only fed her during Vital Stim therapy. Vital Stim is a non-invasive external electrical stimulation therapy to help muscle strengthening and swallowing. It was during this feeding time, we noticed when we gave Gianna foods high in carbohydrates/sugars, she would have these larger, longer tonic clonic seizures where she would turn blue.

As parents, we felt she had to have an underlining condition where she couldn't process these types of foods. With the help of her Metabolic Doctor, this finally led us to the Diagnosis of CDG. At age 2 1/2, Gianna was diagnosed with CDG. (Congenital Disorders of Glycosylation) Type 1/subtype unknown. Age 8, Gianna was Diagnosed with CDG1k (subtype k).

Brief Summary on Current Developments in Therapy

By Eva Morava

- Mannose therapy in MPI-CDG (approved therapy in US)
- D-galactose therapy in PGM1-CDG (approved therapy in Europe), PGM1-CDG, SLC35A2 and SLCA39A8 (experimental therapy in US, Tulane IRB 14-517339, also NCT02955264)
- Liver transplantation in MPI-CDG, CCDC115-CDG, ATP6VAP1-CDG (approved therapy in Europe)
- Heart transplantation in DOLK1-CDG (approved therapy in Europe)
- Bone marrow transplantation in PGM3-CDG (approved therapy in US)

Experimental Clinical Therapy Trial in Progress:

- GlcNAc & Uridine therapy in PGM3-CDG (NCT02511041 status suspended new participants for analysis of data right now)
- Manganese therapy in SLC39A8-CDG (trial in Germany)
- ManNAc therapy in GNE-CDG (NCT02346461 NIH Activ) Also NCT02731690 Aceneuroamic acid (Sialic acid) Recruiting Ultragenix
- D-galactose dietary trial for different types of CDGs, for patients with any genetically proven CDG, which has endocrine, hepatic, and/or hemostatic involvement (trial at Tulane Medical Center, Tulane IRB 14-517339, also recruiting NCT02955264)

Upcoming Pre-Clinical Trials:

- Enzyme therapy with PMM2-CDG in animal model (no date on expected clinical trials
- Man1P liposomal therapy in animal model (clinical trial Phase 1 is planned in about 18 months)

We encourage the patients to contact their metabolic specialist before any dietary use of sugars, available over the counter. For more information e-mail emoravakozicz@tulane.edu at Tulane University Medical Center.

CDG Awareness Day

By Andrea Berarducci

May 16, 2016 was the first recognized Congenital Disorders of Glycosylation (CDG) Awareness Day throughout the United States!

Through extensive written campaign efforts, a total of 48 State Proclamation requests were submitted by CDG CARE State Delegate Volunteers. As a result, 25 Governors proclaimed that May 16, 2016 be recognized as Congenital Disorders of Glycosylation (CDG) Day across their respective States and that all citizens were urged to join in observance of this Day.

The States which supported May 16, 2016 CDG Awareness Day efforts include: Arkansas, Arizona, Colorado, Connecticut, Delaware, Georgia, Illinois, Indiana, Louisiana, Maine, Minnesota, Mississippi, Missouri, New Hampshire, New Mexico, Oklahoma, Oregon, Pennsylvania, South Carolina, Texas, Utah, Vermont, Washington, West Virginia, and Wisconsin.

Additionally, global efforts to raise CDG Awareness were successful and extensive with over 15,000 people reached through social media platforms! A petition containing over 5,000 signatures of support has been submitted to the World Health Organization to request that May 16th be recognized as the annual World Congenital Disorders of Glycosylation (CDG) Awareness Day.

If you would like to join in these efforts and are interested in participating as a CDG CARE State Delegate Volunteer, or are planning an awareness event on or around May 16, 2017, please send an email to: awareness@cdgcare.com

Three New CDG Subtypes

By Fiona Waddell, Journalist and Patient
Reviewed by Eva Morava, MD, PhD

TMEM199-CDG

TMEM199-CDG is a congenital disorder of glycosylation caused by defects in the transmembrane protein 199. A transmembrane protein functions as a gateway to permit the transport of specific substances across the biological membrane.

This CDG is a subgroup, which attributed to disturbed regulation and function of the Golgi system. The Golgi packages proteins into membrane-bound vesicles inside the cell before the vesicles are sent to their destination. TMEM199-CDG is an example of a CDG purely affecting the liver.

The four reported patients from three families showed mild liver symptoms and increased LDL-cholesterol. Because of low serum ceruloplasmin, the protein that carries copper in the blood, and mild liver copper accumulation there is some resemblance to Wilson's disease.

CCDC115-CDG

CCDC115 (Coiled-Coil Domain Containing 115) deficiency is one of the latest reported CDG. This subtype appears to have a role in regulation and function of the Golgi system as well.
Five patients with CCDC115 showed neurological symptoms, three patients showed decreased blood clotting factors, five patients had mild to moderate dysmorphic features and one patient developed psychomotor disability with seizures or low muscle tone combined with jerks or twitches and behavioral problems such as aggressiveness, agitation and psychotic behavior at age 25. Two patients have had a liver transplant, one at 3 years and 10 months old and the other one at 8 years old. The first rejected the donor liver twice and died at the age of 9. The second patient is doing well and has normal transferrin tests, which are blood tests to test for CDG.
The most affected patient died at 7 months of age. She showed failure to thrive, poor muscle volume, redundant skin, intermittent episodes of low blood sugars and high levels of ammonia in the blood, abnormal blood clotting factors and anaemia. After she died, her liver was analysed and showed cirrhosis due to severe inflammation of the bile ducts in the liver.
CCDC115-CDG has some resemblance to TMEM199-CDG, but in addition to the (more severe) liver disease, there is also neurological involvement and dysmorphism in most reported patients.

ATP6AP1-CDG

ATP6AP1 deficiency causes immune abnormalities, liver disease, cognitive impairment and abnormal protein glycosylation. This CDG was described in eleven male patients from six different families.
Recurrent bacterial infections were associated with hypogammaglobulinemia, or a reduced ability of the immune system to fight infections.
Patients with liver failure showed a broad spectrum ranging from mild hypertransaminasemia, or elevated liver enzymes indicating liver damage, to end-stage liver failure. Two babies had high levels of bilirubin in their blood. There was also leukopenia, or a reduced level of white blood cells. The six patients with the p.E346K mutation presented a more severe phenotype, including epilepsy, mild intellectual disability, behavioral abnormalities and early death due to liver failure.

E. Jansen, Radboud UMC and his team discovered the three new subtypes.

CONGENITAL DISORDERS OF GLYCOSYLATION WORLD CONFERENCE

The power of advancing patient-oriented research united

FAMILIES AND PROFESSIONALS

United Shaping the Future for CDG

July 15-16, 2017 in Leuven, Belgium

More information available here!

CDG CARE Global Corner

News from Europe!

Authors: Dr Rita Francisco **(**CDG Patient Advocacy Group Manager and researcher for Portuguese Association for CDG (APCDG) and Vanessa Ferreira (APCDG founder and volunteer, coordinator of the international research network for CDG (CDG & Allies PPAIN)

European Reference Network on Hereditary Metabolic Diseases (MetabERN)- an initiative that will improve overall quality and provision of care on CDG and related rare metabolic diseases.

The MetabERN is supposed to be the European Reference Network for the Metabolic diseases. The MetabERN is responding to the call for the establishment of European Reference Networks (ERNs) launched by the European Commission as laid down in the Directive on the patients' rights in cross-border healthcare. For more information about MetabERN visit HERE.

The MetabERN will be composed by a Multidisciplinary Team (MDT), with 1681 physicians (from 18 countries) taking care of more than 40000 patients (1/3 adults and 2/3 pediatric) with 7 disease categories. **We managed to have CDG, as one of these categories. Patients with a CDG are almost 1% of the total.**

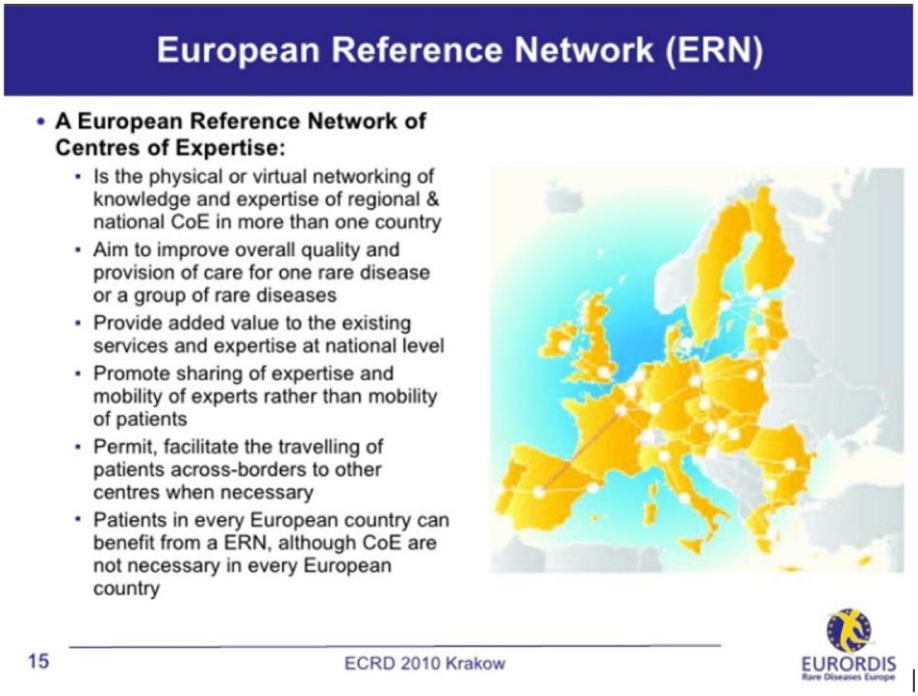

Figure : What is an European Reference Network (ERN), goals and benefits for rare diseases. Full presentation is available HERE.

Importantly, EURORDIS developed European Patient Advocacy Group (EPAG) for each ERN disease grouping. These ePAGs bring together elected patient representatives from EURORDIS member organisations and ensures that the patient voice is heard throughout the ERN development process. The CDG community is currently represented by Dr Rita Francisco, our CDG Patient Advocacy Group Manager (she is researcher among our association, APCDG). The application for MetabERN has been done on the 21st June 2016. The first screen, for the eligibility, ended up with a positive result. The second screen will be done from a technical committee, in October. It is a difficult recognition to be obtained, but let's hope it will be positive too!
The aim of the MetabERN will be focused on:

- prevention and screening
- diagnosis/new diseases diagnosis
- management
- epidemiology
- education
- virtual counselling
- dissemination
- clinical trials
- patient empowerment
- research

#CDGNews

#CDGNews: CDG One-to-One interview with Andrea Berarducci - CDG Mother and Advocate. In this interview Andrea talks about receiving a CDG Diagnosis, Family Life and her role as an Advocate. A testimony of strength and love! Not to be missed! Full interview available at http://bit.ly/2eAJen8

A motivational campaign for CDG community was launched!

The campaign **#CDGBelieve/#CDGAcredita** was launched. It aims at *sharing motivational quotes* that may help families to overcome the *feeling of isolation. Follow the campaign on* Facebook (SindromeCDG page) and related social networks (@CDG_Portugal, LinkedIN). Below you can see an example of posts we are spreading among all social networks.

CDG CARE (Community Alliance and Resource Exchange) is a nonprofit organization founded by parents seeking information and support for a group of disorders known as Congenital Disorders of Glycosylation (CDG).

Our mission is to promote greater awareness and understanding of CDG, to provide information and support to families affected by CDG, and to advocate for scientific research to advance the diagnosis and treatment of CDG.

Visit us on the web at www.cdgcare.com **or send an e-mail to** info@cdgcare.com**.**