ISSUE NO. 96 WINTER 2023

Chromosome Disorder Outreach Newsletter

Letter from the President

Dear Friends of CDO,

As we approach the end of another year, we find ourselves reflecting on the incredible journey we've shared and the meaningful impact we hope CDO has made in the rare disorder community. Your support has been the driving force behind our ability to continue for over 31 years, and we are immensely grateful for your dedication to our mission. In 2023, your generosity allowed us to expand our genetic counseling team, we now have 2 geneticists and 2 genetic counseling students working to help families. This increases CDO's ability to provide even more detailed and accurate information quickly to the newly diagnosed who sometimes may have to wait months for specialists appointments. Our personalized Ask the Doctor and Library programs have also provided positive impacts on those affected by rare chromosome or gene disorders.

None of this would have been possible without your belief in our cause and your willingness to stand with us in making a difference. As we look ahead to the coming year, we are excited about the opportunities and challenges that await.

We hope that if you have time, you too will consider becoming part of our team. Volunteering can provide an immensely fulfilling experience. Volunteers have the opportunity to directly impact the lives of individuals with very rare disorders in positive ways. If you would like to join us, please reach out to let us know your interests, what specific skills you possess and your availability and we will find the perfect role for you. Your contribution no matter now big or small will help CDO in our ongoing efforts to raise awareness and understanding of rare chromosome and gene disorders. Contact CDO at info@chromodisorder.org for more information. And thank you for considering this opportunity to bring a brighter future to the rare disorder community.

And in the spirit of the season, we wish you and your loved ones joy, peace, and fulfillment. May the coming year bring even more reasons for hope and celebration. Thank you for being an integral part of the CDO family. We are profoundly grateful for your support and look forward to another year of collaboration, growth, and positive change. With warm wishes,

Warmest wishes, Linda Sorg, CDO President

Phone: (561) 395-4252 Email: info@chromodisorder.org

The 2024 CDO Calendar

Perfect holiday gift that supports CDO

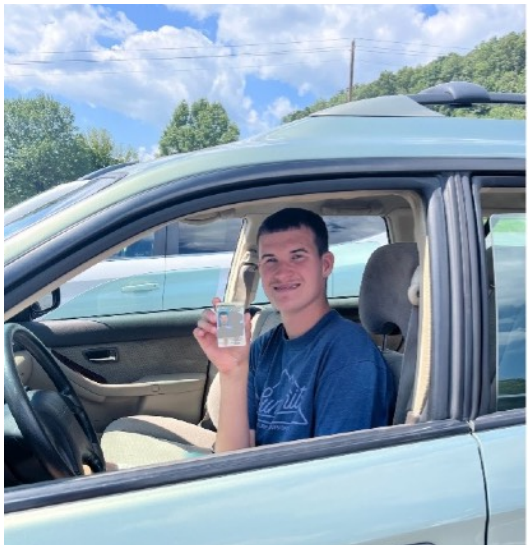
We Do It For You

CDO is a Great Nonprofit

New Media/ Books

What to read and watch

Luke's Journey of Hope, Love, and Perseverance:
By Luke’s Mom



On November 19, 2006, Luke embarked on a remarkable journey as he entered this world, becoming the cherished firstborn of my husband Brian and me. My name is Chrissy, and I am honored to share the inspiring story of Luke's journey—a tale of hope, love, and unwavering perseverance. This narrative is dedicated to all parents navigating the challenges of raising a child with a disability, serving as a beacon of encouragement and a testament that with determination, the impossible can be achieved.

From his earliest days, Luke's life seemed to follow the typical path of babyhood—filled with adorable blue ribbons, snug cuddles, and toy trucks. However, as time passed and milestones came and went, I, a special education teacher in a small town in Pennsylvania, USA, began to sense that something was amiss. The milestones Luke was meant to reach were delayed, and my intuition told me that he needed specialized attention.

Amidst doctor's appointments and reassurances that "he's just a boy" and "it takes time," my motherly instincts remained steadfast. It was a pivotal moment when I decided to bring my own Mom along to Luke's next doctor visit, determined to secure a referral to a neurodevelopmental specialist. Armed with the support of another strong woman, we advocated for Luke's needs, and the referral was finally granted.

That first visit to the neurodevelopmental specialist was fraught with apprehension. Tears flowed as I grappled with the uncertainty and "what ifs." Accepting the news that your child has a disability is an emotionally turbulent experience, but within the darkness, a glimmer of light emerged. During our hours of research, I stumbled upon Emily Perl Kingsley's poignant poem "Welcome to Holland." It became a source of solace during those early days in the realm of disabilities. Despite my background in special education, this was my son, and I resolved to be his steadfast advocate.

The diagnosis finally emerged—Luke had a rare chromosome disorder known as 48 XXXY syndrome. The medical community had limited knowledge of this condition, and we were essentially treading uncharted waters. Armed with this knowledge, we refused to let limitations define our son's potential. We embraced therapies, interventions, and resources that promised to nurture Luke's growth.

Through countless doctor's appointments, therapies, and insurance battles, we championed Luke's development. We demanded the best educational environment, inclusive opportunities, and a support system that saw beyond his challenges. Every time we were told "he cannot," we defiantly responded with "he can, he will."

As Luke progressed through school, his triumphs multiplied. He exceeded expectations, walking, talking, and engaging in tasks that his diagnosis said he shouldn't. Guided by the mantra of "you can do anything," he blossomed into a young man with an indomitable spirit. Today, Luke stands at the threshold of the tenth grade, an embodiment of resilience and determination. He mows lawns, participates in Unified Special Olympics Bocce, he manages the school's varsity baseball team, and recently completed driver's education to earn his Pennsylvania driver's license—a feat that seemed unfathomable given his diagnosis. The journey was undoubtedly arduous, filled with obstacles and doubts, but Luke's story stands as a testament to the power of unwavering parental love and advocacy.

To parents currently facing similar challenges, remember that you are your child's greatest advocate. Luke's story reminds us that with determination, love, and perseverance, incredible strides can be made. The road ahead might be filled with bumps, but each hurdle is a chance for your child to shine. Every success, no matter how small, is a step toward a brighter future. As Luke continues to defy odds and break barriers, his story radiates hope to families facing adversity. Believe in your child's potential, and you'll find that the journey is as extraordinary as the destination. Let us all be inspired by Luke's journey, reminding us that in the face of adversity, hope prevails, love conquers, and perseverance leads to remarkable achievements.

LASTEST RESEARCH

For more information see….

chromodisorder.org

Important new research articles are selected monthly by Dr. Iosif Lurie, MD PhD and summarized for publication on our website.

22q11.2 Microdeletion

22q11.2 microdeletion is the most common microdeletion syndrome in humans; it is associated with congenital heart defects, palate abnormalities, developmental delay, immune deficiency, facial dysmorphisms, and more. A standard of prenatal screening is NIPT, which screens for chromosomal anomalies has begun to include microdeletion syndromes such as 22q11.2 since 2015. Newly published article provides a literature review to provide up-to-date guidelines for 22q11.2 screening and diagnosis testing in the prenatal period.

Langer-Giedion Syndrome (LGS)

Langer-Giedion syndrome (LGS), also known as Type II Trichorhinophalangeal syndrome (TRPS), is a rare disorder noted by chromosomal deletions at 8q24. LGS is characterized by the presence of multiple exostoses and mild-to-moderate intellectual disability, in addition to the classic TRPS

manifestations of distinct craniofacial and skeletal abnormalities. Researchers in this newly published article aim to better differentiate phenotypes between the different types of TRPS.

9p Deletion Syndrome

9p deletion syndrome is a rare autosomal dominant disorder characterized by deletion in the short arm p of chromosome 9; its main manifestations are intellectual disability and craniofacial abnormalities, but there have been some patients with reported cardiac anomalies. Researchers analyze a cohort of 10 patients with a molecular diagnosis of 9p deletion syndrome to further characterize its cardiac phenotypes.

Ring Formation on Chromosome 7

Ring formation on chromosome 7, r(7), is when the two ends of that chromosome fuse together, forming a circular structure. It is rare and characterized by growth and developmental delay, speech delay, intellectual disability, seizures, cardiovascular anomalies, dermatological abnormalities, cranial/facial anomalies, and genital/skeletal system abnormalities; Researchers introduce a new r(7) patient in this newly published research article and advocate for early genetic testing.

Did *You Know?*

Brochures: CDO adds new original brochures to our website each month. These brochures cover chromosome deletions, duplications and syndromes associated with specific disorders. Visit chromodisorder.org/library to view or download the more than 50+ brochures now available.

CDO Library: CDO adds 40-50 new research publications each month to our library. A few articles added recently included discussions about 3q29 deletion, 1q32 duplication, 8q21 deletion and 17q21.31 deletion. For a complete listing of all new publications added monthly to our library please visit chromodisorder.org/cdo-news and for more information on any article email info@chromodisorder.org.

2024 CDO Calendar: The 2024 CDO calendar, filled with 12 months of member's artwork and inspiration quotes is available at our Zazzle store. A small portion of all proceeds go back to support the work of CDO.

Additional Resource: Angel Flight NE - AngelFlightNE.org - coordinating free air transportation for patients and their families seeking medical care when travel via car or public transportation is impossible due to distance, health concerns or financial hardship. Angel Flight pilots donate their time, planes and most of all their hearts to serving their community and patients in need. *Flight Requests - 800-549-9980*

Ask the Doctor

CDO's geneticists answer hundreds of questions from members and website visitors each year. Below is a sampling of a few recent inquiries. Some details have been changed to preserve privacy.

To learn more about our program, view archived questions and answers or submit an inquiry, visit chromodisorder.org/ask-the-doctor or email askthedr@chromosdisorder.org

Q: Do you have any information on 8q13.2 duplication? I would like to know if this duplication could be causing the symptoms my child is experiencing.

A: In the literature there is only one case of duplication 8q13.2 that is compatible with the duplication found in this child. Addis et al. (2018) who studied patients with rolandic epilepsy found that one of their patients had 0.25 Mb duplication (67.996-68.249). Of course, there is no evidence that dup 8q13.2 and epilepsy in their patient were causally related. DECIPHER (a collection of unpublished patients with chromosomal imbalances) does not have any reports of similar duplications. In my opinion the tiny duplication of 8q13.2 in this patient is a benign familial variant unrelated to any clinical manifestations.

Q: I'm looking for information on 20q13.33 duplication. Thank you.

A: This patient has a 3.07 Mb duplication in the distal segment of 20q13.33. The clinical consequences of such a duplication are virtually unknown. There are dozens of reports of duplications of the distal 20q13.33 in association with deletions of different chromosomes (mostly due to familial translocations) but we cannot use these patients for comparison because their clinical manifestations could be caused by this associated imbalance. Information about "pure" duplications 20q13.33 is very limited. Only once (Souto et al.) duplication 20q13.33 was the object of publication. In all other cases patients with dup 20q13.33 were just briefly mentioned among other patients examined by the authors. For example, Chen et al. examined patients with patent ductus arteriosus (type of heart defect), and one of them had dup 20q13.33. Cucinotta et al. examined patients with autism, and two of their patients had different duplications within 20q13.33. Moreover, almost all these patients had duplications less than 1 Mb (and this patient has a 3 Mb duplication). All available clinical information about other patients is presented in an attached table.

DECIPHER (a collection of unpublished reports on patients with chromosomal abnormalities) has only five patients with pure duplications 20q13.33. Information about DECIPHER patients is presented in the same table. Unfortunately there are no other available publications about pure duplications of this segment.

Q: I'm hoping to find information on 1q31.1q32.1 to better understand my child's disorder.

A: This patient has a 13.7 Mb deletion in the 1q31.1q32.1 segment (190.043-203.768). This segment contains many genes, at least two of which definitely cause genetic disorders.

The gene CDC73 is responsible for hyperparathyroidism-jaw tumor (HPT-JT) syndrome and parathyroid carcinoma. Most patients with these conditions have point mutations in the CDC73 gene, but there are publications where these disorders are caused by deletions of these genes. Articles provided for reference.

The second important gene is the NYS7 gene, which can cause nystagmus (see the articles Hecht et al. and Sun et al.in the CDO library). Of course, not all persons with a deletion of this gene will have nystagmus (as well as not everybody with a CDC73 gene deletion will have HPT-JT). This patient's official report shows that the genes BRINP3 and ZBED6 were also affected. As far as I know, deletions of these genes have not been implicated in the origin of human disorders.

Only a few articles present a description of patients with relatively large deletions of this segment (see articles in the CDO library by Carter et al., Hyder et al., Kaur et al. [patient CDL-042-99P in their report], Milani et al., Takarada et al.).

There are several publications discussing patients with small deletions in this area that have not been reported in detail but only briefly mentioned among other patients examined by the authors. Some of these patients [with non-overlapping deletions within 190 Mb-204 Mb segment] had autism (7 patients in Cucinotta et al. research, and the patients Alayadhi et al., Calderoni et al., Chan et al.). I am not sure however that the small deletions in this area of 1q were causally related to autism. Manifestations in other briefly reported patients do not add any significant information regarding the clinical picture in such patients.

Iosif Lurie, M.D., Ph.D. Medical Geneticist CDO Medical Advisor

CDO has many articles in our library. For more information on any article please email info@chromodisorder.org

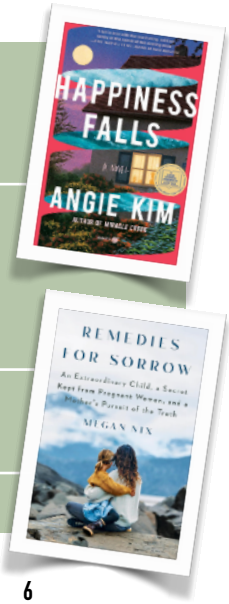
MEDIA CORNER

HAPPINESS FALLS BY ANGIE KIM

A nuanced story about bias, ableism, racism, family dynamics and language.

REMEDIES FOR SORROW BY MEGAN NIX

A lyrical parent's memoir about learning her child's disabilities were caused by a virus.



Chromosome Disorder Outreach
You Are Not Alone.

CDO is a 501C3 registered charity and does not employ professional fundraisers. All donations fund programs benefiting those with rare chromosome and gene disorders.