ISSUE NO. 88 FALL 2020

Chromosome Disorder Outreach Newsletter

Letter from the President

CDO Looks Forward

Dear Everyone,

We know it's been a hard year. For many of our members, 2020 has thrown challenge on top of challenge. But we are looking forward and looking to help, even if that help starts with providing a smile. Sometimes, something as simple as a piece of art, made with love and color and hard work, makes us smile. These works of art, and the love that went into them, are celebrated every year in CDO's calendar. In this issue, we celebrate one of our artists and the joy his art brings him and his family. Then in 2021, we can all share in that joy.

And a quick ask, if you are able, please consider supporting CDO with a year-end donation. Any amount is gratefully appreciated and is tax deductible even for those who do not itemize, up to $300.00. This is a little known benefit of the CARES relief act passed in March. If you do itemize, the CARES act provides a tax break too. Check with your tax professional for more details. Supporting small charities like CDO can really make a difference. Please help us continue our mission and make a positive contribution in a year that has been so difficult.

Warmest wishes, Linda Sorg, CDO President

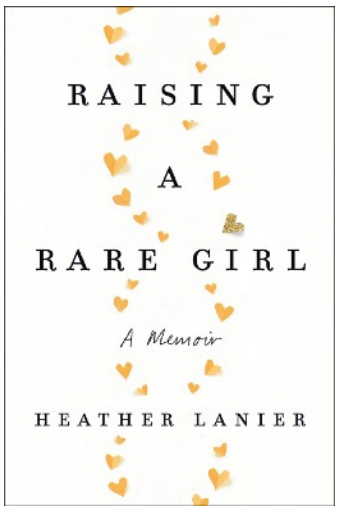
Phone: (561) 395-4252 Email: info@chromodisorder.org

The 2021 CDO Calendar
Coming soon… great holiday gift

We Do It For You
CDO is a 2020 Great Nonprofit

Latest Research Summaries
New summaries from Dr. Lurie

CDO IS HONORED TO BE ABLE TO SHARE AN EXCERPT FROM RAISING A RARE GIRL: A MEMOIR BY HEATHER LANIER, COURTESY OF PENGUIN PRESS.



"You see that top part there?" the young geneticist asked my husband and me in his kind voice. "That cotton-ball top?"

I nodded.

"Fiona's missing some genetic material on that cotton-ball top."

I'd never seen the fourth chromosome. I'd never heard its' end described benignly as a cotton ball. It was like a cloud or the tail of a rabbit. Fluffy, harmless.

The resident called this a "genetic deletion" and told us that the bit of genetic material had been missing in either the sperm or the egg that conceived my one-year-old daughter, Fiona. In other words, the missing bit had existed before her conception. It had existed prior to my DHA pills and hypnosis birthing tracks and organic grocery bills. It had existed before the dawn of her creation. If it had come from my egg, it had even existed before my own birth.

The resident continued. "We know Wolf Hirschhorn syndrome occurs in one out of 50,000 births. And it appears at the same rate across cultures. So it's nothing environmental. Okay? There's nothing you could have done differently. It just happens. Is this your first?" he asked.

My husband and I nodded.

"Congratulations!" he said heartily.

About Fiona's condition, the geneticist told us what I'd already read on the Internet. He described the facial features characteristic of people with her syndrome: high forehead, small chin, wide-set eyes. I nodded.

"She'll probably always be small," he said. "No matter how many calories you give her. Okay?.... And she probably won't learn to crawl or walk when other kids do. Okay?"

I nodded. I was trying to let each word settle into the various cracks inside me—the ones that held my aches and hopes and fears.

Then he said, "Most people with Wolf-Hirschhorn syndrome have intellectual disabilities to some degree."

It was the fall of 2012, one year before the *Diagnostic and Statistical Manual of Mental Disorders* replaced "mental retardation" with "intellectual developmental disorder." Our cherubic resident could have just as easily used *mental retardation*. But he didn't. And I noted the effect inside me. *Mental retardation* would have conjured images of my childhood elementary school, designed as a series of separate circular buildings. Long hallways connected each circle, and the kids who used wheelchairs or walked staggeringly or slurred when they spoke or didn't speak at all—they were taught in a different circle. Had the

doctor said *mentally retarded*, I would have envisioned this isolated circle, a pitiful and ostracized future for Fiona. But *intellectual* brought to mind a monocle. A *New Yorker* article. Attending a Gloria Steinem lecture. *Disability* could mean: an impairment that limits activity. So this is what I immediately grasped about the supine and onyx-eyed four-month-old who was still waking me three-plus times a night: attending a Gloria Steinem lecture while wearing a monocle and holding this week's *New Yorker* might pose a challenge for her.

I could live with that.

Looking back, I see the brilliance of the resident's language. "A genetic deletion," he called it, rather than "a genetic defect." A deletion was descriptive, something I did in a Word document daily, rather than "defect," which called to mind a broken part on a factory line. And he'd said "genetic anomaly" rather than "abnormality." An anomaly was a rarity, an outlier. In simulations of the universe, a planet like Earth is a statistical anomaly, and yet look at all the life it sustains.

This is when I first experienced disability as a flexible reality, bent and twisted by our notions of the body—and which bodies we think are worthy of living.

On this afternoon, the geneticist's language offered the not-so-common impression that my kid could be both significantly disabled and 100% right. This is not a standard view from the medical world. Among my fellow Wolf-Hirschhorn syndrome parents, I've heard horror stories. One woman received her daughter's diagnosis in utero and was told by her OB that she "should" terminate. At 26-weeks pregnant, she was given a three out-of-state locations to call immediately. (She never did.) Another mother also pregnant, met with a geneticist who repeatedly used the word "burden," explaining that her daughter would not only be a burden to the family but to society. "They basically made us feel like crap for NOT wanting to terminate," the mother told me. Plenty of parents recalled a diagnosing doctor using the words "vegetable" and "low quality of life." In one of the more disturbing stories, one mother only days after giving birth was shown a handout about the syndrome that featured a picture of a dead fetus. In the soupy, soft, tender hours postpartum, I cannot fathom processing such a message. She was told that her son would probably be "vegetative" and have "little to no personality." The doctor handed her and her husband information about a home for medically fragile children and said that they could leave their son at the hospital.

There is no good scientific reason for a doctor to be so absolute. He had access to the same 2008 peer-reviewed article I'd found online, which stated that *Intent to communicate appears to be present in most individuals with WHS* and *Slow but constant improvement has been observed over time in all individuals with WHS*. Nine years later, the mother shares a video online of her kid clapping and writes, "Here's my supposedly 'vegetative' child dancing at his school performance last week." But nine years before, the message she received was that, regardless of whether her boy lived or not, he would not really be alive. "It was a horrible time in my life," the mother wrote.

In the poker game of doctors' words, we were dealt aces.

"We won't put limits on her, okay?" the resident said. "We'll help her be all that she can be."

The resident did a powerful thing that day: through language and framing, he took my daughter's life back from a culture that might label her as less-than, and he returned that life to us. The person with the final word would be Fiona, who was lying in a onesie on the examining table, mesmerized like most babies by the ceiling lights.

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: Regarding 6q23.3 deletion with a diagnosis uncertain. Could it be Angelman Syndrome?

A: The deletion in this patient involves only one gene, AHI1. The "central" part of this gene is absent, whereas its "beginning" and "end" are not affected. It's evident that this gene cannot function normally.

In the literature I found only 2 reports on patients with similar deletions of 6q23.3: Dailey-Schwartz et al. found 0.017 Mb deletion (135.716-135.733) in one of their patients with hypoplastic left heart syndrome. Krutzke et al. reported 0.08 Mb deletion (135.712-135.794) in the patient with multiple congenital anomalies. This patient, however, had two other deletions: 4.88 Mb deletion in 15q11.2q13.1 and 0.46 Mb deletion in 5q14.2. Definitely, the loss of the AHI1 gene could not cause these defects.

Mutations of the AHI1 gene may cause Joubert syndrome. This syndrome is an autosomal recessive condition. It means that damage (a mutation or deletion) of both copies of this gene is necessary to produce any harm. In this situation I recommend examining the AHI1 gene on the intact chromosome 6. If there is a mutation of this gene clinical findings (including ataxia) may be attributed to Joubert syndrome. If, however, there is no mutation of another AHI1 gene deletion 6q23.3 can't explain the child's problems.

Angelman syndrome is caused by various abnormalities of the UBE3A gene on chromosome 15, but the records submitted by the family show neither methylation defects nor a deletion of UBE3A. Sometimes causes of Angelman syndrome are not evident, but currently other genetic factors responsible for this syndrome are not known.

FAMILY STORY

The Jacksons

To share your family story, email info@chromodisorder.org

Darius Jackson is my 29 year-old, young adult son born with Chromosome Deletion 13q 31-32. Shortly after his birth, my husband and I were given his chromosome disorder diagnosis. I remember that moment as if it was yesterday, but I can't tell you all that was said after hearing, "your son has a rare chromosome disorder. And there's not much information and not sure what you can expect…."

We are grateful, Darius' growth and development exceeded above and beyond our expectations! But like many other families of special needs children, we have an enormous challenge and tremendous task in trying to create a productive and happy life for our son.

His life started out with early intervention including physical, occupational, and speech therapy at 3 months old. Darius is intellectually delayed. His speech was delayed, and we discovered later he had a hearing loss in his right ear. Features on his right side like his thumb don't bend, his right ear is low set, and his eye color is blue. Our family is African American and Indian descent, so blue eyes are unique! But I'm told not unheard of. Other characteristics include short stature, immature balding, and flat feet. His speech is limited but has improved with consistent speech therapy. Darius is verbal and articulates as best he can. It's difficult at times to understand what he's saying, and this can frustrate him.

Living in New York City can be an advantage for a child with a disability because of its varied services, and it allows independence. Before this global pandemic, Darius was independent in taking the express bus to his private day program at JCC Manhattan, a social and recreational program designed to enhance social skills in an integrated community through cultural, athletic and educational opportunities. He's been employed at the Disney Store for five years, handing out baskets to customers and doing some product placement on shelves with a job coach twice a week, which he also travelled to by bus independently.

With the onset of Covid-19, his schedule came to a squeaking halt, and he's now zooming his activities including a baking class he attended every Saturday, which he loved.

Darius loves sports and could name many minor league baseball teams. He's a Boston Red Sox fan - don't ask me why! We still don't understand since our family are Yankee fans! It's been difficult for him not going to a game this year.

One of Darius' greatest triumphs and milestones was attending a four year college-based certificate program for young adults with intellectual disabilities called Career & Community Studies, where I learned what my son was able to do! Darius to this day, still amazes me. He is a quiet, vibrant, funny, and resourceful young man. He is an only child but has a few cousins.

Darius has grown leaps and bounds despite his disability, and we are so grateful. Now, is the next chapter, we are nervous....yet hopeful. My desire is to have Darius living in a supported community, where he will continue to strive and have some independence with the support his needs. I hope sharing Darius' story will encourage other families.

Sincerely,
Delores Jackson, Darius' mom

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.

New Chromosomal Research:

Population prevalence of copy number variants (CNVs)

Estimates of the population prevalence and inheritance patterns of recurrent copy number variants (CNVs) associated with neurodevelopmental disorders are lacking. This article presents a first glimpse.

It is well known that chromosome microdeletions or microduplications in several areas (1q21.1, 3q29, 15q11, 15q13, 16p11.2, etc) are associated with a wide range of neurodevelopmental disorders. At the same time in many cases the same microdeletions or microduplications can be found in the healthy parents of affected kids. However, the prevalence of such copy number variants (CNVs) in a general population remains unknown.

The authors studied the prevalence of several CNVs potentially causing neurodevelopmental disorders in a large cohort of unselected Norwegian families (mother-father-child). Participation in the study was offered to all pregnant women at 17 weeks of pregnancy, 41% agreed to participate. Families of non-Norwegian descent were excluded. A total analysis of 12,252 families examined showed CNVs in 59 newborns. So basically 1 out of every 200 newborns in Norway has one such CNV. Approximately 2/3 of these CNVs (39/59) were inherited, ~1/3 occurred de novo. Out of 59 CNVs found in newborns 25 were deletions and 34 were duplications. The percentage of inherited cases was higher in patients with duplications compared to kids with deletions. There were 13 de novo deletions and only 7 de novo duplications.

Mothers and fathers of infants had CNVs with the same frequency (43 found in mothers and 44 in fathers). However, most inherited CNVs were of maternal origin (most likely there is a selection against sperm cells with CNVs).

Deletions 1q21.1 and proximal deletions 16p11.2 were found in 6 cases, each (~1:2000), deletions 15q13.3 in 5 (1:2500), duplications 15q11.2 and deletions 17q12 in 3 (~1:4000). Although this data is preliminary it is the first glimpse of population prevalence of copy number variants.

https://chromodisorder.org/latest-research-articles/copy-number-variants/

Smajlagić D. et al. Population prevalence and inheritance pattern of recurrent CNVs associated with neurodevelopmental disorders in 12,252 newborns and their parents. “Eur. J. Hum. Genet.” 2020 (ahead of print).

SUPPORT CDO

DONATE NOW

If you can, please help support CDO during this difficult time.

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CDO ARTIST SPOTLIGHT

Meet Christian… a blossoming artist

Twenty year-old Christian (duplication 7q11.23 and autism) returns as an artist for the 2021 CDO Calendar. His first submitted in 2012 (see below). His works are completed at school, with the majority presented to his mom as gifts for holidays. CJ's school, the Able Academy in Naples, Florida celebrates and encourages student work, as does his family. CJ's mother, his biggest fan, believes he expresses his emotions, without anxiety, through his art. His proud mom, Melissa, shares, "I believe his artwork promotes the most positive feedback that he gets from peers and is his primary source of pride." Find another beautiful piece of his work in the 2021 calendar. Chromosome Disorder Outreach is so proud to share these masterpieces!

Research Study Opportunity

Chromosome Disorder Outreach Inc. Disclaimer: Please always contact your personal healthcare provider if you have questions or concerns. CDO accepts no responsibility for the misuse of information contained within our many publications. Any research study posting is provided as a courtesy only and does not imply endorsement or recommendation by CDO.

Using genomic analysis to define the molecular causes of symptoms in patients with Chromosome 9 P Minus Syndrome

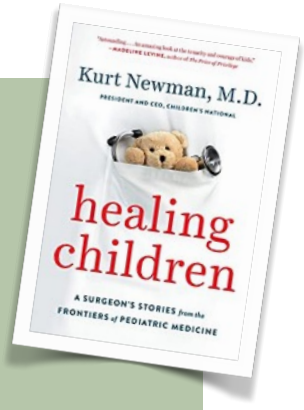
Research Site: Washington University School of Medicine, St. Louis, Missouri USA

The goal of our research project is to identify the specific genes that are deleted in people with 9 P Minus Syndrome and correlate these genetic abnormalities with specific characteristics of each affected person to gain insights needed to develop therapeutic strategies. Each individual who participates in this research project (or her/his parent or legal guardian) will need to provide informed consent, a detailed summary of her/his medical and family histories by providing medical records or access to medical records, and specific characteristics through a standardized examination and/or questionnaire, and a blood sample drawn from the arm and placed in a special blood tube that we will provide. DNA will be extracted from each person's blood sample and state of the art gene code deciphering (called whole genome sequencing analysis) on as many as 100 affected people will be used to determine the exact location of the deleted region of the 9th chromosome in each person. We anticipate that our analysis will help us identify a core set of deleted genes that are consistently associated with specific characteristics of people with 9 P Minus Syndrome. Once the set of deleted genes is in hand, we will use genetic methods, including gene editing technology, to develop new insights into how the missing genes function to alter cells. These studies will be supplemented using blood cells that we will immortalize and store from the original blood sample to investigate, at a molecular level, how the deletion of these genes causes the specific characteristics observed in chromosome 9 P minus patients.

Contact: F. Sessions Cole, M.D. (**fcole@wustl.edu**)

BOOK CORNER

Healing Children: A Surgeon's Story from the Frontiers of Pediatric Medicine,
Kurt Newman, M.D.



From an NPR interview with Dr. Newman: "We want to do more for kids, and there are so many exciting discoveries. The frontier of pediatric medicine is so alive with new ideas and innovation. That's what drives us …"

Chromosome Disorder Outreach
You Are Not Alone.

CHROMOSOME DISORDER OUTREACH

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Family Helpline: (561) 395-4252 or info@chromodisorder.org

CDO is a 501C3 charitable organization.

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