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LETTER FROM THE PRESIDENT

Dear Members -

CDO was recently contacted by the *Chan Zuckerberg Initiative* which among other programs has created the *Rare As One Project*. This project partners with the rare disease community to lift up patient-led research and provide support in the form of tools, grants, training and capacity building. Unfortunately as CDO does not have a staff scientist at this time we were not eligible to apply for this project. But that does not mean we cannot reach out to the *Rare as One Project* coordinators and let them know more about what we do and hope to accomplish in the years ahead. Just in the last 12 years we have registered more than 7000 individuals and families from 75 countries. New cytogenetic techniques are now allowing for the recognition of previously undetected anomalies which further ensures our membership will continue to grow. Although CDO is not directly involved in any research for chromosome or gene mutation disorders, we are willing to collaborate with researchers on their chromosome disorder studies and any clinical manifestations. Members and their families benefit too - as any new treatment information is learned, that knowledge is passed along.

Additionally CDO has a library which includes at least 7,500 publications on different forms of chromosomal pathology. And new information is received weekly. Remember, information packets are available to all members. CDO also condenses and publishes important new research data on our website monthly. As time goes by, we continue to learn more and more about these rare disorders.

Thank you all for your continued support of CDO and rare disorder research.

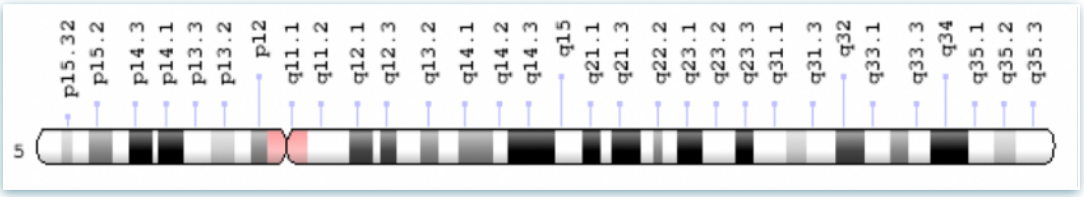
Best wishes, Linda Sorg

And a huge thank you too to Dr. Iosif Lurie for his expertise and knowledge of chromosome disorder pathology - the information he has provided to our members over the years has been invaluable.

New Research

Chromosome 5

Corrêa T, Feltes BC, Riegel M. Integrated analysis of the critical region 5p15.3-p15.2 associated with cri-du-chat syndrome. Genet. Mol. Biol. 2019, ahead of print.



Cri-du-chat syndrome (CdCs) is caused by a deletion of the distal part of the short arm of chromosome 5. The clinical characteristics of CdCs are well known and include a cat-like cry, psychomotor delay, intellectual disability, microcephaly and dysmorphic facial features. Many patients have also abnormalities in the heart and other systems. However it is still unclear which genes or combination of genes may be responsible for these defects. Analyzing six patients with typical manifestations of the syndrome, the authors found that all six had 10.8 Mb as the smallest area of overlap (SRO) in 5p15.33p15.2 segment. This area of 5p contains 44 genes.

Further analysis (including topological analysis) showed that genes SLC6A3, TPPP and CCT5 from SRO region may be responsible for neuronal development. The changes to the SLC6A3 and TPPP-coded proteins could result in neuronal changes associated with hyperactivity, anxiety, and depression. Moreover, SLC6A3 also interacts with CCT5 and is associated with processes that include memory and learning.

The deficiency of genes CTNND2, TERT, and MED10 may be the primary contributor in regards to the behavioral and cognitive impairments seen in CdCs patients. These three genes affect processes related to neurogenesis, DNA repair, and apoptosis.

Network analysis indicated that the genes MTRR, CEP72, NDUFS6, MRPL36, and MED10 may be associated with the development of congenital heart defects, microcephaly, and other abnormalities in CdCs. These genes were found to be associated with processes that included DNA repair, cell cycle control, apoptosis, ATP synthesis, and electron transport.

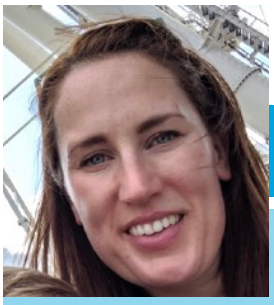
Chromosome 22

Lundin J, Markljung E, Baranowska Körberg I, et al. Further support linking the 22q11.2 microduplication to an increased risk of bladder exstrophy and highlighting LZTR1 as a candidate gene. Mol Genet Genomic Med. 2019, v. 7 (6), e666.

Bladder exstrophy is a rare birth defect resulting in the malformation of the bladder and urethra. It is part of the bladder exstrophy-epispadias complex (BEEC). In several previously published reports the children with bladder exstrophy were found having duplications of 22q11.2 area (although the vast majority of patients with dup 22q11.2 do not have this defect).

The authors performed array comparative genomic hybridization (array-CGH) of 76 Swedish patients with BEEC and found three patients with 22q11.2 microduplications, including inherited and de novo microduplications (occurring spontaneously and not inherited from parents). Increase of dup 22q11.2 among patients with BEEC is highly significant statistically.

The authors also analyzed the protein coding genes in 22q11.2 region of twenty BEEC patients without 22q11.2 duplications. One patient had a missense variant in the LZTR1 gene, predicted to be pathogenic. Previous studies in mouse models have also identified the LZTR1 gene as a potential gene that contributes to the BEEC phenotype. The authors concluded that the LZTR1 variant should be considered a prospective candidate gene in the genetic component of BEEC.



Meet CDO's Newest Board Member: Kathy Wiens

I'm located in Quebec, Canada and work in the field of occupational health. In 2015, my son was born with many health issues that were found to be related to a rare chromosome mutation of the TBX1 gene on chromosome 22. I have found connecting with other families to be incredibly rewarding and am happy to volunteer with CDO to help continue their mission. - Kathy

Volunteers Needed!

Please help CDO compile statewide listings of resources for our members. If you have been successful in navigating and locating the resources of your particular state, please share all that you have learned with CDO. We will then organize this data in a state by state guide and post it on our website and Facebook pages to help others. Contact info@chromodisorder.org if you can help.

Thank you!

ASK THE DOCTOR

12q21 Deletion and Growth Hormone Therapy

QUESTION:

As of right now my son is only having issues with growth, he is delayed in walking and talking but is getting therapy. However the doctors here say that he needs to undergo a 3 hour test for growth hormone, but from what I have read children with this rare chromosome disorder do not always have a hormone problem, but I read it has been given and helped with growth. This is why I'm reaching out because everything is so new to me, I am sure also with more information on this i will be able to learn more.

ANSWER:

I could not find any publications regarding the effects of growth hormone therapy in patients with deletions of 12q21. Growth delay is a common manifestation for many chromosomal disorders, and the existing literature usually shows a positive response for growth hormone therapy in many other forms of chromosomal pathology. Most likely such a therapy will be effective also for this patient. Of course the action of growth hormone is limited to growth velocity and such a therapy will not affect the other manifestations of this disorder.

Iosif Lurie, M.D., Ph.D. (New articles on this deletion are available in the CDO library.)

1q21.1 Deletion Prenatal Diagnosis

Question: Recent genetic testing through microarray came back with a 1q21.1 microdeletion: However, follow-up ultrasounds show no anatomical issues. All measurements are normal and that of a normal baby. Given limited research in this space, we would like to know if there have been cases of child with normal prenatal ultrasound but post birth the child had disorders such as developmental delays, behavioral problems, etc. associated with 1q21.1 micro deletion? Any additional information you can provide and /or uidance is much appreciated.

ASK THE DOCTOR… CONTINUED

ANSWER:
There is a strong association between del 1q21.1 (including "proximal" deletions as in this case) and a wide spectrum of neurodevelopmental disorders [developmental delay, autism, schizophrenia, etc].

The presence of such a deletion, however, does not guarantee that this person will have such conditions. In several families similar deletions were inherited from clinically normal parents. Cytogenetic testing of the parents may be important: if one of them has the same deletion it will decrease the probability of neurodevelopmental disorders in the child (although will not be able to exclude it completely).

Several new articles providing further information about the possible effects of deletion 1q21.1 are now in the CDO Library.

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

STEM cell therapy

QUESTION:
Just wondering if you can possibly answer a question please. My daughter is 7 and has a chromosome deletion. This has caused severe speech and language and global development delays, etc. Can stem cell therapy work for children with a chromosome deletion?

ANSWER:
1) In my opinion stem cell therapy theoretically may be helpful for conditions when the patient's problems are caused by the gene(s) constantly producing abnormal proteins or not producing normal proteins. For example, this might be helpful for the treatment of hemophilia which is due to mutations in the normal proteins necessary for blood clotting. They are either not produced (or their production is very low).

When we are dealing with chromosomal pathology the situation is more complicated because many genes are active mostly in developing tissues (brain, heart, kidneys, etc.), and even if the patient receives a new set of these genes, the damage which occurred in embryonic development cannot be repaired. For example, if the patient has polydactyly (six fingers) due to a deletion a new set of genes will not restore the normal structure of his/her hand. For this reason I do not think that stem cell therapy may be helpful for persons with chromosomal deletions or duplications (at least in the near future).

2) I am not sure whether stem cell therapy has been approved for treatment of any hereditary disorders. -Iosif Lurie M.D., Medical Geneticist, CDO Medical Advisor

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PODCAST CORNER

Mama Bear Podcast - Special needs parents discussing the beautiful highs and sometimes extreme lows that can come with parenting on such a unique journey.

Parenting Special Needs - Podcast from Parenting Special Needs Magazine.

DNA Today - A Genetics Podcast - Information on advancements in genetics with a wide variety of topics and speakers.

Patient Stories with Grey Genetics - The August 6 episode will feature Leah Moore, who shares her experience as a mother to a child with Cri Du Chat syndrome. In her interview, Leah expresses the challenges she faced raising a child with intellectual disabilities. You can listen on your podcatcher of choice or simply visit the Grey Genetics website to download this episode.

CHALLENGING CHROMOSOMES WITH COURAGE: JASE

Our names are Joe and Tori Smith. Our son, Jase, was diagnosed with a rare chromosome disorder. In all our research, we came across your foundation [CDO] and contacted you all. After the support and information given to us and reaching out to other parents, we realized there is not a lot of funding. We decided to do a fundraiser in honor of our son with all net proceeds to be donated to the Chromosome Disorder Outreach. Our hope is that all families can be one step closer to a better understanding of chromosome disorders and specifically Xq28 duplication.

Jase was born on September 18, 2015. By all appearances, he was a completely normal and healthy baby. At seven weeks old, he was admitted to UNC Hospital for pyloric stenosis and underwent surgery on his stomach. By the time he was 1 1/2 years old, he had multiple ear and respiratory infections causing him to be hospitalized on many occasions. Up to this point he was still not talking or crawling. His pediatrician kept telling us to just wait it out, and then finally Jase was referred to an early childhood development coordinator where he received therapy. We then were referred to the CDC autism center in April 2017 where he was diagnosed with autism. Then we were referred to a geneticist at UNC hospital to make sure there were no other underlying issues. In September 2018, he was diagnosed with Xq28 duplication. Jase is affected in many ways such as speech delay, flaccid muscles, respiratory and immune system issues as well as the most recent diagnosis of SVT, a heart condition. Jase is a strong loving boy who when not sick enjoys life to the fullest. He touches the hearts of everyone he meets - leaving an everlasting memory. He works hard every day with all his therapists to try and overcome the odds. We want to take the the time again to thank you for your hard work and dedication with research. We will continue to be in touch with any new updates. We have included a check which is all the money we made selling BBQ plates along with a motorcycle ride as well as a few pictures of Jase so you can see one of the faces you are working to help.

Sincerely, The Smith Family

Joe and Tori Smith's fundraiser raised over $6,700.00 in support of Chromosome Disorder Outreach! These funds will go towards maintaining our genetic consulting program which is overseen by Medical Geneticist, Dr. Iosif Lurie, M.D., PhD. CDO locates information and provides analysis on the rarest of chromosome and gene disorders. We are working hard to continue to expand this program. We cannot thank the Smith family enough for all their hard work and efforts. And wish them and their son, Jase, the very best.

CDO MEMBER MEETINGS

"Member Meetings" are a new feature the Board of Directors has added to our closed/private Facebook Support Group.

Long time board member Heidi Lerner will be run the meeting. She will do a LIVE video in the Facebook group one time a month. Heidi will introduce a topic for discussion about a week prior to the meeting. We would also like to hear from our members regarding issues they would like to discuss. Interacting during the LIVE video should be a great experience for our members.

CDO is a non-profit organization providing support & information to individuals and families diagnosed with any rare chromosome disorder. Information contained in this newsletter should be used for informational & supplemental purposes only. Please always contact your personal healthcare provider if you have questions or concerns. CDO accepts no responsibility for the misuse of information contained herein.

CDO has been Top Rated for several years running. Help us get there again in 2019!
If you love our work then tell the world! Stories about us from people like you will help us make an even bigger impact in our community. GreatNonprofits – the #1 source of nonprofit stories and feedback – is honoring highly regarded nonprofits with their 2019 Top-Rated List. Won't you help us raise visibility for our work by posting a brief story of your experience with us? All content will be visible to potential donors and volunteers. It's easy and only takes 3 minutes! Go here to get started! https://greatnonprofits.org/reviews/write/chromosome-disorder-outreach-inc