

How to Conquer a Chromosome Abnormality— What is the treatment potential for some with a chromosome abnormality?



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Special points of interest:

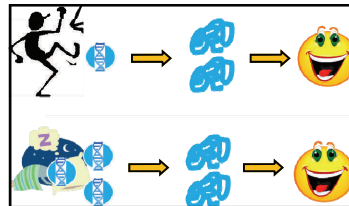
- * Changing gene expression
- * Identifying treatments
- * Getting Answers

What can be done—changing gene expression

What treatment is available for persons with chromosome abnormalities? We recognize that you cannot replace the missing chromosome nor remove the extra chromosome. However, treatments can be devised to counteract the effects of the chromosome abnormality—especially if you know the genes involved. This seems simple and straightforward yet has not been

done for chromosome abnormalities.

When we talk about treatments, we intend the term to be used very broad-



ly in the mechanisms used to achieve the goal. What we fundamentally need to do is to change gene expression. For deletion conditions, we need to upregulate some genes to make one gene do the work of two. For duplication conditions, we need to make three or four genes pull back and reduce output to the normal level of two genes.

Treatments

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There are many known ways to change gene expression. This is not a new concept. We each actually have the ability to change gene expression through diet. One example is alcohol dehydrogenases. As many of you have learned, if you rarely have a drink of alcohol, you quite easily begin to feel the effects. In contrast, if you drink the same amount of alcohol every day for two or three weeks, you no longer feel the effects of a single glass of alcohol. This is because of a very simple mechanism of increasing the production of the key proteins called alcohol dehydrogenases that break down and metabolize alcohol.

There are also drugs that we know can

affect the production of key proteins. For example, some adults take a medication called a statin which is used to treat certain disorder of lipid metabolism. Statins very specifically increase expression of important proteins that help the body get rid of this undesirable fat.

There are also experiential forms of treatment that have benefits. For example, the early use of hearing aids in children with hearing impediments has substantial long-term cognitive benefits.

There are also targeted means of improving outcomes. For example, there are computer programs such as Fast ForWord® which have been

shown to be beneficial in individuals with auditory processing disorders.

While these treatments are not necessarily specific for children with chromosome 18 abnormalities, there is no reason to believe that they would not be beneficial in children that have these conditions.

Treatments

Chemical

- *Dietary—alcohol dehydrogenases
- *Drug—statins

Experiential

- *General—early use of hearing aids
- *Targeted—Fast ForWord® for auditory processing disorders

Getting Answers

“We can devise treatments to counteract the effects of a chromosome abnormality—especially if we know the genes involved.”

We see parallel roads that together will get us to the answers we seek. First is a clinical assessment which provides a variety of useful information. First, it allows us to understand the deficits. Secondly, it helps us identify some potential productive roads of treatment or intervention. In addition, when the children are followed for a prolonged period of time, we begin to understand the natural history. That is, we learn what happens when this two-year-old becomes an eight-year-old or an 18-year-old. The most common questions clinicians are asked by families of children with chromosome abnormalities are: Will my child grow up to be healthy? Will my child be able to

graduate from high school? Will my child be able to have a family? We only learn the answers to these questions by following children for a very long period of time.

The second aspect of getting answers is the molecular assessment. This assessment allows us to obtain a well-defined understanding of where the actual genetic defect is located on the gene. Over time, this will help us understand what are likely consequences of a particular genetic defect. And finally, by correlating the clinical features with the molecular features, we can identify which genes are most important—that critical eight or ten genes that are responsible for the majority

of the phenotypic features. Then we can begin to identify what treatments could conceivably benefit—such as medications or other forms of intervention.

Getting Answers

Clinical Assessment

- *Descriptive > treatment (management)
- *Natural History

Molecular Assessment

- *Define molecular defect
- *Mechanisms of rearrangements

Correlation of Clinical & Molecular

- *Finding key genes
- *Understanding mechanisms of disease > treatment



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Our Motto

To provide individuals and families affected by chromosome 18 abnormalities with comprehensive medical and educational information with a focus on treatment options.

For more information, you may contact the authors and principal investigators of the Chromosome 18 Clinical Research Center at the phone numbers or email shown to the left.

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Information provided by The Chromosome 18 Clinical Research Center to:



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We are on the web!

<http://pediatrics.uthscsa.edu/centers/chromosome18/>