Medicine
UNIVERSITY OF TORONTO

STUDY OF THE WILLIAMS SYNDROME INVERSION IN CHROMOSOME REPLICATION

PARTICIPANT INFORMATION SHEET

What is the goal of this study?

We previously found an inversion (or flipping) of the region on chromosome 7 that is commonly missing in people with Williams-Beuren syndrome (WBS). This form of chromosome 7 (WBSinv-1) is found in up to 5% of the general population, but is found in parents of children with WBS at a much higher frequency (between 25 and 30%), suggesting that it is a risk factor for the deletion.

We would like to gather more information in order to better understand the effect of the WBSinv-1 chromosome on the type of cell division by which germ cells are produced. It is the swapping of segments between chromosomes during this cell division that results in the deletion, or sometimes duplication, of the WBS region. We would like to know whether carriers of the WBSinv-1 chromosome have more germ cells (eggs and sperm) that carry either a deletion or duplication of the WBS region, so increasing their chance of having a child with the WBS deletion or duplication.

This study aims to determine how the WBSinv-1 chromosome affects chromosome recombination by studying germ cells in carriers and non-carriers of the WBS inversion. The frequency of the WBSinv-1 chromosome is much higher in parents of children with WBS, which is why we are asking for participants from WBS families.

Who can participate?

An accurate way to look at recombination events is to look directly at the germ cells themselves, and the only easily accessible germ cells are sperm. If you are the **father of a child with WBS**, we are asking whether you would be willing to consider participating in a new study to try to determine how the inversion affects the WBS region. Your child should have a confirmed molecular diagnosis of WBS (a positive FISH test).

What does this study involve?

Part A. Testing for the WBSinv-1 chromosome

1. ***A blood sample from you***
   We will initially require you to donate a 10 ml blood sample so that we can test for the WBSinv-1 chromosome. At the present time we are unable to test for the inversion using any other method. The blood sample can be drawn by your family physician and we will provide a FedEx number for shipment to our laboratory.

2. ***A consent form signed by you***
   The consent form outlines the study, what will happen to your blood sample, and any potential risks or benefits associated with participation. This study has been reviewed and approved by the University of Toronto Research Ethics Board.

3. ***Result of WBSinv-1 testing***
   Should you be found to carry the WBSinv-1 chromosome, we will invite you to donate a semen sample for our study (see Part B). If you are found not to carry the WBSinv-1 chromosome, you may still be invited to donate a sperm sample for this study, as we need to study sperm from both carriers and non-carriers of the inversion.
   You may request to view the results of your inversion test results be reported to you, or you may request that the results of inversion test remain anonymous.

Part B. Study of sperm in WBSinv-1 carriers

1. ***A semen sample from you***
   The semen sample is produced by masturbation at your home. The sample is sent to Calgary where we will look at chromosome 7 using fluorescent dyes. Using cytogenetic techniques to label the region of chromosome 7 with fluorescent dyes, we will study more than 20,000 individual sperm cells from a single sample. If you decide to enroll in this study, we will send you a sterile container for the sample, detailed instructions for sample preservation and shipping to the laboratory and postage-paid shipping materials.

2. ***A consent form signed by you***
   This consent form outlines the study, what will happen to your semen sample, and any potential risks or benefits associated with participation. This study has been reviewed by the University of Toronto Research Ethics Board and the consent form has been approved by both of them.

3. ***A summary of your medical and environmental history***
   We will ask you to share information about anything in your history that may have had an effect on the chromosomes in your germ cells (sperm). This would include things such as smoking history, alcohol consumption, and any previous medical treatment such as radiation. This information will help us to exclude the influence of any other factors when we look at your sperm cells.

Why is this study important?

Although we know that carrying the WBSinv-1 chromosome increases the risk of the WBS region undergoing deletion or duplication, we do not know extent of this increased risk. Neither do we know whether other chromosome rearrangements occur, since these may result in chromosomes that are not compatible with fetal development, and result in miscarriage. Looking directly at thousands of sperm will give us unique insight into what kinds of chromosome rearrangements occur, and how their frequency is altered in carriers of the WBSinv-1 chromosome.

In the short term, we will generate an accurate measure of the frequency of deletion or duplication of the WBS region at 7q11.23 in germ cells from people with, and without, the WBSinv-1 chromosome. We will also identify other chromosome 7 rearrangements, if they occur.

In the long term, this information will help us to generate more accurate risk factors for having a child with the WBS deletion, in individuals who carry the WBS inversion, and in individuals who do not. We also hope that the study will be applicable to other syndromes where inversions pre-dispose to the loss or gain of genes.

Where can I get more information?

For further information or for a copy of the study consent forms, and details of how to participate please contact:

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