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Child & Family Research Institute
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INVITATION:
You have been invited to participate in this research study because you or a family member have been diagnosed with a genetic condition or have an X chromosome abnormality. Each participant is to receive his/her own consent form.

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

Before you decide, it is important for you to understand what the research involves. This consent form will tell you about the study, why the research is being done, what will happen to you during the study and the possible benefits, risks and discomforts.

If you wish to participate in this study, you will be asked to sign this form.

Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

BACKGROUND
Females have 2 X chromosomes and Males have 1 X chromosome. Most genes on the X chromosome are only meant to function with one copy being active. X-chromosome inactivation (XCI) is a normal mechanism for compensating for the extra X chromosome in females. XCI involves the inactivation of most genes (not all) on one of the two X-chromosomes. In an individual the process is generally random (one X is activated in 50% of the cells and the other X is activated in the other 50% of the cells). Mosaicism is the term used to describe two different populations of cells. Mosaicism within an individual for an activated or inactivated X chromosome is common because it is generally a random process. However sometimes one tissue type may show the normal random (non-skewed) XCI but a different tissue type may show non-random (skewed) XCI., Non-random XCI can be linked to presentation of X-linked disorders in females or other genetic conditions, and is used as a marker for other conditions like cancer. This non-random XCI is termed XCI Skewing.

For decades, XCI has been routinely assessed using a method associated with the Androgen Receptor (*AR*) gene. The AR gene is located on the X-chromosome q arm. Most chromosomes have a long arm designated “q” and a short arm designated “p”. The AR method relies on a process that is uninformative in some cases and does not always correlate with the few other assays for XCI that have been developed. Our goal is to develop new assays along both arms of the X-chromosome that can be implemented in a routine diagnostic lab like the BC Children’s Hospital Molecular Genetics Lab in a reliable manner, as well as to further our understanding of the interpretation of skewing results. This research is important for predicting outcomes in carriers of mutations on the X.

PURPOSE:
The goal is to develop several novel assays along both the X p and q chromosome arms, such that not only can non-random XCI be assessed in multiple tissue types but also the direction of skewing at different regions along the X-chromosome arms.

WHAT THE STUDY INVOLVES:
Participation involves release of medical/health records related to the genetic diagnosis or X chromosome abnormalities in you or a family member (lab/pathology report on any tissues, ultrasound reports, Medical Genetics/Specialty consult notes). The medical records allow us to verify the results we derive from the analyses.

Participation also involves donation of any samples sent to pathology for analysis and donation of four tubes (approximately 2 teaspoons) of blood from each family member. Obtaining samples from various tissue systems in an individual may help to confirm if tissue mosaicism is related to the condition's presentation.

The total amount of time needed is approximately 20 minutes. Each participant is to receive his/her own consent form.

POSSIBLE HARMS & DISCOMFORTS:
There may be some discomfort associated with the placement of the needle for blood withdrawal and occasionally bruising, swelling, feeling faint or dizzy and/or the rare chance an infection may result. Disclosure of genetic or tissue marker research data could result in discrimination by employers or insurance providers toward you or your biological (blood) relatives. The chance that research data would be released is estimated to be small. All counseling will reside with the original health care provider that requests the study.

RESULTS:
Results will be provided to a participant's referring health care provider when requested to confirm a clinical diagnosis or for reproductive health counselling. We do not have an estimated turn around time for the results as this study is unfunded and completed on a volunteer basis by lab personnel. When results are provided, the counselling regarding results will reside with the original health care professional who requested the study. Results will only be provided to the requesting health care provider. The health care provider will contact you to inform you that the results are available. It is up to the health care provider to determine whether results will be provided by an in person appointment or whether a phone appointment is sufficient. No information regarding paternity will be provided.

BENEFITS
Participation in this study may help to further our understanding of the X chromosome and associated conditions.

REMUNERATION
There will be no payment for your participation in this research study.

WITHDRAWING CONSENT: Your participation in this research is entirely voluntary. If you decide to enter the study and later decide to withdraw at any time in the future, there will be no penalty or loss of benefits to which you are otherwise entitled, and your future medical care will not be affected. If you wish for your stored blood samples/data to be destroyed upon your withdrawal, you may contact the principal investigator of the study, at 604.875.3015. The investigator may decide to discontinue the study at any time, or withdraw you from the study at any time. If you choose to enter the study and then decide to withdraw at a later time, all data collected about you during your enrolment in the study and up to the time of withdrawal will be retained for analysis.

CONFIDENTIALITY:
In Canada genetic information as a form of personal information is protected legally by privacy and discrimination Acts. Your confidentiality will be respected. No information that discloses your identity will be released or published without your specific consent to the disclosure. However, research records and medical records identifying you may be inspected in the presence of the Investigator or his or her designate, Health Canada, and the UBC Research Ethics Boards for the purpose of monitoring the research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law. The medical records allow us to verify the results we derive from the analyses. We will be collecting personal identifiers such as year and month of birth because many genetic factors are associated with age and prevent sample mis-handling.

You will be assigned a unique study number as a subject in this study. Only this number will be used on any research-related information collected about you during the course of this study, so that your identity [i.e. your name or any other information that could identify you] as a subject in this study will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate (research co-ordinator, lab manager, lab technician). The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law. The list that matches your name to the unique study number is in a password protected electronic file. The electronic file is kept on the lab server only accessible with an authorized computer login and password.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected and also give you the right of access to the information about you that has been provided to the Robinson lab and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request.

Your de-identified samples and DNA will be stored in Dr. Robinson's laboratory at the Child & Family Research Institute (CFRI). The de-identified samples labelled with the unique study code will be stored until it is used entirely for the study objectives or until such DNA is withdrawn. The laboratory is in a secure building accessible only by photo key card. De-identified DNA samples will be studied at the CFRI. De-identified samples may be sent to other co-investigators on this study for analysis, but the sample/DNA will not be used for any purposes other than those outlined in this consent. At no point will any identifiable data associated with the de-identified sample be sent to outside investigators. Your de-identified samples will not be sold and will not be used for commercial purposes.

Any data or samples, sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries *[for example, the Patriot Act in the United States]* dealing with protection of information may not be as strict as in Canada. However all data and or samples, that might be transferred outside of Canada will be re-coded (this means it will not contain your name or personal identifying information) before leaving the study site. By signing this consent form, you are consenting to the possible transfer of your information and samples, to organizations located outside of Canada. Dr. Robinson will obtain the proper ethics approval prior to transfer of data or samples outside of Canada.

Signing this consent form in no way limits your legal rights against the sponsor, investigators, or anyone else. Your rights to privacy are also protected by the *Freedom of Information and Protection of Privacy Act of British Columbia.* This Act outlines rules for the collection,

protection, and retention of your personal information by public bodies, such as the University of British Columbia and its affiliated teaching hospitals. Further details about this Act are available upon request.

WHO DO I CONTACT IF I HAVE ANY QUESTIONS OR CONCERNS ABOUT PARTICIPATION IN THIS STUDY?

If you have any questions about your participation in this study contact the Robinson Lab at 604.875.3015.

WHO DO I CONTACT IF I HAVE ANY QUESTIONS OR CONCERNS ABOUT MY RIGHTS AS A SUBJECT?

If you have any concerns or complaints about your rights as a research subject and/or your experiences while participating in this study, contact the Research Subject Information Line in the University of British Columbia Office of Research Services by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598).

SUBJECT'S ASSENT (> 14 years of age) TO PARTICIPATE IN RESEARCH

I have had the opportunity to read this consent form, to ask questions about my participation in this research, and to discuss my participation with my parents/guardians.** All my questions have been answered. I understand that I may withdraw from this research at any time, and that this will not interfere with the availability to me of other health care. I have received a copy of this consent form. I assent to participate in this study.

The parent(s)/guardian(s)** and the investigator are satisfied that the information contained in this consent form was explained to the child** to the extent that he/she is able to understand it, that all questions have been answered, and that the child** assents to participating in the research.

□ A member of Dr. Robinson's research team may contact me in the future for follow-up related to this study.

□ A member of Dr. Robinson's research team may contact me in the future regarding potential future research and for general information.

Print name of subject		Signature	Date
Print name of person obtaining consent	Study Role	Signature	Date

CONSENT TO PARTICIPATE:

· *I have read and understood the subject information and consent form.*
· *I have had sufficient time to consider the information provided and to ask for advice if necessary.*
· *I have had the opportunity to ask questions and have had satisfactory responses to my questions.*
- *I understand that all of the information collected will be kept confidential and that the result will only be used for scientific objectives.*

· *I understand that my participation in this study is voluntary and that I am completely free to refuse to participate or to withdraw from this study at any time without effecting my participation in the main study and without changing in any way the quality of care that I receive.*
- *I authorize access to my health record and samples as described in this consent form.*
- *I understand that I am not waiving any of my legal rights as a result of signing this consent form.*

· *I understand that there is no guarantee that this study will provide any benefits to me*
· *I have read this form and I freely consent to participate in this study.*
· *I have been told that I will receive a dated and signed copy of this form.*

□ A member of Dr. Robinson's research team may contact me in the future for follow-up related to this study.

□ A member of Dr. Robinson's research team may contact me in the future regarding potential future research and for general information.

Print name of subject		Signature	Date
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