Consent to Participate in a Research Study

Participant – Genetic Analysis

Study Title:

Molecular and Genomic Analysis of Autism Spectrum Disorder and Related Conditions

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Study Sponsor or Funder:

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Introduction

Throughout this form, "we" represents the SickKids researchers.

We would like to invite you to take part in our research study. This consent form describes the research study and what it means to participate. This consent form may have words that you do not understand. Please ask the study staff to explain anything that you do not understand. Please take as much time as you need to think about your decision to participate or not, and ask any questions you have. If it is helpful to you, you are encouraged to discuss the study with family, friends, your personal physician, other health professionals, or any members of your community that you trust. All participation is voluntary, and you are not under any obligation to participate.

Why am I being asked to participate?

You are being invited to participate in this study because you have, or a member of your family has Autism Spectrum Disorder (ASD) and/or a related condition.

Why is this study being done?

This multicenter research study is being done because we want to better understand what causes ASD and related conditions. All the information we collect from this research study will be kept in an international database. We know that genetics plays a role in the cause of ASD, so this study will involve genetic research. Genetic research involves isolating your genes from your sample(s). Every person has their own unique set of genes, or "genome". Genes carry the information that helps to determine your characteristics. Genes are made up of DNA; between people, the DNA sequence of a gene can vary slightly. These differences in DNA sequence are called variants. These variants may or may not be harmful. Genes are passed down from parents to children, but sometimes genes can change between generations or because of other factors (e.g., environment). Genetic research is being done in this study to help us find genes that may put us at risk of developing ASD and/or related conditions.

Specifically, we are looking for "genetic variants" in children with a diagnosis of ASD and/or related conditions. These differences to the sequence of the DNA can cause an error in the instructions for that specific gene. As a result, the body may not grow, develop or function properly. Similarly, a difference in how the DNA is turned on and off, referred to as an "epigenetic alteration", can prevent a gene from providing the required instruction that the body needs. By finding the genetic variants or epigenetic alterations involved, we hope to improve our knowledge of ASD and/or related conditions. This in turn, may help us (1) find different subtypes of ASD and related conditions (2) develop better ways to identify children at risk for these conditions earlier and (3) provide more effective support, intervention and medical care to children with ASD and related conditions. Genetic findings may also shed light on new targets for developing drug treatments.

What will happen in this research study?

Your participation in this study will involve providing a biological sample (blood and/or saliva and/or cheek swab) for genetic testing (described in detail below). If you previously had genetic testing, such as whole exome sequencing or whole genome sequencing, we may request to obtain that existing data for inclusion in our study if you and the testing organization or company agree to this. Additionally, we will need to collect "phenotype" information (details that describe physical, behavioural, or medical characteristics) about you/ your family. An example of phenotype information is noting whether you have a diagnosis of ASD and/or related condition. This information will help researchers identify patterns and make connections with the genetic data. To collect phenotype information about you/ your family, we will:

- Request to review your health chart from SickKids, as well as any additional institutions/ clinics, if available. We will collect information about your developmental, medical, and family histories as it relates to your diagnosis of ASD and/or related condition.
- Ask you to complete some questionnaires (between 4-7 questionnaires depending on your age) that will take about 1 hour to complete, at your leisure. The questionnaires are standardized forms that ask about your development and behaviour in order to provide us with basic phenotype information from all participating families.

What samples will be collected as part of this study?

A small blood sample (5-10mL or 1-2 tablespoons) or other biological sample (saliva and/or cheek swab) will be taken from you by a trained health care professional. DNA will be isolated from the sample collected. The DNA from your sample will be assigned a research code. This coded sample will be stored indefinitely in our research lab and may be used in future tests related to ASD and/or related conditions, as new technology becomes available.

If a sample was previously collected at SickKids or another hospital, we will ask the respective clinical lab (e.g. SickKids' Genome Diagnostic Lab) to check if there are any leftover samples. If a sample is available, by signing this consent form you allow us to request the sample(s) be released to this study. In addition, if a cord blood sample from you was previously stored at a biobanking company, we may request to obtain that existing sample for inclusion in our study if you and the company agree to this. This cord blood sample may be used to look at the pattern of epigenetic changes in your genetic data which can vary in different types of blood samples.

What type of research will be done on my samples?

In this study, your research sample will undergo genetic testing, which may include the following:

1. Whole Genome Sequencing or Whole Exome Sequencing: This analysis allows us to test all your genes at the same time (using one single experiment) to find variants in your DNA sequence.
2. Microarray testing: This analysis allows us to look for missing or extra sections of DNA, referred to as "copy number variants".
3. Epigenetic analysis: This analysis allows us to look for changes in the pattern of how genes are turned on and turned off, referred to as "epigenetic regulation".

Your samples may be used to create a living sample called a "cell line" that can be grown in the lab. This allows researchers to have an unlimited supply of your cells in the future without asking for more samples from you. Cell lines allow us to have a source of your DNA.

These technologies will provide researchers with an enormous amount of data. To help researchers make sense of the data, this data along with your health information describing the ASD and/or related condition (i.e. phenotype) will be stored in a large international genomic database housed in the "cloud" (i.e. online). Researchers (both academic and from for-profit commercial companies such as pharmaceutical companies) studying ASD and related conditions from anywhere in the world could ask for access to the international genomic database housed in the "cloud". This online database aims to promote access to many different types of researchers and provides research communities with a centralized resource to test ideas without repeating DNA collection and sequencing efforts.

For-profit companies may be interested in obtaining your biological samples such as your DNA and your cell lines. Below are your options for sharing your biological samples with for profit companies:

Future Research of Biological Samples – DNA/Cell Lines with for-profit companies:	
_____ Initials	Yes, you can share my cell lines with for-profit commercial companies such as pharmaceutical companies.
_____ Initials	No, you cannot share my cell lines for-profit commercial companies such as pharmaceutical companies.

It is important to understand that the genetic testing analysis for this study is focused on the individual with ASD and/or related condition in the family. Your biological family members, such as your parents and siblings, may be asked to participate to help us understand the importance of variants found in the individual with ASD and/or related condition. Your family members will be consented separately. Additionally, we

may use your sample to perform some functional experiments (e.g. looking at gene expression) to help interpret the effect of the variant.

How will my information and sample be stored?

All information and samples collected about you will be "de-identified" by replacing your identifiable information (e.g. name) with a "study number" prior to sharing. Your de-identified genetic and phenotype data will be sent to and stored in an international, online central repository (storage place), which are sometimes called data banks. These data banks will store your information indefinitely and allow other researchers to access your data for more research studies. We have put in place safeguards to protect the confidentiality of your identity when sharing research data, including genomic sequence data and/or phenotype information, with local and international researchers and databases.

Sharing of your samples and data is a mandatory part of this research study:

Your de-identified samples (e.g. DNA, cell lines), genetic sequencing data (e.g. whole exome sequencing, whole genome sequencing), and phenotype data (e.g. ASD diagnosis, development notes) will be shared with researchers as approved by the REB. This is a mandatory part of the study, which means it is required for the research study. If you do not consent to the mandatory parts of the study, you cannot be part of this study. This information will be shared two ways:

1. **Controlled-access Database for Coded Genomic and Research Data**
   Your "de-identified genetic and phenotype data will be available to anyone who requests and is approved to access the data bank. Because genetic and phenotype data may contain potentially rare or sensitive information, which when taken together increases the chance of identification, we will review the applicant and put agreements (signed contract) in place. The Data Access Compliance Office will review all applications for access to verify that the proposed study has received ethics approval from the relevant committee (when required) and that the study fits within the objectives of the REB approved international database. Applicants may include researchers at universities, hospitals, government agencies and some for-profit companies around the world who may be conducting research projects not only related to ASD, but also on other medical conditions. The coded data in the controlled-access database is stored on a cloud server that meets international security and safety standards and may be stored in different countries.

2. **Open-access Database for Anonymized Genomic Information**
   Your genetic data (e.g. whole genome sequencing) will be "anonymized" meaning that all personal identifiers (e.g. name, address), as well as any research codes will be removed and it will no longer be possible to link your genomic information with other information (e.g. medical information). However, it will be possible to tell which genomic information comes from the same family, without identifying the family. This anonymized genetic data will be publicly available to anyone without restriction. This is known as open access. Although only experts will know how to interpret this information, there is a chance that somebody could connect you with the information from the study of the sample you give. Researchers who access the open-access database may be conducting research projects not only related to ASD, but other types of research, including research on other medical conditions.

What if the researchers discover something about me?

Primary Findings:

We will tell you if the research genetic analysis identifies a genetic variant believed to be **associated with ASD and/or related condition**. Sometimes, the genetic finding is also associated with another health condition where the ASD is part of a larger genetic condition with additional health risks. Sometimes, the genetic finding associated with ASD and/or related condition may also reveal information about carrier status. People who are "carriers" of a genetic disorder are not affected by the disorder but have a chance of having a child with that specific genetic disorder. Knowledge of carrier status can be important for future family planning. For our study, these are all considered primary findings if the results are related to ASD and/or related condition.

If we identify a primary finding, the study clinician or genetic counsellor will discuss these findings with you. The study team will make appropriate referrals to discuss these findings. These findings will have to be verified in a clinical lab before the information is used for your health care and other important decisions. It is important that you understand that results from research may take a very long time (e.g. several years) and the turnaround time for results is very difficult to predict. This is due to the fact that the genetic testing used in this study is very new and generates a lot of data. It takes researchers time to sort through the complex information to make sense of the meaning, which depends on what is known in the scientific literature. Additionally, our understanding of the relevance of genetic results can change over time as new information becomes available and therefore, meaningful results may not become available until years into the study.

Incidental Findings:

It is important that you understand that although we may test your genome, we will not be reviewing all of this information in detail. Our research analysis is focused on genetic changes associated with ASD and related conditions. However, there is a small chance we may find a genetic variant unrelated to your ASD and/or related conditions, and we may learn something about you that you didn't expect. This is called an incidental finding. **Incidental findings are information that was discovered unintentionally.** Some incidental findings may be **medically actionable or medically non-actionable.**

Medically actionable finding:

This type of incidental finding means there is a high chance of a health problem AND treatment and/or screening is available for this health problem. If we discover medically actionable findings or if any new clinically important information about your health is obtained as a result of your participation in this study, we will let you know. We will only talk to you about those medically actionable findings that we think are likely to have a major effect on health. Seeing a medical specialist could be helpful as there might be specific health recommendations for you and/or family member(s). We will work with you, your family and your doctor(s) during this process. Because many of these variants are passed from parent to child, identification of one of these variants in you could have implications for biological (blood) family members' (such as parent(s) and siblings) health as well.

All medically actionable findings will be discussed with you. However, because these findings were done through research testing, the tests will need to be validated in a clinical laboratory before the information is used for your health care and other important decisions.

Medically non-actionable findings:

There are also medically non-actionable findings. These findings may indicate there is a high chance for a disease but there is currently no treatment and/or screening available (e.g., Alzheimer's or Huntington's

Disease). We will not return these findings to you; we do not return information on incidental findings that are not medically actionable. We will not place this information into your medical records at SickKids.

Future Contact:

We will contact you in the future to give you general updates about our study (e.g. newsletters), a new genetic research test with results and/or to tell you about additional studies that may be of interest to you. We ask that you keep your contact information up-to-date by informing us of any changes to your address or phone numbers.

What are the risks, harms or discomforts of the study?

Genetic Testing

When you give your biological sample for genetic testing, you are sharing genetic information, not only about yourself, but also about biological (blood) relatives who share your genes or DNA. While the study team will take precautions to protect your confidentiality, we cannot guarantee that other members of your family will respect your privacy.

Genetic information can never be fully de-identified. Procedures have been put into place that are designed to make it very difficult for the results from genetic research to be linked to you. Due to the rapid pace of technological advances in genetics, there may be a risk that the genetic information in the samples could be linked back to you. Not unique to genetic studies, there is also a risk of unintentional release of information. The potential re- identification or unintentional release of your information could lead to loss of privacy against you or your biological relatives. The potential future use of genetic information is unknown and therefore not all potential future risks are known. You should be aware that genetic information cannot be protected from disclosure by court order.

The potential psychological and social risks of participating and receiving genomic information are not fully known at this time. It may be upsetting to learn about genetic causes and medically actionable findings which may result in a new diagnosis or "label" for you. Because parent(s) and children can share genetic variants, the discovery of harmful variants in your genome may lead to identifying the same variants in your family members' genome. It may be upsetting to learn that other members of your family share harmful genetic variants with you. If the results of genetic tests do not fit with the information that you have given about your family, it may be that the test is faulty, or that the family information that you gave is wrong. For example, this might happen if the parents do not mention that their child was adopted, or that the biological father is different from the apparent father (this is known as non-paternity).

Sample Collection

Blood - there is a possibility of pain, bruising, swelling or infection. These discomforts are minimal and brief.

Cheek swab - there is a possibility of bleeding if too much pressure is applied. This discomfort is minimal and brief.

Saliva – there are no anticipated risks, harms or discomforts.

Questionnaires

There is an inconvenience of time related to filling out the questionnaires (~1hr) at the start of the study, but there is no time restriction for completing these questionnaires. While filling out the questionnaires, you may experience some anxiety, emotional and/or psychological distress due to the nature of the questions. You can choose to skip or not answer any question. If your responses indicate that there is a

serious risk of harm to yourself or others, confidentiality will be broken in order to protect you or another person. If we feel that you need urgent care as result of participating in this research study, we will intervene according to routine clinical care practices.

Are there benefits from being in the study?

To individual subjects:

You may or may not benefit directly from participating in this study. It is possible that we may be able to identify the genetic reason for ASD and/or related conditions in your family. This information may lead to helping doctors know what medical concerns to watch out for, change treatment plans, and determine the risk for you and other family members.

To society:

We hope that the information learned from this study will improve the understanding of ASD and related conditions and can be used in the future to benefit patients with a similar disease and/or health condition. The international databases that catalog data from this study may also allow for research beyond ASD and may help in the understanding of other medical conditions.

How will my privacy be protected?

We will respect your privacy. No information about you will be given to anyone or be published without your permission unless the law requires us to do this. Our funders (Genome Canada, Autism Speaks, Networks of Centres of Excellence of Canada, Canadian Institutes of Health Research, and the Ontario Ministry of Research and Innovation) are also committed to respecting your privacy.

If you decide to participate in this study, the SickKids research team will collect personal health information about you, including things learned from the study procedures. They will collect only the information they need for this study. The research team will also collect some personal information about you (name, address, phone number, email) for the purposes of contacting you. This personal information will not be shared outside of the SickKids research team.

All information collected about you will be "de-identified" by replacing your identifiable information (i.e. name) with a "study number". Only the "study code key" can connect the information collected about you to your identity. The study code key will be safeguarded by the SickKids research team. Even though the risk of identifying you from the study data is very small, it can never be completely eliminated.

The following people may come to the hospital to look at your personal health information to check that the information collected for the study is correct and to make sure the study followed the required laws and guidelines:

- Representatives of the SickKids Research Ethics Board and/or Research Quality and Risk Management team

The research team will keep any personal health information about you in a secure and confidential location for 7 years after the study ends and then destroy it according to SickKids policy.

Can I choose to leave the study?

It is your choice to take part in this study, participation is voluntary. You can change your mind at any time during the research study. The study team may ask why you are withdrawing for reporting purposes, but you do not need to give a reason to withdraw from the study if you do not want to. Withdrawal from the

study will not have any effect on the care you or your family will receive at SickKids. If you decide to leave the study, you can contact the Principal Investigator or a member of the study team to let them know.

Will I be paid and/or reimbursed if I join this study?

We will reimburse you for your parking expense or public transit expenses for visiting SickKids for blood collection, consenting or feedback as part of your participation in this research study. If you stop taking part in the study, we will pay you for expenses incurred up until that point.

It is possible that a commercial product may be developed as a result of this study. You will have no rights to nor receive royalties from any products that may be created as a result of this study or any future research studies using this research study data.

Will information about this study be available online?

A description of this study will be available on http://www.tcag.ca/projects/index.html. This website will not include information that can identify you. You can search this website at any time.

What if I am injured during/in this study?

If you suffer an injury from participation in this study, medical care will be provided to you in the same manner as you would ordinarily obtain any other medical treatment. In no way does signing this consent form waive your legal rights or release the study doctor(s), sponsors or involved institutions from their legal and professional responsibilities. If you require treatment for any injuries or illness related to your participation in the study, you should contact the study doctor immediately.

How will I be informed about new information?

We may learn new information during the study that you may need to know. We may also learn about things that might make you want to stop participating in the study. If this happens, you will be notified about any new information in a timely manner. You may also be asked to sign a new consent form that describes these new findings if you decide to continue in the research study.

What are my rights when participating in a research study?

You have the right to receive all information that could help you make a decision about participating in this study. You also have the right to ask questions about this study at any time and to have them answered to your satisfaction. Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form, you do not give up any of your legal rights against the study doctors, sponsors or involved institutions for compensation, nor does this form relieve the study doctors, sponsors or their agents of their legal and professional responsibilities.

You will be given a copy of this signed and dated consent form prior to participating in this study.

Will I receive study results?

Research results will be shared through journal publications, academic conferences, and the family information day. When the results of this study are shared, your identity will not be disclosed. Since this study is ongoing, research results will be shared as they become available.

Overall study results (aggregated results from all participants) will be available on our study website http://www.tcag.ca/projects/index.html). Individual family results will be discussed with you and your family as outlined above.

Who can I call if I have questions about the study?

If you have any questions during your participation in this research study you can contact the Principal Investigator, Stephen Scherer at 416-813-7613 or the research contact, Barbara Kellam at 416-813-7654 x301289 listed at the beginning of this consent form.

Research Ethics Board Contact Information

The study protocol and consent form have been reviewed by the SickKids Research Ethics Board (REB). If you have any questions regarding your rights as a research participant, you may contact the Office of the Research Ethics Board at 416-813-8279 during business hours.

Consent to Participate in a Research Study

Study Title: Molecular and Genomic Analysis of Autism Spectrum Disorder and Related Conditions

By signing this research consent form, I understand and confirm that:

1. All of my questions have been answered,
2. I understand the information within this informed consent form,
3. I allow access to my medical records and specimens as explained in this consent form,
4. I do not give up any of my legal rights by signing this consent form,
5. I have been told I will be given a signed and dated copy of this consent form.
6. I agree to take part in this study.

I consent to participate in this study.

Print name of participant	Participant signature	Date (DD/MM/YYYY)
Print name of person who obtained consent	Signature	Date (DD/MM/YYYY)
	Role of person obtaining consent	

If participant does not read English,
Please check the relevant box and complete the signature space below:

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to, and appeared to be understood by the participant.

☐ The person signing below acted as a translator for the participant during the consent process.

Language: _____

Name (print)	Signature	Date (DD/MMM/YY)

Optional Parts of Research Study

Study Title: Molecular and Genomic Analysis of Autism Spectrum Disorder and Related Conditions

Complete the following section only if you have biological samples (e.g. DNA, cord blood) or genetic data stored at another institution/lab.

If you have a DNA sample stored at another hospital, do you consent to the study team requesting access to this existing sample for use in this study?

Access to DNA samples from another hospital:	
_____ Initials	No, you cannot access DNA samples stored at another hospital
_____ Initials	Yes, you can request access to stored DNA samples and conduct research on these samples My DNA sample is stored at _____ [Name of hospital]

If you previously had genetic testing, such as whole exome sequencing or whole genome sequencing, do you consent to the study team requesting access to this existing data for use in this study?

Access to existing genomic data:	
_____ Initials	No, you cannot access existing genomic data for inclusion in this study.
_____ Initials	Yes, you can request access to existing genomic data and conduct research on this data My genomic data is stored at _____ [Name of organization/company/study]

If you have a cord blood sample stored elsewhere, do you consent to the study team requesting access to this existing sample for use in this study?

Access to cord blood samples from other companies/labs:	
_____ Initials	No, you cannot access cord blood samples stored at other companies or laboratories.
_____ Initials	Yes, you can request access to stored cord blood samples and conduct research on these samples My cord blood sample is stored at _____ [Name of company/laboratory]