



Consent to Participate in a Research Study

Parents or Guardian Consenting for Child – 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

As your child's Parent/Substitute Decision Maker, you are being asked to provide informed consent on behalf of your child. If your child gains the capacity to consent for themselves, consent will be sought from them and your consent for them will end. Throughout this form, "we" represents the SickKids researchers.

We would like to invite your child 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 allow your child 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 allow your child to participate.



Why is my child being asked to participate?

Your child is being invited to participate in this study because your child, 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 child's genes from their 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 child's 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 your child 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 your child/ your family. An example of phenotype information is noting whether your child has 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 your child/ your family, we will:

- Request to review your child's health chart from SickKids, as well as any additional institutions/ clinics, if available. We will collect information about your child's developmental, medical, and family histories as it relates to your child's diagnosis of ASD and/or related condition.
- Ask you to complete some questionnaires (between 4-7 questionnaires depending on your child's age) that will take about 1 hour to complete, at your leisure. The questionnaires are standardized forms that ask about your child's 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 your child by a trained health care professional. DNA will be isolated from the sample collected. The DNA from your child's 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 from your child 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 your child 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 child’s genetic data which can vary in different types of blood samples.

What type of research will be done on my child’s samples?

In this study, your child’s 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 child’s genes at the same time (using one single experiment) to find variants in your child’s 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 child’s 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 child’s cells in the future without asking for more samples from your child. Cell lines allow us to have a source of your child’s 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 child’s 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 child’s biological samples such as your child’s DNA and your child’s cell lines. Below are your options for sharing your child’s biological samples with for profit companies:

Future Research of Biological Samples – DNA/Cell Lines with for-profit companies:	
<hr/> Initials	Yes, you can share my child’s cell lines with for-profit commercial companies such as pharmaceutical companies.
<hr/> Initials	No, you cannot share my child’s 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 child’s biological family members, such as 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 child's sample to perform some functional experiments (e.g. looking at gene expression) to help interpret the effect of the variant.

How will my child's information and sample be stored?

All information and samples collected about your child will be "de-identified" by replacing their identifiable information (e.g. name) with a "study number" prior to sharing. Your child's 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 child's 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 child's identity when sharing research data, including genomic sequence data and/or phenotype information, with local and international researchers and databases.

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

Your child's 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, your child cannot be part of this study. This information will be shared two ways:

1. Controlled-access Database for Coded Genomic and Research Data

Your child's "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 child's 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 child's 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 your child with the information from the study of the sample that was provided. 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 my child?

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 child’s 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 child’s 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 child’s ASD and/or related condition, and we may learn something about your child 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 child’s health is obtained as a result of your child’s 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 your child 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 your child 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 child’s 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 child's 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 for your child. 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 provide permission to give your child's biological sample for genetic testing, you are sharing genetic information, not only about your child, but also about biological (blood) relatives who share your child's genes or DNA. While the study team will take precautions to protect your child's 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 your child. 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 your child. Not unique to genetic studies, there is also a risk of unintentional release of information. The potential re-identification or unintentional release of your child's information could lead to loss of privacy against your child or their 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 your child. Because parent(s) and children can share genetic variants, the discovery of harmful variants in your child's genome may lead to identifying the same variants in their family members' genome. It may be upsetting to learn that other members of your family share harmful genetic variants with your child. 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:

Your child 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 your child 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 child's privacy be protected?

We will respect your child's privacy. No information about your child 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 child's privacy.

If you decide to give permission for your child to participate in this study, the SickKids research team will collect personal health information about your child, 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 your child will be "de-identified" by replacing your child's identifiable information (i.e. name) with a "study number". Only the "study code key" can connect the information collected about your child to their identity. The study code key will be safeguarded by the SickKids research team. Even though the risk of identifying your child 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 child's 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 your child 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 have my child leave the study?

It is your choice, and your child's, to decide to take part in this study, participation is voluntary. You and your child can change your mind at any time during the research study. The study team may ask why you are withdrawing your child for reporting purposes, but you do not need to give a reason to withdraw your child from the study if you do not want to. Withdrawal from the study will not have any effect on the care your child or your family will receive at SickKids. If you decide to have your child leave the study, you can contact the Principal Investigator or a member of the study team to let them know.

Will my child be paid and/or reimbursed if they 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 or your child 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 your child. You can search this website at any time.

What if my child is injured during/in this study?

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

How will my child be informed about new information?

We may learn new information during the study that you and your child may need to know. We may also learn about things that might make you and your child want to stop participating in the study. If this happens, you and your child will be notified about any new information in a timely manner. You and your child 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 child's rights when participating in a research study?

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

By signing this form you do not give up any of your child's 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 your child's participation in this study.



Will my child 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 child's 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 child's 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 child's rights as a research participant, you may contact the Office of the Research Ethics Board at 416-813-8279 during business hours.



Consent for my Child 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 child's medical records and specimens as explained in this consent form,
4. I do not give up any of my child's legal rights by signing this consent form, I have been told I will be given a signed and dated copy of this consent form.
5. I agree to allow the person for whom I am responsible to take part in this study.

I consent on behalf of _____ to participate in this study

Print name of parent/guardian Parent/guardian 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/MM/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 your child has biological samples (e.g. DNA, cord blood) or genetic data stored at another institution/lab.

If your child has 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:	
<hr/> Initials	No, you cannot access my child's DNA samples stored at another hospital
<hr/> Initials	Yes, you can request access to my child's stored DNA samples and conduct research on these samples My child's DNA sample is stored at _____ [Name of hospital]

If your child 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:	
<hr/> Initials	No, you cannot access my child's existing genomic data for inclusion in this study.
<hr/> Initials	Yes, you can request access to my child's existing genomic data and conduct research on this data My child's genomic data is stored at _____ [Name of organization/company/study]

If your child has 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:	
<hr/> Initials	No, you cannot access my child's cord blood samples stored at other companies or laboratories.
<hr/> Initials	Yes, you can request access to my child's stored cord blood samples and conduct research on these samples My child's cord blood sample is stored at _____ [Name of company/laboratory]