The INVESTICATE project: Identification of New Variation, Establishment of Stem cells, and TIssue Collection to Advance Treatment Efforts

Information and Consent Form for Parents

Project Title: The INVESTICATE project

Principal Researchers: Dr. Carl Ernst, Ph.D., Douglas Institute, Research center, McGill University.

Protocol Number: 15/14

Institutions: Douglas Mental Health University Institute

Project financed by: McGill University, Department of Psychiatry

1. INTRODUCTION

We are conducting a research project on children with a neurodevelopmental disorder and members of their family. Examples of neurodevelopmental disorders are autism spectrum disorders, intellectual disabilities, and seizure disorders, among others.

We are soliciting your participation, as well as the participation of your child/children in this research project because at least one of your children has been diagnosed with a neurodevelopmental disorder, and the genetic tests that were made may or may not have revealed any identifiable mutation. His or her doctor has referred you to our research team.

2. VOLUNTARY PARTICIPATION

Your participation, as well as your child/children's participation, is entirely voluntary. This consent form tells you about the research project. Before agreeing that you and your child/children participate in this research project and signing the consent form, please take the time to read, to understand and to attentively consider the following information. You can also discuss it with other family members, or someone else you trust.

This document can contain words that you do not understand. Please do not hesitate to ask either the principal researcher or any other member of the research team and let them explain any word or information that is not clear.

When children under 18 years old are solicited to participate in a genetic research project, their parents need to provide consent for them. At the end of this form, we will thus request your consent for your own participation, as well as for the participation of your child/children.

3. DESCRIPTION OF RESEARCH PROJECT

The purpose of this research project is to analyze the DNA of families in which at least one member is diagnosed with a neurodevelopmental disorder and for which genetic testing may or may not have revealed any identifiable mutation. In this research project, we will use new tools that are developed in research and that are not available in most health care systems to study DNA

DNA is a molecule that contains all the transmissible genetic information which directs the cellular activity of our bodies. DNA provides a set of instructions that determine certain hereditary characteristics of an individual such as the color of their eyes or their blood type. The technology that we will use in this research project will allow us to obtain a large amount of genetic information, but we do not know yet the significance of all this information. We are hoping that this research project will help us further our knowledge on genetic information that may be related to neurodevelopmental disorders

4. WHO CAN PARTICIPATE TO THE RESEARCH PROJECT?

Participation in this study is dependent on an individual having a neurodevelopmental disorder. Inclusion of other family members in the study can significantly ease our understanding of the disease, so we also request participation from parents and related siblings, though this is not essential. Other family members related to the person with the neurodevelopmental disorder are also welcome to participate.

5. PROCEDURE OF THE RESEARCH PROJECT

We will request that DNA samples already collected at the hospital be sent to Dr. Ernst's lab at the Douglas Mental Health University Institute in Montreal, Quebec for analysis. If fibroblasts (from skin biopsies) have been collected these will also be requested. We will also request a urine sample from all family members willing to participate.

5.1 Blood samples

If your blood or your child/children's blood has not been already collected at the hospital for extraction of DNA, a sample of blood will be drawn from a vein in your arm as well as your child/children's) arm one time. This sample will be used for extraction of DNA. We will try to minimize the amount of blood taken and this will be determined by you or your child/children's age, weight, and health condition, but will be less than 10 mL for parents and less than 4 mL for children. This is less than 1 tablespoon of blood. If your blood and/or your child/children's blood has already been collected for DNA extraction, we will request a DNA sample from the hospital where the blood was collected.

5.2 Urine samples

We require a urine sample from your child, yourself and any other family member willing to participate in the study. We will provide you with a collection pot for this, and we need about 100ml of urine. We will isolate cells from urine so that we can study your son or daughter's illness. Specifically, we can use cells present in urine to isolate DNA and to make stem cells, which can be converted into any cell type in the body and offer a powerful tool which may help to understand your child/children's neurodevelopmental disorder. Stem cells will be able to develop into brain cells. Because each cell of the human body has its own blueprint, studies in brain development require brain cells to better understand disease. Our hope in these experiments is to model your child's disease in the proper cell type. Brain cells created from your child/children will be tested to try to understand the reason for the disease. Sometimes it can be helpful to collect urine cells from parents or siblings. This can allow us to compare urine-derived brain cells from an affected child to skin-derived brain cells from an unaffected sibling or parent.

These brain cells also provide us with the ability to assess new molecules and medications that may one day be able to treat neurodevelopmental disorders. While we are highly unlikely to provide any molecule of significance to your child, we do aim to test molecules that may reverse some features of disease in these cell models. While this project is aimed at therapeutic intervention, there are many hurdles to overcome and thus success in this area is likely to be very limited.

5.3 Skin biopsies (optional)

If you and/or your child/children has/have not had a skin biopsy taken at the hospital that referred you to us, we may request some of you to have a skin biopsy. This is not required for this project but can help us better understand neurodevelopmental disease by establishing comparison cells from the same family. At the end of this form, we will ask for your consent to undergo a skin biopsy. You are always free to accept or refuse to do it. If your child/children has/have had a skin biopsy taken at the hospital that referred you to us, we will request a sample from this biopsy.

Skin biopsies involve taking a very small piece of skin and are done routinely by doctors everyday in hospitals across Canada. A small (1mmX 1mm X 1mm, about the size of the tip of a pencil) piece of skin will be taken by a physician, after application of an anesthetic to a patch of skin, usually under the arm. After the application of a topical anesthetic cream, a small pen-like tool will be applied to the skin and excise a circular piece of skin, to a depth of 1mm, resulting in minor bleeding. You and/or your child may feel some minor discomfort in this area after the anesthetic has worn off, usually about 15 minutes after the procedure. Most procedures do not leave a scar, however it is possible that a mark is visible on this area of you or your child's skin even years later.

Skin cells are made up of fibroblast cells which are used by hospital testing centers to investigate your child/children's illness. We will use these skin cells to make stem cells, which are capable of becoming any cell type in the human body and offer a powerful tool which may help to understand your child/children's neurodevelopmental disorder. Those stem cells will then be able to develop into brain cells. Because each cell of the human body has its own blueprint, studies in brain development require brain cells to better understand disease. Our hope in these experiments is to model your child's disease in the proper cell type. Brain cells created from your child/children will be tested to try to understand the reason for the disease. Sometimes it can be helpful to collect skin cells from parents or siblings. This can allow us to compare skin-derived brain cells from an affected child to skin-derived brain cells from an unaffected sibling or parent.

These brain cells also provide us with the ability to assess new molecules and medications that may one day be able to treat neurodevelopmental disorders. While we are highly unlikely to provide any molecule of significance to your child, we do aim to test molecules that may reverse some features of disease in these cell models. While this project is aimed at therapeutic intervention, there are many hurdles to overcome and thus success in this area is likely to be very limited.

5.4 Duration of the research project

The complete project will last at least 15 years, though the total time per individual from DNA sequencing to creation of stem cells will take approximately three years.

5.5 Scope of the research project

Recruitment and DNA storage will occur at the Douglas Mental Health University Institute in Montreal, Quebec, Canada; however your (and your child/children's) DNA samples, cells grown from urine, and fibroblasts may be analyzed outside the Douglas Hospital Research Center but without any information that can identify them.

5.5 Access to medical records

The research team may want consult medical records in order to obtain additional information which could be pertinent to the research project. We will ask for your authorization to access your file and your child's/children's medical records. You are always free to accept or refuse to provide access.

6. STORAGE OF DNA AND FIBROBLAST SAMPLES

6.1 Identification of samples

All information, DNA samples, and fibroblast samples collected over the course of this research project will remain strictly confidential according the guidelines set by the law. In order to protect your identity and the confidentiality of the samples, only a code number will identify you. The sample will not be identified by name. The key linking your name to your code number will be kept by the principal researcher, in the case there is a need to link back the samples to you or your child/children. This can only be done by the principal researcher or by another individual designated by them.

6.2 Length of storage

Your DNA and fibroblast samples and your child/children's DNA and fibroblast samples will be stored at the Douglas Mental Health University Institute, for up to 7 years following the end of the research project, unless you provide consent for future use of your samples in another Information and Consent Form where a new length of storage will be described to you. At any time during this period you and your child/children may withdraw your participation and the sample and related information will be destroyed.

7. BENEFITS

You will receive no benefits from this study.

8. RISKS

8.1 Physical risks

Although the taking of the blood or fibroblast samples cause no serious problems for most people, it may cause some bleeding, bruising, malaise, dizziness, infection and/or discomfort at the injection site.

8.2 Socio-economic risks

One of the risks associated with this research project relates to the disclosure of the results or the disclosure of your participation and your child/children's participation to third parties. Mere participation in genetic research projects could compromise or diminish chances and the chances of your family of obtaining insurance (life insurance, disability, mortgage, or health) or certain types of employment.

9. CONFIDENTIALITY

9.1 Security of the data

During your participation and the participation of your child/children in this research project, the principal researcher and his team will collect and record the information concerning each of you in a separate study file. Only the data required to meet the scientific goals of the project would be collected.

This information could include information contained in your medical files or the medical files of your child/children (if you have granted access) concerning your past and present health condition, your lifestyle, as well as the results of the tests and other data relating to your samples. Your study file will also contain other information such as your name, sex, date of birth and ethnic origin.

All of the information obtained about you and your child/children and the results of the research project will remain strictly confidential to the extent prescribed by law. In order to protect your identity and the confidentiality of your information, only a code number will identify you. The key to the code linking your name to your study file will be kept by the principal researcher. Your information will be coded, encrypted and kept under lock and key. The study file will be kept at the Douglas Mental Health University Institute under the responsibility of Dr Carl Ernst. You and your child/children's participation in and the results of this study will not be included in your medical records. The results of this research project may be published or communicated in other ways, but it will be impossible to identify you or your child/children.

The research we are conducting may necessitate the release of samples to other researchers, including those outside of the Douglas Mental Health University Institute. At any point, your samples will be coded and will not be able to be linked to you by anyone else but the Principal Researcher, who has the key that links the code to your identity.

9.2 Third party access to study results

Unless you have provided specific authorization or where the law permits or a court order has been obtained, you and your child/children's personal results will not be made available to third parties such as employers, governmental organizations, insurance companies or educational institutions. This also applies to your spouse, other members of your family and your genetic counsellor, unless they are already involved in this study. Medically relevant results (i.e. mutations in genes known to be associated with a neurodevelopmental disorder) from this project will be communicated to you and anyone else you would like present at that time, via your genetic counsellor.

However, for the purposes of ensuring the proper management of the research, it is possible that a person mandated by the Research Ethics Board of the Douglas Mental Health University Institution, or the Douglas Mental Health University Institution, or a representative of Health Canada, may consult the research data as well as your medical records. All these individuals agree with the privacy policy.

You have the right to consult your study file in order to verify the information gathered and to rectify it if necessary, as long as the principal researcher or the Douglas Mental Health University Institution holds this information.

10. COMMUNICATION OF RESULTS

You can communicate with the research team at any moment in order to obtain information on the general progress of the research project.

One objective of this study is to identify mutation(s) in your child's DNA that may be associated with disease. Please note that, in most cases, we will not identify a mutation that is known to cause neurodevelopmental disease. However, if we do identify a clinically relevant mutation known to be associated with a neurodevelopmental disorder in your child, we will ask you, at the end of this form, if you want to be informed of the inheritance of this mutation, i.e., whether it came from both parents, one parent, or occurred sporadically. For your child/children participating in this study who do(es) not have a neurodevelopmental disease, we will wait until he/she becomes an adult and ask him/her if he/she wants to know if he/she is a carrier.

We do not routinely screen for incidental findings (mutations that may have some outcome on your health other than the ones we are looking for) in DNA, either from your child or from any other family members, so we will not have any data concerning how your genetic make-up make affect your health. However, there is a remote possibility of finding information not related to neurological disorders and that such information may be clinically significant: if this information affects your child during childhood and adolescence this information will be returned to you through the genetic counsellor. if this information affects you as an adult participant, we will ask you , at the end of this form, if you agree for this information to be communicated to the referring genetic counsellor.

11. GENETIC COUNSELLING SERVICES

At any time, you may request information about genetic counselling, if you do not already have one. We will guide you to appropriate genetic counselling.

12. COMMERCIALIZATION/RENUNCIATION

The analysis of your DNA sample, cells from urine, and/or fibroblasts may contribute to the creation of commercial products from which neither you nor your child will receive financial benefit.

13. CONFLICT OF INTEREST

There is no conflict of interest on the part of the researchers, collaborators or institutions involved in this research project.

14. RECRUITEMENT OF OTHER FAMILY MEMBERS

Over the course of the study, it is possible that we may ask you or a person you will designate, to contact other members of your family to offer them the opportunity to participate in the study. The researchers and their medical team cannot personally contact your family members for recruitment purposes. DNA and clinical information from other family members can sometimes provide important information about your child/children's illness, for example, by ruling out genetic mutations that are rare but unrelated to disease.

15. FREEDOM TO PARTICIPATE AND PERIOD OF REFLECTION

You and your child/children's participation is completely free and voluntary. The quality of medical services available to you will not be affected by your decision. You may take the time necessary to reflect on your decision and discuss your participation in the project with persons close to you before giving us your answer.

You and your child/children are free to withdraw from the study at any time while the samples remain coded (15 years). If you withdraw, the DNA sample will be retraced and destroyed. After said period samples will be remove from all identification and they cannot be remove.

16. COMPENSATION FOR EXPENSES INCURRED AND INCONVENIENCES

Any costs incurred by your participation in this research project will not be reimbursed, and you will not receive any compensation for your participation in this research project.

17. COMPENSATION IN CASE OF INJURY AND RIGHTS OF THE PARTICIPANTS

If you or your child/children should suffer any injury or prejudice as a result of your participation in this research project, you will receive the appropriate care and services for your medical condition without any charge to you.

By accepting to participate in this research project, you are not waiving any of your legal rights nor discharging the researchers, the institution or their civil and professional responsibility.

18. RESOURCE PERSONS

18.1 Members of the research team

If you have any questions concerning the research project or if you are experiencing a problem which you believe is related to your participation in the research project, you can communicate with the principal researcher responsible for the project, Carl Ernst, by phone at 514-761-6131, ext 3382.

For any additional information concerning the progression of the research project or for any change in address, please communicate with the project coordinator, Annie Bachiet, at 514-761-6131, ext 3376.

18.2 Ombudsman, ethics committee or authorized person

If you would like to discuss your participation with an individual not directly involved in the project, we invite you to contact the Service Quality and Complaints Commission, Toll Free Number : 1 844 630-5125 or by email at commissariat.plaintes.comtl@ssss.gouv.qc.ca

19. CONTROL OF THE ETHICAL ASPECTS OF THE RESEARCH PROJECT

The Research Ethics Board of the Douglas Mental Health University Institute approved this research project and is responsible for ensuring its monitoring. Any change or amendment made to the information/consent form or to the research project must first be approved by the Research Ethics Board.

20. CONSENT

20.1 Consent of parent 1 as a participant to the research project

Name of Participant (parent 1)_____

Consent to provide a sample of your skin: Providing a skin biopsy is not required for this research project but can help us better understand neurodevelopmental disease by establishing comparison cells from the same family. If you have not had a skin biopsy taken at the hospital that referred you to us, do you consent to undergo a skin biopsy for this research project, or if you have already had a skin biopsy, do you accept to give a sample of this skin biopsy for this research project?

YES or **NO** (please circle)

Consent to provide a urine sample: Do you consent to providing a urine sample for this research project?

YES or **NO** (please circle)

Consent to be informed of the inheritance of a mutation: If we do identify a clinically relevant mutation known to be associated with a neurodevelopmental disorder in your child, do you want to be informed of the inheritance of this mutation, i.e., whether it came from both parents, one parent, or occurred sporadically?

YES or **NO** (please circle)

For Clinically Significant Incidental Findings for Adult Participants: do you agree to be informed through a genetic counsellor?

YES or **NO** (please circle)

Consent to be re-contacted in the scope of this research project: We may wish to re-contact you in some cases, for example because we may need additional health information, or to invite other family members to participate in the study. Do you authorize us to re-contact you in the scope of this research project?

YES or **NO** (please circle)

Consent to be re-contacted for other research projects: A new consent will be necessary for the use of your coded DNA and information, as well as the use of your child/children's coded DNA and information in other research. May we re-contact you:

- To request your participation and/or the participation of your child/children in future research project?

  YES or **NO** (please circle)

- To ask for your permission to use your remaining samples and associated data, and/or your child/children's remaining samples and associated data in a future research project?

  YES or **NO** (please circle)

- To ask for your permission to put your remaining samples and associated data, and/or your child/children's remaining samples and associated data in a bank for future research projects?

YES or **NO** (please circle)

Consent to participate in this research project:

I have reviewed the Information and Consent Form. I acknowledge that the research project was explained to me, that my questions were answered to my satisfaction, and that I was given sufficient time to make a decision.

I agree to participate in this research project according to the conditions stated above. A dated and signed copy of the present Information and Consent Form was given to me.

Name of parent 1_____

Signature _____Date _____

20.2 Consent of parent 2 as a participant to the research project

Name of Participant (parent 2)
_____

Consent to provide a urine sample: Do you consent to providing a urine sample for this research project?

YES or **NO** (please circle)

Consent to provide a sample of your skin: Providing a skin biopsy is not required for this research project but can help us better understand neurodevelopmental disease by establishing comparison cells from the same family. If you have not had a skin biopsy taken at the hospital that referred you to us, do you consent to undergo a skin biopsy for this research project, or if you have already had a skin biopsy, do you accept to give a sample of this skin biopsy for this research project?

YES or **NO** (please circle)

Consent to be informed of the inheritance of a mutation: If we do identify a clinically relevant mutation known to be associated with a neurodevelopmental disorder in your child, do you want to be informed of the inheritance of this mutation, i.e., whether it came from both parents, one parent, or occurred sporadically?

YES or **NO** (please circle)

For Clinically Significant Incidental Findings for Adult Participants: do you agree to be informed through the genetic counsellor?

YES or **NO** (please circle)

Consent to be re-contacted in the scope of this research project: We may wish to re-contact you in some cases, for example because we may need additional health information, or to invite other family members to participate in the study. Do you authorize us to re-contact you in the scope of this research project?

YES or **NO** (please circle)

Consent to be re-contacted for other research projects: A new consent will be necessary for the use of your coded DNA and information, as well as the use of your child/children's coded DNA and information in other research. May we re-contact you:

- To request your participation and/or the participation of your child/children in future research project?

  YES or **NO** (please circle)

- To ask for your permission to use your remaining samples and associated data, and/or your child/children's remaining samples and associated data in a future research project?

  YES or **NO** (please circle)

- To ask for your permission to put your remaining samples and associated data, and/or your child/children's remaining samples and associated data in a bank for future research projects?

  YES or **NO** (please circle)

Consent to participate in this research project:

I have reviewed the Information and Consent Form. I acknowledge that the research project was explained to me, that my questions were answered to my satisfaction, and that I was given sufficient time to make a decision.

I agree to participate in this research project according to the conditions stated above. A dated and signed copy of the present Information and Consent Form was given to me.

Name of parent 2 _____

Signature _____Date _____

20.3 Consent of parents as legal representatives of child 1

Name of Participant (minor child 1)_____

If we cannot access your child's medical file, can we discuss your child's medical history and prognosis with their care provider or genetic counsellor?

YES or **NO** (please circle)

Consent to provide a urine sample from your child: Do you consent to providing a urine sample for this research project?

YES or **NO** (please circle)

Consent to provide a sample of your child's skin: Providing a skin biopsy is not required for this research project but can help us better understand neurodevelopmental disease by establishing comparison cells from the same family. If your child has not had a skin biopsy taken at the hospital that referred you to us, do you consent that your child undergoes a skin biopsy for this research project, or if your child has already had a skin biopsy, do you accept to give a sample of your child's skin biopsy for this research project?

YES or **NO** (please circle)

Consent of legal representative for the participation of minor child in this research project:
In my capacity as a legal representative, I took notice of the Information and Consent Form. I acknowledge that the research project was explained to me, that my questions were answered and that I was given sufficient time to make a decision.

I was informed that the principal researcher of the research project will transmit to my child treating physician pertinent information, should these be clinically validated. I understand that the research team will try to contact my child at the age of majority to obtain his/her consent for participation.

After consideration, I agree that my child participate in this research project according to the conditions stated above.

Name of legal representative _____

Signature of legal representative _____
Date _____

Name of legal representative _____

Signature of legal representative _____
Date _____

16.4 Consent of parents as legal representatives of child 2

Name of Participant (minor child 2)_____

If we cannot access your child's medical file, can we discuss your child's medical history and prognosis with their care provider or genetic counsellor?

YES or **NO** (please circle)

Consent to provide a urine sample: Do you consent to providing a urine sample for this research project?

YES or **NO** (please circle)

Consent to provide a sample of your child's skin: Providing a skin biopsy is not required for this research project but can help us better understand neurodevelopmental disease by establishing comparison cells from the same family. If your child has not had a skin biopsy taken at the hospital that referred you to us, do you consent that your child undergoes a skin biopsy for this research project, or if your child has already had a skin biopsy, do you accept to give a sample of your child's skin biopsy for this research project?

YES or **NO** (please circle)

Consent of legal representative for the participation of minor child in this research project:
In my capacity as a legal representative, I took notice of the Information and Consent Form. I acknowledge that the research project was explained to me, that my questions were answered and that I was given sufficient time to make a decision.

I was informed that the principal researcher of the research project will transmit to my child treating physician pertinent information, should these be clinically validated. I understand that the research team will try to contact my child at the age of majority to obtain his/her consent for participation.

After consideration, I agree that my child participate in this research project according to the conditions stated above.

Name of legal representative _____

Signature of legal representative _____
Date _____

Name of legal representative _____

Signature of legal representative _____
Date _____

16.5 Consent of parents as legal representatives of child 3

Name of Participant (minor child 3)_____

If we cannot access your child's medical file, can we discuss your child's medical history and prognosis with their care provider or genetic counsellor?

YES or **NO** (please circle)

Consent to provide a urine sample: Do you consent to providing a urine sample for this research project?

YES or **NO** (please circle)

Consent to provide a sample of your child's skin: Providing a skin biopsy is not required for this research project but can help us better understand neurodevelopmental disease by establishing comparison cells from the same family. If your child has not had a skin biopsy taken at the hospital that referred you to us, do you consent that your child undergoes a skin biopsy for this research project, or if your child has already had a skin biopsy, do you accept to give a sample of your child's skin biopsy for this research project?

YES or **NO** (please circle)

Consent of legal representative for the participation of minor child in this research project:
In my capacity as a legal representative, I took notice of the Information and Consent Form. I acknowledge that the research project was explained to me, that my questions were answered and that I was given sufficient time to make a decision.

I was informed that the principal researcher of the research project will transmit to my child treating physician pertinent information, should these be clinically validated. I understand that the research team will try to contact my child at the age of majority to obtain his/her consent for participation.

After consideration, I agree that my child participate in this research project according to the conditions stated above.

Name of legal representative _____

Signature of legal representative _____
Date _____

Name of legal representative _____

Signature of legal representative _____
Date _____

21. SIGNATURE OF THE PERSON WHO OBTAINED THE CONSENT

I hereby certify that we have explained to the research subjects and research subject's legal representatives (parents), the terms of the present Information and Consent Form, that we have answered the questions that the research subjects and the research subject's legal representatives had in that respect, and that we have clearly indicated that they remain free to put an end to their participation or the participation of the person they represent without suffering any prejudice.

I hereby certify that I have explained to the minor research subject in an adapted language that he can comprehend the research project. He understood and did not oppose. I hereby commit myself to respect any refusal.

_____

Name and signature of the person who obtains the consent

_____

Date

22. SIGNATURE AND COMMITMENT OF THE RESEARCHER IN CHARGE OF THE PROJECT

I hereby certify that the research project, as well as the conditions of participation, was described to the participants. A member of the research team answered any questions and explained that participation was completely free and voluntary.

I commit myself, as well as the research team, to respect what was agreed upon in the Information and Consent Form and to give a signed copy of this form to the adult participant and legal representative.

Name: _____

Signature of researcher: _____ Date: _____

20. ETHICS COMMITTEE APPROVAL

This consent form was approved by the ethics committee at the Douglas Mental Health University Institute on March 2016.