**Genetic Studies of the Placenta**
**Control Consent**

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**Background:** Pregnancy complications such as low birth weight or maternal pre-eclampsia (a condition which involves high blood pressure in the mother) can result from abnormal development of the placenta. Although women who screen positive on the Maternal Serum Screen (MSS) are at a slightly elevated risk for these complications in their pregnancy, most go on to have a normal amniocentesis result and a normal term birth. The causes of low birth weight, maternal preeclampsia, or abnormal maternal serum screen are mostly unknown and there are no prenatal tests to predict which pregnancies are at high risk of later complication.

One possible explanation for these complications is that cells with an abnormal number of chromosomes are present but only in the placenta. This is called placental mosaicism. Mosaic trisomy occurs when two populations of cells are present in a certain tissue. The first population of cells is what we expect to see in healthy individuals with each cell containing 46 chromosomes. The second is a cell line carrying 47 chromosomes (for example in mosaic trisomy 16 we will see some cells with three chromosome 16's instead of just two). When looking at chromosomes found in cells of the placenta from healthy pregnancies, about 5% have mosaic trisomy. Mosaic trisomy isolated in the placenta usually leads to a healthy birth, but can increase the risk for neonatal death, low birth weight, and maternal complications such as high blood pressure.

Another possible explanation for these complications is that there are errors regulating how genes that control placental growth are being turned on and off. One indirect measure of this on/off switch for gene regulation involves a chemical modification to the DNA (the material our genes and chromosomes are made of) in and around the gene. This chemical modification is termed DNA methylation.

**Aim:** Our aim is to determine whether or not placental trisomy, or errors in DNA methylation, contribute to abnormal outcome associated with unexplained screen positive MSS, poor fetal growth, or preeclampsia. Through the characterization of placental abnormalities we hope to be better able to predict pregnancy risks using such prenatal screens.

**Procedure:** You are being invited to participate in this study as a control because you have received screen negative MSS results and have had an uncomplicated pregnancy. Participation will require about one hour.

PART 1: Detailed clinical follow-up which will involve the review of birth records, tissue sampling from the placenta and/or cord blood after birth of the baby, completion of a brief questionnaire and a blood sample from you. Cells from the

placenta will be tested for the presence of trisomy using a DNA based method. Four 4mL tubes (approximately 3 teaspoons) of your blood will be drawn and collected for genetic studies of DNA.

PART 2: After the birth of your baby a sample of your baby's cells from the inside of the cheek may be obtained using a swab to compare methylation differences to the placenta.

**Risks:** There may be some discomfort associated with the placement of the needle for blood withdrawal and occasionally bruising, swelling, feeling faint or dizzy and/or the rare chance an infection may result. There are no anticipated risks to your baby from obtaining a cheek swab.

**Benefits:** Participation in this study will help to further our understanding of prenatal screening, placental mosaicism and placental DNA methylation. There is no direct benefit to the individual from participating in this study.

**Remuneration:** There will be no remuneration for your participation in this research study.

**Confidentiality:** Your confidentiality will be respected. Only the research team members involved will know the name of the participants in this research project. The samples will be coded with a number upon receipt and the list of names will be kept under lock and key in the office of the principal investigator. The samples are therefore identifiable only to the investigators. De-identified coded placental and blood DNA samples will be studied at the Child and Family Research Institute (CFRI). Also, de-identified coded placental DNA samples will be sent to Dr. Ding for further analysis not possible at CFRI. The names of the subjects will not be used in any discussion or correspondence about the data. Some of the information obtained from this study will be used in scientific publications, but the identity of the subjects will not be revealed. The findings of this study will not appear in medical records or patient charts. No information that discloses your identity will be released or published without your specific consent to the disclosure. However, research records and medical records identifying you may be inspected in the presence of the Investigator or his or her designate by Health Canada and the UBC Research Ethics Boards for the purpose of monitoring the research. No records which identify you by name or initials will be allowed to leave the Investigators' offices.

As the study goals will take several years to complete and as it is often difficult to anticipate future advances in science that open up new research questions, leftover DNA from blood, the placenta and the cheek swab may be banked for further genetic research related to the general objectives of this proposal that may arise in the future. DNA will be stored in the laboratory of the principal investigator, labeled with the code, until it is used entirely or until such DNA is withdrawn. The laboratory is in a secure building accessible by photo identification only. Subjects can request DNA samples be destroyed or withdraw from the study at any time by contacting the principal investigator. No further consent will be sought for these future studies. These DNA samples will not be sold and will not be used for commercial purposes.

Signing this consent form in no way limits your legal rights against the sponsor, investigators, or anyone else. Your rights to privacy are also protected by the *Freedom of Information and Protection of Privacy Act of British Columbia.* This Act outlines rules for the collection, protection, and retention of your personal information by public bodies, such as the University of British Columbia and its affiliated teaching hospitals. Further details about this Act are available upon request.

You understand that your participation in this study is entirely voluntary and that you may refuse to participate without jeopardizing your present or future care at Children's and Women's Hospital of British Columbia. You also understand that you may withdraw from this study at any time, by contacting the principal investigator, at which time your DNA sample will be destroyed. Your signature on this form signifies that you consent to participate in this study after reading the above information. You have been given the opportunity to discuss pertinent aspects of this research study and to ask questions. You have also received a signed and dated copy of this consent form for your own records.

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

Please check one box below.

☐ PART 1

☐ PART 1 & 2

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| Subject Name (please print): | Subject Signature: | Date: |

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| Investigator Name (please print): | Investigator Signature: | Date: |