Subject's Name: _____
Medical Record #_____

Georgia Regents University

CONSENT FOR SUBJECT AND NORMAL CONTROL FOR PARTICIPATION IN RESEARCH PROTOCOL

Protocol/Study Title:	Developmental Gene Discovery Project—Mapping and Identifying New Genes in Uterine and Vaginal Development Identifying New Genes Causing Birth Defects in Children
Name of Principal Investigator (PI):	Lawrence C. Layman, M.D.
PI address:	Georgia Regents University BB7514, 1120 15th St. Augusta, GA 30912
PI telephone number:	(706) 721-3832
Name(s) of Sub-investigators (sub-I):	Hyung Goo Kim, PhD., Phone: (706) 721-5764 Lynn P. Chorich, M.A., Phone: (706) 721-7591 Megan E. Sullivan, B.S., Phone: (706) 721-7591 Viji Sundaram, M.D., Phone: (706) 722-4434
Sponsor:	This study is sponsored by Georgia Regents University

INVITATION TO TAKE PART IN RESEARCH: You are invited to take part in a research study. You have been invited to participate as a healthy control (have no developmental disorder).
☐ _____

You have been invited to participate as a subject (have a developmental disorder).
☐ _____

This document will tell you about:

- important information about the study
- what will happen if you decide to take part in the study
- the purpose of the study
- and the potential risks and benefits of taking part in the study.

The study doctor and/or study staff will:

- discuss the study with you and
- answer all of your questions.

Taking part in this study is voluntary. Please take the time to read this form carefully. Please ask any questions you may have before you agree to take part in the study. If you decide to take part in this study you will be asked to:

- sign this form
- put your initials on each page.

PURPOSE OF STUDY:

What is the Purpose of This Study?

The purpose of this study is to determine the genetic cause for disorders that affect human growth, development, and reproduction. There are reasons to believe that these conditions can be inherited in families, and we are interested in trying to find out if changes in genes cause these disorders.

INFORMATION ABOUT PEOPLE TAKING PART IN THE STUDY:

Some chromosomal abnormalities or gene mutations may disrupt the function of genes required for normal growth and development. By identifying these genes in people with specific developmental defects (birth defects), we hope to reach a greater understanding of how the human body grows and develops. You will be asked to provide some personal information to the researchers about yourself, such as demographic information including race, sex and date of birth, family history, and contact information. You will also be asked to have your medical records reviewed to be sure your diagnosis fits this study.

Why am I being asked to take part in this study?

You have been asked to participate in this research study because you are a healthy control or you have one or more developmental abnormalities (a birth defect or developmental defect such as _____), chromosome problem, cancer, or a reproductive problem such as _____ .

How many people are expected to take part in this study?

You will be one of at least 3150 people internationally participating in this study.

If I take part in this study, can I take part in other studies?

If you participate in this study, you may also participate in other studies.

Can I take other medication while I am taking part in the study?

You may participate in this study if you are on medications. Please inform the study team about any of your medications.

STUDY PROCEDURES:

What will happen to me in the study?

Consent for giving blood:

You will be asked to give about 30 milliliters (two tablespoons) of blood from a vein in your arm one time. From this blood, your white blood cells will be isolated so DNA can be extracted. Some of your white blood cells will be grown to create a permanent cell line which will provide a long-term supply of DNA, RNA (RNA is copied from DNA and gives the code to make proteins), and protein. Your DNA will be analyzed and compared with either the DNA from an affected person or healthy control. The healthy control DNA sequence should be normal compared to someone with a known developmental disorder. These studies are important to establish if a real gene variant exists in someone with a developmental disorder.

Risk: There will be some minor discomfort from having blood drawn and there is a chance of a bruise forming where the needle was stuck. There may be more risks that are not known or not expected.

Time Required for Participating: The only time required will be having a blood sample drawn.

My blood may be used for the research study: ☐ Yes _____ ☐ No_____

Consent for cheek swab collection:

You will be asked to do a mouth/saliva swab from which DNA can be extracted. Your DNA will be analyzed and compared with either the DNA from an affected person or healthy control. The healthy control DNA sequence should be normal compared to someone with a known developmental disorder. These studies are important to establish if a real gene variant exists in someone with a developmental disorder.

Risk: There will be no discomfort from the mouth swab. There may be more risks that are not known or not expected.

Time Required for Participating: The only time required will be doing the actual cheek swab.

My cheek swab may be used for the research study:
☐ Yes _____ ☐ No_____

Consent for a skin biopsy:

You will be asked to give consent for a skin biopsy to grow cells so that your chromosomes and gene function can be studied to see if they could cause your condition(subject) or to compare to an affected

subject (healthy control). Sometimes chromosomes in the blood are not the same as in the skin. Skin biopsies may be performed in several different ways. Yours will be performed by:

_____ 1) Numbing the skin with a local anesthetic, then using a small punch biopsy, which will remove a small piece of skin. The skin will be covered with a band-aid or tape, and a stitch will be placed if needed.

_____ 2) Since you will be having surgery, a small piece of skin taken from the incision will be removed or skin that would otherwise be thrown away will be used.

Skin cells will be grown to create a cell line which will provide a long-term supply of DNA or RNA (RNA is copied from DNA and gives the code to make proteins) and may be used to check my chromosomes. For subjects: your DNA will then be studied to see if there are changes in the DNA (genetic variants) that may be the cause of the disease or be a marker for the disease, which might help us find the responsible gene. For healthy controls: your DNA will be used to compare to subject DNA.

Risk: There will be some minor discomfort from having a skin biopsy and there is a chance of a bruise forming and a small chance of infection. If you have a bleeding problem, or a suppressed immune system, or a circulatory problem, you will not have this performed since it could lead to healing problems. There may be more risks that are not known or not expected.

Time required for Participating: The only time required will be having the skin biopsy performed.

I will have a skin biopsy for the purposes of the research study: ☐ Yes_____ ☐ No_____

Consent for tissue collection:

You will be asked to allow a small piece of tissue (relevant to the research) that would otherwise be discarded during surgery to be collected for use in the study. Your DNA, RNA, and/or protein will be extracted from the tissue and compared to an affected person or healthy control. These studies are important to establish if a real gene variant is confirmed in someone with a developmental disorder.

For subjects: your tissue DNA/RNA/protein will then be studied to see if there are changes that may be the cause of the disease or be a marker for the disease. This might help us find the responsible gene. For healthy controls: your tissue DNA/RNA/protein will be used to compare with that of a subject.

Risk: There will be no additional risks to you to have a small piece of discarded tissue taken during surgery that already would have been removed. There may be more risks that are not known or not expected.

Time required for Participating: There will be no extra time required in the surgery to have the tissue taken after it is removed by the surgeon.

I will allow a small piece of discarded tissue to be taken for the purposes of the research study:
☐ Yes_____ ☐ No_____

Consent for Giving a Semen analysis:

You will be asked to provide a semen analysis for evaluation so that the function of your sperm may be studied:

____ for an evaluation of your infertility. Once the laboratory is finished with the specimen, it will be provided for this study instead of being discarded.
____ You are supplying this sample for the purpose of the present study and it will not have a full semen analysis because you have had other ones performed.

From your sperm, DNA can be extracted. Some of sperm cells will be used to study your DNA or RNA (RNA is copied from DNA and gives the code to make proteins) and may be used to check your chromosomes.

For subjects: your DNA will then be studied to see if there are changes in the DNA (genetic variants) that may be the cause of the disease or be a marker for the disease, which might help us find the responsible gene.

For healthy controls: your DNA will be compared to subject DNA. There will be no discomfort from having a semen analysis done.

Risk: There is no health risk and there is no discomfort from having a semen analysis done.
Time required for Participating: The only time required will be providing the semen specimen.

I will provide a semen sample for the purposes of the research study:
☐ Yes_____ ☐ No_____

IMAGING CONSENT:

You may be asked to be photographed or recorded for research purposes.

☐ Yes _____ **I give my consent to be photographed** ☐, or recorded ☐ during my participation in this research study. I understand these images will only be used for analysis and research documentation. I also understand my image may appear in publications, presentations, or teaching material outside the health system. Although my name will not be used, I understand these images may show my face or any part of my face or body. If they do show my face, people may be able to identify me in these pictures or tapes. If the eyes are not essential for documentation purposes, an effort will be made to block them.

I understand that I have a right to revoke my consent to be photographed, videotaped, or to have other images taken in writing at any time to Dr. Lawrence C. Layman, Georgia Regents University, OB/GYN, IMMAG, BB7514, 1120 15th Street, Augusta, Georgia 30912. I understand I may request cessation of photography, videotaping or other imaging during the taping process. I understand that if I wish to revoke this consent, it will apply to the use of my images in the future, but will not apply to previously made publications or presentations. I understand my photographs, videotapes or other images are considered protected health

information and will be maintained in a protected and secure manner as part of my confidential research record. Lawrence C. Layman, M.D., who can be reached at (706) 721-3832, will answer any further questions I may have at any time concerning the study. If I have any questions or concerns about the 'rights of research subjects', I may contact the Institutional Review Board at 706-721-1483. In case of emergency, Dr. Layman may be reached at (706) 721-3832.

☐ No_____**I do not want photographs, videotaped images, or other images taken of me.**

INJURY AS A RESULT OF THE STUDY

Because of Georgia Regents University policy, the institution is not able to offer financial compensation should you be injured as a result of participating in this research. However, you are not precluded from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research, including the institution.

The possible risks, which are very minimal, of taking part were described to you and talked about with your study doctor. Medical treatment will be provided if you become injured because you are taking part in the study. These costs will be paid by the study.

FOR HEALTHY CONTROLS: You realize that there is a very small chance that you might have a mutation in the gene being studied even though you have no developmental disorder. You will be given the opportunity to decide if you would like to be identified and have this result discussed with you. If you choose to be contacted, arrangements will be made with the researchers to discuss your findings and to determine if further medical care is recommended.

☐ I want to know if I have an abnormal result. _____ Subject's Initials

☐ I do not want to know if I have an abnormal result. _____ Subject's Initials

BENEFITS:
The results of this research will not directly benefit you, but will help researchers identify people at risk for developmental disorders (birth defects) and may provide an understanding of why some people have birth defects. The results of this research may also help researchers identify people at risk for developmental disorders before the disease develops and may provide an understanding of why certain people have birth defects.

ALTERNATIVE TREATMENTS AND THERAPIES: The alternative is not to participate in the study.

ENDING THE STUDY

Can I stop taking part in the study?
You may withdraw your consent to stop taking part in the study at any time. If you withdraw your consent, there will be no penalty. If you decide to stop taking part in the study for any reason, you must contact the study staff immediately at 706-721-7591.

If I withdraw from the study, can information about me still be used and/ or collected?
If you stop taking part in the study the study staff will not collect any more information from you. The information that the study staff had about you before you decided to stop being in the study can be used.

Can the study doctor remove me from the study?

Yes, the study doctors may stop your taking part in the research study if he or the sponsor decides to stop the study, or if you are not eligible to take part in the study.

FINANCIAL INFORMATION:
You will neither be paid nor charged anything for participating in this project. You will be responsible for the costs of transportation to participate in the study.

USE OF GENETIC SAMPLES

There is a new federal law called the Genetic Information Nondiscrimination Act (GINA). This law was created to protect you. This law makes it illegal for any of the following to discriminate against you based on your genetic information:

• health insurance companies

• group health plans

• employers with 15 or more employees

A person's genetic tests that are tests that are used to assess:

- genotypes
- mutations
- or chromosomal changes

The law defines 'genetic information' as information about:

- an individual's genetic tests (including genetic tests done as part of a research)
- genetic tests of the individual's family members (defined as dependents and up to and including 4th degree relatives)
- genetic tests of any fetus of an individual or family member who is a pregnant woman, and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology
- the manifestation of a disease or disorder in family members (family history)
- any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or family member.

Genetic information does not include information about the sex or age of any individual.

Routine tests such as complete blood counts, cholesterol tests, and liver function test are not protected under GINA.

The new law (GINA) prohibits group and individual health insurers from:

- using a person's genetic information in deciding if that person is eligible or the amount of their insurance premiums
- from requesting or requiring that a person undergo a genetic test

The new law (GINA) prohibits employers with 15 or more employees from using a person's genetic information in making employment decisions such as:

- hiring
- firing
- job assignments
- or any other terms of employment

The new law (GINA) does not:

- prevent health care providers from recommending genetic tests to their patients
- mandate coverage for any particular test or treatment
- prohibit medical underwriting based on current health status
- cover life, disability, or long-term care insurance
- apply to members of the military

CONFIDENTIALITY:

How will the researchers protect my privacy and keep information about me confidential (private)?

Any study information about you will be kept private and will only be given out with your permission. If the results of this study are published, your name will not be used. Your research records will be private to the extent allowed by law. In order to make sure the research is done properly, the Institutional Review Board (IRB – the Board that oversees research at Georgia Regents University) may need access to information about your participation in this study. If you sign this consent form, you are giving us permission to collect, use and share your health information.

Research records that identify you will be kept private.

-Subject information will be kept in a locked drawer in a locked office or laboratory.
-Computer identification will kept in a secured site that can only be accessed by the investigators
-Any remaining sample of DNA, RNA, or protein will be kept in a locked refrigerator or freezer until it is used.

You will not be identified in study records or publications disclosed outside Georgia Regents University.

If you have questions or concerns about the privacy of your information please contact the Georgia Regents University Privacy Officer at (706) 721-5631, or through our Toll Free Hotline, 1-800-576-6623. Written inquiries or complaints may be emailed to: privacy@gru.edu or mailed to the: Privacy Officer c/o the Institutional Review Board, Georgia Regents University, Room CJ-2103, 1120 15th Street, Augusta, Georgia, 30912.

Eliminating Potential Risks of Sample/ Data Storage:

For your protection, all samples will be stored without identifying patient information. All collected samples will be coded; the codes will be kept in locked files and a secured database, and will be known only to the investigators.

PRIVACY NOTICE AND AUTHORIZATION TO USE OR RELEASE (DISCLOSE) HEALTH INFORMATION

If I take part in the study what confidential information about me will be collected, used and shared with others?

If you agree to be in this study, the investigators will collect health information that identifies you. We may collect the results of tests, questionnaires and interviews, such as the Subject Clinical Questionnaire. The protected health information that may be used and disclosed includes:

- All information collected during the research described in this informed consent document;
- All protected health information in your medical records that is related to the research
- All protected health information collected and maintained by your physicians and other healthcare providers.

We will only collect information that is needed for the research. This information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, use and share your health information. This permission is called authorization.

<u>Banking and Future Use of DNA, RNA, Protein Samples and Cultures</u>

The DNA, RNA, and protein from blood and/or cells from tissue samples taken from you may be made available to Georgia Regents University and other scientists engaged in research, which may ultimately lead to the development of medical processes. The sample may also be made available to public and private organizations that are participating in research with the Georgia Regents University and/or Georgia Regents Medical Center. Georgia Regents University and/or Georgia Regents Medical Center make no commitment to provide financial compensation or property rights to you.

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No".

1. Do you give permission for some of your DNA or cells that were left over from this research to be used for future research studies related to this study?

☐ **Yes** **Subject Initials_____**

☐ **No** **Subject Initials_____**

2. Do you give permission for some of your DNA or cells that were left over from this research study to be used for future research studies not related to this study?

☐ **Yes** **Subject Initials_____**

☐ **No** **Subject Initials_____**

Who will collect, use, and share my confidential information and samples?

Lawrence C. Layman, M.D., Hyung Goo Kim, PhD., Lynn P. Chorich, M.A., (Department of Obstetrics & Gynecology, Georgia Regents University) and other investigators involved in this research, may share your PHI and/ or results of your study with other researchers. In addition, your records may be reviewed in order to meet federal or state research regulations. Reviewers may include authorized representatives from National Institutes of Health (NIH), the Institutional Review Board (IRB – the Board that reviews research at the Georgia Regents University), and others. If your research record is reviewed by any of these groups, they may also need to see your entire medical record.

In addition, the researchers may also share your health information without your written permission to people who are planning a future research project, so long as any information identifying you does not leave our facility.

Information about people who have died may be shared with researchers using the information of deceased persons, as long as the researchers agree not to remove from our facility any information that identifies these individuals.

Data from this study may be used in medical publications or presentations. The information will be de-identified so that individual subjects cannot be recognized and the information will no longer be considered Protected Health Information (PHI).

Please be aware that once private information is disclosed, it is subject to re-disclosure by the recipient and can no longer be considered protected.

Can I review a copy of my confidential information that has been collected, used or shared with others under this authorization?

If your research records are used for decisions related to your clinical care, then you have the right to review this information and request changes. This is limited to information about your treatment, and does not include information related to procedures or tests that are for research purposes only. You may access this information only after the study analysis is complete. You have the right to know who has and who will see your records.

To request this information, or for any questions related to the privacy of your health information, you may contact the Enterprise Privacy Officer at 706 721-5631, or through our Toll Free Hotline, 1-800-576-6623. Written inquiries or complaints may be emailed to: privacy@gru.edu or mailed to the:

Enterprise Privacy Officer , Georgia Regents University, C/O GRU IRB Office, Pavilion III, CJ-2103, 1120 15th Street, Augusta, Georgia, 30912.

What happens to me if I cancel my authorization?

If you change your mind about being in the study, you may withdraw at any time. If you want to stop, you need to send a letter to the researcher at the following address: Dr.Lawrence C. Layman, Georgia Regents University, OB/GYN, BB7514, 1120 15th St, Augusta, GA 30912. Your letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

Georgia Regents University may not refuse to treat you whether or not you sign this authorization.

How long will my confidential information be used and shared with others?

The information that is collected for research will be analyzed for many years and it is not possible to know how long this analysis and follow-up will take. Therefore, you are allowing access to this information indefinitely.

Am I required to sign this consent and authorization and allow the researchers to collect, use, and share my confidential information with others?

You do not have to sign this Authorization.

Contact Information for Answers to Your Questions:

Your participation in this study is voluntary. You may take back your consent and withdraw from the study now or at any time in the future. This decision will not change your status as a non-research patient. It will not result in a penalty or loss of care or other benefits.

You have read this form that serves as an informed consent document. This form also serves as your authorization for Georgia Regents University and/or to use and release (disclose) your PHI in the manner described as a study participant. You have been given the opportunity to ask questions about the information on this form. If you have questions later, you can contact Dr. Lawrence Layman at 706-721-3832. You will be given a signed copy of this form for your records.

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

You can ask questions about the study at any time. Please contact Dr Layman at 706-721-3832 if you have questions about:

- More information of the study
- Study procedures
- Leaving the study before it is finished
- Expressing a concern about the study
- Any other questions you may have about the study

Who can I contact to discuss problems, concerns, or questions I may have about the research?

Contact the Georgia Regents University Institutional Review Board at (706)-721-1483 to discuss problems, questions, complaints, obtain information, offer input or find out about your rights as a research subject.

Who can I contact if I have questions about the privacy of my health information because I am taking part in the study?

If you have questions or concerns about the privacy of your information please contact the Enterprise Privacy Officer at 706 721-5631, or through our Toll Free Hotline, 1-800-576-6623. Written inquiries or complaints may be emailed to: privacy@gru.edu or mailed to the: Enterprise Privacy Officer , Georgia Regents University, C/O GRU IRB Office, Pavilion III, CJ-2103, 1120 15th Street, Augusta, Georgia, 30912.

Who can I contact if I have a research emergency or questions about the research study?

Dr. Layman, 706-721-3832

Date of Expiration of Authorization:

The information that is collected for research will be analyzed for many years and it is not possible to know how long this analysis and follow-up will take. Therefore, you are allowing access to this information indefinitely.

Voluntary Participation:

Taking part in this research study is voluntary and your choice. You may withdraw from the study at any time simply by refusing to have your blood drawn, a skin biopsy performed, and/ or a semen analysis. You do not need to give a reason. You will not be treated differently if you choose not to take part in the study. If you stop, contact the study staff immediately. Withdrawing from the study will not affect your other medical care. Information that the study staff had about you before you decided to stop being in the study can be used.
Lawrence C. Layman, M.D., who can be reached at (706) 721-3832, will answer any further questions you may have at any time concerning the study, the procedures, and any injuries that may appear to be related to the research. If you have any questions or concerns about the 'rights of research subjects', you

may contact the Institutional Review Board at (706) 721-1483. In case of emergency, Dr. Layman may be reached at (706) 721-3832.

What documents will be given to me if I decide to be in the study?

- This "Research Informed Consent Document"

STATEMENT OF CONSENT:

I have read this form and the information in it was explained to me. I agree to take part in this research study. All of my questions were answered. My taking part in the study is voluntary. I will receive a copy of this form for my records. I am not giving up my legal rights by signing this form.

_____
Subject's Name (print)

_____ _____
Subject's Signature Date and Time(00:00)

_____
Legally Authorized Representative or Parent/Guardian's Name (print)
(*If applicable only)*

_____ _____
Legally Authorized Representative or Parent/Guardian's Signature Date and Time(00:00)
(*If applicable only)*

_____
Witness' name (print)

_____ _____
Witness' signature Date and Time(00:00)

My signature indicates that I was present during the informed consent process and that informed consent was given freely by the subject or their legally authorized representative. My signature also indicates that I was present when the subject or their legally authorized representative signed the form.

INVESTIGATOR STATEMENT

Subject's Name: _____
Medical Record #_____

I acknowledge that I have discussed the above study with this participant and answered all of his/her questions. They have voluntarily agreed to participate. I have documented this action in the subject's medical record source documents or research chart source documents, as applicable. A copy of this signed document will be placed in the subject's medical record or research chart, as applicable. A copy of this document will be given to the subject or the subject's legally authorized representative.

_____
Printed name of investigator obtaining consent

_____ _____
Signature of investigator obtaining consent Date andTime(00:00)