The Children's Hospital *of* Philadelphia®

Informed Consent Form and HIPAA Authorization

Study Title: Identifying biomarkers of adverse health in early and late puberty using a computational 'multiomics' approach

Version Date: [redacted]

Principal Investigator: [redacted] [redacted]

Lead Investigator: Diana Cousminer, Ph.D. [redacted]

You and your child may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study and the risks and possible benefits of participating.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time.

In the sections that follow, the word "we" means the study doctor and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

Why are you being asked to take part in this study?

You are being asked to take part in this research study because you are a healthy adolescent girl who experienced your first period before you were 10 or after you were 13. Your parents will also participate in this study.

What is the purpose of this research study?

The purpose of this research study is to determine differences in girls who had earlier or later puberty within the normal range.

How many people will take part?

About 20 children and their parents will take part in this study.

What is involved in the study?

This study involves a visit to the Children's Hospital of Philadelphia to measure your body size, body composition, and heart function and to collect a blood sample.

How long will you be in this study?

If you agree to take part, your participation will last the day of the study visit. Your parents' participation will last for approximately 1 hour and will be limited to completing questionnaires.

What are the study procedures?

The study involves the following tests and procedures.

Pregnancy Test: You will be asked to take a pregnancy test before starting this study. The results will be shared with you and not with your parent(s). We strongly encourage you to share the results with your parents. If you are found to be pregnant, you will not be able to continue participation in the study. About 2 teaspoons of urine will be needed.

Blood Sample: We will ask you to fast overnight and provide a 16 mL blood sample (about 3 teaspoons) to test markers called genotypes that provide information about your genes. Additionally, the blood sample will be tested for markers that provide information about your cardiometabolic health. Your blood specimen will be given a special coded number and will not contain your name or any other identifying information about you. You will be provided with time to eat after the blood draw.

Pubertal Assessment: You will be asked questions about your current pubertal status (the changes in your body as you become more mature) and pubertal history, including several questions regarding menstrual periods. These questions are intended to establish when you had puberty and whether your puberty happened within a normal, healthy range.

Body Size Assessment: We will measure your height, weight and waist circumference. It will take approximately 5 minutes to complete these measurements.

Blood Pressure Assessment: We will measure your blood pressure using a standard arm cuff. It will take approximately 5 minutes to complete this measurement.

Body Composition Assessment- DXA Scan: We will use a DXA scanner to measure the amount of fat, lean and bone tissue in your body. This method uses a very low-powered X-ray beam to scan your entire body. The results are analyzed by a computer, which provides an estimate of the amount and density of your bones, fat mass and muscle mass. The test is done while you are lying on the soft tabletop of the DXA machine. The whole body scan takes less than 5 minutes. The radiation used in this machine is very minimal. This is the standard method for measuring bone mineralization and body composition, and is considered safe for children.

Body Composition Assessment - p-QCT Scan: A method called peripheral quantitative computed tomography (p-QCT) will also be used to measure the amounts of fat, lean, and bone tissue in your body. This instrument uses a low-energy X-ray beam to measure the density of bone in the forearm and the lower leg. It is different from DXA because it measures the hard outer layer of bone (cortical bone) and the inner layer of bone (trabecular or "spongy" bone). The lower leg will be measured three times. We will also measure your forearm using a high-resolution p-QCT scanner. The radiation exposure for each scan is low, and each individual scan takes less than 5 minutes. Together, the scans take approximately 30 minutes. These p-QCT tests are the most advanced and accurate method of measuring bone health and are considered safe for children.

Pulse Wave Velocity and Analysis Assessments: These methods are used to assess your cardiovascular health by scanning the flexibility of the walls of major arteries in your neck and upper leg, and also provide data on your blood pressure. These scans are taken while

you are lying down, after 5 minutes of rest. These scans are non-invasive and are considered safe for children.

Questionnaires: We will ask you and your parent(s) to you to complete questionnaires. The child questionnaires will ask questions about family background, sleep patterns, eating patterns, and physical activity patterns, and bone fracture history. The parent questionnaires will ask questions about birth-related and neighborhood-related demographics, sleep patterns, physical activity patterns, dietary behavior, self-reported height and weight, and puberty history.

NOTE: Parents are eligible to complete the parental questionnaires if they are the biological parent or a legal guardian of the child participant. Parents will be excluded from completing the parental questionnaires if they do not have knowledge of the child participant's birth history or if they do not currently live in the same household as the child participant.

What will we do with the genetic test results?

The genetic tests that will be part of this study, and in future studies, are for research purposes only. They are not clinical tests. You will not receive any results from any of these tests.

Sharing genetic results

You will have the option to allow the investigators to share or use your genetic data for future research (e.g. the NIH database for Genome-Wide Association Studies). The shared information will not include information that can identify you. This information will include information about your measurements and genes. If you withdraw consent for sharing your information or samples, it will be removed and will no longer be used for future research. However, data and samples that have already been shared with other researchers cannot be taken back.

What are the risks of this study?

Taking part in a research study involves inconveniences and risks. If you have any questions about any of the possible risks listed below, you should talk to your study doctor or your regular doctor.

While in this study, you are at risk for the following side effects:

Risks associated with the body composition assessment.

The small amount of radiation from the DXA and p-QCT scans is not needed for your medical care. You will get the radiation only because you are taking part in this study. Radiation can increase the risk of cancer after many years, but at a dose much higher than you will get. Because of the low dose of radiation you will get, it is very likely that you will not see any radiation effects at all.

All female participants will be asked to provide a urine sample for pregnancy testing prior to the whole DXA scan. Adolescents who are pregnant are ineligible to participate in this study.