Official Title: Molecular Transducers of Physical Activity Consortium (MoTrPAC)
NCT03960827
IRB Approval Date: 02/18/2025

UNIVERSITY OF CALIFORNIA, IRVINE
CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT

Molecular Transducers of Physical Activity Consortium (MoTrPAC) – Pediatric Study

Lead Researcher
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STUDY LOCATION(S):
Pediatric Exercise and Genomics Research Center (PERC)
UCI Institute for Clinical Translational Science (ICTS)

STUDY SPONSOR(S):
NIH

SPONSOR MASTER PROTOCOL NUMBER:

In the instance of parental permission, "You" refers to "Your child

SUMMARY OF KEY INFORMATION:

The information provided in this box includes a brief yet complete summary of key information about the research, presented first as required by the federal regulations. Some sections that require additional information may be repeated later in this document.

Participation is Voluntary
You are being asked to participate in a research study. Participation is completely voluntary. Please read the information below and ask questions about anything that you do not understand. A researcher listed above will be available to answer your questions.

Study Purpose
The Molecular Transducers of Physical Activity Consortium (MoTrPAC) is a national research study with the goal of discovering the molecular pathways that link exercise to health. We know that being physically fit helps children to grow and develop in the best way possible. We do not know exactly how exercise makes kids healthier. This research will help us to use exercise in ways that can make children and adults healthier.

Study Procedures
All participants will complete a series of health and fitness assessment sessions consisting of health history, physical fitness evaluation, measurement of body composition and bone health, and exercise tests. We will obtain blood samples before and after an exercise test.

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Institutional Review Board
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A sub-group of low-active participants will be asked to participate in a longer term intervention phase of the study. These selected volunteers will be placed randomly into either: 1) An endurance exercise training group or 2) a comparison group (no supervised exercise training). At the end of the intervention phase the participants will repeat the health and fitness assessment sessions.

Expected Duration

Health and fitness assessment sessions only (12-14 hours):
5 visits at the UCI Pediatric Exercise and Genomics Research Center (PERC). This will involve a total of 12-14 hours which will be completed over no more than 30 days (see Health and Fitness Assessments Visits table below for details on each visit). The number of screening and health and fitness assessment study visits will be allowed to vary to accommodate your schedule. In a case of a technical failure (e.g., computer crash or IV mal functioning) the participant may be asked to resume the study in another visit.

Participants selected for the intervention phase (up to 14 weeks):
An additional 12 weeks of intervention (exercise or no-exercise control group) which will be completed in up to 14 weeks if some training sessions are cancelled because of the participant's vacation, colds, etc. Health and fitness assessment sessions will be repeated at the end of the intervention phase and completed within 2 weeks.

Risks of Participation

The more notable risks of participation include:
Risks of exercise testing: fainting, dizziness, muscle soreness.
Risks associated with blood draws: brief pain, mild bleeding at site where blood was drawn and bruising.
Should there be a breach in confidentiality of your data, there is a slight risk that your private medical information could be shared with individuals who are not members of the study team.

Benefits to Participants

You will not directly benefit from participation in this study. You will receive information about your level of fitness, information about your body composition, and how to improve endurance fitness. This information can help you in guiding your own exercise programs to improve fitness and health.

Benefits to Others or Society

The scientists and physicians will use the results of the study to better understand how exercise can improve health. This knowledge will be translated to improve the ways in which health care providers guide patients and the public in the use of exercise to improve health.

Alternative Procedures or Treatments

There are no alternative treatments or procedures available. The only alternative is not to participate in this study.

WHY IS THIS RESEARCH STUDY BEING DONE?

The purpose of this research study is to learn more about how the human body changes in response to exercise. While we have a general understanding that exercise is good for health, we do not fully understand what it is about exercise that benefits health. While other scientists have tried to study this, the results in many cases have not led to clear answers. In some cases, the number of children studied was too small to reach definite answers and/or the latest and best research tools were not used.

The vision of this study is to overcome these challenges. UCI PERC has been assigned by the NIH to study children and adolescents, but we are part of a much larger national consortium studying adults that is working together in this research. Thus, our plan is that the results of the study will provide transformative new insights into how exercise influences health across the lifespan.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
At UCI (the only MoTrPAC site to assess children and adolescents), approximately 320 youth participants will be enrolled to the health and fitness assessment sessions. A sub group of 170 participants will be asked to participate in the intervention phase (endurance exercise training or no exercise comparison group) as well.

AM I ELIGIBLE TO PARTICIPATE IN THIS STUDY?
Inclusion Requirements for the Overall Study
You can participate in this study if you are 10-17 years of age and

- you and your parent or legal guardian are willing to provide informed consent and assent to participate in the study
- you are able to read and speak English well enough to provide informed assent and understand instructions
- determined to be in good health by pre-participation medical history review performed at PERC
- have body mass index (BMI) greater or equal to 5th percentiles but less than 95th percentiles of healthy children
- Your weight is ≥ 66 lbs (30kg)

Exclusion Requirements for the Overall Study

You cannot participate in this study if you (are)

- using medication on a daily/weekly basis
- using illegal drugs or abuse alcohol (self-report)
- pregnant or breastfeeding
- use marijuana (self-report)
- use tobacco (self-report)
- Body weight change (≥5%) weight lost (self-report) over the preceding 2 months or plan to lose or gain weight during the study
- have a past history of chronic diseases (e.g., cancer, diabetes, autoimmune diseases Inflammatory bowel disease (IBD), juvenile idiopathic arthritis, cystic fibrosis)
- have evidence of disease, disability or other condition that would impair participation in physical activity as determined by a study clinician
- donated blood in the past 3 months (self-report)
- COVID-19 infection
- Hospitalization for COVID-19 infection in the past 12 months
    - Individuals who tested positive for COVID-19 but were not hospitalized must be symptom-free at least 14 days (without a negative antigen test) or symptom-free for at least 7 days with a negative antigen test on the day of the study visit. A PCR test can be used if antigen tests are not available.

Additional Exclusion Requirements for the Endurance Exercise Training Intervention Phase Only

1. Participation in a structured/regular high intensity endurance sports ≥4 times per week in the 9 months prior to randomization to the intervention phase.
2. Only one member of a household can participate.

HOW LONG WILL THE STUDY GO ON?

Screening and Health and fitness assessment sessions only:

4-5 visits at the UCI Pediatric Exercise and Genomics Research Center (PERC). This will include a total of 12-14 hours which will be completed over no more than 30 days. The number of screening and physical fitness assessment study visits will be allowed to vary to accommodate your schedule.

Participants selected for the endurance exercise training group:

- Health and fitness assessment sessions as described above, then
- Twelve-weeks of exercise training consisting of three 70-min exercise sessions per week. The 12 weeks of training can be completed in up to 14 weeks if some training sessions are cancelled because of the participant's vacation, acute illness, etc.
- Health and fitness assessment sessions will be repeated during weeks 11-12 of the training intervention and 2-3 days following the last training session.

Participants selected for the comparison group:

- Health and fitness assessment sessions as described above, then
- No required exercise for the participants over the 12-week interval
- Health and fitness assessment sessions will be repeated during weeks 11-12 of the intervention. and during the week following the intervention.

WHAT PROCEDURES ARE INVOLVED WITH THIS STUDY?

Initial screening

↓

Study orientation and informed consent and assent

↓

Screening to establish eligibility [health history, puberty and physical activity questionnaires, height, weight, blood pressure and electrocardiogram (ECG) measurements]

↓

Eligible participants enrolled

↓

Health and fitness assessments visits (cardiorespiratory fitness, muscle strength, body composition, physical activity, health related behaviors questionnaires and familiarization with exercise tests)

↓

day washout (no intense exercise or testing)

↓

Acute endurance exercise challenge with blood sampling

↓

Establish eligibility for endurance exercise training phase

↓

Randomization to endurance exercise training or no exercise Intervention comparison group

↓

Intervention phase (approximately 12 weeks)

↓

Repeat health and fitness assessment visits

↓

day washout (no intense exercise or testing)

↓

Repeat acute endurance exercise challenge with blood sampling

Before you can participate in the main part of the study...
You will need to have "screening" exams, tests or procedures. The screening process helps the researchers decide if you meet the study requirements listed below. The screening procedures include:

- Review this informed consent document and discuss what is involved in this study.
- Provide your contact information and basic information.
- Tell us about your medical history and any medicines and supplements (vitamins and minerals) that you are taking or have taken in the last 3 months.
- Have your height, weight, and waist measured.
- Have a blood pressure and resting heart's electricity activity (ECG) measurements.
- Complete a physical activity questionnaire and a standard puberty assessment.
- Obtain clearance to perform physical activity
- Become familiar with laboratory exercise testing.

Some screening questionnaire may be conducted by Zoom including consent/assent. In this case the consent, assent forms will be e-mailed/mailed to you prior to the Zoom session. You will bring the signed consent/assent form to the first UCI visit. You will also have the option to complete some of study questionnaires by Zoom.

During the main part of the study...
1. If the screening exams, tests and/or procedures during Visit 1 show that you can continue to be in the study, and you choose to take part, then you will have the following procedures and tests done.

   This is a process/procedure flow table of the overall study and the procedures will be explained in detail below.

Procedures, duration and location for all participants:

	Health and Fitness Assessments Visits		
Study Visits^	**Activities**	**Approximate participant time**	**Location**
Visit 2 Health and fitness assessments	• Body Composition (DXA) • Laboratory fitness test (Peak VO_2) • Food Frequency Questionnaire (FFQ) • Orientation for physical activity monitoring	• 20 min • 45 min • 30 min • 10 min	PERC
Visit 3 Health and fitness assessments and familiarization	• Leg and hand grip strength assessments • Questionnaires • Familiarization - practice cycling intensity	• 45 min • 30 min • 30 min	PERC

Visit 4 Acute exercise challenge familiarization	• Familiarization - practice cycling intensity • 1-day 24-hour dietary recall	• 30 min 15 min	PERC Home
Visit 5 Acute exercise challenge with blood sampling	• Clinical blood labs • Acute endurance exercise challenge (with blood sampling*)	• 6-7 h	PERC

^ The number of screening and health and fitness assessment study visits may vary to accommodate the schedules of participants.

* Blood will be collected before, during and in multiple time points during the 4-h recovery following the endurance exercise challenge. Each blood draw ~ 20ml or about 4 teaspoons. Total volume ~ 130ml or less than ½ cup. Additional blood samples may be collected for safety or other study needs when and necessary, but no more than 5ml/kg per accepted standards for healthy children and adolescents.

Determine eligibility for endurance exercise training study: Training (n=120); Control (n=50)

12 Week endurance exercise training intervention (see below) or no exercise comparison group (see below) (includes adherence calls and monitoring visits)

Study Visits^	**Post Intervention Physical Fitness Assessment Visits** **Activities**	**Approximate participant time**	**Location**
Visit 1 Post-intervention health and fitness assessments and familiarization	• Weight, height • Body composition (DXA) • Laboratory fitness test (Peak $\dot{V}O_2$) • Questionnaires • Familiarization for exercise challenge	• 5 min • 20 min • 45 min • 30 min • 25 min	PERC
Visit 2 Post-intervention health and fitness assessments and familiarization	• Leg and hand grip strength assessments • Questionnaires • Familiarization - practice cycling intensity	• 45 min • 30 min • 30 min	PERC

Visit 3 Post-intervention acute exercise challenge familiarization	• Familiarization - practice cycling intensity • 1-day dietary recall	• 30 min • 15 min	PERC Home
Visit 4 Post-intervention acute exercise challenge with blood draws	• Acute endurance exercise challenge (with blood sampling*)	• 6-7 h	PERC

^ The number of assessment study visits will vary to accommodate the schedules of participants.
* Blood will be collected before, during and in multiple time points during the 4-h recovery following the endurance exercise challenge. Each blood draw ~ 20ml or about 4 teaspoons. Total volume ~ 130ml or less than ½ cup and no more than 5ml/kg per accepted standards for healthy children and adolescents.

Health and Fitness Assessment Visits

PERC Laboratory Visit 2: Body Composition, Fitness Assessment, Questionnaires

This visit will take about 2 hours. During this visit you will:

- Have bone density and body composition (amounts of lean, fat, and bone tissue) measured by DXA. You will be asked to lie on your back while a very low dose x-ray passes through you. You may be asked to change into an exam gown for this test. If not completed during Visit 2, this assessment can be done during Visit 3 or 4.
- Complete a test of the fitness level of the heart and lungs (peak $\dot{V}O_2$ test) on a stationary bicycle for about 8 to 12 minutes. During this time, we will increase the work rate progressively according to your age and fitness level. You will only exercise until you reach your limit of tolerance, that is, when you signal that you do not want to continue to exercise.
    - You will wear a nose clip and breathe through a mouthpiece during the test. You will also wear monitors to measure the heart's electricity activity (ECG) and blood pressure during the test.
- Complete questionnaires about mood, diet, health and other health-related behaviors.
- Be asked to take home a small device that measures movement while participating in daily activities and sleeping. You will be asked to wear this device around your wrist for seven days. You will be asked not to do anything outside of your normal daily activities.

Visits 3 and 4: Muscle Strength, Familiarizations with Exercise Challenge, Questionnaires

Visits 3 will take about 2 hours and visit 4 about 45 min. During these visits you will:

- Complete a test of lower body muscle strength using specialized equipment.
- Squeeze a grip strength device to assess muscle strength in your hand.
- Complete exercise challenge familiarizations to prepare you for the acute exercise challenge visit. You will be asked to pedal on the stationary bicycle in different intensities. You will breathe through a mouthpiece and wear a nose-clip.
- 1-day 24-hour dietary recall will be completed at home prior to the acute endurance exercise challenge visit.

Visits 5: Exercise Challenge with Blood Sampling

Visit 5 (Exercise Challenge) will be completed at PERC at least 2-3 days after the last familiarization for the exercise challenge. This visit will take a total of about 6-7 hours. For this visit:

- You will be asked to not eat or drink anything but water for 8 hours prior to the arriving for your appointment
- A small plastic tube will be inserted into your vein in your arm or hand vein by trained physicians and/or nurses with experience in pediatric procedures of this nature. In this way, the research team can get blood samples without having to perform many "sticks." If you wish, you can ask the research team to put a special numbing cream or a spray on your arm or hand before the small plastic tube is inserted.
- A fasting blood sample for metabolic and lipid panel (measuring, for example, sugar and fat in the blood) will be drawn (~1 tablespoon).
- Following the blood draw a light snack will be served and you will rest for about 20-30 minutes.
- You will be asked to pedal on the stationary bicycle for 2, 20-minute periods of exercise, with 2 minutes of rest in between (a total of 40 minutes). The work rate is calculated to be equivalent to the work rate corresponding to about 65% of your maximal effort. You will breathe through a mouthpiece and wear a nose-clip. Heart rate and blood pressure will be measured

- Blood samples will be taken through the plastic tube in your arm or hand vein before exercise, during, immediately after exercise and up to 4 h after exercise. About 20 ml or 4 teaspoons per sample and no more than 130 ml of your blood in total will be collected (up to approximately 9 tablespoons, per accepted standards for healthy children and adolescents).
- At the end of the session you will get a light meal.

Randomization to Intervention Study: either 1) Endurance Exercise Training Group or 2) Comparison Group (no supervised exercise training)

A subgroup of participants (see above for inclusion/exclusion criteria) will be selected to participate in an intervention study and will be randomly assigned (like flipping a coin) to one of two groups:

- Endurance exercise training group - about 70% of selected study participants will be in this group
- Comparison group - about 30% of selected study participants will be in this group

You will be assigned at random (by chance alone) to participate in the training program or be in a control no-exercise group. Neither you nor the study physician will pick the group to which you will be assigned.

Intervention Groups

- Endurance Exercise Training Group – If you are assigned to this group, you will be asked to perform exercise sessions in schools and/or PERC 3 times per week, approximately 70 min/session, for approximately 12 weeks. If you are 10-12 y/o participant (elementary school student) you will be trained in a form of circuit training (e.g., endurance activity stations: cycle ergometer, steppers, individual jump rope, pacer, sliders). If you are a high school or a middle school student, you will exercise on a variety of ergometers (for example: stationary bike, treadmill, elliptical and rowing machine) based on a target HR obtained from your testing in the lab. Each week, at least two of the sessions will be performed on a stationary bike. During the sessions, we will ask you to wear a monitor to measure your heart rate and we will ask questions about how you are feeling. You will be asked to not change your physical activity level (apart from the exercise sessions) or diet for the entire 12-week training program.
- Comparison Group –If you are assigned to this group, you will not take part in the exercise training sessions during this study. You will be asked to not change your physical activity level or diet for the entire 12-week training period.
- All participants from both groups - You will be asked to wear an activity monitor for at least one-week interval to track your level of physical activity. The activity monitoring will occur 3 times during the 12-week period (i.e., weeks 4, 8 and 12). At these visits, you will again be queried about any changes in you structured exercise or dietary patterns and changes in health status or medication use. You will be reminded to not change your usual physical activity and diet.
- At the end of the 12-week intervention phase you will be asked to repeat the health and fitness assessment sessions and acute endurance exercise challenge on the cycle with blood sampling.

RETURN OF RESULTS

During this study some of the study results (e.g., fitness level, body composition and lipid panel) will be provided to you. You will not have access to certain medical information and test results collected for the study. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to the study physician and other physicians who treat you.

WHAT ARE THE POSSIBLE SIDE EFFECTS OR RISKS RELATED TO THE STUDY?
You should talk to the research team about any side affects you experience while taking part in the study.

Possible risks and side effects related to the procedures include those which are:

Exercise Testing
Less common:
- Muscle soreness (mild)

Unlikely:
- Fainting (moderate)
- Dizziness (mild)

Rare:
- Chest pain (moderate)
- Irregular heartbeat (moderate)

Blood Sampling
Common:
- brief pain

Less common:
- Developing a bruise or bump (mild)

Unlikely:
- bleeding at site where blood was drawn
- feeling faint or light-headed

Endurance Exercise Training.
Common:
- Minor discomfort and/or shortness of breath (mild)

Less common:
- Muscle, joint strains and soreness (mild)

Rare
- Irregular heartbeats (moderate)
- Falls (mild to moderate)
- Possible exercise-induced bronchoconstriction (having difficulties to breath following exercise) in a participant with no previous history of exercise induced asthma (moderate)
- Muscle injury and broken bones (moderate to severe)

ECG
Rare:
Possible skin irritation from removal of electrodes

Activity monitor
No known risks

Unknown risks: There may be risks related to the research that we don't know about yet. However, you will be informed of any additional risks to which you may be exposed, and any changes that are made to the study, as a result of any newly-identified risks.

Randomization: You will be assigned to a study group by chance (like a coin flip). You may not be assigned to the study group that you had hoped you would be.

Psychological discomforts: Some of the procedures may cause embarrassment or anxiety, or the questions the researchers ask you may be upsetting or make you uncomfortable. If you do not wish to answer a question, you can skip it and go to the next question. If you do not wish to participate you can stop.

Radiation: During this study you will have DXA scans of your body. These scans are solely for the purpose of this research and you would not have these scan(s) if you decide not to participate in this research study. A DXA scan uses radiation to create pictures of the structures inside the body. The total radiation dose that you will receive from a scan of this type is about 2.5 mRem per scan or <5.0 mRem for two scans. A millirem is a unit used to quantify radiation dose. The total radiation dose will be about the same as a typical New York City-to-Los Angeles trip in a commercial airplane.

There are no known health effects associated with this amount of radiation exposure, and no radiation remains in the body after the scan. If you are especially concerned about radiation exposure, you should discuss this with the researcher listed at the top of this form.

Pregnancy Testing in Minors: If you are a female and have had your menses (started having periods) you will have some of your urine collected before the DXA scan for the purposes of pregnancy testing. Pregnancy test strip will be used to determine pregnancy. Per California Law, pregnancy test results will be provided to the parents only with permission from the child.

Whole Genome Sequencing (WGS): WGS generates an extremely large amount of information about people, including factors that will contribute to their future medical conditions. Specifically, the gene profile can help us understand the response to exercise. It can provide insight into how exercise influences the health of individuals and their biological family. It is possible that WGS data gathered for one purpose could reveal important information, perhaps unanticipated and unplanned for, years later. Since this is done for research and not clinical purposes, the NIH has decided that the results will be de-identified and will not be reported to the participants.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?
You will be paid up to $280 for completing the health and fitness assessment sessions which includes acute endurance exercise challenge with blood sampling. For the intervention study, the endurance exercise training group will receive up to an additional $570 upon completion of all study assessments. The comparison group will receive up to an additional $380 when all aspects of the research are completed. If you decide to withdraw from the study or are withdrawn by the research team, you will receive compensation for the visits and/or procedures that you have completed.

The US Internal Revenue Service (IRS) requires UCI to report compensation in excess of $600 per calendar year. Since you may receive compensation in excess of $600 per calendar year, your name and social security number will be collected and released to the UCI Office of Accounting to process the Form 1099-Misc for IRS tax-reporting purposes.

Reimbursement
You will not be reimbursed for any out of pocket expenses, such as parking or transportation fees.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?
There is no cost to you for participation in this study. If a health condition is identified as part of the assessments conducted for this study, you may be responsible for the cost of any medical follow-up.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?
It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number listed at the top of this form.

If you are injured as a result of being in this study, UCI will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call UCI Human Research Protections [redacted] or [redacted] or by e-mail at [redacted]

Federal and state privacy laws give patients the right to access information about their care and treatment contained in their medical record. During this study, you may not be able to access certain information related to this study in your EMR until the study is complete to ensure that the study remains unbiased. By consenting to participate in this study, you are also consenting to this possible temporary withholding of your records. If necessary for your care, this information will be provided to you or your physician.

WHAT HAPPENS IF I WANT TO STOP TAKING PART IN THIS STUDY?
You are free to withdraw from this study at any time. **If you decide to withdraw from this study, you should notify the research team immediately**. The research team may also end your participation in this study if you do not follow instructions, miss scheduled visits, the study sponsor decides to stop the study or your safety and welfare are at risk.

If you experience any of the side effects listed above, if your health worsens, or if you are injured during the research, you may need to be withdrawn from the study, even if you would like to continue. The research team will make this decision and let you know if it is not possible for you to continue. The decision may be made to protect your safety and welfare, or because the research plan does not allow people who develop certain conditions to continue to participate.

If you withdraw or are removed from the study, the researcher may ask you to *complete an exit telephone interview.*

Withdrawing from study participation will in no way compromise the relationship you have with your medical/health care provider or the ongoing care you receive. If you leave the study early, you may request that any unused biospecimens be destroyed and/or that your de-identified data be removed from the various databases where it is deposited. It is important for you to realize that once your de-identified data or samples have been shared, we cannot control research that is done with them. Also, once data have been analyzed and published, these data (with personal identifiers removed) cannot be withdrawn.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT?

Subject Identifiable Data
Identifiable information collected about you will be removed and replaced with a code. A list linking the code and your identifiable information will be kept separate from the research data.

Data Storage

Research data will be maintained in paper format in a secure location at UCI.

Research data will be stored electronically on a computer in an encrypted file and is password protected.

Research data will also be stored electronically on a secure computer or network in an encrypted file with password protection.

Data Retention
The researchers intend to store your research data and/or biospecimens in a repository indefinitely. The researchers may continue to use and share your information and information obtained from analyses of your biospecimens indefinitely. Also the use and sharing of your de-identifiable biospecimens will continue until the specimens are gone. Please note that the researchers of the MoTrPAC study include not only the researchers at UCI but also scientists from the NIH, universities involved in the MoTrPAC consortium, and other universities and centers who may be approved to use the de-identified data.

Your individual genomic data and health information will be put in a controlled-access data repository. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the repository must agree not to attempt to identify you.

The researchers intend to keep the research data for seven years after all children enrolled in the study reach the age of majority (age 18 in California).

There is no direct benefit to you from placing your genetic information in the repository. Allowing researchers to study your genetic information may lead to a better understanding of how genes affect health. This may help other people in the future.

WHO WILL HAVE ACCESS TO MY STUDY DATA?
The research team, authorized UCI personnel, the study sponsor NIH, and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to your study records to protect your safety and welfare.

While the research team will make every effort to keep your personal information confidential, it is possible that an unauthorized person might see it. We cannot guarantee total privacy.

Future Research Use
The de-identified data will be stored by the NIH and made available to researchers for further analyses to discover the molecular pathways that link exercise to health. You will not be informed about any of the specific research studies that might be conducted with your information and biospecimens. This means that your information and biospecimens could be used in research in which you might not have chosen to participate (i.e. without your additional consent).

Sharing for Future Research
Any information or biospecimens shared for future research will not include your name or other personal identifying information.

Clinical Trials.gov
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time." This statement must be added, and it should be noted that the study-specific registration number will be provided upon request.

Certificate of Confidentiality

To help us protect your privacy, we have obtained **a** Certificate of Confidentiality from the National Institutes of Health (NIH). With this Certificate, researchers cannot be forced to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the NIH which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

Medical Care

If you agree to participate in this research study, a signed copy of this consent document and the privacy authorization form may be filed in your electronic medical record (EMR) and your study participation may be added to your EMR. This information will be used for your care and treatment and for healthcare operations, which may include billing and payment.

Federal and state privacy laws give patients the right to access information about their care and treatment contained in their medical record. During this study, you may not be able to access certain information related to this study in your EMR until the study is complete to ensure that the study remains unbiased. By consenting to participate in this study, you are also consenting to this possible temporary withholding of your records. If necessary for your care, this information will be provided

ARE THERE OTHER ISSUES TO CONSIDER IN DECIDING WHETHER TO PARTICIPATE IN THIS STUDY?

Use of Biospecimens

Biospecimens such as blood collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research, and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them.

Genetics In the event of an unexpected breach of confidentiality, a federal law called the Genetic Information Non-Discrihmination Act (GINA) will help protect you from health insurance or employment discrimination based on genetic information obtained about you. In California, state law (CalGINA) requires that employers with 5 or more employees may not use your genetic information, obtained from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. However, these laws do not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

If you would like more information about the federal GINA law go to:
http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf or CalGINA:
http://www.leginfo.ca.gov/pub/11-12/bill/sen/sb_0551-0600/sb_559_bill_20110906_chaptered.pdf

Investigator Financial Conflict of Interest
No one on the study team has a disclosable financial interest related to this research project.

Future Contact
The study team would like your permission to contact you for future research. Please initial your level of permission below:

_____Yes, UCI researchers may contact me in the future to ask me to take part in other research studies.

_____No, UCI researchers may **not** contact me in the future to ask me to take part in other research studies.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?
If you have any comments, concerns, or questions regarding the conduct of this research, please contact the research team listed at the top of this form.

A 24-hour number is also listed on the top of this form to report any health concerns or unanticipated problems you may experience after normal hours or on weekends.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any suggestions, problems or concerns you may have about the study, please contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

What is an IRB? An Institutional Review Board (IRB) is a committee made up of scientists and non-scientists. The IRB's role is to protect the rights and welfare of human subjects involved in research. The IRB also assures that the research complies with applicable regulations, laws, and institutional policies.

HOW DO I AGREE TO PARTICIPATE IN THIS STUDY?
You should not sign and date this consent form until all of your questions about this study have been answered by a member of the research team listed at the top of this form. You will be given a copy of this signed and dated consent form, and the attached "Experimental Subject's Bill of Rights" to keep. **Participation in this study is voluntary.** You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with UCI or your quality of care at the UCI Medical Center.

If, during the course of this study, significant new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the research team listed at the top of the form.

Your signature below indicates you have read the information in this consent form and have had a chance to ask any questions you have about this study.

Note: If the research described in this form involves your protected health information (PHI), you will be asked to sign separate UC HIPAA Research Authorization form for the use of your PHI.

I agree to participate in the study.

Subject Signature	**Date**
Printed Name of Subject	
Legally Authorized Representative/Guardian Signature	***Date***
Printed Name of Legally Authorized Representative/Guardian	***Relationship to Subject***
Signature of Person Obtaining Informed Consent	**Date**
(For research that is greater than minimal risk, this individual must be listed on Page 1 of this consent)	
Printed Name of Person Obtaining Informed Consent	

WFU School of Medicine
Institutional Review Board
IRB Number: IRB00097219
Meeting Date Approved 2/18/2025
Version Valid Until: 5/21/2025

A witness signature is required on this consent form only if: ***(Researchers: check which one applies)***

IMPORTANT! If no witness signature is required, this witness signature section of the consent form may be left blank.

☐ Consent is obtained from the subject via the Short Form process, as approved by the IRB.
☐ The subject has decision-making capacity, but cannot read, write, talk or is blind.
☐ The subject's guardian/legally authorized representative (LAR) cannot read, write, talk or is blind.
☐ The IRB specifically mandated a witness signature for this study (e.g., high risk and/or invasive research procedures).

For the witness:
I confirm that the information in this consent form was accurately explained to and understood by the subject or legally authorized representative and that informed consent was given freely.

_____ _____
Witness Signature **Date**
Note: The witness must be impartial (i.e. not a member of the subject's family, not a member of the study team).

_____
Printed Name of Witness

UNIVERSITY OF CALIFORNIA, IRVINE
Experimental Subject's Bill of Rights

The rights listed below are the right of every individual asked to participate in a research study. You have the right:

1. To be told about the nature and purpose of the study.

2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.

5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.

7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.

9. To receive a copy of the signed and dated written consent form and a copy of this form.

10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

- -

If you have any concerns or questions regarding the research study you should contact the research team listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact the UCI's Human Research Protections unit in the Office of Research by calling [redacted] or [redacted] Monday – Friday, 8 am – 5 pm; or by e-mail at [redacted]; or by writing us at [redacted].

University of California Irvine Health
Permission to Use Personal Health Information for Research

Study Title (or IRB Approval Number if study title may breach subject's privacy):

Molecular Transducers of Physical Activity Consortium (MoTrPAC) – Pediatric Study

Principal Investigator Name: Shlomit Radom-Aizik Ph.D

Sponsor/Funding Agency (if funded): NIH

A. What is the purpose of this form?

State and federal privacy laws protect the use and release of your health information. Under these laws, the University of California or your health care provider cannot release your health information for research purposes unless you give your permission. Your information will be released to the research team which includes the researchers, people hired by the University or the sponsor to do the research and people with authority to oversee the research. If you decide to give your permission and to participate in the study, you must sign this form as well as the Consent Form. This form describes the different ways that health care providers can share your information with the researcher, research team, sponsor and people with oversight responsibility. The research team will use and protect your information as described in the attached Consent Form. However, once your health information is released by UC Irvine Health it may not be protected by the privacy laws and might be shared with others. If you have questions, ask a member of the research team.

B. What Personal Health Information will be released?

If you give your permission and sign this form, you are allowing your health care provider to release the following medical records containing your Personal Health Information. Your Personal Health Information includes health information in your medical records, financial records and other information that can identify you.

☐ Entire Medical Record

☐ Ambulatory Clinic Records
☐ Progress Notes
☐ Other Test Reports
☒ Other (describe):

☐ Lab & Pathology Reports
☐ Dental Records
☐ Operative Reports
☐ Discharge Summary
☐ Consultations

☐ Emergency Department Records
☐ Financial Records
☐ Imaging Reports
☐ History & Physical Exams
☐ Psychological Tests

Legal First and Last Name
Date of Birth
Gender
Mobile Number
Race
Ethnicity
Home Address
Date of Consent
(Ensure Medical Record Number) is correct

(Description of Other Health Information)

C. Do I have to give my permission for certain specific uses?

Yes. The following information will only be released if you give your specific permission by putting your initials on the line(s).

_____I agree to the release of information pertaining to drug and alcohol abuse, diagnosis or treatment.

_____I agree to the release of HIV/AIDS testing information.

_____I agree to the release of genetic testing information.

_____I agree to the release of information pertaining to mental health diagnosis or treatment.

D. Who will disclose and/or receive my Personal Health Information?

Your Personal Health Information may be shared with these people for the following purposes:

1. To the research team for the research described in the attached Consent Form;
2. To others at UC with authority to oversee the research
3. To others who are required by law to review the quality and safety of the research, including: U.S. government agencies, such as the Food and Drug Administration or the Office of Human Research Protections, the

research sponsor or the sponsor's representatives, or government agencies in other countries.

E. How will my Personal Health Information be shared for the research?

If you agree to be in this study, the research team may share your Personal Health Information in the following ways:

1. To perform the research
2. Share it with researchers in the U.S. or other countries;
3. Use it to improve the design of future studies;
4. Share it with business partners of the sponsor; or
5. File applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

F. Am I required to sign this document?

No, you are not required to sign this document. You will receive the same clinical care if you do not sign this document. However, if you do not sign the document, you will not be able to participate in this research study.

G. Optional research activity

If the research I am agreeing to participate in has additional optional research activity such as the creation of a database, a tissue repository or other activities, as explained to me in the informed consent process, I understand I can choose to agree to have my information shared for those activities or not.

☐ I agree to allow my information to be disclosed for the additional optional research activities explained in the informed consent process.

H. Does my permission expire?

This permission to release your Personal Health Information expires when the research ends and all required study monitoring is over.

I. Can I cancel my permission?

You can cancel your permission at any time. You can do this in two ways. You can write to the researcher or you can ask someone on the research team to give you a form to fill out to cancel your permission. If you cancel your permission, you may no longer be in the research study. You may want to ask someone on the research team if canceling will affect your medical treatment. If you cancel, information that was already collected and disclosed about you may continue to be used for limited purposes. Also, if the law requires it, the sponsor and government agencies may continue to look at your medical records to review the quality or safety of the study.

J. Signature

Subject

If you agree to the use and release of your Personal Health Information, please print your name and sign below. You will be given a signed copy of this form.

_____
Subject's Name (print)—*required*

_____ _____
Subject's Signature Date

Parent or Legally Authorized Representative

If you agree to the use and release of the above named subject's Personal Health Information, please print your name and sign below.

_____ _____
Parent or Legally Authorized Representative's Name (print) Relationship to Subject

_____ _____
Parent or Legally Authorized Representative's Signature Date

Witness

If this form is being read to the subject because s/he cannot read the form, a witness must be present and is required to print his/her name and sign here:

_____
Witness' Name (print)

_____ _____
Witness' Signature Date

WFU School of Medicine
Institutional Review Board
IRB Number: IRB00097219
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