Additional Preclinical Animal Study Sites (PASS) for MoTrPAC

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National Institutes of Health

Office of Strategic Coordination - The Common Fund

What is MoTrPAC?

MoTrPAC has the following goals:

- Assemble a comprehensive map of the molecular changes that occur in response to exercise and when possible relate these changes to the benefits of physical activity
- Develop a user friendly database that any researcher can access to develop hypotheses for additional studies regarding the mechanisms whereby physical activity improves and/or preserves health

MoTrPAC: Exercise Studies in Humans and Rodents

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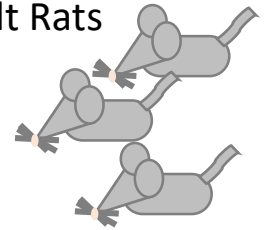
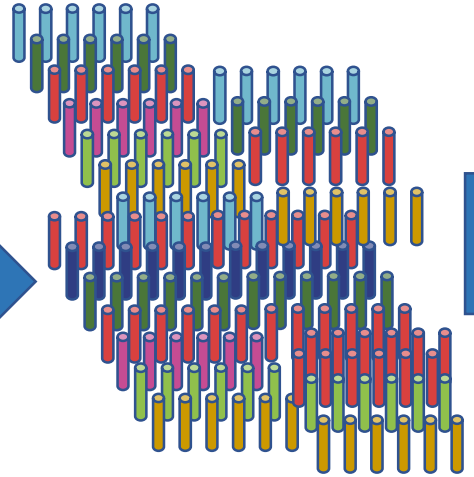
~2000 Healthy Human volunteers
M/F, age 12-elderly, all fitness levels

Participant characteristics
Age, sex, body comp, fitness, response to training

Acute Endurance/Resistance PA
Before/after 12 wks training

Adult Rats





Tissue Samples

Metabolomics,
transcriptomics, genomics,
epigenomics, proteomics

Molecular Transducers of Physical Activity

Participant characteristics

Genes
Proteins
Peptides
Lipids
Sugars
Hormones
Epigenetics
mRNA
ncRNA
exosomes

Clinical Phenotype Data

Molecular Data

Structure of MoTrPAC

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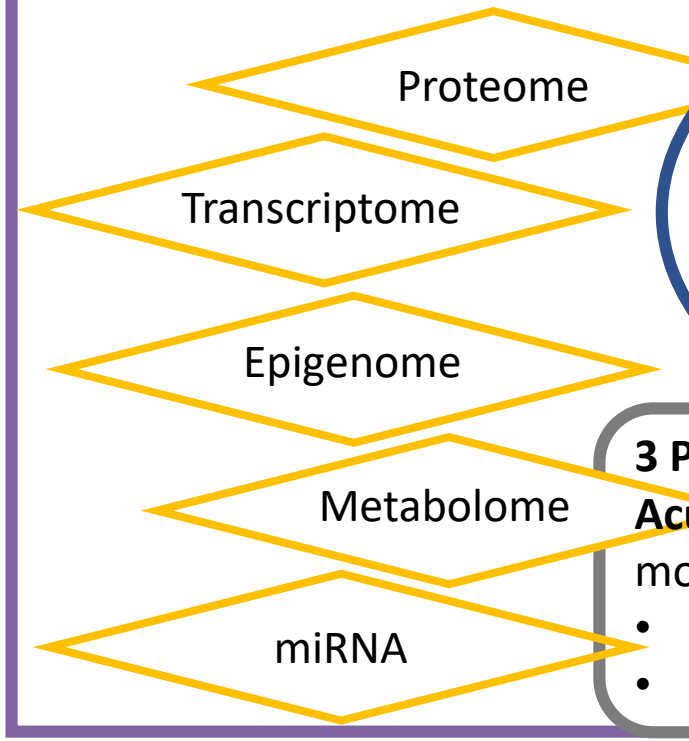
Chemical Analysis Sites (CAS)
5 Proteomics/Metabolomics and 2 Genomics Centers

Clinical Centers
7 Centers (6 adult, 1 pediatric) for physical activity (PA) study in healthy human subjects for discovery of molecular transducers of PA in blood, muscle, fat

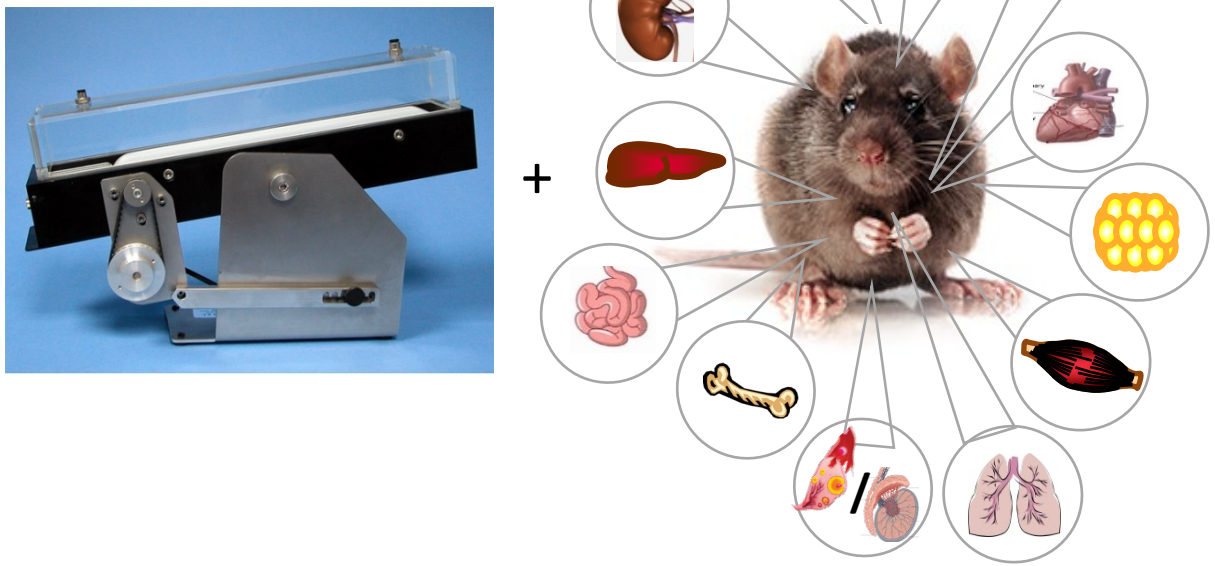


Consortium Coordination Center
- Coordination
- Protocol Development
- Standardization
- Tissue Repository
- Pilot Funding

Bioinformatics Center
- Bioinformatics
- Data standards
- Data storage/retrieval
- Data analysis

3 Preclinical Animal Study Sites: F344 rats, Acute and Training exercise. Allow molecule discovery in many tissues
- Find target tissues and pathways
- Test hypotheses regarding mechanisms

PASS (Animal) Protocol



- Acute and exercise training of Fischer 344 rats, 6-month cohort + 18-month cohort
  - For acute bout – collecting tissues at 7 post-acute exercise time points: immediately post-exercise (IPE), 0.5, 1, 4, 7, 24, and 48 hours after exercise
  - For trained--tissues will be collected from rats trained for 1, 2, 4, or 8 weeks; tissue collection will be 48 hours after the last exercise bout
- Tissues will be analyzed using transcriptomics and epigenomics (RNA-seq, ATAC-seq, methyl capture/RRBS), metabolomics (targeted and untargeted), proteomics (global and phospho)
- First data release expected Fall 2019

Proposed PASS2 FOA

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- Investigate the molecular mechanisms of action of compounds mobilized in response to exercise, initially identified by the consortium PASS protocol
- Applicants will have access to consortium data, and may request consortium samples for their research
- Additional exercise studies or tissue collection are not part of this RFA
- Up to $6 million available to support up to 4 awards

- Awardees must work collaboratively as full MoTrPAC consortium members to help deliver program goals

- Analysis of additional tissues/organs from animals substantially broadens the impact of MoTrPAC: indicates how tissues (not available from humans) are responding and adapting to exercise