Investigating Skeletal Muscle Metabolic Adaptations underlying Aerobic Fitness Gains Following High Intensity Interval Training in a Rat Model of Pulmonary Arterial Hypertension

Mary Talley[1], Rachel Novack[1], Tsungai J Chingombe[1], Tim Lahm[2,3], Irina Petrache[2,3] Mary Beth Brown[1] [1]Department of Physical Therapy, Indiana University School of Health and Rehabilitation Sciences, [2]Pulmonary and Critical Care, Department of Medicine, [3]Indiana University School of Medicine, Indianapolis, Indiana

Rationale: In patients with pulmonary arterial hypertension (PAH) a shift from oxidative to a less efficient non-oxidative (glycolytic) metabolism in skeletal muscle is believed to contribute to the reduced exercise tolerance hallmark of the disease. As seen for other cardiopulmonary diseases, exercise training (ExT) may ameliorate this “glycolytic switch” in PAH and improve exercise capacity. Previous studies in this lab showed an improved metabolic profile of skeletal muscle in PAH rats following an ExT protocol of continuous running at moderate relative intensity, 60 minutes at 75% of maximal aerobic capacity (VO_2Max). High intensity interval training (HIIT) has been shown in healthy individuals as well as in patients with cardiovascular disease to promote favorable cardiac and skeletal muscle adaptations and greater improvements in aerobic capacity versus customary continuous training. This study tests the hypothesis in a PAH rat model that HIIT will result in preserved aerobic capacity and a greater attenuation of skeletal muscle glycolytic shift than that observed with continuous moderate intensity exercise. Methods: Male Sprague-Dawley rats received either monocrotaline (MCT, 40 mg/kg, s.q.) to induce PAH (n= 8), or saline, for healthy controls (n=4). After 2 wks, with MCT-induced PAH well-established, 6 wks of treadmill HIIT was initiated for a subset of PAH animals (PAH-ExT, n= 6) and healthy controls (CON-ExT, n=2). The HIIT runs were alternated between 2 to 3 minutes of high intensity exercise (85% VO2max reserve) and active recovery intervals between 2 to 3 minutes (10 m/min, 0° incline) VO2max was assessed at baseline, and in pre-training and post-training via analysis of expired gases during incremental treadmill running. Preliminary results: MCT-induced decrement in VO2max was attenuated by HIIT. Abundance of membrane glucose transporter Glut-1, a marker of glycolytic metabolism, is currently being evaluated in soleus cryosections with immunofluorescent staining. Findings are being compared to historical data for PAH and healthy rats from a study protocol that differed only by training approach-continuous instead of HIIT.

Mentors: Mary Beth Brown, Department of Physical Therapy, IU School of Health and Rehabilitation Sciences, IUPUI; Tim Lahm, Pulmonary and Critical Care, Department of Medicine, IU School of Medicine, IUPUI