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Conference Details

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Total Expense (USD):750 Location:San Diego, CA

Conference Title: Plant and Animal Genomics (PAG) 2018

Communication Title: Proteome and Transcriptome Profiling of Equine Myofibrillar Myopathy Identifies Diminished Peroxiredoxin 6 and Enhanced Cysteine Metabolic Pathways

ABSTRACT

Arabian horses are adept at endurance races, routinely competing in distances of 50 to 100 miles. Exertional rhabdomyolysis (ER), literally the dissolution of skeletal muscle with exercise, is a common occurrence in endurance horses affecting 4 to 18% of competitors. To date, however, genetic causes of ER have not been identified in the Arabian horse breed. Recently, our lab has identified a muscle disease with a suspected genetic predisposition in Arabian horses called myofibrillar myopathy (MFM). MFM causes muscle stiffness, exertional muscle pain and is characterized by myofibrillar disarray and ectopic protein aggregates of unknown origin. To investigate the pathophysiology of equine MFM, we compared the skeletal muscle proteome and pre-and 3h post-exercise transcriptome of gluteal muscle in MFM and control Arabian horses using isobaric tags for relative and absolute quantitation (iTRAQ) for protein and RNA-Seq analyses for transcriptome quantification. Proteome analysis revealed significantly lower content of antioxidant peroxiredoxin 6 (PRDX6, ↓4.14 log2 fold change [FC]), sarcomere protein tropomyosin (TPM2, ↓3.24x) and higher fatty acid enzyme carnitine palmitoyl transferase (CPT1B, ↑3.49x) in MFM vs. control muscle at rest. Differential expression (DE) between case/control horses were evaluated using Edge R and pathway analysis performed using Cytoscape and Cluego. Three hours after exercise, 191 genes had DE in MFM vs. control muscle with a remarkably focused >1.5 log2 FC in genes involved in sulfur compound and cysteine metabolism. RNA-Seq analyses identified 284 genes as DE in MFM vs. control at rest with > 1.5 log2 FC in pathways for structure morphogenesis, fiber organization, tissue development and cell differentiation. Results indicate that, in MFM horses, characteristic myofibrillar disarray was represented by DE expression of genes in pathways involved in muscle structure/fiber organization and tissue regeneration and that protein aggregation may arise from oxidative damage to sarcomeric and cytoskeletal proteins as a result of diminished cysteine rich antioxidants such as peroxiredoxin 6 and a limited capacity to reduce free radicals generated through fatty acid oxidation during exercise. The data presented here is pioneering in that it uses for the first time a combined proteomic and transcriptomic approach to determine that pathomechanism for a newly described equine myofibrillar myopathy (MFM), a major cause of concern in endurance horses.

COMMUNICATION OUTCOMES

My research as an MSU postdoc, involves working with researchers, clinical practitioners, graduate and undergraduate students to study the underlying causes of muscular/neurological diseases using an equine as a model. The equine model is a very robust model for studying muscle morphology and function as these subjects are natural athletes, with large muscle mass for sampling. To study these changes into muscle physiology and structure, I use proteomics, transcriptomics and genomics to identify, query and establish underlining SNPs, genes, and pathways that contribute to the etiology of equine myofibrillar myopathy (MFM).
I have been invited to give oral presentations about the research undertaken in our lab on two days v at the Plant and Animal (PAG) 2018 conference in San Diego, CA, which is the largest Agricultural-genomics conference in the world. The first talk is going to be presented at the equine workshop, where the overall integrated approach using proteomics and transcriptomics analysis will be discussed as well as its value in elucidating the biological mechanisms driving MFM disease pathobiology and characterization. I will be addressing researchers and clinical practitioners to disseminate my findings and interact with current and future collaborators to bring new perspectives to our small community. This talk will provide me with a suitable platform needed for such a beneficial exchange of ideas as well as explore future collaborations and research.

The second talk will be hosted during the proteomics workshop at PAG 2018, showcasing the use of proteomics to the genomics community as cross-platform tool to better understand biology. With the integration of proteomics and transcriptomics, I will be providing an example of such a study using the equine model to use cross platform tools for meta-data integration and biology.

My ultimate objective from this conference is to develop novel collaborative opportunities to further my research network and incorporate new approaches and ideas for implementing scientific knowledge to understand muscle health and disease.