Skeletal Muscle Proteomic Signature In Pulmonary Arterial Hypertension

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Introduction: Most pulmonary arterial hypertension (PAH) patients exhibit severe dyspnea and fatigue resulting in restricted exercise capabilities and poor quality of life. Numerous observations suggest that exercise limitation in PAH is not solely due to cardio-pulmonary impairment, but that other determinants such as skeletal muscle abnormalities are involved. In order to better understand the origins of exercise limitation in PAH, we studied the proteomic signature of skeletal muscle impairment in PAH.

Methods and results: Muscle proteins from 4 idiopathic PAH patients and 4 matched controls were extracted following quadriceps muscle biopsy. Fractioned peptides were then tagged using an isobaric Tags for Relative and Absolute Quantitation (iTRAQ, ABsciex) specific for each patient. Tagged peptides were then mixed, fractioned, identified and quantified using mass spectrometry quantitative method. Over 900 proteins were identified using iTRAQ analysis, among them, 9 were under-expressed and 7 were over-expressed in all iPAH patient quadriceps. More than 75% of the under-expressed proteins are involved in oxidative metabolism and most other highlighted proteins play a role in myogenesis. In addition, structural differences between control and PAH skeletal muscles were explored by electronic microscopy. PAH skeletal muscles had decreased mitochondrial density and impaired mitochondrial structure resulting in abnormal metabolism. Finally, PAH skeletal muscles had impaired micro-vessels structure and decreased in their density.

Conclusions: Proteomic data allowed us to highlight proteins that could be responsible for exercise limitation in PAH. Taken together with electronic microscopy experiments, these data suggest that as shown in both the lungs and the right ventricle (RV), impairment of oxidative metabolism is also present in skeletal muscles of PAH patients. Similarly to the RV, metabolism unbalanced is associated with abnormal mitochondria and micro-vessels. In addition to shedding light on exercise limitation in PAH, this study might lead to the discovery of an early and less invasive diagnostic method for PAH.

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pas de conflit d'intérêts à déclarer