Label free proteomic analysis of Duchene and Becker muscular dystrophy revealed decrease of proteins involved in sarcomere organization.

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Introduction - Muscular Dystrophies (MD) represent a heterogeneous group of hereditary diseases characterized by progressive loss of muscle tissue leading to weakness and degeneration of skeletal muscles mostly occurring due to structural alterations in Dystrophin-Glycoprotein Complex (DGC) such as in Duchenne Muscular Dystrophy (DMD) and Becker Muscular Dystrophy (BMD). The Dystrophin-Glycoprotein Complex (DGC) is the major structural element present in the muscle fibers and is responsible for maintaining the stability and integrity of the fibers through a network that couples the extracellular matrix components to the cytoskeleton. Like all degenerative diseases, MDs have no cure, and for this reason, clinical and experimental studies have focused on characterizing putative therapeutic targets to increase the time and quality of life for patients.

Methodology - In this work, skeletal muscle tissue samples from 4 DMD and 3 BMD patients obtained by biopsy, as well as from 3 non-dystrophic patients, were used. The tissues proteins extracts were hydrolysed according to the \"filter-aided sample purification\" (FASP) protocol and analysed using Easy1000 nanoLC system (Thermo Fisher) coupled to a Quadrupole Orbitrap mass spectrometer (Q Exactive Plus, Thermo Scientific) to qualitatively and quantitatively characterize the proteomic profile of DMD and BMD using a label free proteomic methodology. Database searches and identification of peptides and proteins were conducted using the Proteome Discoverer v2.5.0.400.

Results and discussion - Our GO analysis showed that the molecular signature of muscle tissue is related to biological processes associated with cellular energy metabolism, such as energy derivation by oxidation of organic compounds, generation of precursor metabolites and energy, and cellular respiration. We also observed an enrichment of molecular functions related to cell structure and RNA binding, such as structural molecule activity, cytoskeletal protein binding, and RNA binding. In fact, the human phenotypes most related to the proteomic signature were associated with abnormal circulating metabolite concentration, abnormal muscle physiology and muscle weakness. Comparing DMD vs. Control and BMD vs. Control we found proteins with abundance differences statistically significant related with sarcomere organization and ubiquitination. We would like to highlight two proteins with decreased abundance in both DMD and BMD, compared to control: Myomesin-2 (MYOM2; P54296) and Myozenin-2 (MYOZ2; Q9NPC6), these proteins have a pivotal function in sarcomere organization.

Conclusion

- Quantitative analysis showed that Becker and Duchenne muscular dystrophy significantly alter the abundance of proteins related to sarcomere organization, as myomesin-2 and myozenin suggesting them as putative therapeutic targets.

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