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Bioinformatics tools for the systems biology of dysferlin deficiency

Abstract:

The aim of this project was to build and apply tools for the analysis of muscle omics data, with a focus on Dysferlin deficiency. This protein is expressed mainly in skeletal and cardiac muscles, and its loss due to mutation (autosomal-recessive) of the *DYSF* gene, results in a progressive muscular dystrophy (Limb Girdle Muscular Dystrophy type 2B (LGMD2B), Miyoshi myopathy and distal myopathy with tibialis anterior onset (DMAT)). We have developed various tools and pipelines that can be applied towards a bioinformatics functional analysis of omics data in muscular dystrophies and neuromuscular disorders. These include: tests for enrichment of gene sets derived from previously published muscle microarray data and networking analysis of functional associations between altered transcripts/proteins. To accomplish this, we analyzed hundreds of published omics data from public repositories. The tools we developed are called CellWhere and MyoMiner.

CellWhere is a user-friendly tool that combines protein-protein interactions and protein subcellular localizations on an interactive graphical display. It accepts a list of genes and generates a protein-protein interaction network graph organized into subcellular locations to mimic the structure of the cell. Localization annotations acquired from the manually curated public repositories, Gene Ontology and UniProt (Swissprot), are mapped to a smaller number of CellWhere localizations. Protein-protein interactions and their scores are acquired from the Mentha interactome server. CellWhere can be accessed freely at https://cellwhere-myo.rhcloud.com

MyoMiner is a muscle cell- and tissue-specific database that provides co-expression analyses in both normal and pathological tissues. Many gene co-expression databases already exist and are used broadly by researchers, but MyoMiner is the first muscle-specific tool of its kind. High-throughput microarray experiments measure mRNA levels for thousands of genes in a biological sample and most microarray studies are focused on differentially expressed genes. Another way of using microarray data is to exploit gene co-expression, which is widely used to study gene regulation and function, protein interactions and signaling pathways. These co-expression analyses will help muscle researchers to delineate muscle pathology specific protein interactions and pathways. Changes in co-expression between pathologic and healthy tissue may suggest new disease mechanisms and therapeutic targets. MyoMiner is a powerful

muscle specific database for the discovery of genes that are associated in related functions based on their co-expression and is available at https://myominer-myo.rhcloud.com.