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A Short History of Skeletal Muscle Proteomics

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Abstract

Proteomics is the study of proteins using high-throughput techniques and relies on a combination of genomics, mass spectrometry and protein biochemistry. The human genome contains of approximately 20,000 genes that are transcribed into mRNA and then can be translated in to proteins Researchers can test hypotheses regarding individual mRNA or proteins using techniques such as Northern blots (for mRNA expression) or Western blots (for protein abundance). This 'reductionist' approach, where biology is reduced to individual questions, has been the mainstay of biological research. However, data arising from hypothesis-led studies clearly indicates that biology is not organised or controlled by isolated events Rather, biological systems are organised as complex networks and multiple interactions occur to bring about physiological changes. Therefore, more comprehensive (eg '-omic') analysis techniques are required in order to advance our understanding of biological systems.

The proteome is cell-specific and dynamic, responding on a minute-by-minute basis to changes in cell environment. Consequently, the proteome reflects the particular stage of development and current environmental condition the cell finds itself experiencing with regard exercise proteomics, report proteomic studies have mostly focused on striated muscle responses to endurance training, which are associated with health benefits underpinned by improvements in aerobic capacity. Over the past decade, researchers have studied the ability of proteomics analysis on skeletal muscle and the development of techniques. In this review we will point out some of the studies related that contributed to skeletal muscle proteomics

Keywords: Skeletal Muscle; Proteomics; 2DGE; MALDI-TOF; LC-ESI-MS/MS

Introduction

In theory, proteomics techniques should be able to characterise and measure the relative abundance of each myofibrillar protein species (ie encompassing isoforms, splice-variants and post-translational states) simultaneously [1]. This more comprehensive analysis circumvents the need to reduce the description of muscle to its relative proportion of 3 fibre types Burniston and Hoffman (2011) [2].

Studies Related

The first study to report proteomic analysis of skeletal muscle was reported the effects of atrophy in rat slow twitch muscle Since this initial publication there have been many studies in skeletal muscle animal and human-a summary of proteomic studies investigating muscle of laboratory animals is presented in Table 1 [3]. In particular 2DGE has been used to catalogue the proteins expressed in striated muscle Early investigations produced 2D gel maps of mouse mixed-fibre gastrocnemius muscle, and compared archetypal muscles such as rat extensor digitorum longus (EDL) and soleus that comprise predominantly fast- or slow-twitch fibres, respectively [4,5]. Mean while Hojlund et al. [6] used 2DGE of human vastus lateral is to observe proteins with potential roles in type 2 diabetes Furthermore 2DGE of human samples has been used to provide more detailed information regarding proteome changes due to aging, obesity and exercise training [7-10]. Gelfi et al. [7] in their study of 2D gel map of human vastus lateralis muscle provide a valuable resource for the definition of functional properties of muscle fibres. These and other proteome mining works provide important catalogues of accessible muscle proteins and extend earlier biochemical and histochemical studies describing muscle diversity.

Author, Year	Sample	Technique
Isfort, et al. 2000 [3]	Rat soleus denervation	2DGE, MALDI-TOF
Sanchez, et al. 2001 [4]	Mouse skeletal muscle	2DGE, MALDI-TOF
Yan, et al. 2001 [11]	Rat skeletal muscle	2DGE, MALDI-TOF
Le Bihan, et al. 2004 [12]	Mouse skeletal muscle	SELDI-TOF
Donoghue, et al. 2005 [13]	Rabbit skeletal muscle electro-stimulation	2DGE, MALDI-TOF
Piec, et al. 2005 [14]	Rat skeletal muscle ageing	2DGE, MALDI-TOF
Okumura, et al. 2005 [15]	Rat skeletal muscle	SDS-PAGE, 2DGE, MALDI-TOF
Gelfi, et al. 2006 [6]	Rat soleus & gastrocnemius ageing	2-DGE, LC-ESI-MS/MS
Guelfi, et al. 2006 [16]	Rat skeletal muscle acute exercise	2DGE, LC-ESI-MS/MS
O'Connell, et al. 2007 [17]	Rat skeletal muscle ageing	2DGE, MALDI-TOF
De Palma, et al. 2007 [18]	Rat skeletal muscle hypoxia	2D DIGE, LC-ESI-MS/MS
Donoghue, et al. 2007 [19]	Rabbit tibialis anterior electro-stimulation	2DGE, MALDI-TOF
Burniston 2008 [20]	Rat Plantaris exercise	2DGE, MALDI-TOF/TOF
Doran, et al. 2008 [21]	Rat skeletal muscle ageing	2D DIGE, MALDI-TOF
O'Connell, et al. 2008 [22]	Rat gastrocnemius ageing	2DGE, MALDI-TOF
Moriggi, et al. 2008 [23]	Rat skeletal muscle dytrophy	2D DIGE, MALDI-TOF
Gannon, et al. 2008 [24]	Rat gastrocnemius ageing	2DGE, MALDI-TOF
Gannon, et al. 2009 [25]	Rat gastrocnemius ageing	2DGE, MALDI-TOF
Donoghue, et al. (2010) [26]	Rat skeletal muscle ageing	2DGE, MALDI-TOF, LC-ESI-MS/MS
Lewis & Ohlendieck 2010 [27]	Mouse skeletal muscle dystrophy	2DGE , LC-ESI-MS/MS
Mullen & Ohlendieck 2010 [28]	Rats gastrocnemius diabetes	2DGE, LC-ESI-MS/MS
Mullen & Ohlendieck 2011 [29]	Rat gastrocnemius diabetes	2DGE, LC-ESI-MS/MS
Macedo, et al. 2012 [30]	Mouse skeletal muscle	MALDI-TOF/TOF
Malik, et al. 2013 [31]	Rats soleus & Human vastus lateralis	LC-ESI-MS profiling, LC-ESI-MS/MS, SRM
Burniston, et al. 2014 [32]	Rat soleus, artificial selection	2D DIGE, LC-ESI-MS/MS

Table 1: Summary of proteomic studies on animal skeletal muscle.

Two-dimensional gel electrophoresis (2DGE), Matrix-assisted laser desorption ionisation (MALDI), Surface-enhanced laser desorption ionisation (SELDI), Time of flight (TOF), Tandem time of flight (TOF/TOF), Liquid chromatography (LC), Electrospray ionisation (ESI), Mass spectrometry (MS, Tandem mass spectrometry (MS/MS), Difference in-gel electrophoresis (DIGE), Selective reaction monitoring (SRM).

Proteomic Techniques

The use of 2DGE offers robust comparative analysis of protein species, which represent different post-translational states of a protein [33]. However, 2DGE requires a significant level of skill is laborious and has a number of technical limitations, including difficulties in resolving proteins at the extremes of the mass and pH scales, and a limited dynamic range. Therefore, there is currently a drive to move away from 2DGE and develop simpler (SDS-PAGE) or more automated HPLC workflows. In muscle proteomics, the time efficiency of orthogonal SDS-PAGE and HPLC separations has been investigated [34]. The combination of SDS-PAGE with HPLC coupled directly to electrospray ionisation (ESI) tandem mass spectrometry (MS/MS), known as GeLC-MS/MS is of particular utility in skeletal muscle protein identification [35]. Several studies have applied the GeLC-MS/MS technique in proteomic research [36] used GeLC-MS/MS and reported combination of proteomic and transcriptomic analyses. In 2008, Hojlund and colleagues catalogued almost 1,000 proteins in the human skeletal muscle proteome using GeLC-MS/MS and Norheim, et al. [37] used this method for identification of proteins secreted by skeletal muscle cells *in vitro.*

Burniston & Hoffman, (2011)[2] pioneered the application of proteomic techniques to investigate cardiac and skeletal muscle responses to endurance exercise. Further to standard proteomic techniques using 2DGE [20], they have developed specific methods for analysing muscle proteins [2,8,38] using sub-fractionation and solution-based protein separations (ie 1D HPLC). The current researches further develops this workflow by specifically investigating the myofibrillar sub-proteome using liquid chromatography separation of proteins with real-time tandem mass spectrometry and create a more robust analysis platform for measuring differences in the abundance of dozens of important myofibrillar proteins based on quantitative label-free mass spectrometry techniques.

Conclusions

More than a decade of research exploring the proteomic analysis of skeletal muscle has provided very promising results; only the future will determine more advance proteomic techniques will successfully use by all researchers.

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