ELSEVIER

Journal of Chromatography B, 771 (2002) 155–165

JOURNAL OF
CHROMATOGRAPHY B

www.elsevier.com/locate/chromb

Review

Proteomic analysis of striated muscle

Robert J. Isfort*

Research Division, Procter & Gamble Pharmaceuticals, Health Care Research Center, 8700 Mason-Montgomery Road, Mason, OH 45040-9317, USA

Abstract

The techniques collectively known as proteomics are useful for characterizing the protein phenotype of a particular tissue or cell as well as quantitatively identifying differences in the levels of individual proteins following modulation of a tissue or cell. In the area of striated muscle research, proteomics has been a useful tool for identifying qualitative and quantitative changes in the striated muscle protein phenotype resulting from either disease or physiological modulation. Proteomics is useful for these investigations because many of the changes in the striated muscle phenotype resulting from either disease or changes in physiological state are qualitative and not quantitative changes. For example, modification of striated muscle proteins by phosphorylation and proteolytic cleavage are readily observed using proteomic technologies while these changes would not be identified using genomic technology. In this review, I will discuss the application of proteomic technology to striated muscle research, research designed to identify key protein changes that are either causal for or markers of a striated muscle disease or physiological condition. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Reviews; Proteomics; Striated muscle

Contents

1. Introduction ... 155
2. Proteomic analysis of striated muscle ... 156
3. Value of proteomic analysis in understanding striated muscle biology ... 162
4. Conclusions ... 164
References ... 164

1. Introduction

Striated muscle has several major functions in the body including movement, storage of amino acids, and storage of energy. Diseases of striated muscle can have profound physiological effects including loss of movement and metabolic disequilibrium. These effects are often lethal and thus research is focused on understanding the underlying molecular causes of various striated muscle diseases including muscular dystrophies, myopathies, striated muscle metabolic disorders and neural muscular diseases. In addition to striated muscle diseases, research is also focused on understanding normal physiological processes of striated muscle including contraction, development, differentiation, metabolism, and neuro-

*Tel.: +1-513-622-1899; fax: +1-513-622-1195.
E-mail address: isfortrj@pg.com (R.J. Isfort).

1570-0232/02/$ – see front matter © 2002 Elsevier Science B.V. All rights reserved.
PII: S1570-0232(02)00056-9

muscular biology. One area of active research involves understanding the physiological, biochemical and molecular processes involved in the storage and release of amino acids. Collectively these processes are known as atrophy or wasting (the release of stored amino acids from muscle) and hypertrophy (the storage of amino acids). Striated muscle atrophy, induced by diverse stimuli such as disuse, immobilization, nerve damage, sepsis, and starvation, is a process in which selective protein loss occurs [1–5]. While each atrophy-inducing mechanism has its own unique initiation signal, it is generally believed that a common mechanism for protein loss occurs. During atrophy, loss of a subset of striated muscle proteins including contractile proteins occurs. In contrast, striated muscle hypertrophy is a process of increased protein mass resulting in increased function. Striated muscle atrophy occurs by decreasing protein synthesis and increasing protein degradation while hypertrophy results from the opposite activities [6–9]. Mechanistically, this occurs by altering gene transcription, mRNA translation and proteolysis including modulating the calpain, lysosomal and ubiquitin-mediated proteolytic systems [6–9].

Proteomics refer to a collection of technologies with the common goal of separating and identifying proteins in complex biological samples. One of the most widely used proteomic technologies is two-dimensional gel electrophoresis (2DGE). 2DGE involves separating a complex protein mixture first by charge using isoelectric focusing then by size using SDS–PAGE. Coupling these two technologies allows for the separation of hundreds to thousands of proteins into discrete spots. Importantly, 2DGE can be performed quantitatively so that the relative amount of the separated proteins can be measured. When 2DGE is coupled with a protein identification technology, such as Edman sequencing or mass spectrometry, proteins of interest can be identified and an understanding of the biological significance of the protein changes can be determined. In addition to 2DGE, several other proteomic technologies are currently undergoing evaluation including ICAT [10], MALDI–MS [11] and coupled chromatography [12]. These technologies are still in the optimization and validation phase and thus have not been widely applied to research topics of interest in striated muscle.

2. Proteomic analysis of striated muscle

During the past 30 years, many proteomic analyses of striated muscle have been performed. The earliest studies, particularly those by Giometti and coworkers [13–16] used 2DGE in addition to protein identification technologies to quantitatively compare changes in the protein phenotype from normal and diseased striated muscle. These pioneering studies demonstrated the potential of using proteomic technology to characterize the striated muscle protein phenotype and identify protein markers of disease states. Studies by Lorkin and Lehmann [17] investigated the use of proteomic technology (2DGE) for determining the mechanisms involved in a toxicological effect—halothane-induced malignant hyperthermia. Heizmann and coworkers [18] used proteomic technology to identify proteins useful in distinguishing type I from type IIA and type IIB muscle fibers. Studies by Murakami and coworkers [19] and Yablonka-Reuveni and coworkers [20] demonstrated the application of proteomic technology in identifying protein markers useful in differentiating cardiac, striated and smooth muscle as well as myoblast from fibroblast isolated from embryonic striated muscle. Following these pioneering studies in the 1970s and 1980s, a plethora of scientific research on striated muscle using proteomic technologies occurred. Many studies focused on identifying the molecular mechanisms involved in muscular dystrophies by identifying differences in the protein phenotype of dystrophic muscle when compared to normal muscle [21,22]. In addition, studies were conducted which were designed to identify changes in the protein phenotype from muscle undergoing atrophy resulting from nerve damage [23–26]; sepsis [27]; hindlimb suspension [28,29]; limb immobilization [30–32]; congestive heart failure [33]; spaceflight [29]; and age-related striated muscle atrophy (also known as sarcopenia) [34,35]. In contrast to striated muscle atrophy, studies were undertaken to identify changes in the protein phenotype in striated muscle undergoing hypertrophy resulting from either reweighting [28] or chronic electrical stimulation [36,37]. In all these studies, the intention of the proteomic analysis was to identify markers related to the specific physiological condition or disease state under investigation. Unfortunately, quantitative

proteomic analysis was not performed in most of these studies since rigorous quantitative analysis technology has only recently been introduced and was not available at the time these studies were performed. In addition to the use of 2DGE for characterizing changes in the protein phenotype during disease and following physiological modulation of striated muscle, 2DGE has been used extensively to characterize individual proteins in striated muscle extracts, particularly protein isoforms with minor differences in either molecular mass or charge. For example, myosin heavy and light chains, tropomyosins, C-protein, troponin T, dihydropyridine receptor subunits, proteasome subunits, actin binding proteins, desmin, dystrophin associated proteins and enolase [37–52].

Proteomic technology, in particular 2DGE has been used to catalog the proteins expressed in striated muscle. Several studies of this type have been performed including the pioneering studies of Giometti and coworkers [13–16] in which muscle proteins were separated using 2DGE with approximately 20 different proteins identified. Recently, two studies have been published that have attempted to utilize 2DGE in conjunction with mass spectrometry to generate a more complete striated muscle protein map. Yan and coworkers [53] identified 74 different proteins using these techniques while Sanchez and coworkers [54] identified 141 proteins. Importantly, all three studies identified not only novel proteins but also variants of specific proteins which migrated differently using 2DGE. Table 1 contains a list of published striated muscle proteins identified using proteomic technology. The study by Sanchez and coworkers [54] is part of the SWISS-2D PAGE database of two-dimensional electrophoresis reference maps from mouse samples and can be accessed at http://www.expasy.ch/ch2d/. At this site can be found both a listing of all identified striated muscle proteins and a striated muscle protein 2D gel image and map. It is noteworthy that in the approximately 20 years between the studies of Giometti and coworkers and Yan/Sanchez and coworkers, the efficiency in the resolution and identification of striated muscle proteins using proteomic technology has increased over 700%.

One area of striated muscle biology that is currently undergoing intense investigation is the loss and gain of striated muscle protein following either decreased or increased use. Atrophy or wasting (loss of muscle mass and function) and hypertrophy (gain of muscle mass and function) are normal physiological phenomena that are poorly understood at the molecular level and thus particularly attractive subjects for proteomic analysis. As discussed above, in the past, several proteomic analyses have been performed on striated muscle undergoing atrophy and hypertrophy; however these studies were not performed using modern proteomic technologies resulting in poor quantitative analysis and relatively few identified protein changes [24,26,27,31–36]. Recently, we have performed a series of quantitative proteomic analysis on striated muscle undergoing atrophy induced by either hindlimb suspension, limb immobilization or denervation in addition to hypertrophy induced by hindlimb reweighting following hindlimb suspension [23,28,30]. In these studies care was taken in the study design and execution to ensure that strict statistical criteria could be applied, allowing for the measurement of significant quantitative changes in protein levels following perturbation. In particular, triplicate samples/time point were analyzed; samples were prepared using well characterized dissolution agents designed to minimize sample alteration during preparation; 2DGE was performed using optimized conditions carefully controlling for all potential variables including variations in electrolyte quality, gel-to-gel casting variations, run condition variations and protein staining; data analysis was automated as much as possible in order to avoid operator bias; data accuracy and consistency was checked by highly trained and experienced analysts; rigorous statistical analysis of the data was performed; and protein identification was performed using highly sensitive MALDI–TOF technology with the protein identification checked, when possible, using Edman protein sequencing technology. The results of these analyses were the observation of 73 protein changes in rat soleus muscle following denervation-induced atrophy, 17 protein changes in rat soleus muscle following limb immobilization-induced atrophy, 29 protein changes in rat soleus muscle following hindlimb suspension-induced atrophy, and 15 protein changes in rat soleus muscle following reweighting. Because of the quantitative nature of the data, study-to-study comparisons could be made allowing for the identifi-

Table 1
Striated muscle proteins identified using proteomic technologies

Protein	p*I*	MW	Reference
Aconitate hydratase, mitochondrial	7.4	82 399	[53]
Actin, alpha	5.2	41 817	[13–16,23,25,28,30,53,54]
Actin, aortic smooth muscle	5.2	41 775	[53]
α-Actinin	5.2	41 817	[13–16]
Albumin, serum	5.8	65 904	[13–16,31,32,34,53,54]
Aldehyde dehydrogenase, mitochondrial	6.3	50 388	[54]
Aldolase	8.3	39 352	[13–17,34]
Aldose reductase	6.3	35 666	[53]
Alpha crystallin B chain	6.8	20 089	[23,28,30,53,54]
Antioxidant protein 2	6.2	26 047	[23,28,30,54]
Apolipoprotein A-I	5.2	23 915	[54]
ATP synthase alpha chain	8.3	55 267	[53]
ATP synthase alpha chain, mitochondrial	7.6	50 806	[54]
ATP synthase beta chain, mitochondrial	5.0	51 710	[23,28,30,53,54]
ATP synthase D chain, mitochondrial	6.2	18 632	[53]
Beta enolase	6.2	46 894	[13–16,23,28,30,34,53,54]
C-protein	6.4	68 737	[13–16]
Carbonic anhydrase III	7.0	29 300	[23,28,30,53,54]
Calmodulin	4.0	13 627	[54]
Calreticulin	4.5	60 352	[54]
Cofilin 2	7.7	18 709	[53]
Contraception associated protein 1	6.3	21 800	[53]
Creatine kinase	6.6	43 019	[13–16,34,53]
Creatine kinase, M chain	6.6	43 019	[53,54]
Creatine kinase, sarcomeric mitochondrial	7.3	42 116	[54]
Cypher 2	9.2	31 430	[53]
Cytokeratin	5.3	41 076	[54]
Cytochrome C oxidase polypeptide VA, mitochondrial	5.0	12 485	[54]
Cytochrome C oxidase polypeptide VB, mitochondrial	5.9	12 589	[54]
Desmin	5.3	53 837	[13–16,23,28,30,54]
Dystrophin	5.5	350 000	[21]
Endoplasmin	4.9	96 873	[54]
Eukaryotic translation elongation factor 1 alpha 1	9.1	50 454	[53]
Fatty acid binding protein, heart	5.3	13 125	[23,28–30,54]
Five finger-containing phosphoinositide kinase	6.1	173 259	[54]
Fructose-bisphosphate aldolase A	8.0	39 728	[54]
Fructose-bisphosphate aldolase C	6.8	35 468	[54]
Fructose-bisphosphate aldolase, muscle	8.4	39 220	[53]
78-kDa Glucose-regulated protein	5.0	72 255	[54]
Glutathione *S*-transferase GT8.7	8.1	26 655	[54]
Glutathione *S*-transferase P1	7.7	24 612	[54]
Glyceraldehyde 3-phosphate dehydrogenase	8.4	35 705	[13–17,34,53,54]
Glyceraldehyde 3-phosphate dehydrogenase, cytoplasmic	5.8	37 462	[53]
Heat shock protein 60 precursor	5.9	60 965	[23,28,30]
Heat shock cognate 71-kDa protein	5.4	70 871	[53,54]
Heat shock 27 protein	6.1	22 893	[53]
Heat shock protein HSP-90 beta	5.0	85 913	[54]
Heat shock 47-kDa protein	8.8	44 778	[53]
Hemoglobin alpha chain	7.8	12 050	[54]
Hemoglobin beta-1 chain	7.8	12 050	[13–16,54]

Table 1. Continued

Protein	p*I*	MW	Reference
Isovaleryl-CoA dehydrogenase	6.4	40 985	[54]
Lactate dehydrogenase B	5.7	36 612	[23,28,30]
L-Lactate dehydrogenase M chain	7.0	33 645	[54]
Malate dehydrogenase, mitochondrial	8.4	33 124	[53]
Mitochondrial matrix protein, P1	5.3	59 312	[54]
Mitochondrial stress-70 protein	5.3	69 611	[54]
Myoglobin	7.2	13 885	[13–16,34,54]
Myosin regulatory light chain 2, striated muscle isoform	4.8	18 838	[53,54]
Myosin regulatory light chain 2, ventricular/cardiac muscle isoform	4.9	18 749	[53]
Myosin-binding protein H	5.8	63 743	[54]
Myosin heavy chain	8.6	225 037	[13–16]
Myosin heavy chain, cardiac muscle alpha isoform	5.3	141 926	[54]
Myosin light chain 1, striated muscle isoform	5.0	20 548	[13–16,23,25,28–30,40,53,54]
Myosin light chain 1, slow twitch muscle B/ventricular isoform	5.0	22 025	[13–16,25,29,40,53]
Myosin light chain 2, slow twitch			[25,29,40]
Myosin light chain 2, fast twitch	4.8	18 969	[29,40,53]
Myosin light chain 2, cardiac	4.9	18 880	[23,28,30]
Myosin light chain 3, striated muscle isoform	4.5	13 044	[29,40,54]
NADPH-cytochrome P450 reductase	5.3	72 255	[54]
Natural killer cell surface protein P1-40	6.5	12 962	[54]
Nucleoside diphosphate kinase B	6.8	14 905	[54]
P20	6.1	17 504	[23,28,30]
Parvalbmin alpha	5.0	11 794	[34,53,54]
Peptidyl-prolyl *cis-trans* isomerase A	7.0	14 967	[54]
Phosphatidylethanolamine binding protein	5.5	20 801	[53]
Phosphoglycerate mutase, muscle form	8.8	28 755	[53,54]
Phosphoglycerate kinase 1	7.6	42 000	[54]
Phosphoglucomutase	6.1	59 755	[23,28,30,54]
Protein disulfide isomerase	4.8	57 681	[54]
Protein disulfide isomerase ER-60	5.8	56 578	[54]
Proteasome beta chain	5.4	24 715	[54]
Pyruvate carboxylase	6.2	118 405	[54]
Pyruvate kinase, M1 isozyme	6.7	57 686	[53]
Pyruvate kinase, M2 isozyme	6.7	56 578	[54]
60S Acidic ribosomal protein P2	4.4	14 089	[54]
40S Ribosomal protein SA	4.8	42 583	[54]
Serotransferrin precursor	6.8	74 517	[53,54]
Skelemin	6.0	174 181	[54]
Superoxide dismutase [Cu–Zn]	6.1	14 326	[54]
T-complex protein 1, epsilon subunit	5.7	59 607	[54]
T-lymphoma invasion and metastasis inducing protein 1	6.1	172 342	[54]
Thioredoxin peroxidase 1	5.3	21 784	[53]
Translationally controlled tumor protein	4.7	24 152	[54]
Triosephosphate isomerase	6.5	26 790	[13–16,27,53,54]
Troponin C, striated muscle	3.9	18 512	[13–16,54]

Table 1. Continued

Protein	p*I*	MW	Reference
Troponin I, fast striated muscle	8.3	24 560	[54]
Troponin T	6.2	30 750	[23,28,30]
Troponin 1, fast striated muscle	8.9	21 197	[53]
Tropomyosin	4.7	28 720	[13–16]
Tropomyosin alpha chain, striated/cardiac muscle	4.8	28 709	[53,54]
Tropomyosin alpha chain, smooth muscle	4.7	32 675	[53]
Tropomyosin beta chain, striated muscle	4.7	32 850	[53]
Tubulin alpha-1 chain	5.1	56 111	[54]
Tubulin beta-5 chain	4.9	53 246	[54]
Ubiquitin	8.9	17 983	[53]
UTP-glucose-1-phosphate uridylyltransferase 1	6.8	52 228	[54]
Vimentin	5.1	55 496	[54]
Voltage-dependent anion channel protein 1	9.1	32 740	[54]
Voltage-dependent anion channel	8.6	32 351	[53]

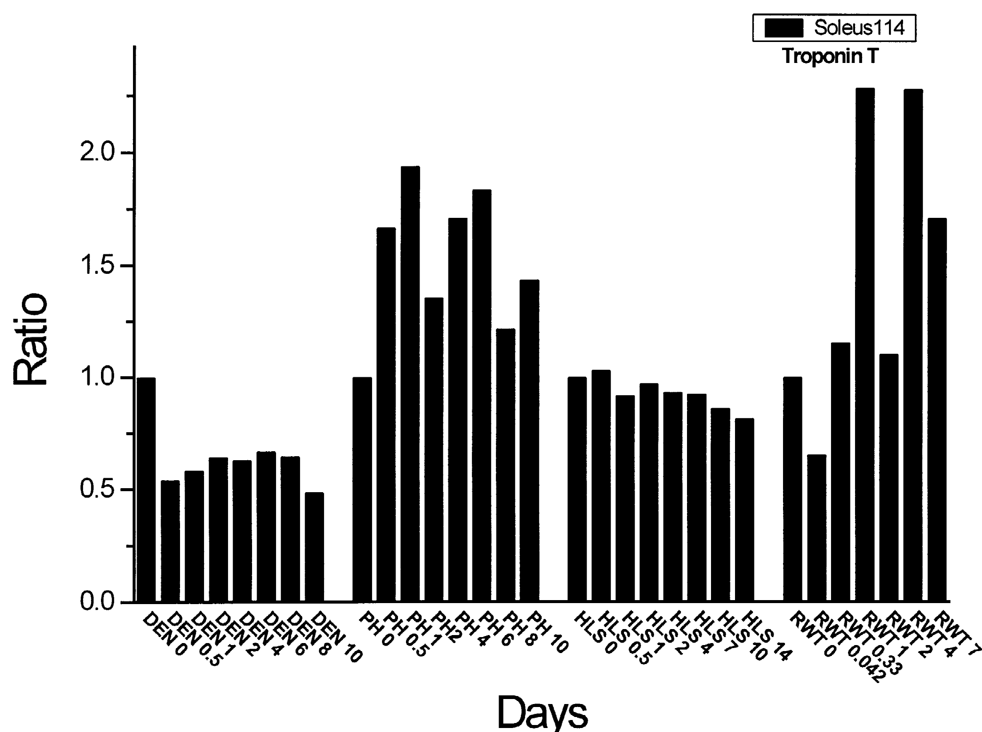

Fig. 1. Analysis of relative levels of soleus protein 114, identified as tropinin T, following either denervation-induced atrophy (DEN), pin-heel limb immobilization-induced atrophy (PH), hindlimb suspension-induced atrophy (HLS), or reweighting following hindlimb suspension-induced hypertrophy (RWT). All data are given as the ratio of soleus protein 114 (troponin T) levels at various times following the induction of atrophy or hypertrophy relative to the corresponding zero time point level. Times are given in days following the induction of atrophy or following reweighting after 21 days of hindlimb suspension. All data are the average of three different soleus muscles/time point.

cation of common protein changes between different atrophy conditions. For example, Fig. 1 demonstrates quantitative changes in soleus protein 114 (identified as troponin T) levels showing a decrease in protein levels 12 h following denervation, an increase in protein levels 12 h following hindlimb immobilization, no change following hindlimb suspension and increased levels following reweighting. Thus changes in troponin T levels appear to be atrophy model-specific. A second example is shown in Fig. 2. Here soleus protein 255 (not yet identified) levels decreased dramatically in denervation and hindlimb suspension atrophies, did not change in limb immobilization, and increased dramatically following reweighting-induced hypertrophy. Thus soleus protein 255 would serve as a marker for hindlimb suspension and denervation-induced atrophy as well as reweighting hypertrophy but is not a marker for limb immobilization-induced atrophy. A third interesting protein change is illustrated in Fig. 3. In this instance, soleus protein 459 (not yet identified) levels increased significantly in denervation, immobilization, and hindlimb suspension-induced atrophies and decreased during reweighting hypertrophy. Thus, soleus protein 459 would serve as an excellent marker of atrophy and hypertrophy and in addition may provide important biological insight into the atrophy and hypertrophy processes. A final example is shown in Fig. 4. Here, soleus protein 333 (identified as the P20 protein) levels decreased significantly in denervation, hindlimb suspension and limb immobilization-induced atrophies and increased during reweighting hypertrophy. P20 is a member of the small heat shock protein family, a family of proteins that have important roles in striated muscle biology including signal transduction, chaperone activities, and maintenance of the quasi-crystalline structure of the contractile apparatus [55–59]. Thus the altera-

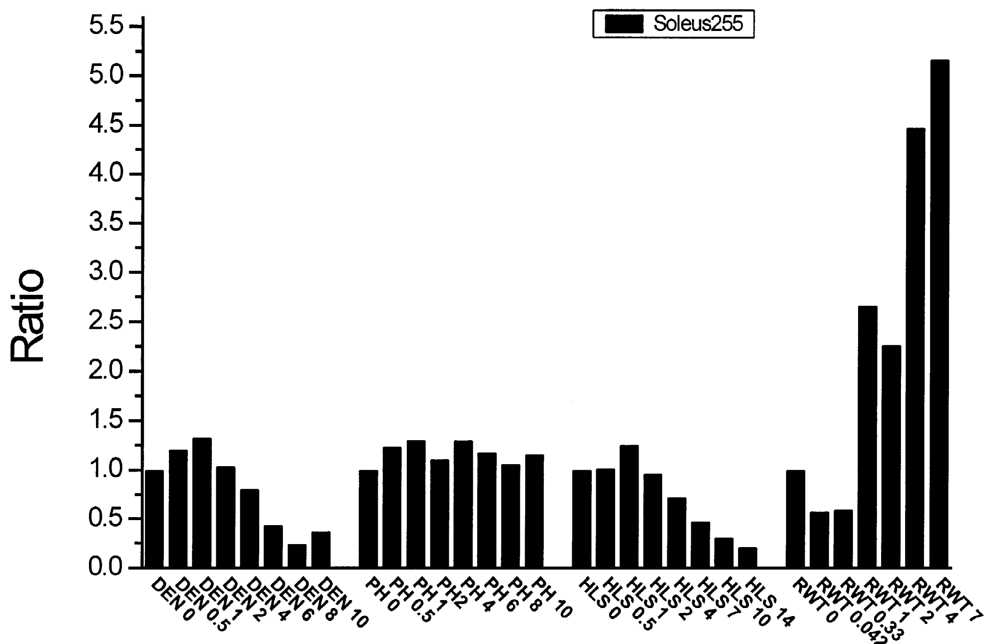

Fig. 2. Analysis of relative levels of soleus protein 255 following either denervation-induced atrophy (DEN), pin-heel limb immobilization-induced atrophy (PH), hindlimb suspension-induced atrophy (HLS), or reweighting following hindlimb suspension-induced hypertrophy (RWT). All data are given as the ratio of soleus protein 255 levels at various times following the induction of atrophy or hypertrophy relative to the corresponding zero time point level. Times are given in days following the induction of atrophy or following reweighting after 21 days of hindlimb suspension. All data are the average of three different soleus muscles/time point.

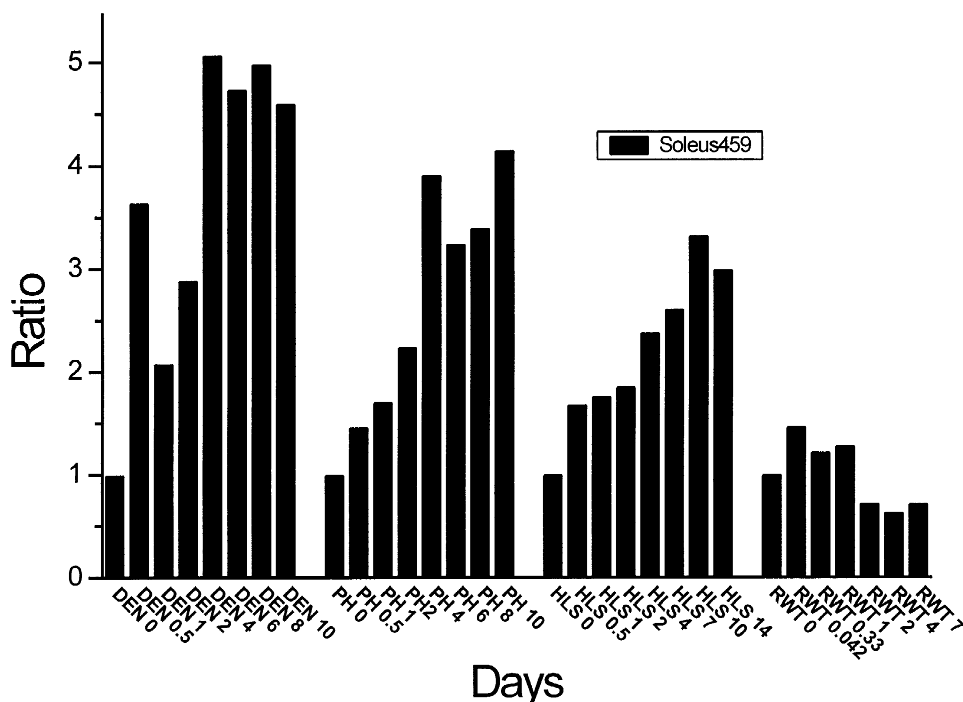

Fig. 3. Analysis of relative levels of soleus protein 459 following either denervation-induced atrophy (DEN), pin-heel limb immobilization-induced atrophy (PH), hindlimb suspension-induced atrophy (HLS), or reweighting following hindlimb suspension-induced hypertrophy (RWT). All data are given as the ratio of soleus protein 459 levels at various times following the induction of atrophy or hypertrophy relative to the corresponding zero time point level. Times are given in days following the induction of atrophy or following reweighting after 21 days of hindlimb suspension. All data are the average of three different soleus muscles/time point.

tions observed with P20 point to an important role for this protein in atrophy and hypertrophy.

3. Value of proteomic analysis in understanding striated muscle biology

As I discussed above, proteomic analysis has been used to evaluate changes in the protein phenotype occurring during striated muscle disease and physiological perturbation. The value of this approach in investigating striated muscle disease lies in the ability of proteomics to provide a comprehensive view of the striated muscle protein phenotype. This in turn allows the investigator to formulate a more comprehensive hypothesis with regards to the biological phenomena under investigation, instead of making smaller disjointed hypotheses based on the observation of a small number of proteins. Thus, in the case of striated muscle diseases such as muscular dystrophy, unknown genetic mutations underlying the disease could be inferred from the loss of specific proteins identified using proteomic technology. In addition, when the underlying genetic mutations for a particular type of muscular dystrophy is known, the effects of loss of this protein on the muscle can be determined by observing changes in the striated muscle protein phenotype over time. In both instances, the use of a comprehensive cataloging technology such as proteomics provides the type and amount of data necessary to identify useful markers of a disease and/or understanding the molecular pathology of the disease state. In both instances, the information gleaned from the proteomic analysis is useful in developing hypothesis that lead to a better understanding of the disease and ultimately measures to alleviate the disease.

In normal physiological processes such as striated

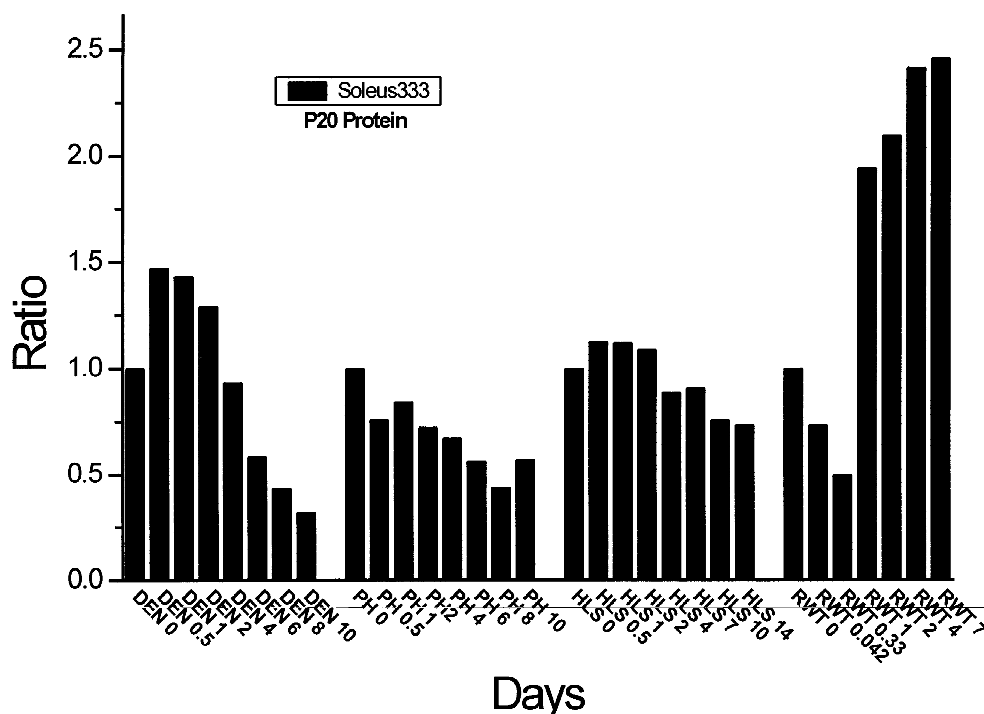

Fig. 4. Analysis of relative levels of soleus protein 333, identified as P20 protein, following either denervation-induced atrophy (DEN), pin-heel limb immobilization-induced atrophy (PH), hindlimb suspension-induced atrophy (HLS), or reweighting following hindlimb suspension-induced hypertrophy (RWT). All data are given as the ratio of soleus protein 333 (P20 protein) levels at various times following the induction of atrophy or hypertrophy relative to the corresponding zero time point level. Times are given in days following the induction of atrophy or following reweighting after 21 days of hindlimb suspension. All data are the average of three different soleus muscles/time point.

muscle atrophy and hypertrophy, proteomic analysis has led to increased understanding of these processes and potential methods for modulating these processes. Of particular importance is the observation of post-translational modification of proteins in striated muscle undergoing atrophy and hypertrophy, in particular proteolysis and phosphorylation of proteins. Thus, proteomics is a technology that allows for quantitative as well as qualitative observation of changes in the protein phenotype. This is particularly important in instances where increases in gene expression do not occur yet activation of enzymatically active proteins does occur.

Improvements in the standard 2DGE continue to be made which still makes this technology extremely useful for proteomic analysis. The ability to mix two samples prior to 2DGE decreases the potential for sample-to-sample variations in the 2DGE analysis. This technological improvement is achieved by differential dye labeling of the two samples to be compared prior to mixing and analysis by 2DGE. Improved separation matrices including immobilized p*I* gradients and improved acylamide polymers have greatly improved the resolution capabilities of 2DGE. Better visualization and post electrophoresis analytical tools have made 2DGE more reproducible, quantitative, sensitive. This allows the identification of a greater range of proteins. For example, image analysis improvements allow the fully automated comparison of two 2DGE gels, thereby increasing the potential to identify subtle shifts in protein migration. In addition, these tools allow rigorous quantification of protein spots, thus greatly improving the analysis of changes in protein quantities of two independent samples. In addition, the coupling of mass spectrometry technology to 2DGE has greatly improved our ability to identify proteins. Mass spectrometry, in particular MALDI–TOF, has

increased the number of proteins that can be identified from 2DGE samples by at least a factor 10 over standard Edman sequencing technology. Automation of protein spot picking and enzymatic digestion coupled to MALDI–TOF allows for the efficient analysis of protein spots, often in a fully automated manner. This increases the throughput of samples that can be analyzed by 2DGE, making the application of 2DGE to studies that include a large sample number feasible. Finally, improvements in analysis software and tools make identifying quantitative and qualitative changes in the protein phenotype easier since analysis of the hundreds or thousands of protein spots from a standard two-dimensional gel can be automated, substantially increasing throughput and reducing operator error. I would expect that future improvements in 2DGE technology will continue to make 2DGE an important proteomic technology.

4. Conclusions

In conclusion, proteomic technology has been applied to striated muscle investigations with the hope of better understanding the mechanisms of striated muscle disease and changes in physiological state. Proteomic analysis using quantitative methodology has allowed the robust evaluation of changes in the protein phenotype as well detection of modulated proteins. What does the future of proteomics hold for scientific investigations into striated muscle diseases and physiological processes? Probably the most significant advances in proteomic technologies lie in the increases in speed and sensitivity promised by mass spectrometry-based methodologies. These technologies, including ICAT and MALDI–MS, should allow researchers improved sample throughput, increased sensitivity and the potential to identify a greater number of proteins than currently used 2DGE-based methods. In addition, mass spectrometry methods should allow the identification of a greater range of proteins since proteins that are not readily resolved using 2DGE, such as membrane proteins and large molecular mass proteins, can be resolved with this technology. Mass spectrometry methods coupled with differential separation or concentration technologies offer even greater protein detection sensitivity since minor proteins can be identified. Future work focused on the application of proteomic technologies with increased sensitivity, throughput, and quantitation will increase the use of proteomics in the study of striated muscle biology.

References

[1] G.J. Herbison, M.M. Jaweed, J.F. Ditunno, Arch. Phys. Med. Rehabil. 60 (1979) 401.
[2] D.F. Goldspink, Biochem. J. 156 (1976) 71.
[3] A.L. Goldberg, J. Biol. Chem. 244 (1969) 3223.
[4] R.J. Zeman, R. Lundemann, J.D. Etlinger, Am. J. Physiol. 254 (1987) E152.
[5] F.W. Booth, P.D. Gollnick, Med. Sci. Sports Exerc. 15 (1983) 415.
[6] K. Furuno, M.N. Goodman, A.L. Goldberg, J. Biol. Chem. 265 (1990) 8550.
[7] G. Boissonneault, R.R. Tremblay, FEBS Lett. 257 (1989) 329.
[8] A. Jakubiec-Puka, J. Kordowska, C. Catani, U. Carraro, Eur. J. Biochem. 193 (1990) 623.
[9] D. Taillander, E. Aurousseau, D. Meynial-Denis, D. Bechet, M. Ferrara, P. Cottin, A. Ducastaing, X. Bigard, C-Y. Guezennec, H-P. Schmid, D. Attaix, Biochem. J. 316 (1996) 65.
[10] S.P. Gygi, R. Beate, R. Aebersold, Curr. Opin. Biotechnol. 11 (2000) 396.
[11] P. Chaurand, M. Stoeckli, R.M. Caprioli, Anal. Chem. 71 (1999) 5263.
[12] T.J. Griffin, S.P. Gygi, B. Rist, R. Aebersold, A. Loboda, A. Jilkine, W. Ens, K.G. Standing, Anal. Chem. 73 (2001) 978.
[13] C.S. Giometti, N.G. Anderson, N.L. Anderson, Clin. Chem. 25 (1979) 1877.
[14] C.S. Giometti, M. Barany, M.J. Danon, N.G. Anderson, Clin. Chem. 26 (1980) 1152.
[15] C.S. Giometti, N.G. Anderson, Clin. Chem. 27 (1981) 1918.
[16] C.S. Giometti, M.J. Danon, N.G. Anderson, Neurology 33 (1983) 1152.
[17] P.A. Lorkin, H. Lehmann, J. Med. Genet. 20 (1983) 18.
[18] C.W. Heizmann, M.R. Celio, R. Billeter, Eur. J. Biochem. 132 (1983) 657.
[19] U. Murakami, K. Uchida, J. Biochem. 98 (1985) 187.
[20] Z. Yablonka-Reuveni, S.K. Anderson, D.F. Bowen-Pope, M. Nameroff, Cell Tissue Res. 252 (1988) 339.
[21] S. Hori, H. Sugiura, T. shimizu, T. Hirabayashi, S. Ohtani, M. Yoshida, K. Miyamoto, H. Tanabe, Biochem. Biophys. Res. Commun. 161 (1989) 726.
[22] R. Kobayashi, I. Toyoshima, O. Masamune, Y. Tashima, J. Biochem. 107 (1990) 51.
[23] R.J. Isfort, R.T. Hinkle, M.B. Jones, F. Wang, K.D. Greis, Y. Sun, T.W. Keough, N.L. Anderson, R.J. Sheldon, Electrophoresis 21 (2000) 2228.

[24] R.C. Iannello, P.L. Jeffrey, Exp. Neurol. 108 (1990) 156.
[25] J.C. Lee, A.M. Braun, J. Neurochem. 54 (1990) 96.
[26] G.A. Nicholson, S. Hawkins, J.G. McLeod, Muscle Nerve 13 (1990) 675.
[27] E.L. Owens, C.J. Lynch, K.M. McCall, N.D. Carter, T.C. Vary, Shock 2 (1994) 171.
[28] R.J. Isfort, F. Wang, K.D. Greis, Y. Sun, T.W. Keough, R.P. Farrar, S.C. Bodine, N.L. Anderson, J. Chromatogr. B (2001) in press.
[29] D.A. Riley, S. Ellis, C.S. Giometti, J.F. Hoh, E.I. Ilyina-Kakueva, V. Oganov, G.R. Slocum, J.L. Bain, F.R. Sedlak, J. Appl. Physiol. 73 (1992) 33S.
[30] R.J. Isfort, F. Wang, K.D. Greis, Y. Sun, T.W. Keogh, S.C. Bodine, N.L. Anderson, Proteomics (2001) in press.
[31] A. Wagatsuma, S. Yamada, Scand. J. Med. Sci. Sports 10 (2000) 205.
[32] A. Wagatsuma, Y. Yamazaki, K. Mizuno, S. Yamada, Acta Neuropathol. 101 (2001) 540.
[33] B.A. Tikunov, D. Mancini, S. Levine, J. Mol. Cell Cardiol. 28 (1996) 2537.
[34] D. Cai, M. Li, K. Lee, K. Lee, W. Wong, K. Chan, Electrophoresis 21 (2000) 465.
[35] D.Q. Cai, M. Li, K.K. Lee, K.M. Lee, L. Qin, K.M. Chan, Arch. Biochem. Biophys. 387 (2001) 202.
[36] S.J. Gilroy, S. Salmons, S.R. Pennington, Electrophoresis 18 (1997) 809.
[37] G.A. O'Brien, J.M. Corbett, M.J. Dunn, D.V. Cumming, A.J. May, M.H. Yacoub, Electrophoresis 13 (1992) 726.
[38] T. Akaishi, H. Yokosawa, H. Sawada, Biochim. Biophys. Acta 1245 (1995) 331.
[39] T. Akaishi, H. Sawada, H. Yokosawa, Biochem. Mol. Biol. Int. 39 (1996) 1017.
[40] R. Billeter, C.W. Heizmann, H. Howald, E. Jenny, Eur. J. Biochem. 116 (1981) 389.
[41] D.D. Bronson, F.H. Schachat, J. Biol. Chem. 257 (1982) 3937.
[42] J.V. Coumans, I. Humphery-Smith, C.G. dos Remedios, Electrophoresis 18 (1997) 1079.
[43] G. Foucault, M. Vacher, T. Merkulova, A. Keller, M. Arrio-Dupont, Biochem. J. 338 (1999) 115.
[44] G.R. Froemming, K. Ohlendieck, Cell Mol. Life Sci. 58 (2001) 312.
[45] H. Furuoka, A. Murakami, M. Tsuchihashi, H. Yokota, T. Doi, Y. Kobayash, T. Matsui, M. Horiuchi, H. Taniyama, Acta Neuropathol. 97 (1999) 177.
[46] C.Y. Guezennec, E. Gilson, B. Serrurier, Eur. J. Appl. Physiol. Occup. Physiol. 60 (1990) 430.
[47] J.J. Pernelle, P.G. Righetti, J.P. Wahrmann, B. Herve, Electrophoresis 11 (1990) 325.
[48] I. Stuhlfauth, F.G. Jennekens, J. Willemse, B.M. Jockusch, Muscle Nerve 6 (1983) 69.
[49] H. Takano-Ohmuro, S.M. Goldfine, T. Kojima, T. Obinata, D. Fischman, J. Muscle Res. Cell Motil. 10 (1989) 369.
[50] H. Yamamoto, Y. Mizuno, K. Hayashi, I. Nonaka, M. Yoshida, E. Ozawa, J. Biochem. 115 (1994) 162.
[51] Y. Yao, M. Kirinoki, T. Hirabayashi, J. Muscle Res. Cell Motil. 15 (1994) 21.
[52] P. Lohse, B. Winter, V. Mouly, M.Y. Fiszman, H.H. Arnold, Dev. Biol. 125 (1988) 229.
[53] J.X. Yan, R.A. Harry, R. Wait, S.Y. Welson, P.W. Emery, V.R. Preedy, M.J. Dunn, Proteomics 1 (2001) 424.
[54] J-C. Sanchez, D. Chiappe, V. Converset, C. Hoogland, P-A. Binz, S. Paesano, R.D. Appel, S. Wang, M. Sennitt, A. Nolan, M.A. Cawthorne, D.F. Hochstrasser, Proteomics 1 (2001) 136.
[55] A. Suzuki, Y. Sugiyama, Y. Hayashi, N. Nyu, M. Yoshida, I. Nonaka, S. Ishiura, K. Arahata, S. Ohno, J. Cell Biol. 140 (1998) 1113.
[56] Y. Sugiyama, A. Suzuki, M. Kishikawa, R. Akutsu, T. Hirose, M.M. Waye, S.K. Tsui, S. Yoshida, S. Ohno, J. Biol. Chem. 275 (2000) 1095.
[57] Y. Wang, A. Xu, G.J.S. Cooper, Biochem. J. 344 (1999) 971.
[58] Y. Wang, A. Xu, G.J.S. Cooper, FEBS Lett. 457 (1999) 149.
[59] Y. Wang, A. Xu, J. Ye, E.W. Kraegen, C.A. Tse, G.J.S. Cooper, Diabetes 50 (2001) 1821.