

Skeletal muscle proteome analysis provides insights on high altitude adaptation of yaks (#525)

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Introduction

The mechanisms of adaptation to high altitudes by mammals received increasing attention. The genomes of several mammals inhabiting plateaus have been sequenced; and a large number of genes related to high-altitude adaptation have been identified [1]. Yak and cattle have been considered as convenient large ruminant subjects for studying adaptation to high altitudes, with previous studies characterizing their enzyme activities and genomics [1,2]. Yak and cattle were estimated to have diverged approximately 4.9 million years ago. Although yak and cattle are different species, their genomes were highly similar, including an identical number of chromosomes (30 chromosomes), similar karyotypes, the extensive synteny of the yak and cattle genomes, with 45% of encoded proteins identical and mean protein similarity approximating 99.5% [1]. In order to characterize the molecular mechanisms of mammalian adaptation to high altitudes, the present study compared qualitative and quantitative differences of proteomes in LT muscles in yak and cattle.

Methods

LT muscles were obtained from three adult male yaks from Hongyuan County, and three adult male bovines from Chengdu Plain of Sichuan. iTRAQ analysis was implemented at Beijing Genomics Institute (BGI, Shenzhen, China). Two independent biological triplicates (yak labeled with reagents 113, 114, 115 and cattle labeled with reagents 116, 119, 121) were applied. LC-ESI-MS/MS proteomic analysis was based on TripleTOF 5600. The MS raw data recovery to MGF was processed via pFind (<http://pfind.ict.ac.cn/downloads.html>). Protein identification and quantification were performed using Mascot 2.3.02 (Matrix Science Inc, Boston, MA). The Gene Ontology (GO) analysis (<http://www.geneontology.org>) was conducted according to method reported previously [3]. For analysis of protein-protein interaction, the differentially expressed proteins were matched against the STRING database (www.string-db.org).

Results

Fifty-two differentially expressed proteins were identified, 20 of which were found to be up-regulated in yak and 32 were up-regulated in cattle. These proteins were classified using GO annotation and were categorized into three major functional groups: molecular function, cellular components, and biological processes. Proteins assigned to each category were presented in Fig. 1. The clusters of interacting proteins were generated using STRING database (Fig. 2). Twenty-four proteins were recognized as key nodes in bi-

ological interaction networks. The central interaction networks were related to myofilaments and regulation of calcium ions. The second cluster included proteins related to cellular energy metabolism. Proteins involved in citric acid cycle, electron transport chain, and oxidative phosphorylation were over-expressed in yak muscles.

Our proteomes analyses of muscle tissues in yaks and cattle revealed that there were 20 up-regulated and 32 down-regulated proteins in the muscle tissue of yaks, most of which were involved in the molecular function of proteins binding, catalytic activity and structural molecule activity. In yaks, energy may be supplied by greater protein catabolism and glycolysis in order to adapt to high altitudes. The work performed here may provide a demonstration on the mechanism of animals' adaptation to high altitude.

Conclusion

The differences in proteome profile of *longissimusthoracis* (LT) muscles of yak (*Bosgrunniens*) and cattle (*Bostaurus*) were investigated employing isobaric tag for relative and absolute quantification (iTRAQ) to understand the cellular level adaptations of yaks to high altitudes. Fifty-two proteins were differentially expressed, among which 20 were up-regulated and 32 were down-regulated in yaks. Gene ontology (GO) annotation revealed that most of the differentially expressed proteins were involved in the molecular function of protein binding, catalytic activity, and structural activity. Protein-protein interaction analysis recognized 24 proteins (involved in structural integrity, calcium ion regulation, and energy metabolism), as key nodes in biological interaction networks. These findings indicated mammals living at high altitudes could possibly generate energy by pronounced protein catabolism and glycolysis compared with those living in the plains.

References

1. Qiu, Q., et al., The yak genome and adaptation to life at high altitude. *Nature Genetics*, 2012. 44(8): p. 946-949.
2. Zhong, C.L., et al., Comparison of aquaporin-1 expression between yak (*Bos grunniens*) and indigenous cattle (*Bos taurus*) in the Qinghai-Tibetan Plateau. *Animal Production Science*, 2017. 57(8): p. 1618-1623.
3. Yang, L.T., et al., iTRAQ protein profile analysis of *Citrus sinensis* roots in response to long-term boron-deficiency. *Journal of Proteomics*, 2013. 93: p. 179-206.

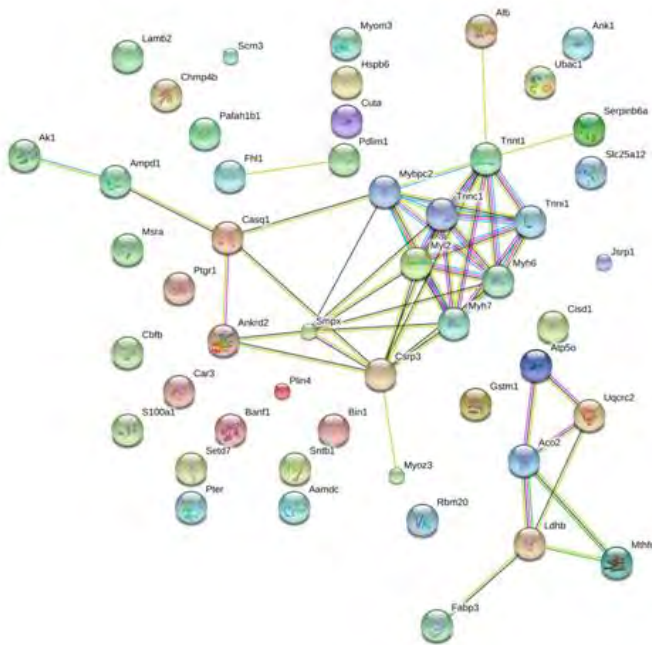


Fig. 2 Protein-protein interaction networks of differentially expressed proteins.

Different clusters of interacting proteins were identified using STRING database. Two networks involved in muscle contraction and nutrient metabolism are shown.

Notes

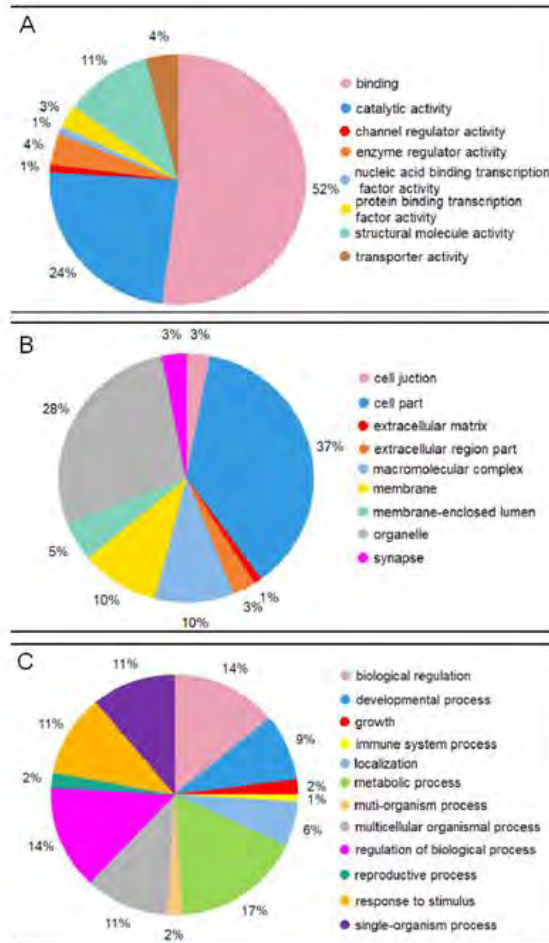


Fig. 1 Classification of 52 differentially expressed proteins in yak *longissimus thoracis muscles ac*

(A) Molecular function, mainly involved in binding and catalytic activity (B) Cellular component, mainly involved in cell part and organelle (C) Biological process, mainly involved in metabolic process and biological regulation.