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Glycogen Synthase Kinase 3β (GSK3β) Regulates Myogenic Differentiation in Skeletal Muscle Satellite Cells of Sheep

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Simple Summary: In this study, we investigated the function of GSK3β in the skeletal muscle satellite cells (SMSCs) of sheep. The overexpression of *GSK3β* inhibited myotube formation and the expression of *MyoD*, *MyoG*, *MyHC1*, and *MyHC2a* genes in sheep SMSCs. Additionally, inhibiting the activity of GSK3β significantly promoted myotube formation as well as *MyoD*, *MyoG*, *MyHC1*, and *MyHC2a* genes at mRNA levels. The present study provides evidence for studying the mechanisms involved in the regulation of sheep SMSCs differentiation by GSK3β.

Abstract: Glycogen synthase kinase 3β (GSK3β) has a vital role in the regulation of many cellular processes. However, the role of GSK3β in muscle cell differentiation in sheep remains unknown. In this study, we investigated the function of GSK3β in skeletal muscle satellite cells (SMSCs) of sheep. An overexpression of *GSK3β* significantly inhibited myotube formation as well as the mRNA levels of myogenic genes (*MyoD*, *MyoG*, *MyHC1*, and *MyHC2a*) in sheep SMSCs. SB216763 treatment had a time-course effect on the phosphorylation levels of sheep GSK3β. In addition, reducing the activity of GSK3β lead to the promotion of sheep SMSCs differentiation as well as the mRNA levels of myogenic genes (*MyoD*, *MyoG*, *MyHC1*, and *MyHC2a*). This study illustrated the function of GSK3β to inhibit myogenesis in sheep SMSCs, which provided evidence for studying the mechanisms involved in the regulation of sheep SMSCs differentiation by GSK3β.

Keywords: sheep; GSK3β; skeletal muscle; satellite cells; SB216763

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1. Introduction

Glycogen synthase kinase 3β (GSK3β) was originally known as a vital enzyme in glycogen metabolism biosynthesis [1,2]. Glycogen Synthase (GS) is an enzyme that is involved in converting glucose to glycogen. Serine 9 phosphorylation of GSK3β leads to a loss of GSK3 catalytic activity [3]. It is well accepted that GSK3β acts as a key and negative regulatory kinase of GS. IGF-1 can regulate the GSK3β activity through the phosphorylation regulation of GSK3β, and GS is the direct substrate of GSK3β. With further study on GSK3β, it was demonstrated that GSK3β is not only an enzyme in glycogen metabolism biosynthesis but also an important regulator of many cell signaling pathways [4]. In mice, GSK3β phosphorylates PPARα at the Ser73 site, thereby inhibiting PPARα activity. This leads to elevate blood glucose levels and severe liver steatosis [5]. Additionally, GSK3β reduces brown adipocyte thermogenesis by inhibiting MAPK to regulate thermogenic gene expression [6]. GSK3β promotes the differentiation of human adipose-derived stem cells, suggesting its potential to regulate stem cell differentiation [7]. Furthermore, a knockdown of GSK3β induces the formation of multiple axons in neurons, whereas the overexpression of *GSK3β* in neurons inhibits axon arborization [8]. These studies demonstrate that GSK3β regulates cell differentiation and metabolism.