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VMP1 Regulated by chi-miR-124a Effects Goat Myoblast Proliferation, Autophagy, and Apoptosis through the PI3K/ULK1/mTOR Signaling Pathway

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Abstract: The production of goat meat is determined by the growth speed of muscle fibers, and the autophagy and apoptosis of myoblast cells is a crucial process in the growth of muscle fibers. The rapid growth of muscle fibers occurs from one month old to nine months old in goats; however, the mechanisms of myoblast cells' autophagy and apoptosis in this process are still unknown. To identify candidate genes and signaling pathway mechanisms involved in myoblast apoptosis and autophagy, we compared the expression characteristics of longissimus dorsi tissues from Wu'an goats—a native goat breed of China—at 1 month old (mon1 group) and 9 months old (mon9 group). Herein, a total of 182 differentially expressed mRNAs (DEGs) in the mon1 vs. mon9 comparison, along with the KEGG enrichments, showed that the PI3K-Akt pathway associated with autophagy and apoptosis was significantly enriched. Among these DEGs, expression of vacuole membrane protein 1 (VMP1)—a key gene for the PI3K-Akt pathway—was significantly upregulated in the older goats relative to the 1-month-old goats. We demonstrated that VMP1 promotes the proliferation and autophagy of myoblasts, and inhibits their apoptosis. The integration analysis of miRNA–mRNA showed that miR-124a was a regulator of VMP1 in muscle tissue, and overexpression and inhibition of miR-124a suppressed the proliferation and autophagy of myoblasts. The PI3K/Akt/mTOR pathway was an important pathway for cell autophagy. Additionally, the activator of the PI3K/Akt/mTOR pathway, the expression of VMP1, and ULK1 were higher than the negative control, and the expression of mTOR was depressed. The expression of VMP1, ULK1, and mTOR was the opposite when the inhibitor was added to the myoblasts. These results show that the PI3K/Akt/mTOR pathway promoted the expression of VMP1 and ULK1. By using adenovirus-mediated apoptosis and proliferation assays, we found that that miR-124a inhibits myoblast proliferation and autophagy, and promotes their apoptosis by targeting VMP1. In conclusion, our results indicated that VMP1 was highly expressed in the LD muscle tissues of nine-month-old goats, and that it was regulated by miR-124a to inhibit myoblast cells' apoptosis through the PI3K/Akt/mTOR pathway, and to promote proliferation and autophagy. These findings contribute to the understanding of the molecular mechanisms involved in myoblast proliferation, autophagy, and apoptosis.

Keywords: goat; longissimus dorsi tissue; apoptosis; autophagy; VMP1; miR-124a

Citation: Liu, Y.; Zhou, Z.; Li, K.; Wang, P.; Chen, Y.; Deng, S.; Li, W.; Yu, K.; Wang, K. VMP1 Regulated by chi-miR-124a Effects Goat Myoblast Proliferation, Autophagy, and Apoptosis through the PI3K/ULK1/mTOR Signaling Pathway. *Cells* **2022**, *11*, 2227. https://doi.org/10.3390/cells11142227

Academic Editor: Maria Pennuto

Received: 11 May 2022
Accepted: 12 July 2022
Published: 18 July 2022