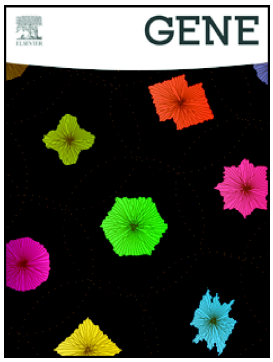


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PII: S0378-1119(18)30690-5
DOI: doi:10.1016/j.gene.2018.06.039
Reference: GENE 42972

To appear in: *Gene*

Received date: 8 May 2018
Revised date: 4 June 2018
Accepted date: 12 June 2018

Please cite this article as: Zengkui Lu, Lixin Du, Ruizao Liu, Ran Di, Liping Zhang, Youji Ma, Qing Li, Enmin Liu, Mingxing Chu, Caihong Wei , MiR-378 and BMP-Smad can influence the proliferation of sheep myoblast. Gene (2017), doi:10.1016/j.gene.2018.06.039

# MiR-378 and BMP-Smad can Influence the Proliferation of Sheep Myoblast

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**Abstract:** MicroRNA (miRNA) is a sort of endogenous ~20-25nt non-coding RNAs, and it can regulate a variety of biological events. We found the miR-378 may involve in regulating the muscle development of sheep during our previous research. However, the molecular mechanism of miR-378 regulating myoblast proliferation still unclear. In this research, we predicted that *BMP2* (Bone morphogenetic protein 2) was the target gene of miR-378 and the BMP-Smad signal pathway that *BMP2* participated in playing an important role in the muscle development. Therefore, we tried to determine whether miR-378 influence myoblast proliferation of sheep through the BMP-Smad signal pathway. The results indicated that inhibit BMP-Smad signal pathway by interfering *Smad4* to promote proliferation of sheep myoblasts; promote BMP-Smad signal pathway by interfering *Smad7* to inhibit proliferation of sheep myoblasts; over-expression miR-378 promotes BMP-Smad signal pathway and myoblast proliferation in sheep; interfering miR-378 inhibits BMP-Smad signal pathway and myoblast proliferation in sheep. However, when both of which functioned at the myoblast, miR-378 could not fully depend on BMP-Smad signal pathway to regulate myoblast proliferation. In sum, both miR-378 and BMP-Smad can influence the proliferation of myoblast, but miR-378 does not target the 3' UTR of sheep *BMP2*.

**Keywords:** miR-378; BMP-Smad; sheep myoblast; myogenic regulation

## 1. Introduction

Muscle development is a highly complex and orderly biological process, and muscle formation is a process that myoblast exit from the cell cycle to express muscle-specific genes. The study finds that *BMP2* belonging to TGF-β (Transforming growth factor-β) superfamily has an extensive biological activity, and it also plays an important role in the skeletal muscle development (Almodovar et al., 2014; Zhang et al., 2014a). BMP signal must be mediated by Smad protein family when it travels from the cell membrane to the cell nucleus (Derynck and Zhang, 2003). The activation process of BMP receptor is the same as that of TGF-β receptor. In the transduction process of BMP-Smad signal, BMP II receptor first binds with BMP ligand, and then binds with BMP I receptor and activates I receptor (Liu et al., 2012). The activated BMP I receptor can make Smad1/5/8 phosphorylate, and the activated TGF-β I receptor can make Smad2/3 phosphorylate. The p-Smad1/2/3/5/8 combines with Smad4 and forms a polymer, and it transferred to the cell nucleus to interact with DNA and proteins, and then regulates the target genes (Miyazawa et al., 2002; Vogt et al., 2014). While as an inhibitive Smad, Smad6/7 can inhibit the signal transduction of R-Smad (Smad1/2/3/5/8). Smad7 can directly bind with TGF-β II receptor, prevent Smad2/3 from phosphorylating, inhibit a phosphorylation of Smad1/5, and thus inhibit the signal transduction ( Lan et al., 2003; Yan et al., 2016). The study finds that Smad1, Smad4, and Smad5 negatively regulate myogenic differentiation, and Smad7 positively regulate myogenic differentiation (Lee et al., 2015; Winbanks et al., 2016; Wrighton et al., 2009). Therefore, BMP-Smad signal pathway plays an important role in the muscle development process.

miRNA is a kind of non-coding RNA with a length of 22 nucleotides; its main function is suppressing the expression on the post-transcriptional level through combining with the 3' UTR (3' untranslated region) of mRNA and degrading the targeted mRNA or preventing its translation (Bartel, 2009). It has been reported that miRNA involved in myoblast proliferation and differentiation, but its regulation and control mechanism is not clear (Zhang et al., 2014b; Shi et al., 2015). In our previous studies, through identifying miRNA of Texel and Ujimqin which is the sheep longissimus dorsi muscle, we find that miR-378 may associated with sheep muscle