Sulforaphane enhances proliferation of porcine satellite cells through suppression of TGF-β signaling pathway. R. Zhang¹, C. Neuhoff², H. Fan², J. Welzenbach³, Q. Yang⁴, M. J. Uddin⁵, M. U. Cinar⁶, D. Tesfaye¹, E. Tholen⁷, C. Looft⁸, K. Schellander⁹ (¹Institute of Animal Science, University of Bonn, Bonn, Germany, ²Department of Basic Medical Science and Center for Cancer Research, Purdue University, West Lafayette, West Lafayette, IN, ³School of Veterinary Science, The University of Queensland, Gatton, Australia, ⁴Faculty of Agriculture, Department of Animal Science, Erciyes University, Kayseri, Turkey, ⁵Department of Medicine, Faculty of Veterinary Science, Bangladesh Agricultural University, Mymensingh, Bangladesh, ⁶School of Veterinary Science, University of Bonn, Bonn, Germany)

Satellite cells, the muscle stem cells, play a critical role in muscle growth, maintenance, and regeneration. A lot of muscle diseases result from defective function of satellite cells. Porcine satellite cells are a good model for studying the role of satellite cells in muscle development. Sulforaphane (SFN), a natural molecule rich in cruciferous vegetables, is a potent inducer for the NF-E2-related factor 2 (Nrf2) signaling and also inhibits the activity of histone deacetylases (HDAC). Our previous study found that SFN epigenetically suppressed the transcription of myostatin in porcine satellite cells. However, the effects of SFN on the proliferation of porcine satellite cells and the related mechanisms are far from understood. In the present study, we report that SFN enhanced the proliferation of the porcine satellite cells and modified the expression of HDACs and inhibited the activity of HDACs. The activity of TGF-β signaling was suppressed by SFN treatment, which was accompanied with up-regulation of Smad7, an endogenous suppressor of TGF-β signaling. Furthermore, we found that SFN increased the mRNA expression of Smad7’s transcription factors and decreased the expression of miRNAs targeting Smad7. The DNA methylation of a studied fragment in Smad7 promoter was not influenced by SFN treatment. SFN has received substantial attention because of its potential application in cancer therapy. The present study, for the first time, investigated the effects of SFN on the proliferation of porcine satellite cells and the underlying mechanism. We found that both mRNA and protein level of Smad7 were greatly increased by SFN. Thus, besides reducing TGF-β1 protein abundance, SFN also inhibits the activity of TGF-β signaling by increasing expression of Smad7. It has been shown that overexpression of Smad7 led to enhanced skeletal muscle differentiation and cellular hypertrophy. In summary, our studies state that SFN enhances the proliferation of porcine satellite cells by suppressing TGF-β signaling through activation of Smad7.

Lipopolysaccharide-induced gene expression of CD14 in TRIF pathway is epigenetically regulated by sulforaphane in porcine pulmonary alveolar macrophages. Q. Yang¹, M. J. Pröll¹, D. S. Wondim¹, R. Zhang¹, D. Tesfaye¹, H. Fan², M. U. Cinar³, C. Grosse-Brinkhaus¹, E. Tholen⁴, C. Looft⁸, A. Islam⁵, M. Höcker¹, K. Schellander¹, M. J. Uddin⁶, C. Neuhoff¹ (¹Institute of Animal Science, University of Bonn, Bonn, Germany, ²Department of Basic Medical Science and Center for Cancer Research, Purdue University, West Lafayette, IN, ³Faculty of Agriculture, Melikgazi Kayseri, Turkey, ⁴Institute of Animal Science, University of Bonn, Bonn, Germany, ⁵Department of Medicine, Faculty of Veterinary Science, Bangladesh Agricultural University, Mymensingh, Bangladesh, ⁶School of Veterinary Science, The University of Queensland, Gatton Campus, Gatton, Australia)

Cluster of differentiation 14 (CD14) is the pattern recognition receptor (PRR) involved in the recognition of bacterial component lipopolysaccharide (LPS) through the MyD88-dependent and TRIF pathway of innate immunity. It may be a modulator to prevent and mitigate the LPS-induced lung inflammation in pigs. However, reports on CD14 activation induced by LPS in TRIF pathway are controversial. Furthermore, the gene expression regulation of CD14 by the epigenetic factor sulforaphane (SFN) is still poorly understood. To identify the epigenetic changes of CD14 mediated with SFN in LPS-induced TRIF pathway, the PAMs model in vitro was investigated. For this, the mRNA expression of CD14 and downstream genes of TRIF pathway were quantified using qPCR. The cytokine levels of tumor necrosis factor-α (TNFα) and interleukin-1β (IL-1β) were measured by enzyme-linked immunosorbent assay (ELISA). The gene expression of the epigenetic enzymes DNA methyltransferase-1...