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Authors: Haolan Yu, Ningning Jiang, XiuHua Yu, Zhitao Zhao, Xiuyun Zhang, Hui Xu



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<AT>The role of TGF $\beta$  receptor 1-smad3 signaling in regulating the osteoclastic mode caused by fluoride

Haolan Yu<sup>1</sup>·Ningning Jiang<sup>1</sup>·XiuHua Yu<sup>2</sup>·Zhitao Zhao<sup>1</sup>· Xiuyun Zhang<sup>1</sup>· Hui Xu<sup>\*1</sup>

<AU>H. Yu·N. Jiang·X. Yu· Z. Zhao · X. Zhang, H. Xu\*  
##Email##huixu@jlu@yahoo.com##/Email##

<AU>

<AFF><sup>1</sup>Department of Regenerative Medical Science, School of Pharmaceutical Sciences, Jilin University, Changchun 130021, People's Republic of China

<AFF><sup>2</sup>First Clinical Hospital, Jilin University, Changchun 130021, People's Republic of China

<PA>1163 Xinmin street, Changchun, Jilin Province, 130021, People's

Republic of China.

<ABS-HEAD>Highlights► Fluoride upregulated 303 miRNAs expression and downregulated 61 miRNAs. ► Fluoride exhibited biphasic effect on osteoclast viability, formation and function. ► Fluoride indicated little effect on expression of RANK protein. ► SB431542 inhibited or aggravated fluoride-regulating osteoclast mode. ► Stimulation of fluoride on Smad3 expression exhibited dose-dependent manner.

<ABS-HEAD>Abstract

<ABS-P>Studies that have focused on the role TGF $\beta$  signaling plays in osteoclast activity are gradually increasing; however, literature is rare in terms of fluorosis. The aim of this study is to observe the role the T $\beta$ R1/Smad3 pathway plays in fluoride regulating cells osteoclast-like cells that are under the treatment of TGF $\beta$  receptor 1 kinase. The RANKL-mediated osteoclast-like cells from RAW264.7 cells were used as osteoclast precursor model. The profile of miRNA expression in fluoride-treated osteoclast-like cells exhibited 303 upregulated miRNAs, 61 downregulated miRNAs, and further drew 37 signaling pathway maps by KEGG and Biocarta pathway enrichment analysis. TGF $\beta$  and its downstream effectors were included among them. Osteoclast viability, formation and function were detected via MTT method, bone resorption pit and tartrate-resistant acid phosphatase (TRACP) staining, respectively.

<ABS-P><ST>Results</ST> demonstrated that different doses of fluoride exhibited a biphasic effect on osteoclast cell viability, differentiation, formation and function. It indicated that a low dose of fluoride treatment stimulated them, but high dose inhibited them. SB431542 acted as T $\beta$ R1 kinase inhibitor and blocked viability, formation and function of osteoclast-like cells

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