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# PTH (1-34) affects bone turnover governed by osteocytes exposed to fluoride

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## Highlight

- Osteocytes endured high dose of fluoride exposure.
- Fluoride inhibited expression of SOST/Sclerostin in osteocytes.
- Fluoride modulated ratio of RANKL/OPG in osteocytes
- Fluoride regulated Wnt/  $\beta$ -catenin signaling in osteocytes.
- PTH(1-34) participated in fluoride-modulating SOST and RANKL expression in osteocytes.

## Abstract

Exposure to fluoride from environmental sources remains an overlooked, but serious public health risk. In this study, we looked into the role osteocytes play on the mechanism underlying fluoride induced osteopathology. We analyzed bone formation and resorption related genes generated by osteocytes that were exposed to varied doses of fluoride with and without PTH *in vitro*. Correspondingly, osteogenesis and osteoclastogenesis related genes were also investigated in rats exposed to fluoride for 8 weeks, and the PTH (1-34) was applied at the last 3 weeks to observe its role in regulating bone turnover upon fluoride treatment. The data *in vitro* indicated that fluoride treatment inhibited Sost expression of mRNA and protein and stimulated RANKL mRNA protein expression as well as the RANKL/OPG ratio in the primary osteocytes. Single PTH treatment played the similar role on expression of these genes and proteins. The PTH combined administration enhanced the action of fluoride treatment on RANKL/OPG and SOST/Sclerostin. The up-regulation of RANKL and decreasing of Sost induced by fluoride and/ or PTH treatment was validated *in vivo* and suggests that osteocytes are a major source of RANKL and Sost, both of which play essential roles in fluoride affecting

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