

Activation of NF- κ B signaling regulates ovariectomy-induced bone loss and weight gain

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<https://hdl.handle.net/2324/7329449>

出版情報 : Kyushu University, 2024, 博士 (歯学), 課程博士
バージョン :
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論 文 名	Activation of NF- κ B signaling regulates ovariectomy-induced bone loss and weight gain (NF- κ B シグナルの活性化が卵巣摘出による骨量減少と体重増加を制御する)			
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論 文 審 査 の 結 果 の 要 旨

Postmenopausal women experience bone loss and weight gain. To date, crosstalk between estrogen receptor signals and nuclear factor- κ B (NF- κ B) has been reported, and estrogen depletion enhances bone resorption by osteoclasts via NF- κ B activation. However, it is unclear when and in which tissues NF- κ B is activated after menopause, and how NF- κ B acts as a common signaling molecule for postmenopausal weight gain and bone loss. Therefore, we examined the role of NF- κ B in bone and energy metabolism following menopause. NF- κ B reporter mice, which can be used to measure NF- κ B activation in vivo, were ovariectomized (OVX) and the luminescence intensity after OVX increased in the metaphyses of the long bones and perigonadal white adipose tissue, but not in the other tissues. OVX was performed on wild-type (WT) and p65 mutant knock-in (S534A) mice, whose mutation enhances the transcriptional activity of NF- κ B. Weight gain with worsening glucose tolerance was significant in S534A mice after OVX compared with those of WT mice. The bone density of the sham group in WT or S534A mice did not change, whereas in the S534A-OVX group it significantly decreased due to the suppression of bone formation and increase in bone marrow adipocytes. Disulfiram, an anti-alcoholic drug, suppressed OVX-induced activation of NF- κ B in the metaphyses of long bones and white adipose tissue (WAT), as well as weight gain and bone loss. Overall, the activation of NF- κ B in the metaphyses of long bones and WAT after OVX regulates post-OVX weight gain and bone loss. This research contains novel findings. Therefore, the candidate deserves to be conferred the degree of DOCTOR OF PHILOSOPHY (Dental Science).