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## Proteasome inhibitors enhance the BMP-2 induced osteoblastic differentiation of periodontal ligament cells

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Proteasome inhibitors are drugs that block the action of proteasomes which mainly functions in the break down of cellular complexes proteins, like *p53* protein. This study investigated the effects of proteasome inhibitor-1 and epoxomicin on osteoblast differentiation in periodontal ligament (PDL) cells and its mechanism. Mouse PDL cells were cultured in DMEM (growth medium containing 10% fetal bovine serum and 1% antibiotics) with proteasome inhibitor-1 or epoxomicin. The cells were pre-treated with TNF- $\alpha$ . After 2 days of TNF- $\alpha$  treatment, they were treated with not only proteasome inhibitors but also BMP-2. Metabolic cell activity after 24 hr was measured using WST-1 assay. Real-time PCR were performed to analyze the expression of several genes involved in osteoblast differentiation. Bone forming ability in cell cultures was characterized by examining alkaline phosphatase (ALP) activity and ALP staining. Activation of phosphor-Smad 1/5/8 and Smad antibodies were determined by western blot analysis. After treatment of TNF- $\alpha$ , BMP-2 with proteasome inhibitor-1 or epoxomicin resulted in the recovery of genes like ALP and bone sialoprotein. Overall, proteasome inhibitors-treated cells increased the expression of ALP and mineralized nodule formation when compared to other controls. Activation of Smad signaling pathway was observed. In the present study, proteasome inhibitors improve the osteoblastic differentiation which was decreased by TNF- $\alpha$ . This suggests that proteasome inhibitors (proteasome inhibitor-1 and epoxomicin) could be a promising therapeutic approach for periodontal diseases.

### Biography

Il-Shin Kim has completed her PhD at the age of 28 years from Chonnam National University School of Dentistry. She is the professor of Honam University. She is interested in oral health education and prevention of periodontal disease.

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