

# Root resorption associated with orthodontic force in IL-1B knockout mouse

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## Introduction

Root resorption (RR) is one of the most common sequelae of orthodontic treatment. A key role for a genetic influence in external apical root resorption (EARR) was described recently, by describing both linkage and linkage disequilibrium between interleukin-1B (*IL-1B*) and EARR in orthodontically treated individuals, accounting for approximately 15% of the variation in EARR<sup>1</sup>. The murine model, which allows for a controlled and reproducible orthodontic mechanical loading was applied to IL-1B knockout (-/-) mice (background strain C57BL/6J) to investigate the role of IL-1B in RR.

## Interleukin-1 $\beta$ and orthodontic tooth movement

Interleukin-1, the term which encompasses three different polypeptides: IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra, has been shown to be a potent stimulus for bone resorption. The presence of elevated levels of IL-1 $\beta$  in the periodontal tissue and gingival crevicular fluids of patients undergoing orthodontic tooth movement implicate a role of this cytokine in the orthodontically induced tooth movement<sup>2-9</sup>. IL-1 $\beta$  has been implicated in the process of bone resorption (catabolic modeling) accompanying orthodontic tooth movement<sup>10-13</sup>. Variation in IL-1 levels among individuals undergoing orthodontic treatment is well documented<sup>8,14</sup>. It is found to correlate with interindividual differences in the amount of tooth translation<sup>8</sup> and may contribute to root resorption susceptibility.

## Purpose of the study

The purpose of this study was to verify the finding in

human subjects that the IL-1B gene is a significant candidate gene that contributes to root resorption.

## Materials and methods

Male inbred mice of the control strain (C57BL/6J) and B6.129-IL-1BtmChaplin strain were used in 4 groups: control untreated (N=7), control treated (N=8), IL-1B null untreated (N=8), IL-1B null treated (N=10). Each of the treated animals received an orthodontic appliance to tip the maxillary left molar mesially (Figure 1). Histological sections of the tooth were used to determine root resorption and TRAP scores.

## Statistical analysis

The Wilcoxon rank sum nonparametric test was used to evaluate differences between groups. To maintain an experiment-wise alpha of 0.05, a corrected alpha,  $\alpha^* = 0.013$ , was utilized.

## Results

Mean root resorption values increased significantly for the groups that received orthodontic treatment in both wild



**Figure 1.** Orthodontic appliance *in situ*.

The authors have no conflict of interest.

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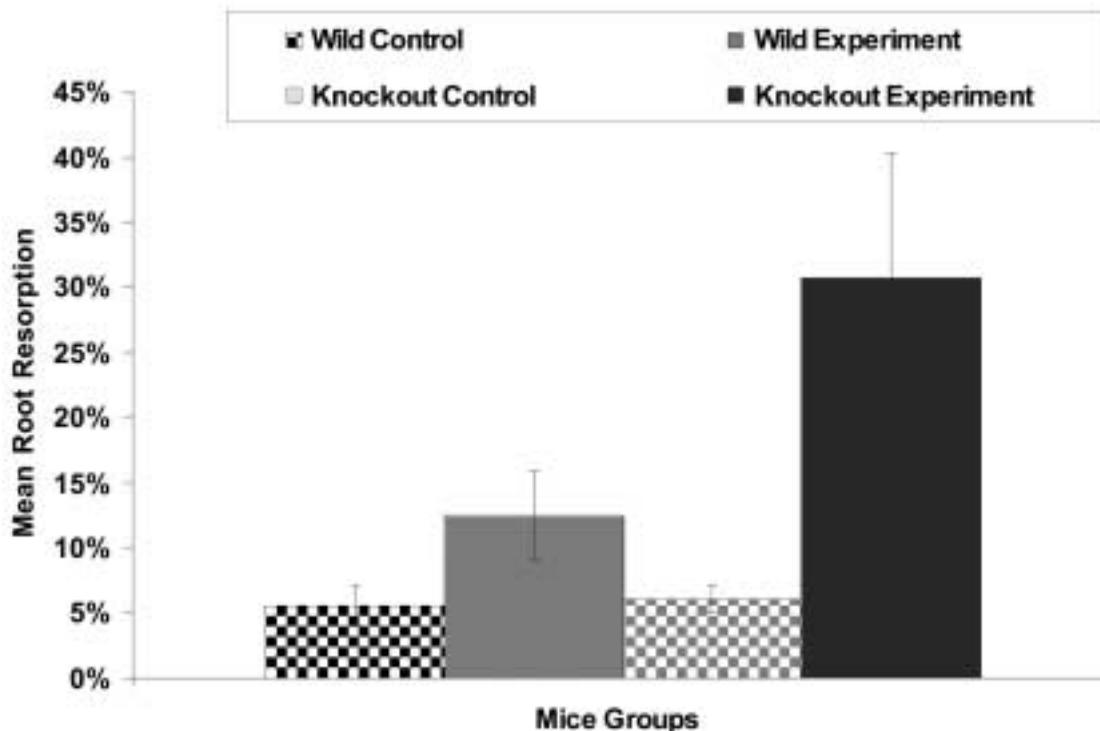


Figure 2. Mean root resorption  $\pm$  one standard deviation.

type and knockout animals. Moreover, there was significant increase in root resorption associated with orthodontic force in treated knockout mice compared to treated wild type mice ( $0.25 \pm 0.095$ ,  $0.07 \pm 0.03$ , respectively) (Figure 2). However, TRAP positive cell counts did not differ significantly between the two treated mouse groups, although the count was slightly lower in the treated IL-1B null group ( $1.9 \pm 0.54$  compared to  $2.4 \pm 0.68$  in the treated C57BL/6J group). There was no significant difference in root resorption between the untreated groups.

### Discussion and conclusions

(1) Absence of IL-1 $\beta$  cytokine activity did not affect baseline root resorption in wild type C57BL/6J mice. (2) Orthodontic force applied for 9 days significantly increased root resorption in both wild type and knockout mice. (3) Absence of IL-1 $\beta$  cytokine activity significantly increased root resorption associated with orthodontic force in male mice of C57BL/6J strain. (4) The increase in root resorption associated with orthodontic force in knockout mice in comparison to wild type was not associated with significant increase in TRAP positive cell count. (5) The present findings support previous clinical findings that IL-1 $\beta$  cytokine is a significant factor in root resorption associated with orthodontic movement<sup>1</sup>. (6) The findings support the hypothesis that excessive root resorption associated with orthodontic tooth movement may be mediated

through a decreased rate of catabolic bone modeling (resorption) of alveolar bone resulting in prolonged stress and strain of the tooth root against the alveolar bone<sup>1</sup>.

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