Introduction
While the current tenet of mechanically related bone adaptation suggests that mechanical signals have to be large in magnitude to stimulate bone formation, recent studies have demonstrated the osteogenic potential of extremely small magnitude high frequency mechanical signals. In addition to the osteogenic character of these high frequency mechanical stimuli, we hypothesize that their presence is also responsible for preventing bone resorption. During daily functional activities, small magnitude but high frequency strain signals are evident in bone in addition to large amplitude strains that are typically associated with these activities. These small strain signals persist over long durations, including passive actions such as standing, and therefore represent a dominant component of bone’s functional strain history. Not surprisingly, therefore, animal models, such as rat-tail suspension, remove this regulatory stimulus, and may be therefore permissive to resorptive activity. Osteoclast differentiation factor (ODF) is a cytokine involved in the recruitment and activity of osteoclasts and in vitro studies have linked its expression to the presence or absence of mechanical strain. Here, we first examined the osteogenic efficacy of low-level high frequency mechanical stimuli and their presence or absence of mechanical strain. Here, we first examined the osteogenic efficacy of low-level high frequency mechanical stimuli and their ability to inhibit bone loss caused by disuse. We then hypothesized that the expression of ODF would be inversely related to altered tissue level bone formation rates.

Materials and Methods
Female 6 months old Sprague-Dawley rats were assigned to controls (n=30), mechanically stimulated (n=21), tail suspension related disuse (n=11), and disuse interrupted by 10 min of daily mechanical stimulation (n=21). All mechanically stimulated (n=21), tail suspension related disuse (n=11), and disuse interrupted by 10 min of mechanical stimulation (n=19). All mechanical stimulation was applied for 28d. Mechanical stimulation consisted of whole body vibration at 90Hz (0.25g). All rats were given injections with demeclocycline prior to study begin and calcein on day 18 of the protocol to determine indices of bone formation. Longitudinal sections of the tibiae were extracted from whole left tibiae (including bone marrow and cartilage), quantitated in three animals of each of the four groups via Northern analysis. RNA densitometry in arbitrary units and normalized to combined 18S and 28S ribosomal RNA. T-tests were used to assess the osteogenic potential of the mechanical signal. BFR/BV between the other three groups was compared by ANOVA followed by a Tukey HSD post-hoc test.

Results
Hindlimb suspension significantly decreased trabecular bone formation rates by 92% compared to controls. Mechanical stimulation at 90Hz was strongly osteogenic (+97%, Fig.1). When this anabolic stimulus was used to combat disuse, the impact of the intervention served to normalize the response back to control values. Disuse increased the expression of ODF by 72% with respect to control values. Mechanical stimulation for 10 min/d decreased ODF mRNA levels by 78% while disuse interrupted by 10 min of daily mechanical stimulation muted this decrease to 49% (Fig. 2). When linear correlation was done with respect to control values) were strongly correlated with altered bone formation rates (r²=0.79).

Discussion
We showed the anabolic potential of extremely low level, high frequency mechanical stimuli when applied for a very short daily duration. Most importantly from a clinical perspective, these signals effectively prevented disuse related osteopenia from occurring, even when the bone was subjected to 23 hours and 50 minutes per day of this high magnitude stimulus for resorption.

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