

# Regulation of bone growth via ligand-specific activation of estrogen receptor alpha

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## Conclusions

- Selective ER $\alpha$  agonist (PPT) or estradiol (E2) treatments decrease tibia and femur longitudinal growth and the height of the tibia growth plate cartilage in female mice.
- Our data show that the estrogenic effects on bone growth and growth plate maturation are mainly mediated via ER $\alpha$ .

## Aim

The aim of the study was to evaluate the effects of estradiol (E2) and selective ER $\alpha$  (PPT), ER $\beta$  (DPN) and GPER-1 (G1) agonists on bone growth and growth plate maturation.

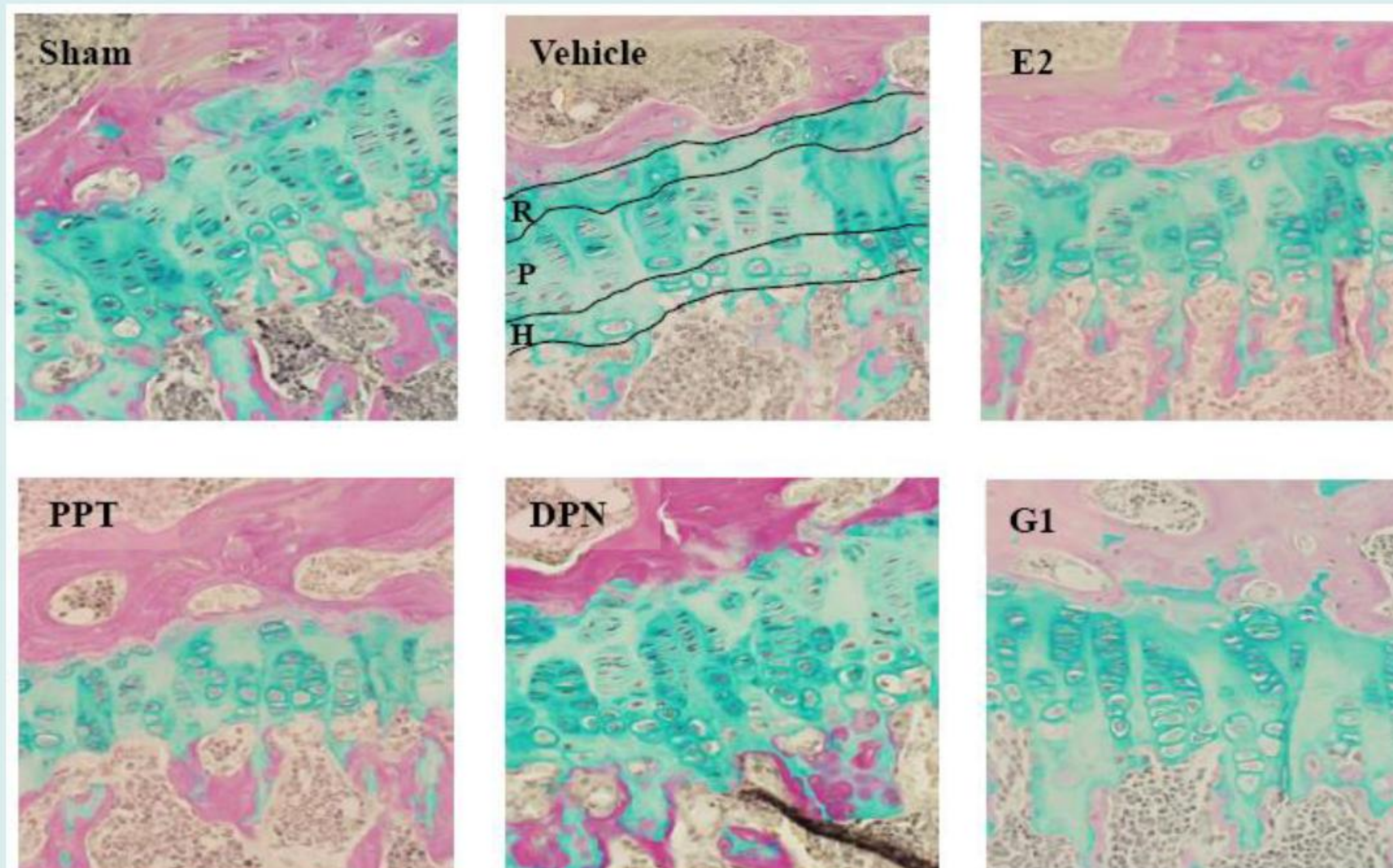


Figure 1. Effects of E2 and selective ER $\alpha$  (PPT), ER $\beta$  (DPN) and GPER-1 (G1) agonists on tibia growth plate length and different chondrocytes zones. R=resting zone, P=proliferative zone and H=hypertrophic zone.

## Introduction

Estrogens are well known to promote bone maturation and at high doses to induce growth plate closure and thereby stop further growth. High-dose estrogen treatment has therefore been used to limit growth in extremely tall girls. However, recent data suggest that this treatment may have severe side effects, including increased risk of cancer and reduced fertility.

## Results

- E2 and PPT treated mice had shorter tibia and femur when compared to vehicle treated controls while those animals treated with DPN and G1 had similar bone lengths as controls (Fig. 1 and 2A).
- The histological evaluation of PCNA staining of tibia growth plate cartilage showed lower proliferation in E2 or PPT treated OVX mice compared to OVX vehicle (Fig. 2B).
- Growth plate height and proliferative zone height were reduced in animals treated with E2 or PPT but not in those treated with DPN or G1 (Fig. 1 and 3).

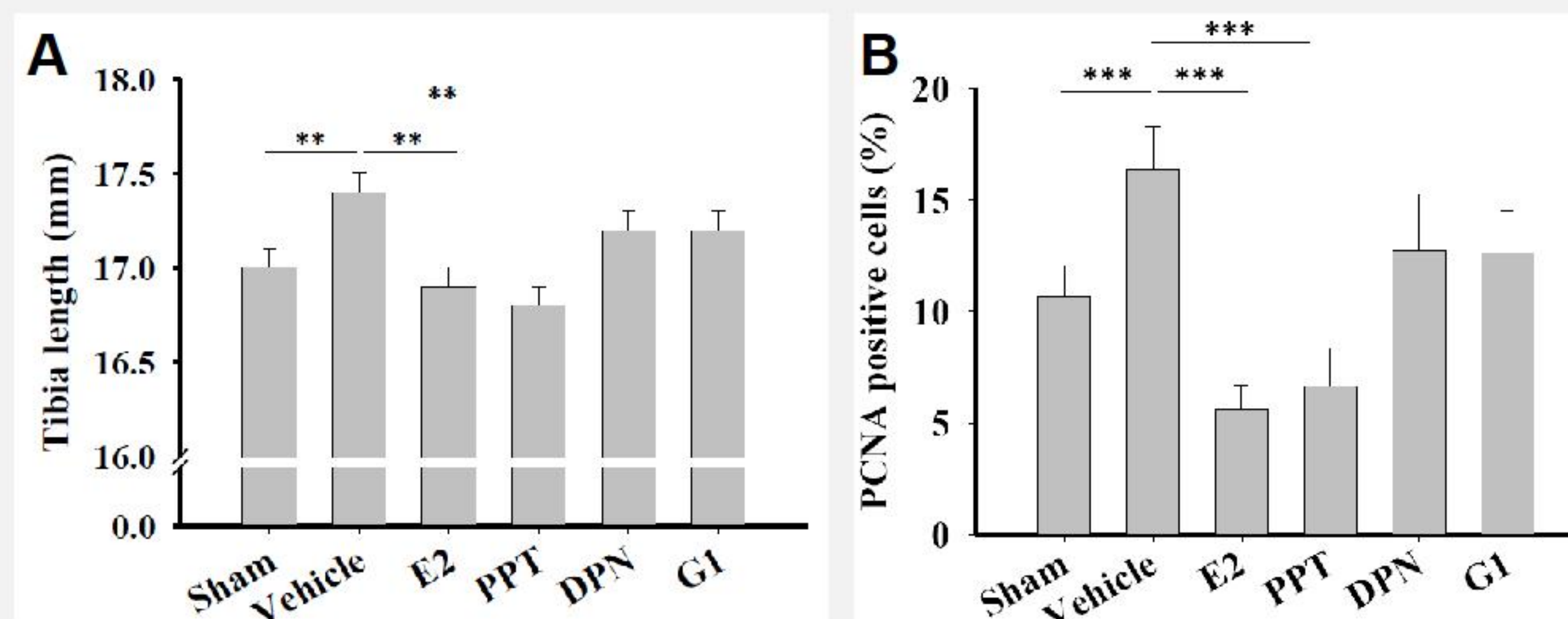


Figure 2. Effects of E2 and selective ER agonists on tibia length and chondrocyte proliferation (A) and on proliferation (B). Values are means  $\pm$  SEM. \*\* $p < 0.01$  and \*\*\* $p < 0.001$ .

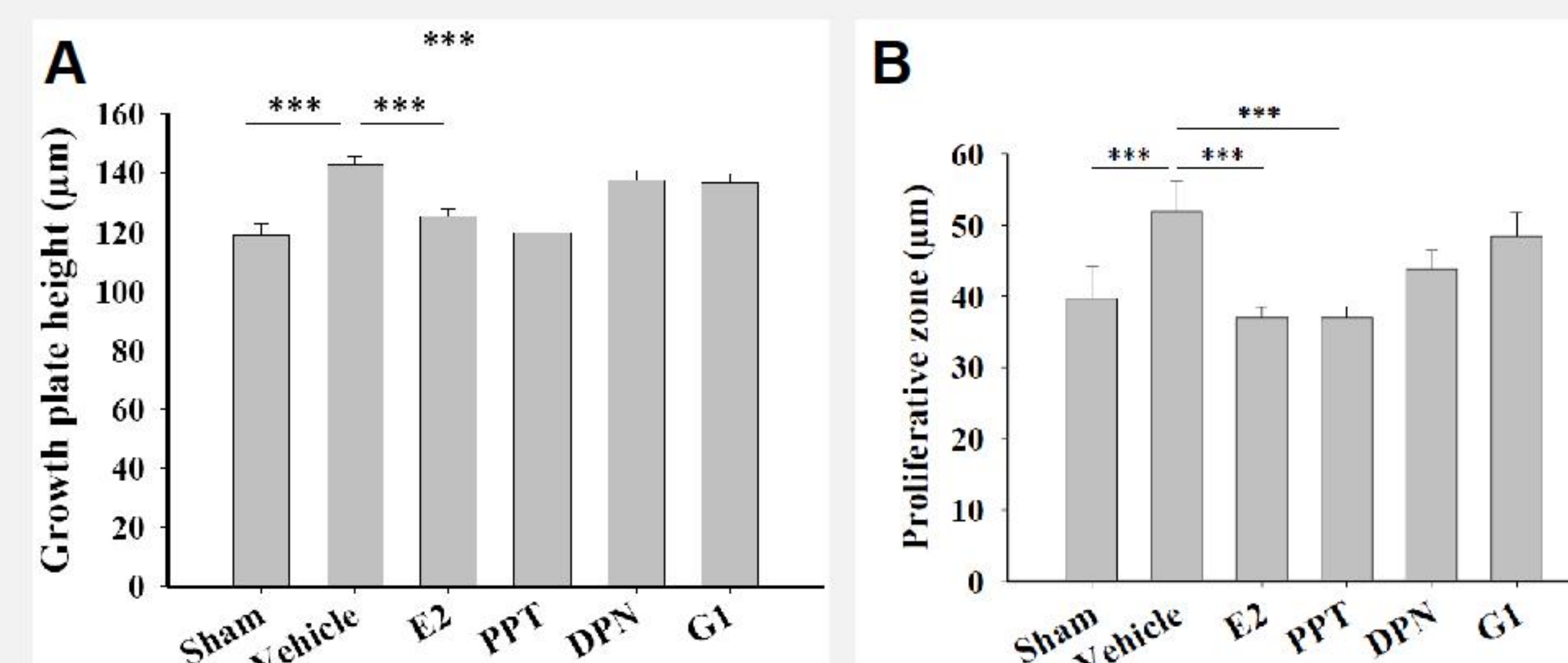


Figure 3. Effects of E2 and selective ER agonists on tibia growth plate height (A) and proliferative zone height (B). Values are means  $\pm$  SEM. \*\*\* $p < 0.001$ .

## Materials and Methods

Twelve-week old ovariectomized female C57BL/6 mice were injected 5 days per week for 4 weeks with E2 (1  $\mu$ g), PPT (175  $\mu$ g), DPN (105  $\mu$ g) or G1 (5  $\mu$ g) per mouse. Tibia and femur lengths were measured after sacrifice and growth plate morphology was analyzed.



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