英语学习与文献汇报

English learning & Literature reviewing

王博伦

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Inhibitory effects of melatonin on titanium particle-induced inflammatory bone resorption and osteoclastogenesis via suppression of NF-kB signaling

褪黑激素通过下调NF-kB信号通路抑制钛颗粒介导的炎性骨吸收

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Full length article

Inhibitory effects of melatonin on titanium particle-induced inflammatory bone resorption and osteoclastogenesis via suppression of NF-κB signaling

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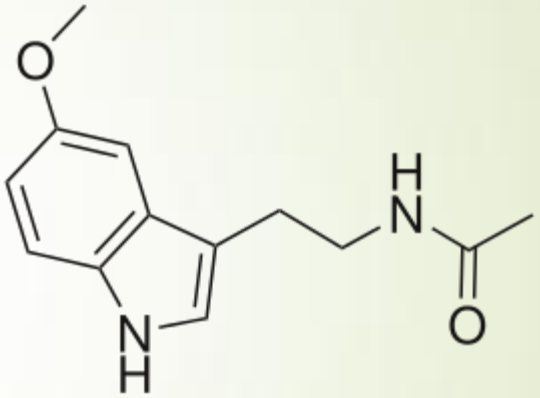
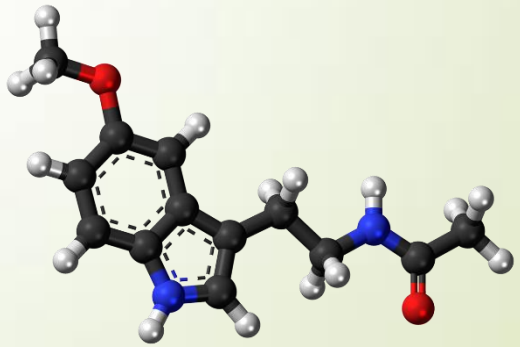
2017 Soochow University（IF=6）

Melatonin是什么？

- Melatonin (MT)
- 褪黑激素
- Melatonin, a hormone produced mainly by the pineal gland, is involved in many physiological and pathological conditions, such as anti-tumor activity, sleep, and circadian rhythms.





Introduction

- 人工关节置换术术后
- Peri-implant osteolysis (PPO) 磨损颗粒介导的假体周围骨溶解
- Ensuing aseptic loosening 无菌性松动发生
- In this study, we hypothesized that melatonin attenuates titanium particle-induced osteolysis by reducing osteoclastogenesis and inflammatory reactions.
- *In vivo* murine calvaria model
- *In vitro bone marrow-derived macrophage (BMM) cell culture systems*

Materials and Methods

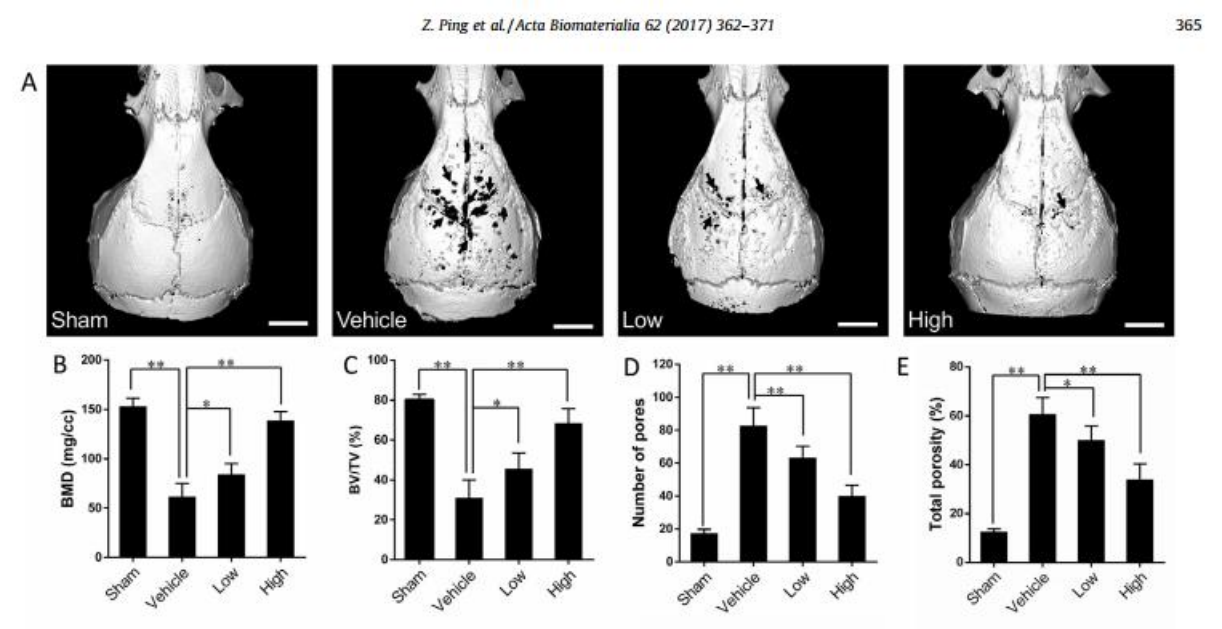
- Ti particles：mean diameter=3.32 ±2.39 μm, 95% less than 4 μm
- *In vivo*：60只7周龄雄性C57BL/6 小鼠建立颅骨磨损颗粒介导的骨质溶解模型。PBS；PBS+Ti；Ti+low- (5mg/kg)；Ti+high- (50mg/kg)
- Radiological analyses：high resolution μCT
- number of pores, bone volume(BV), bone volume/tissue volume (BV/TV) and bone mineral density (BMD)
- Histological and immunohistochemical analysis
- HE, TRAP staining, eroded bone surface area (mm^2) and bone thickness (BT, mm), positive staining cells counted
- ELISA of TNF-a, IL-1, and IL-6

Materials and Methods

- *In vitro*： BMMs were collected from the hind limbs of C57BL/6 mice. To induce osteoclastic differentiation, M-CSF and RANKL were added to the medium.
- Osteoclastic activity assessment： TRAP staining
- Cytotoxicity assay： CCK-8
- Osteoclastic function： Resorption pit assay
- Immunofluorescence of F-actin ring
- Western blot

Results

- Melatonin suppresses Ti particle-stimulated bone loss in vivo



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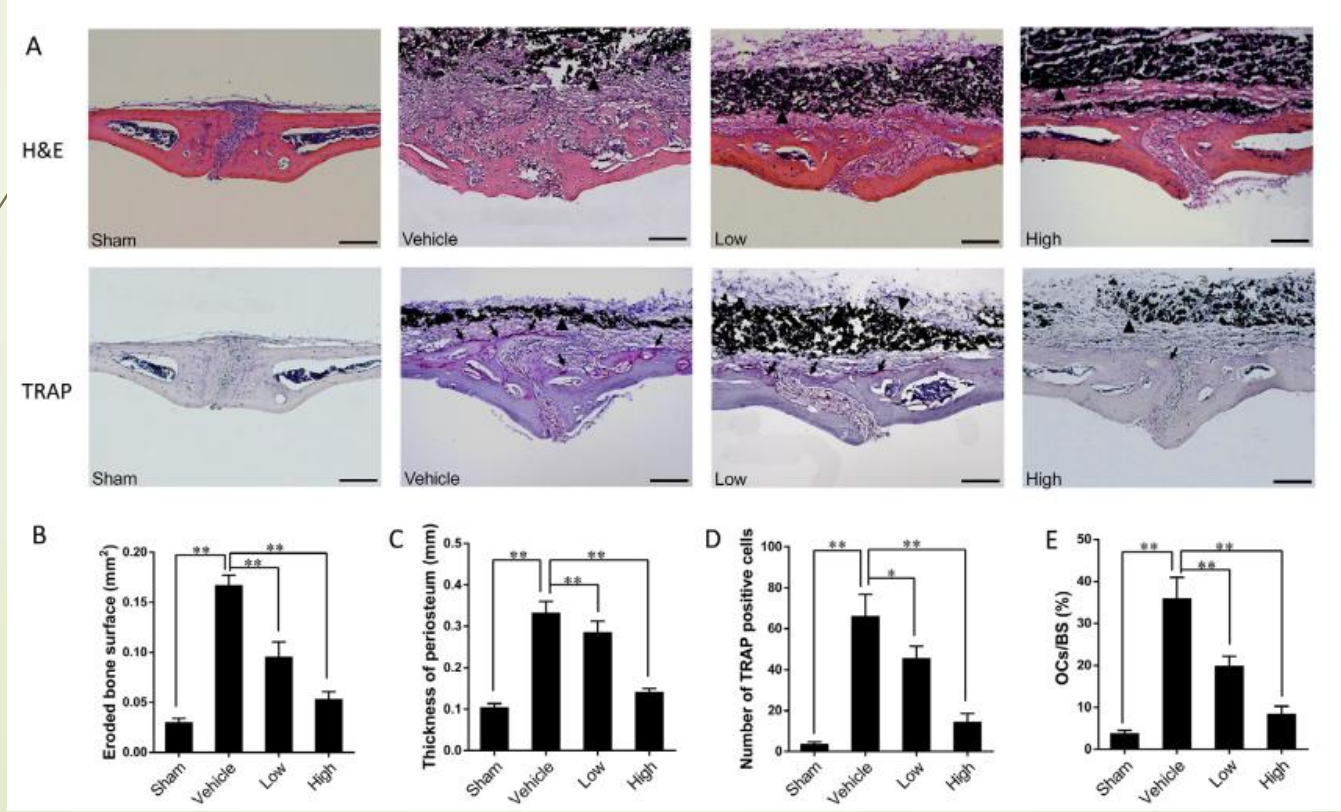
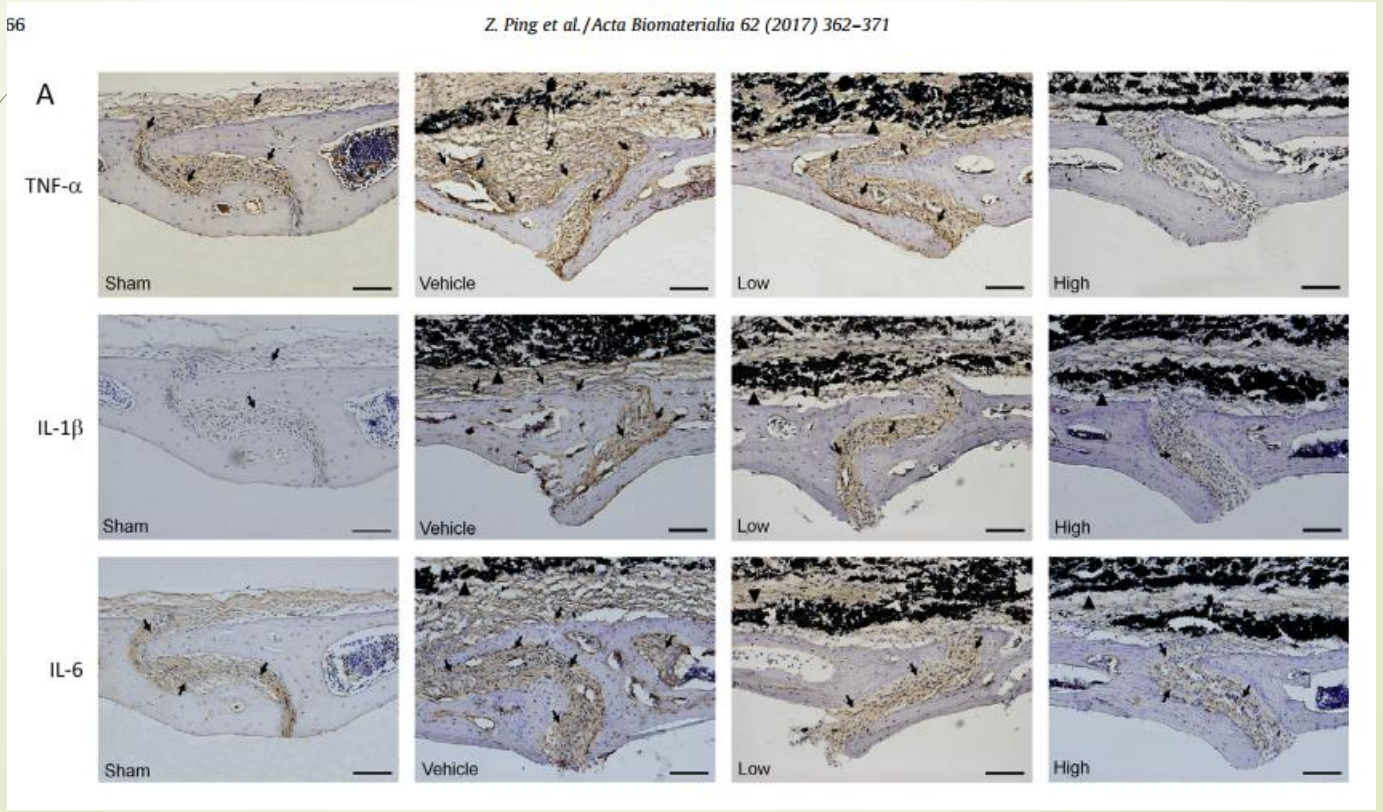


Results

- Melatonin inhibits the release of inflammatory cytokines



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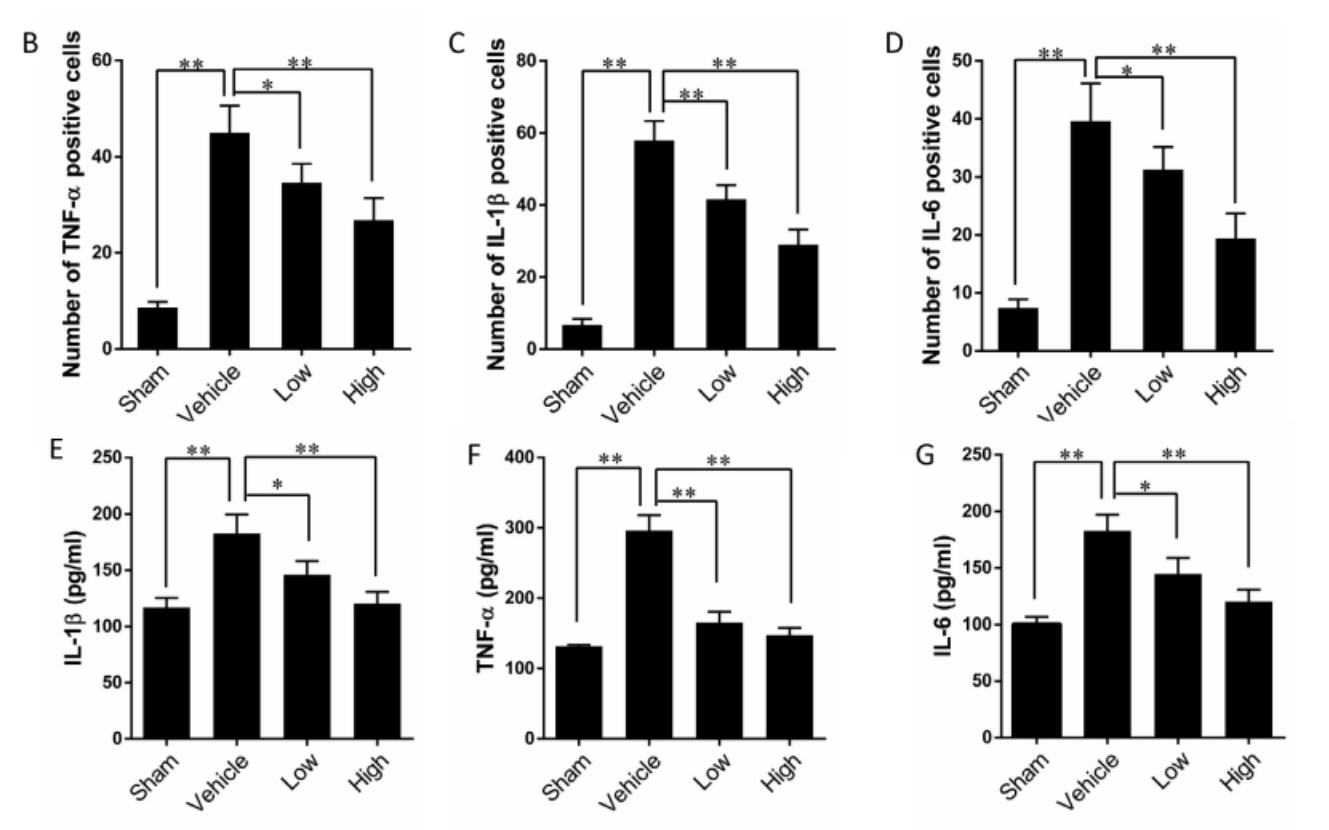
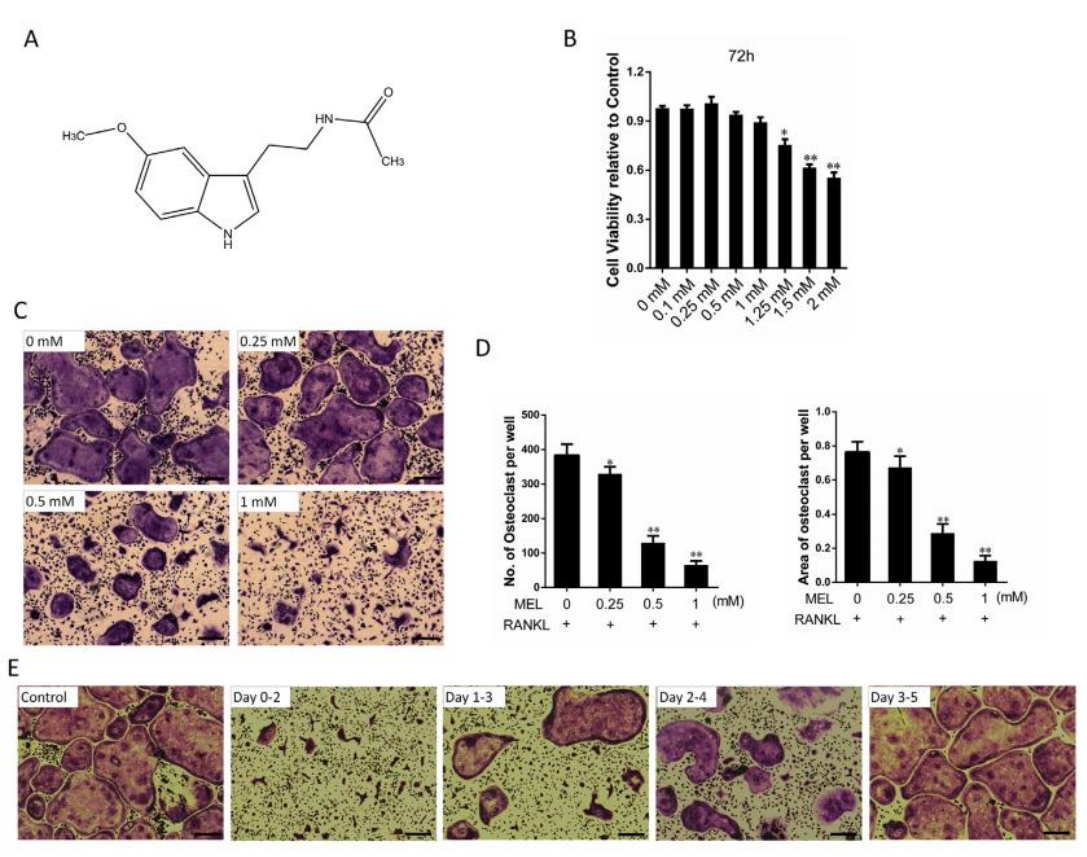


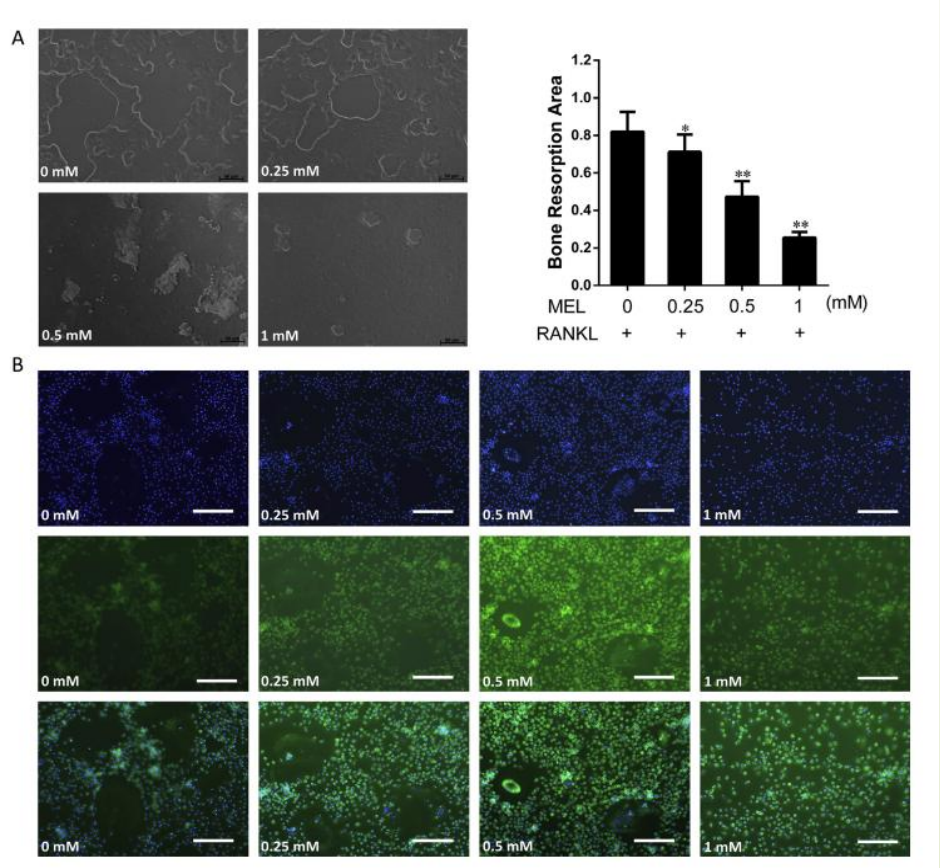
Results

- Melatonin abrogates RANKL-induced osteoclast formation without cytotoxicity in vitro



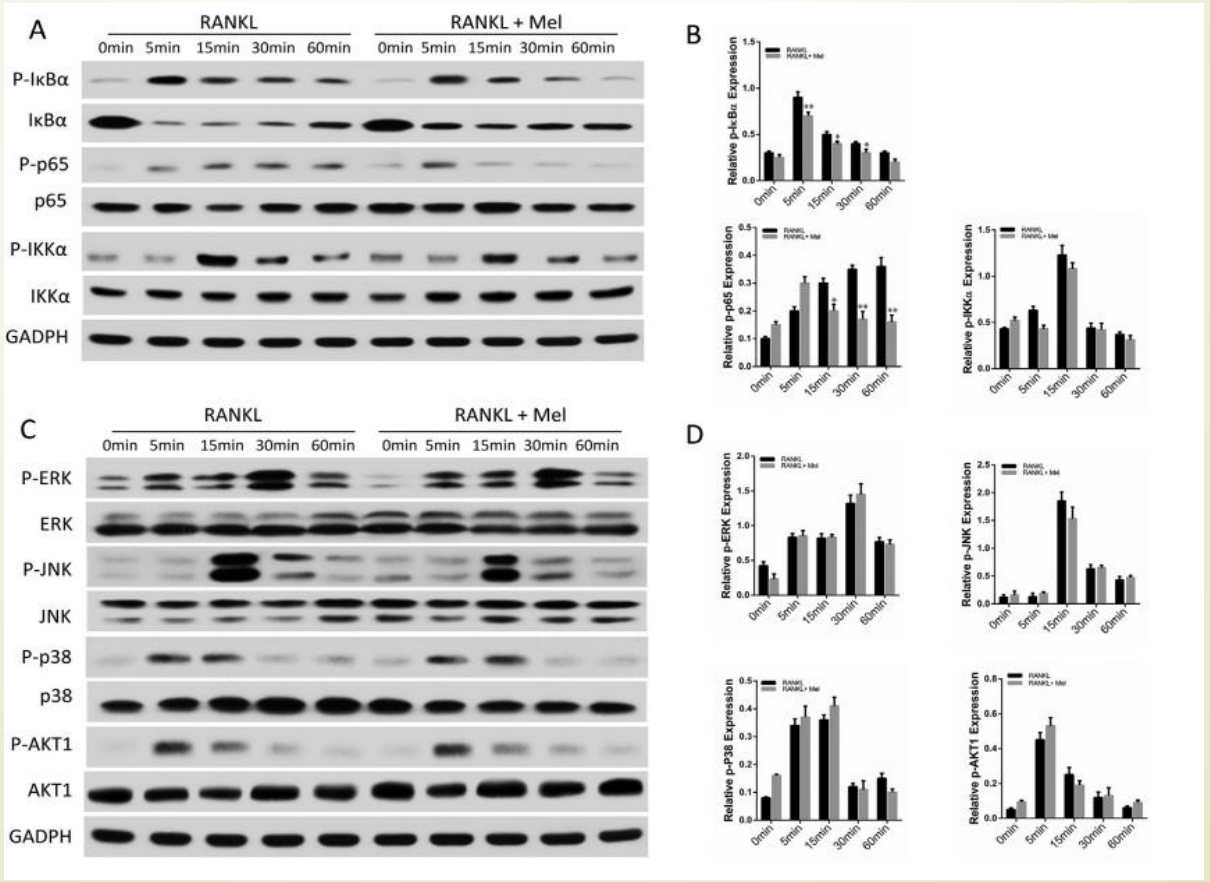
Results

- Melatonin inhibits bone resorption and osteoclastic F-actin ring formation



Results

- Melatonin suppressed the activation of NF-jB signaling pathway



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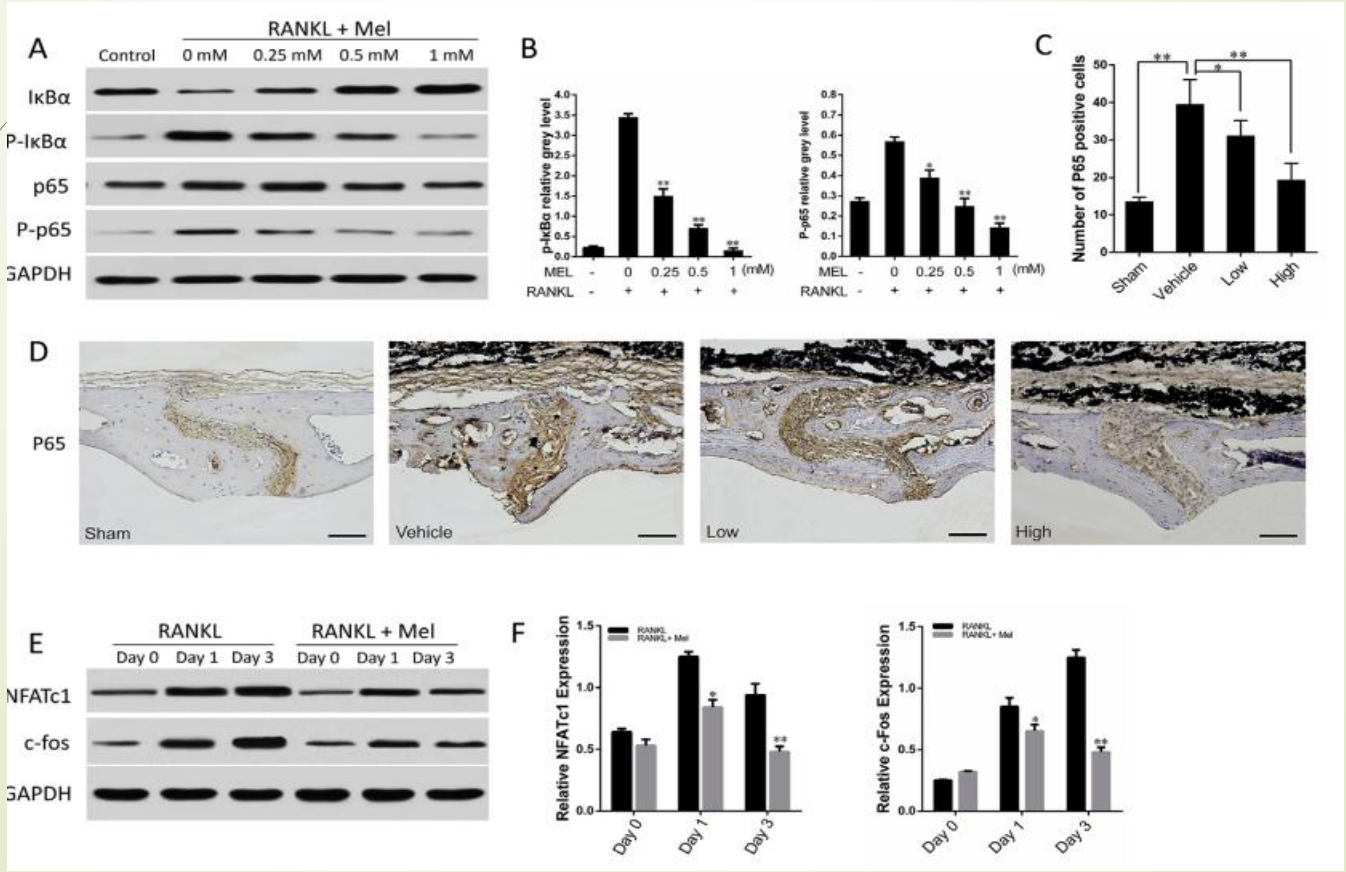

Discussion

- The present study initially verified whether melatonin can inhibit osteoclast formation and function in vivo. Consistent with previous reports [9,13], we found a significantly lower number of mature osteoclasts after melatonin administration.
- Following this, we then sought to establish the concentration-dependent effects of melatonin in osteoclast differentiation when delivered in combination with RANKL in vitro.

Discussion

- Blocking NF-jB signaling has been proposed to be an effective way to prevent osteoclastic activities and particle-induced osteolysis [27,28]. In this regard, we speculated that the observed inhibitory effects of melatonin may occur through abrogation of the NF-jB signaling pathway.
- Melatonin dramatically abrogated the expression of TNF-a, IL-1b, and IL-6 in vivo, and suppressed the levels of these factors in the supernatants of melatonin-treated groups, consistent with a previous study that melatonin normalizes plasma pro-inflammatory cytokines [36]

Discussion

- In conclusion, this study confirmed that melatonin effectively attenuates Ti particle-induced inflammation and bone resorption in vivo and hinders osteoclast differentiation as well as osteoclastic function in vitro, presumably through abrogated NF-jB signaling.

感谢各位老师、师兄弟的收听，欢迎提问！