

Transplantation of parathyroid hormone-treated Achilles tendon promotes meniscus regeneration in a rat meniscal defect model

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COI Disclosure

Presenter's name(s): ©Kazuya Nishino, Yusuke Hashimoto

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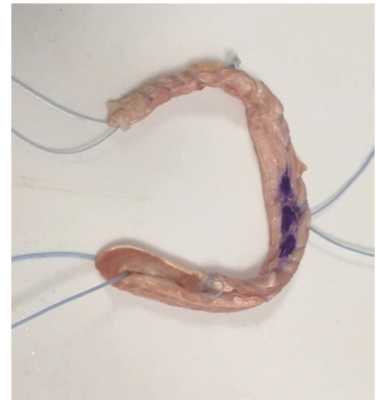
Grants from Japanese Orthopaedic Society of Knee, Arthroscopy and Sports Medicine

Received a drug from Asahi Kasei

Surgery for Meniscal Defect

- Allograft / Artificial meniscus: Limited supply in Japan
- Meniscal reconstruction with **autologous tendon graft**

Histologically differ from native meniscus



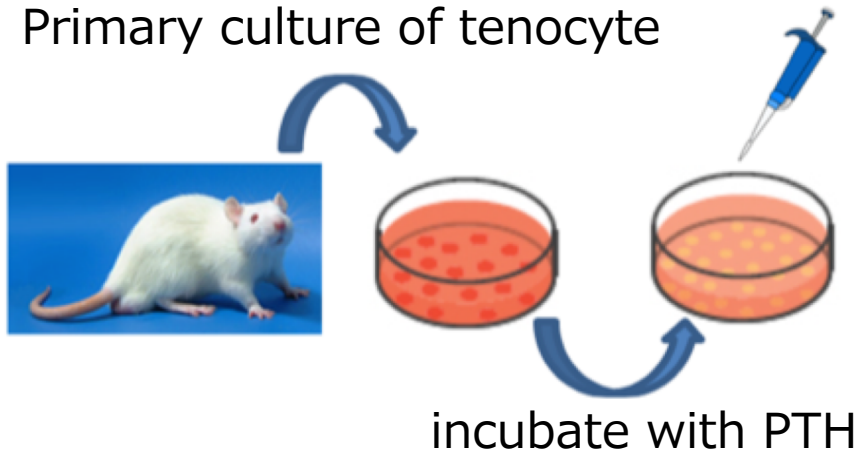
Additional procedure promoting chondrogenesis

Focused on PTH

Methods : *in vitro*

- Achilles tendons excised from, 8-week-old, male Lewis rats.
- Digested with type 1 collagenase

Primary culture of tenocyte



- ✓ 6-well plate ; 1×10^5 /well
- ✓ PTH(1-34) (Teribon , Asahi Kasei)
- ✓ 0 (control), 1nM, 10nM, 100nM
- ✓ Day 28 → Alcian Blue stain
- ✓ Day 14, Day28 → qRT-PCR

target gene : PTH1R, Col2a1, Sox9, Col1a1, RUNX2, Scx

Methods : *in vivo* ①

PTH(1-34) injection for Achilles tendon

- Lewis Rat male 8-weeks-old

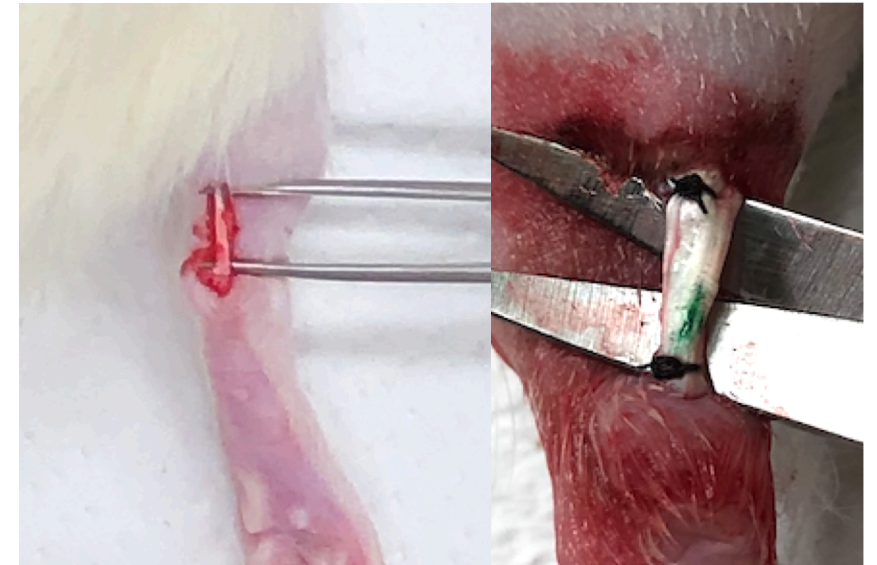
0 μ g (control), 9 μ g, 22.5 μ g, 45 μ g / 15 μ l

↓
Recommended dose treating osteoporosis

N=6 for each group

sacrificed at 4 and 8 weeks

evaluating [cartilaginous matrix
appropriate dose

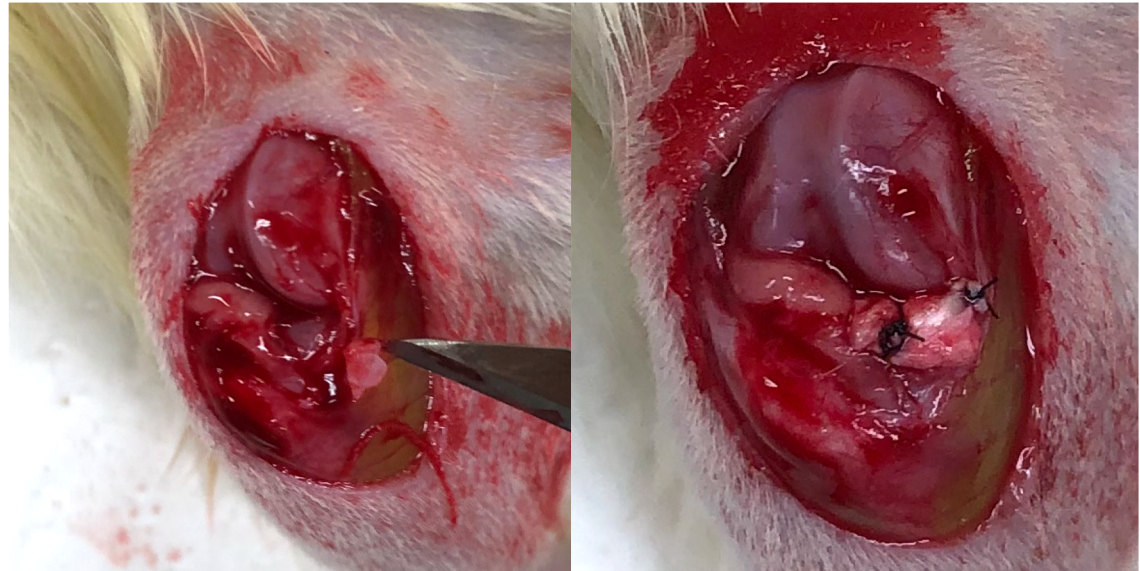


Methods : *in vivo* ② ;

Meniscal Transplantation using PTH(1-34) treated tendon graft

- PTH (1-34) ($9 \mu\text{g}/15\text{ml}$) injected into Achilles tendon
- Transplanted to medial meniscus defect model
- Sacrificed at 4 and 8W

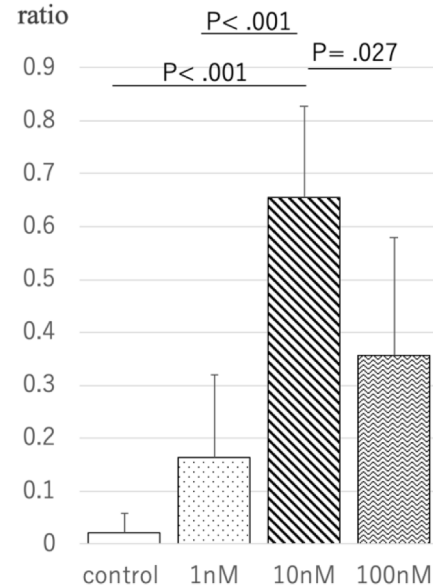
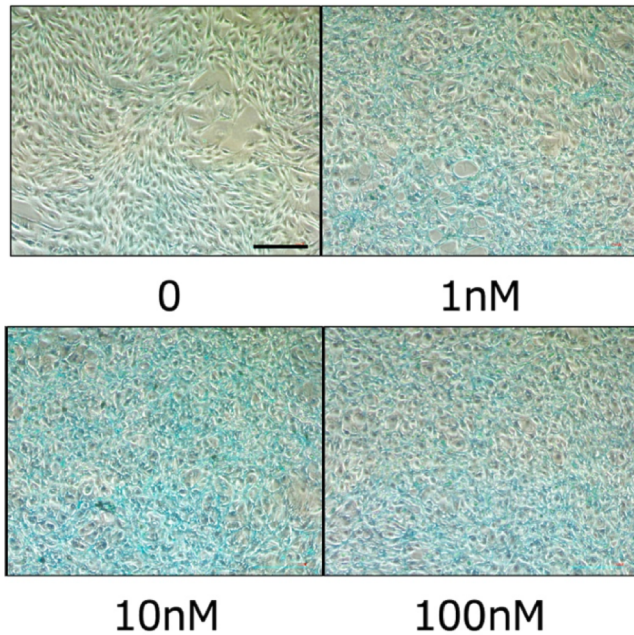
N=6 for each group



Result : *in vitro* ; PTH(1-34) administration

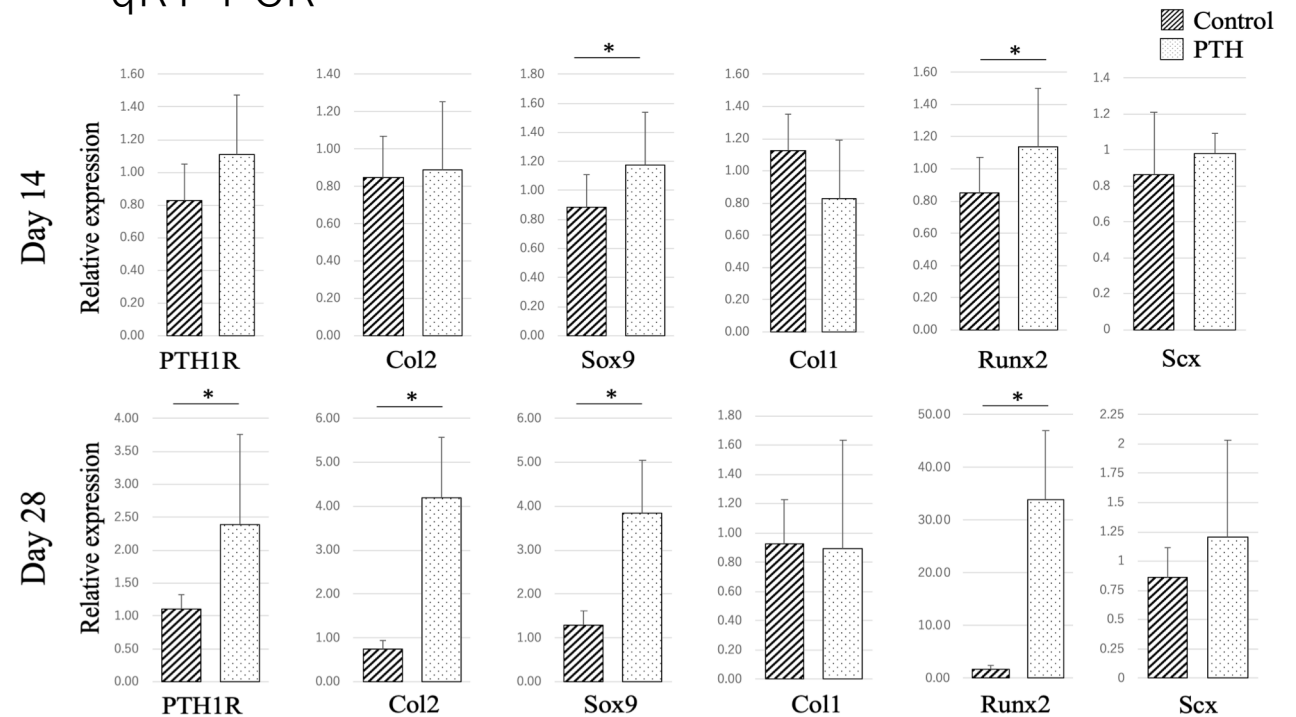
Day 28

Alcian Blue

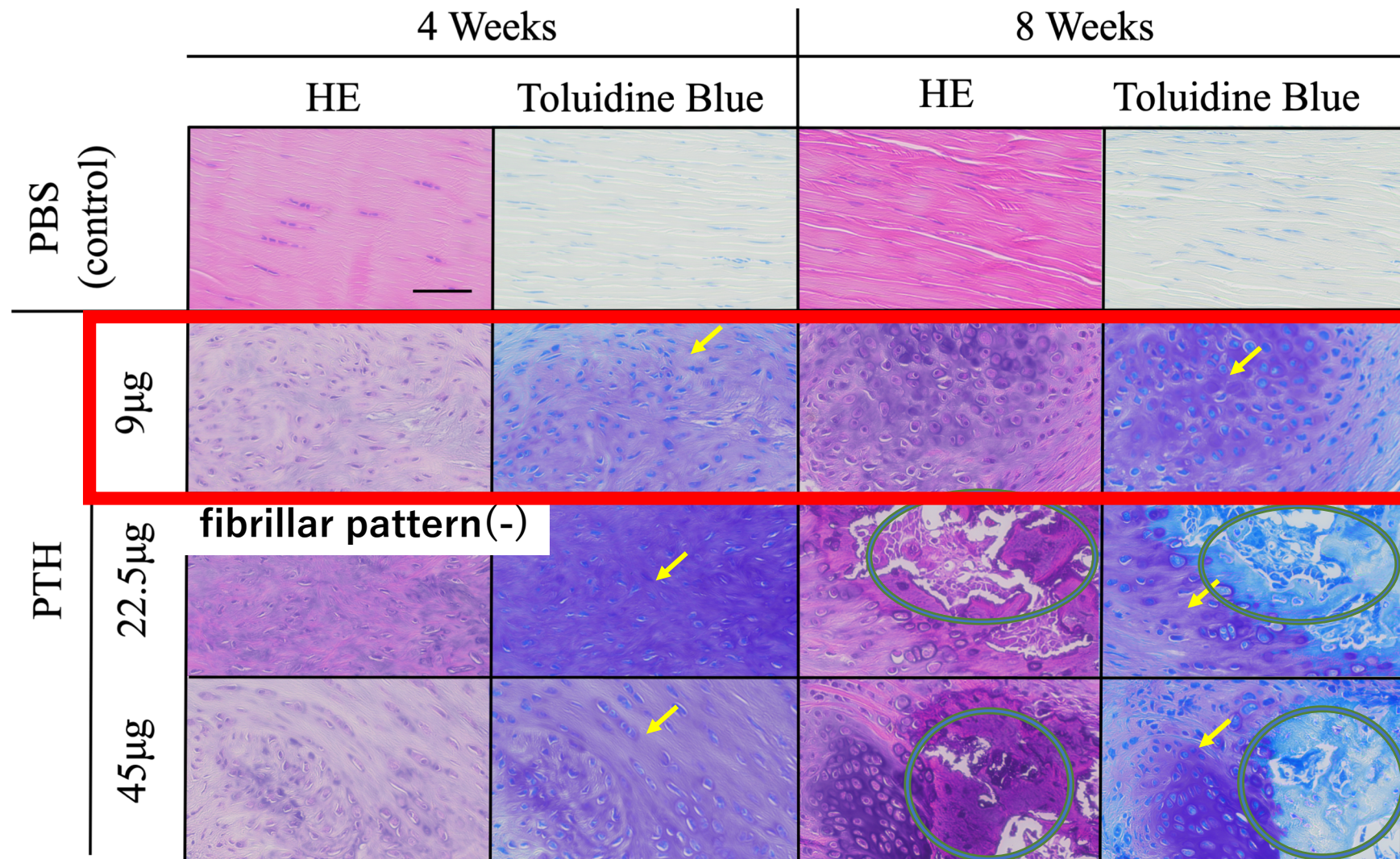


10nM was used for qRT-PCR

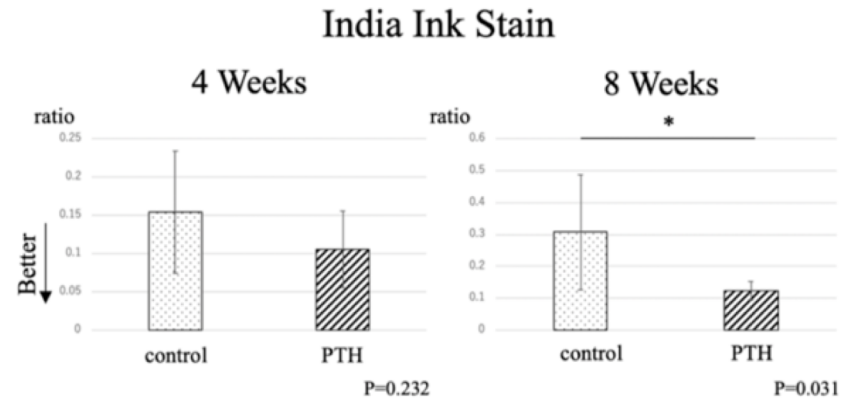
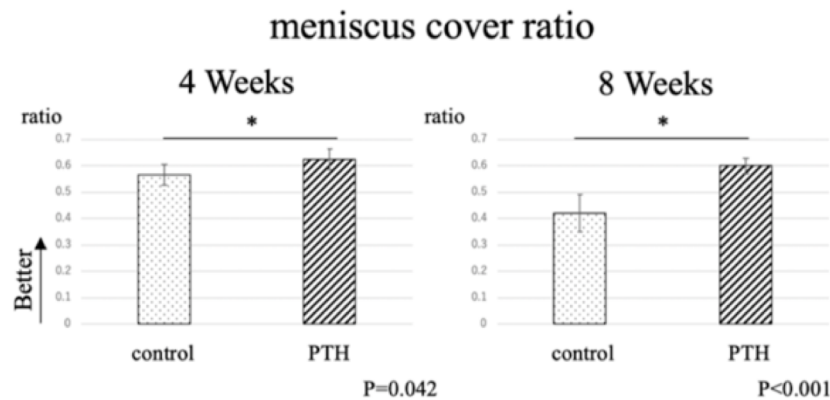
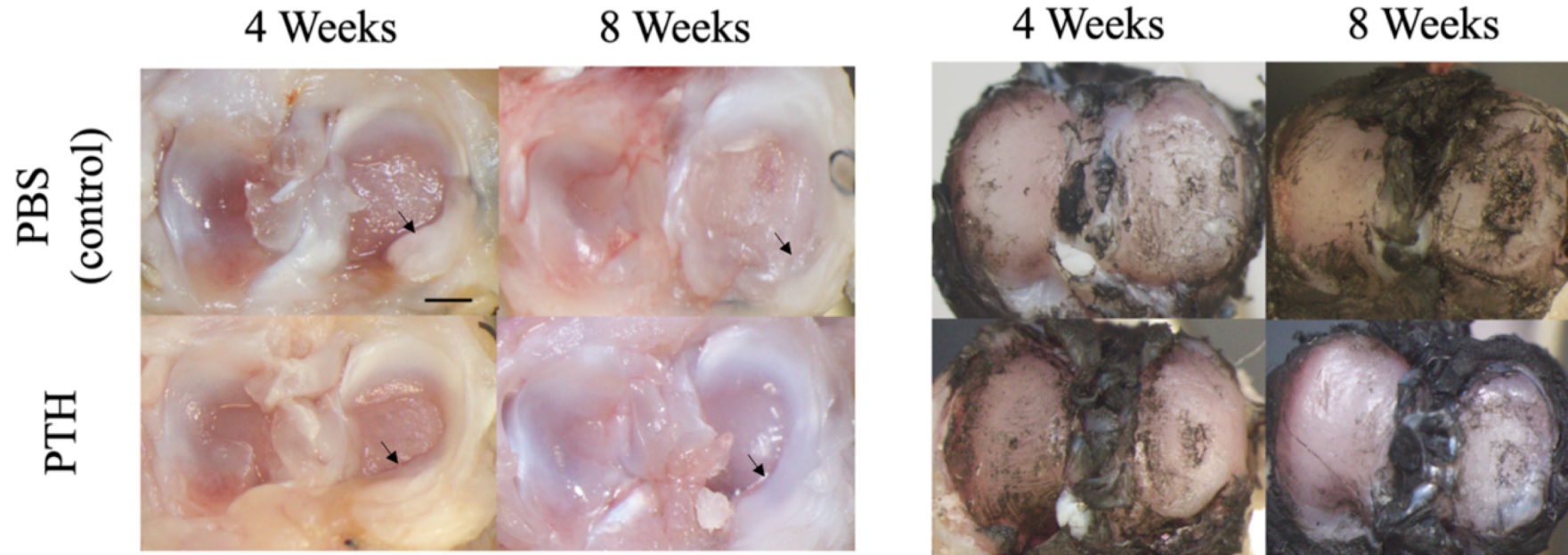
qRT-PCR



in vivo ; Histological examination of rat Achilles tendon treated with PBS or PTH (1-34)

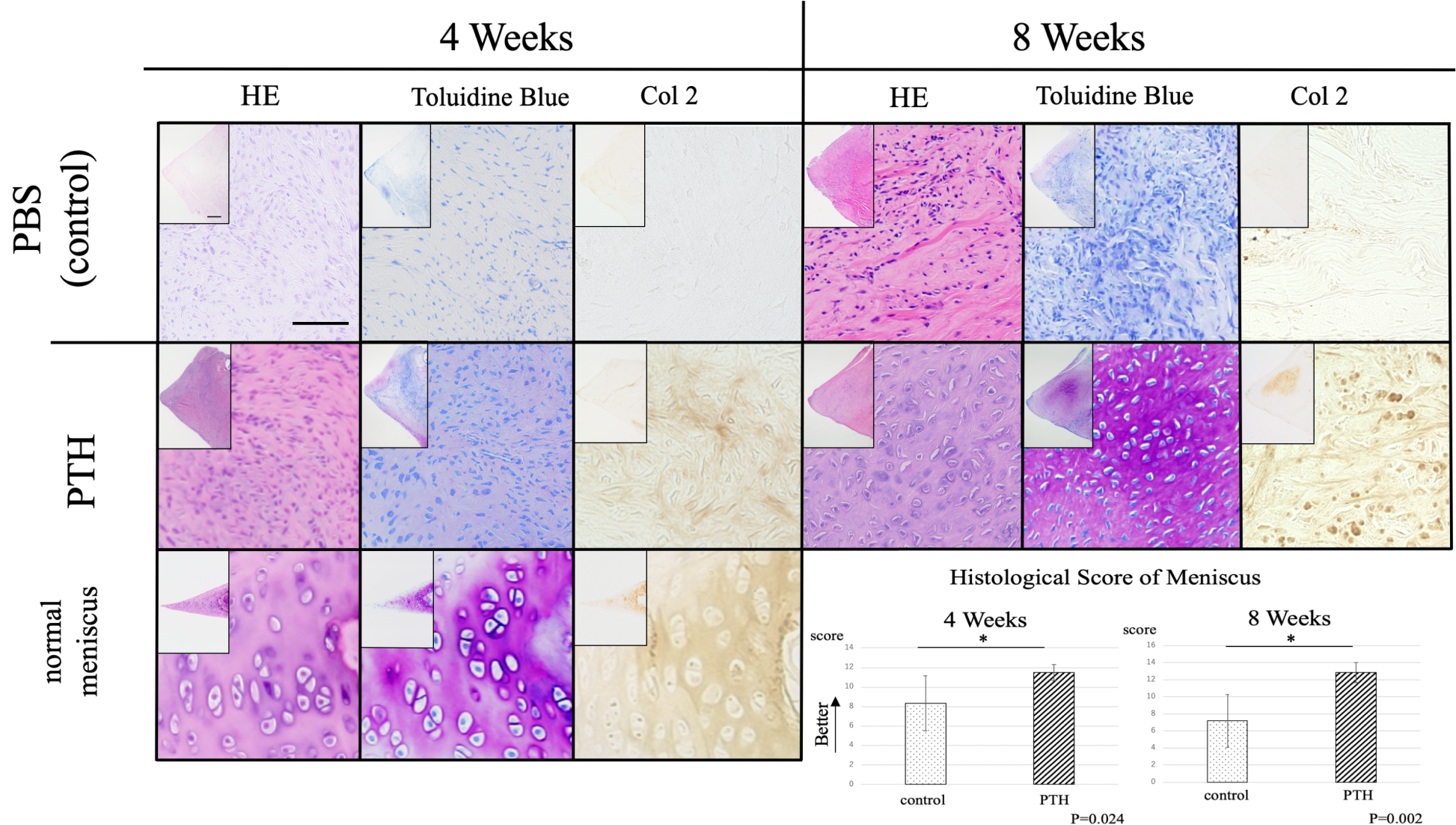


in vivo ; Macroscopic examination of the regenerated meniscus and tibial plateau

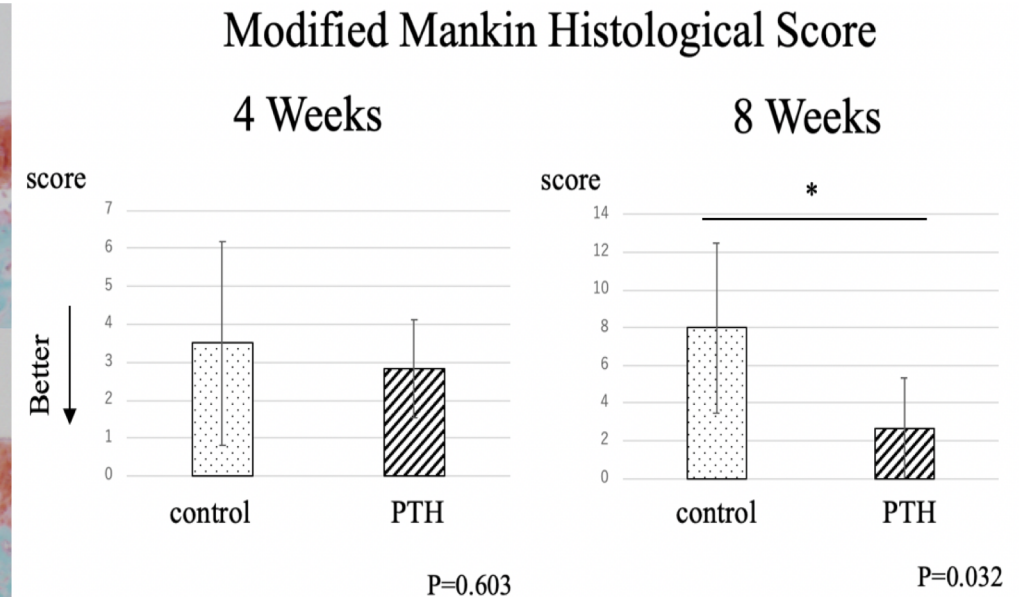
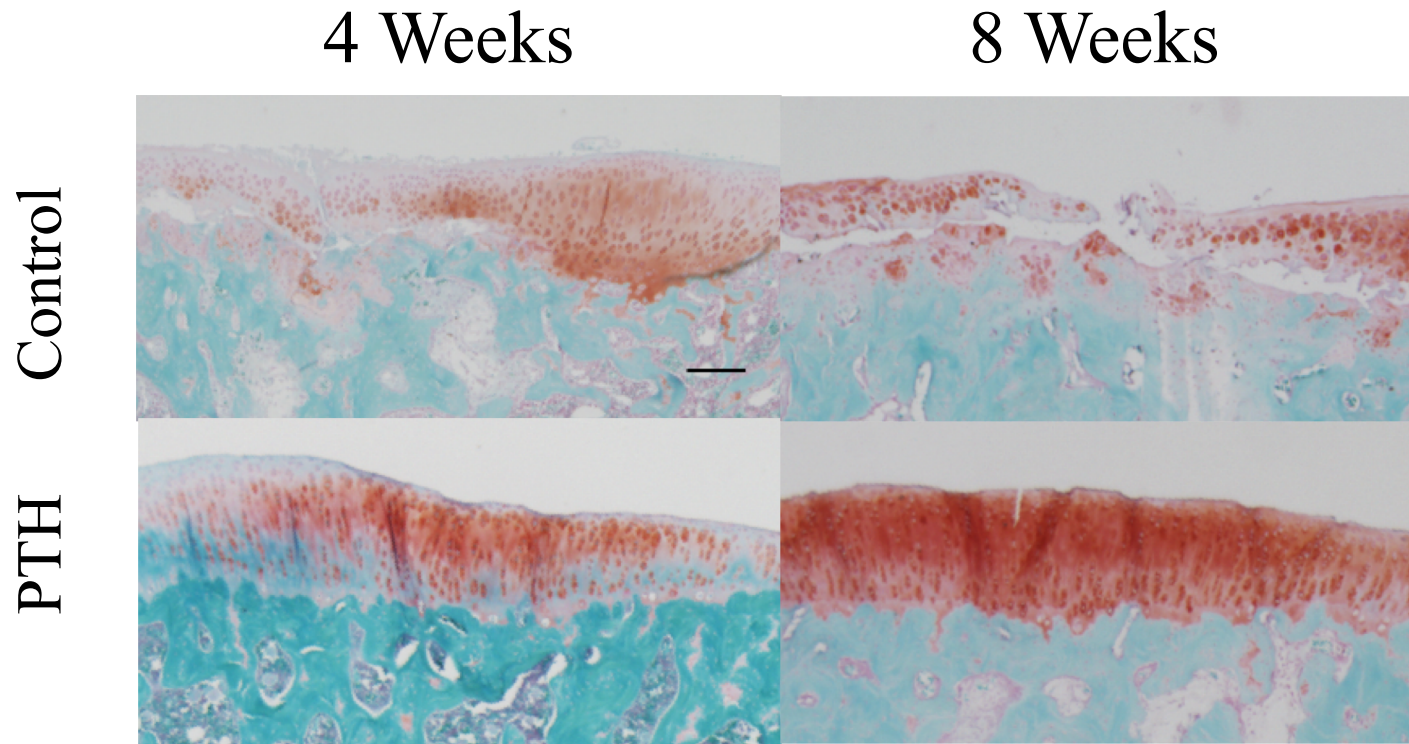


in vivo ;

Histologic analysis of regenerated rat meniscus



in vivo ;
Safranin O staining of the medial tibial plateau

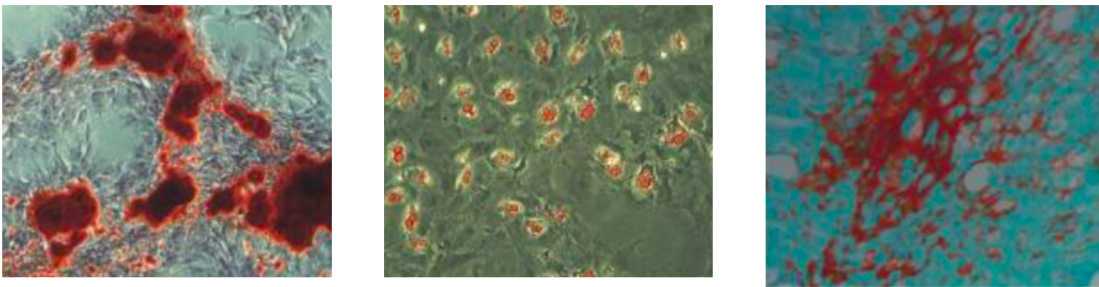


Discussion

- PTH(1-34)(teriparatide) : bone anabolic therapy for osteoporosis
- PTH(1-34) administration **enhances** chondrocyte proliferation
suppresses chondrocyte differentiation

Zang 2014

- The rat Achilles tendon has abundant multipotent stem cells, called **tendon-derived stem cells**



Rui et al, 2010

PTH(1-34) might have stimulated tendon-derived stem cells

Conclusions

- PTH (1-34) **induced cartilage formation** in the rat tendon.
- Transplantation of PTH (1-34)-treated Achilles tendon induced meniscal regeneration and **preserved knee articular cartilage** in a rat meniscal defect model.
- Histologically, the regenerated meniscus showed more cartilaginous matrix content in PTH group.
- PTH (1-34) **stimulated tendon-derived cells** showed promotion of chondrogenic differentiation.