A Novel Heterozygous Mutation in the SLCO2A1 Gene in Family with Primary Hypertrophic Osteoarthropathy
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Background: Primary hypertrophic osteoarthropathy (PHO), also called pachydermoperiostosis is characterized by digital clubbing, pachyderma, and periostosis and the precise incidence and prevalence are still unknown. PHO has been thought to be genetically heterogeneous and both autosomal dominant and autosomal recessive patterns have been suggested. In 2008, homozygous mutations in hydroxyprostaglandin dehydrogenase (HPGD), which encodes 15-hydroxyprostaglandin dehydrogenase (15-PGDH) were identified as a cause of PHO. More recently homozygous mutations in solute carrier organic anion transporter family, member 2A1 (SLCO2A1), the gene encoding the prostaglandin transporter were also identified in 3 Chinese families with PHO. Although as a result of studies that followed, knowledge of the pathomechanism of PHO has greatly improved that increased levels of prostaglandin E2 (PGE2) due to the failure of its degradation are involved, more cases and their genetic backgrounds are needed for the comprehensive understanding of this disease.

Clinical case: The 62-year-old Asian proband, who was born to healthy nonconsanguineous parents visited our clinic for genetic counseling of his son. At 19 years of age, the patient presented with enlarged hand and foot, knee joints swelling and pain and then was referred to neurosurgeon for suspicious of acromegaly. He got hypophysectomy but revealed no tumor lesion in the specimen. Attention was aroused only after periosteal thickening was noticed in the carpal, phalangeal, radial and ulnar simple X-ray, indicating the possibility of PHO. Since he was not the exact diagnosis and treatment of common disorders.

Conclusion: Here we add one more inactivating mutation in SLCO2A1 gene that causes PHO. This novel heterozygous mutation broadens the allelic spectrum of SLCO2A1 mutations. Further clinical study will be needed in order to validate the genotype-phenotype correlations and to develop any therapeutic options of PHO in future. The study of inherited monogenic diseases has contributed greatly to our mechanistic understanding of pathogenic mutations and gene regulation and has provided tremendous knowledge toward the common goal of developing methods for the early diagnosis and treatment of common disorders.

Polyosaccharides of Trametes Versicolor Improve Bone Properties in Diabetic Rats
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This study investigates the effects of Trametes versicolor (L.:Fr.) Pilát (TVP, also known as Yunzhi) on bone properties in diabetic rats. Forty-five 8-week-old male Wistar rats were fed either a chow diet (control, CON) or a high-fat diet throughout the study period of 28 days. Animals in the high-fat-diet group were injected nicotinamide and streptozotocin to induce diabetes mellitus (DM). The DM rats were divided into a group receiving distilled water (vehicle, VH) and another group receiving TVP at 0.1 g/kg-weight by gavage. Compared to the CON group, animals in the vehicle group demonstrated higher degree of hyperglucemia, smaller bone volume of tibia and femur, and lower femoral strength. Compared to the vehicle group, the TVP group demonstrated significantly lower postprandial blood sugar and femoral cortical porosity, increased bone volume of proximal tibia and femoral bone strength, and mitigated DM-induced deterioration of proximal tibial microarchitecture, as shown by reduced trabecular separation and larger trabecular number. The protective effect of TVP on bone properties was mediated through, in part, the improvement of hyperglycemic control in DM animals. Further study is needed to investigate whether TVP's osteoprotective effect is related to any mechanism that directly benefits the bone in rats with DM.

Marine Cartilage Proteoglycan Prevents Degradation of the Bone Quality in Ovariectomized Rats
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Background: Osteoporosis is defined as “Disease of low bone mass and increase the risk of bone fracture”, and the number of estimated patients is 13 million in Japan. Bone strength is estimated by the bone density and quality. Bone quality is affected by bone architecture, turnover, accumulated damage, and mineralization. The bisphosphonates and selective estrogen receptor modulators (SEAM) are thrown for treatment in the current osteoporosis therapies, but effect of these drugs is only reduction of fracture risk and determinative in improvement of the bone density. On the other hand, it is reported that activated vitamin D3 and vitamin K2 improve the bone quality. But the effect of these vitamins is poor, effective therapeutic agents for improvement of the bone quality is required.

Objectives: The objective of this study is to determine the benefits of Salmon cartilage proteoglycan (SPG) diet in ovariectomized rats.

Materials and method: 1. Animal experiments
Fifty 8-week-old female Sprague-Dawley rats were housed individual cages. The rats were randomized into sham or OVX experiments, and underwent either ovariectomy or sham-operation under anesthesia with sodium pentobarbital. The rats were divided into the following five groups.
A) SHAM: sham-operated rats/receive MF
B) OVX: ovariectomized rats/receive MF
C) Ca-less: ovariectomized rats/receive Calcium-lessness Diet
D) 5%SPG: ovariectomized rats/receive MF which includes SPG by the 5 wt%
E) 10%SPG: ovariectomized rats/receive MF which includes SPG by the 10 wt%
The respective groups received free access to water and Diet for 12 weeks, and the rats were sacrificed using intraperitoneal sodium pentobarbital at 12 weeks postoperatively. Whole blood was collected via abdominal aorta, and both side femurs were collected by surgery extraction.
2. Serum Biochemistry analysis
Serum was separated from whole blood by centrifusion. Gla/Glu type Osteocalcin (Takara bio. INC., Japan) and TRAP-5b (DS Pharma Biomedical Co., Japan) were measured by EIA.
3. Peripheral quantitative computed tomography (pQCT) analysis
To evaluate bone strength and density, pQCT sectional images were taken by XCT Research SA+ (Stratec Medizintechnik GmbH Pforzheim, Germany). Densitometric parameters and geometric parameters were analyzed.
4. Histopathological analysis
To evaluate bone inner structure, left side femurs were fixed in the 10% formalin for 48 h and 70% ethanol for 72 h. After Calcium was removed by the 10% EDTA solution for 4 weeks, femurs were embedded in the paraffin (FFPE). HE stain, Azan stain and immunohistochemistry were performed on FFPE sections.

Results: Gla/Glu type Osteocalcin expression showed up-regulation in OVX rats. Gla/Glu type Osteocalcin expression showed down- regulation by SPG treatment, and it was equal to sham-operated rats. Although Bone strength and density showed weak improvement effect by SPG treatment, but it was not significantly. Trabecula showed decrease in OVX rats by histopathological evaluation. Meanwhile, SPG treatment suppressed decrease of trabecula.

Conclusions: It suggested that SPG suppress destroy of trabecula, and prevents deterioration of the bone quality. It is expected that SPG has the preventive effect to the osteoporosis.