factors. The heritable modes concern the more overall variations in shape, like slenderness of the hips, suggesting that subtle shape variations are due to individual environmental factors. Two of the tested OA susceptibility genes associated with variations in hip shape. FRZB, part of the ubiquitous and for cartilage and bone highly relevant Wnt-signaling pathway, associated with an overall change in shape, ranging from broad to slender hips. The influence of the DIO2 variant on mode 5 appears to link OA susceptibility to shallow placement of the head inside the acetabulum, which resembles dysplasia and has previously been recognized as a predisposing factor of OA.

Although independent of OA status, this data shows that SNPs of the tested genes are indeed associated with variations in shape of the hip.

**Aging**

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BACKGROUND OF GENERALIZED OSTEOARTHRITIS; EPIDEMIOLOGICAL ANALYSIS OF THE DISTRIBUTION OF PERI-ARTICULAR OSTEOPHYPES IN HUMAN SKELETONS

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**Purpose:** The concept of generalized osteoarthritis (GOA) was firstly defined by Kellgren and Moore (1952). Peri-articular osteophyte is one of the typical features of joint degeneration; such osteophytes emerge with ageing and develop as the pathological condition of osteoarthritis progresses. By analyzing the distribution of these minor degenerative and proliferative phenomena in general skeletal systems, considerable information on physiological and/or pathological ageing, and the background of GOA was derived.

**Methods:** Three hundred and seventy Japanese skeletons (male 232 and female 138) were examined. All of the six major joints, shoulder, elbow, wrist, hip, knee and ankle in every skeleton were observed macroscopically. Broken parts of the joint surfaces were not evaluated; accordingly 180 skeletons were scored in all of these six joints (male 122 and female 58). Materials ranged from 19 to 92 years of age at the time of death, and the average was 59.7 years old for males and 66.2 years old for females; the latter was significantly higher than that of the former. Using our criteria, the osteophytes were estimated as grade 0, 1, 2, 3 or 4 based on size and degree of proliferation in order to determine osteophyte scores (OS) from 0 to 50 in every skeleton. The scores for the upper extremity (UOS) were calculated by averaging scores for shoulder, elbow and wrist joints in every skeleton; and the scores for the lower extremity (LOS) were calculated by averaging the scores for hip, knee and ankle joints. Averages of all six joint scores in every skeleton were calculated to obtain its total osteophyte scores (TOS).

**Results:** The values for UOS and LOS showed significant correlation. The correlation coefficient in males was 0.78, which was larger than that in females, 0.63. In females, it was noted that the score for LOS was relatively higher than that for UOS, and there were many individuals in whom LOS was higher than those of UOS. In males, there were many individuals in whom UOS was relatively higher than those of LOS (Fig. 1). Fig. 2 is the scatter chart in which TOS was plotted as the longitudinal axis and age as the horizontal axis, and the correlation coefficients between TOS and age in males and females were determined. This chart shows that the average scores for males were larger than those for females but the rate of increase in females was greater than that in males. In males, the correlation coefficient between the TOS and age was 0.59, and in females, that was 0.70. There were some individuals whose TOS was uncharacteristically larger or smaller for their age; especially several males younger than 60 years old and several female older than 60 years old showed higher than expected OS for their age.
which could indicate GOA. The background of GOA was investigated by epidemiological analysis of peri-articular osteophytes of major six joints in a skeletal population.

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AGE-RELATED BEHAVIOR OF COLLAGEN AND PROTEOGLYCAN IN SUPERFICIAL, MIDDLE AND DEEP ZONES OF PATELLAR CARTILAGE: FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR) ANALYSIS OF NORMAL RABBITS

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Purpose: To detect the collagen content and proteoglycan content in the superficial, middle and deep zones of articular cartilage is a trend but still technical challenge. Fourier transform infrared spectroscopy (FTIR) is a powerful tool to investigate the collagen and proteoglycan in cartilage matrix. The FTIR quantifies the collagen content and proteoglycan content on histologic sections, the collagen and proteoglycan can be analyzed in the superficial, middle and deep zones of cartilage. Age-related behavior of the collagen and proteoglycan in each zone of patellar cartilage has not been reported yet. Therefore, the objective of this pilot study is to investigate the behavior of the collagen and proteoglycan in each zone using the FTIR.

Methods: Non-treated five rabbits of various ages (3-week, 8-week, 6-month, 1-year, 2.5-year) were examined. Specimens of patella were removed from each rabbit and all specimens were observed macroscopically and confirmed that the cartilage surface was smooth and glossy. Specimens were then prepared and sagittal sections were cut for histology and for the FTIR. The sections stained with safranin-O/fast green were observed using a light microscope and confirmed that no fibrillation or degenerative change had occurred. The sections for the FTIR were not stained. The integrated area of collagen Amide I (wave, 1590-1720 cm⁻¹) was defined as collagen content. The integrated area of proteoglycan sugar ring C-O absorbance (wave, 985-1140 cm⁻¹) normalized by Amide I area was defined as proteoglycan content. The superficial, middle, deep and whole zones of cartilage were defined as the area from surface to 100 μm depth, 100 μm to 400 μm, 400 μm to 600 μm and surface to 600 μm, respectively. Mean collagen content and mean proteoglycan content of each zone were calculated and compared.

Results: Collagen content in the superficial zone was the lowest in the 3-week animal and the highest in the 6-month animal (Fig. 1A). Collagen content in the middle, deep and whole zones was the lowest in the 3-week animal and the highest in the 2.5-year animal (Fig. 1A). Proteoglycan content in the superficial, middle and whole zones was the highest in the 6-month animal (Fig. 1B). Proteoglycan content in the deep zone was the highest in the 3-week animal (Fig. 1B). Proteoglycan content in the middle, deep and whole zones was the lowest in the 2.5-year animal (Fig. 1B).

Conclusions: The FTIR successfully detected the age-related behavior of collagen and proteoglycan in each zone of patellar cartilage. Because number of animals was limited, further study is needed.

Figure 1. Age-related behavior of collagen content (A) and proteoglycan content (B) in each zone of patellar cartilage.

Animal models

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ORAL TREATMENT WITH THE PLANT EXTRACT OF BRACHYSTEMMA CALYCINUM D. DON REDUCES THE DEVELOPMENT OF CARTILAGE LESIONS IN EXPERIMENTAL DOG OSTEOARTHRITIS: INHIBITION OF PROTEASE ACTIVATED RECEPTOR-2

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Purpose: There is an obvious need for safe and effective new agents that can stop the progression of osteoarthritis (OA). Botanical medicinal products or neutraceuticals used for the treatment of OA in general have been demonstrated to have better tolerability than classical drugs. J&L is a plant extract prepared from Brachystemma calycinum D. don, a plant classically used in Chinese medicine for the treatment of musculoskeletal diseases. The aim of this study was to evaluate the potential protective effect of J&L on the in vivo development of OA lesions in the experimental dog anterior cruciate ligament (ACL) transection model and to document its mechanism of action.

Methods: OA was induced by sectioning the ACL of the right knee in crossbred dogs. There were two treatment groups (n=6-7 dogs/group): placebo and J&L at a therapeutic dosage (200 mg/kg/day), given orally for the entire duration of the study (8 weeks). Macroscopic and histopathological evaluations of cartilage lesions on the femoral condyles and tibial plateaus were performed. Moreover, immunohistochemical analyses of cartilage assessing the levels of iNOS, MMP-13 and protease activated receptor (PAR)-2 were done.

Results: Treatment with J&L reduced the severity of cartilage OA lesions. More specifically it reduced the depth of cartilage lesions on the tibial plateaus with a significant effect on the femoral condyles (p≤0.04). J&L treatment significantly decreased (p<0.02) the histopathological score on both femoral condyles and tibial plateaus; the main effect was observed on structural changes and cellularity. J&L also significantly reduced the level of key inflammatory and catabolic factors, iNOS (p<0.009) and MMP-13 (p<0.003), as well as the level of PAR-2 (p<0.03).

Conclusions: This study demonstrates that the J&L can have a protective effect on the development of experimental OA articular (or joint) structural changes. This effect was associated