the EP4 receptor. To determine the effects of lamin A overexpression on chondrocytes, we transfected human chondrocyte cell lines (HTB94 and C28/I2) with wild-type or progerin-type lamin A protein. Transfected cells displayed markers of early apoptosis, including increased caspase-3 activity decreased cytoplasmic ATP levels loss of mitochondrial membrane potential (JC1 staining), and decreased bcl2 transcription when compared to mock plasmid transfected controls. Surprisingly, we did not detect markers of advanced apoptosis in the transfected cells (TUNEL by microscopy, DNA laddering, PI staining by FACS), suggesting that lamin A induces cellular injury that initiates but does not complete programmed cell death.

Conclusions: This study demonstrates that the progeria-associated protein lamin A is upregulated in OA chondrocytes, where it leads to cellular changes characteristic of early apoptosis. We suggest that nuclear accumulation of lamin A in response to catabolic stress may account for the premature aging phenotype and senescence of OA chondrocytes.

A29 ASSOCIATION OF A SINGLE NUCLEOTIDE POLYMORPHISM IN GDF5WITH CONGENITAL DYSPLASIA OF THE HIP

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Purpose: Congenital dysplasia of the hip (CDH) is an abnormality of the seating of the femoral head in the acetabulum, mainly caused by Shallow acetabulum and lax capsule. CHD is the most prevalent causative factor of secondary hip OA. Genetic factors are considered to play a considerable role in pathogenesis of CDH. GDF5 has been identified being involved in skeletal development and joint morphogenesis in humans and mice, playing a crucial role in the morphogenesis of tendons, ligaments and bones. Recently a functional single nucleotide polymorphism (SNP) (rs143383, T/C) in the 5'-UTR of the growth differentiate factor 5 (GDF5) gene was reported associated with osteoarthritis (OA) susceptibility. Function study showed that allele T of rs143383 mediates a significant reduction of promoter activity in GDF5 gene. As a key role in morphogenesis of skeletal components and soft tissues in and around joints, GDF5 may be involved in the pathogenesis of CDH. To investigate this association, a case-control study was conducted.

Methods: The GDF5 SNP rs143383 was genotyped in 338 children who suffered from CDH disease with radiographic confirmation and 622 control subjects using Taqman assay (7500 Real Time PCR System, Applied Biosystems).

Results: GDF5 was significantly associated with CDH ($P = 0.0037$; OR = 1.40; 95% CI = 1.11−1.75). Significant difference was detected in female samples when stratified by gender ($P = 0.0053$; OR = 1.46; 95% CI = 1.21−1.91), and when stratified by severity ($P = 0.0058$; OR = 1.43; 95% CI = 1.11−1.85).

Conclusions: Our results indicate that *GDF5* is important in the etiology of CDH. This was the first the definite instance that association of the CDH susceptibility was detected.

A30 VARIATION IN SHAPE OF THE PROXIMAL FEMUR WITH RESPECT TO FEMOROACETABULAR IMPINGEMENT AND OSTEOARTHRITIS IN A POPULATION OF RETIRED SOCCER PLAYERS AND CONTROLS

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Purpose: The etiology of Osteoarthritis (OA) is still unclear partly due to the many biomechanical and molecular factors associated with the development of OA. One of these biomechanical factors is the practice of sports among which soccer is considered one of the most harmful.

The high risk for OA among professional soccer players might be caused by a deformation of the femoral head called cam impingement, a type of femoroacetabular impingement. This deformity would occur during adolescence after a long period of excessive sports practice caused by a slipped capital femoral epiphysis. Cam impingement comprises a shortening of the collum femoris and a flattening of the concave surface of the lateral part of the femoral head. In cam impingement the femoral head impinges on the anterior acetabulum and thereby damages the labrum.

We investigated whether anatomical variations resembling cam impingement occur more often among active soccer players than in a general population and if these anatomical variations are associated with OA. The anatomical variations were quantified using a Statistical Shape Model of the proximal femur.

Methods: A Statistical Shape Model (SSM) was created of the shape of the proximal femur and acetabulum in anterior-posterior x-ray images of the hips. The method results in a set of independent modes that together quantitatively describe the total shape, while each mode separately describes a specific characteristic of the shape.

The SSM comprised 83 x-rays of retired soccer players and 51 x-rays of male controls that were taken from the GOAL cohort. GOAL consists of patients with complaints of the hip that were included on their first visit to the physician. The control group and the retired soccer players had similar age, weight and OA levels as measured by Kellgren & Lawrence scores.

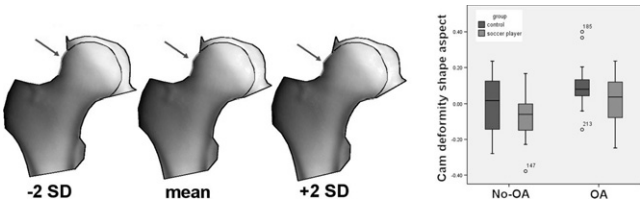
Regression analysis was used to test differences between the groups and the effect of OA (defined as K&L > 1) on each shape aspect.

Results: We did not find any striking differences between the general shape of retired soccer players and the control group.

Subjects with OA showed a significantly different shape of the hip than non-oa subjects, irrespective of group status (soccer player or control). This difference was described and quantified by three distinct and independent shape modes: At OA the femoral head was laterally extended (mode 1); the transition from the superior part of the neck into the head was more gradual (mode 2); and the joint space was narrower (mode 3).

Conclusions: One of the shape aspects (see figure) showed the lateral extension of the femur typical for a cam type deformity. Interestingly, this deformity was stronger in the subjects with OA, but similar between soccer players and controls (see figure). Thus, the relation between cam type impingement and OA does not seem to be specific for soccer players but might be general in all OA populations.

In general, all shape aspects that related to the transition from neck to head showed a relation with OA. Therefore, femoroacetabular impingement might indeed play a role in the development of OA, even if the deformity is mild as is the case for non-clinical cases.



Cam type deformity, quantified in a statistical shape model.

A31 STATISTICAL SHAPE MODELS SHOW DIFFERENCES IN BONE SHAPE BETWEEN PROGRESSORS AND NON-PROGRESSORS IN OAI PROGRESSION COHORT

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Purpose: To examine the difference in bone shape between non-progressors and progressors, as determined by radiographic OA.

Methods: Radiographic OA progression was judged using a decrease in the joint space width, measured at the central point of the medial joint. KneeAnalyzer software (Optasia Medical, Manchester, UK) was used to make semi-automated annotations of the radiographs. JSW was automatically calculated along a parameterized line bisecting the medial compartment, with its origin (x = 0) at the tip of the tibial spine and end (x = 1) at the outer medial edge of the joint. The central JSW (cJSW) was measured at x = 0.5 on this line. Calibration was made by automated location of Synaflexer beads within the image.

Subjects with K-L scores of 2 or 3; medial JSN greater than lateral JSN, and evidence of medial osteophytes were selected from the 12 months OAI progression groups 0.B.1 and 1.B.1. Those with a reduction in cJSW greater than 12% of baseline were classified as progressors (n = 15, 8 female). Subjects whose cJSW changed by 0±3% (n = 15, 7 female) were classified as non-progressors.

The bone shapes for each individual were determined by fitting a 3D statistical model of shape and intensity to the baseline image. Quality of the fitting was assessed visually and by comparison with manual markup.