SAT0560  
FROM A 2-YEAR MULTICENTRE CLINICAL TRIAL IN HIP SHAPE PREDICTS KNEE OSTEOARTHRITIS, A METABOLOMIC ANALYSIS REVEALS THAT OVER ACTIVATION OF THE CONVERSION PATHWAY OF PHOSPHATIDYLCHOLINE TO LYSOPHOSPHATIDYLCHOLINE IS ASSOCIATED WITH KNEE CARTILAGE VOLUME LOSS OVER TIME
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Background: While progression of osteoarthritis (OA) is variable, no tools yet exist to predict disease course.

Objectives: To identify, using a metabolomic approach, serum marker(s) for predicting knee cartilage volume loss over time measured by magnetic resonance imaging (MRI) in a 24 month Phase III clinical trial in patients with symptomatic knee OA.

Methods: 139 knee OA patients who completed the clinical trial according to protocol were selected from a 24 month DMOAD trial studying the effect of leflunomide versus naproxen. MRI was performed at baseline and 24 months. Targeted metabolomic profiling was performed on serum collected at baseline. Metabolite ratios as proxies for enzymatic reaction were calculated and used in the analysis. The levels of 186 metabolites were measured and 152 met the quality control criteria. A metabolome-wide significance level of α=2.3*10^-4 was determined for the metabolomic analysis. A total of 38 limbs from 19 mice were processed to perform histologic analyses: 8 limbs from both strains at 75 w compared with 25 w (p<0.001), confirming the ageing of the joint. When 75 w mice were selected (table 1), the BL6/37 strain showed a significantly increased score in whole joint (p=0.038), femoral condyles (p=0.021) and medial femoral condyle (p=0.015) than BL6/26 strain. Safranin-O-Fast-green ratio value at 75 w was higher in the medial compartment of BL6/26 compared with BL6/37 (both tibial plateau and femoral condyle); however, only the difference detected in the medial compartment of the tibial plateau reached the statistical significance (p<0.001), whilst the differences detected in the femoral condyle borderline the statistical significance (p=0.091).

Abstract SAT0561 – Table 1. Mankin score grading of cartilage destruction in osteoarthritis mice BL6/26 and BL6/37 at 75 w

<table>
<thead>
<tr>
<th></th>
<th>BL6/26</th>
<th>BL6/37</th>
<th>Med. femoral</th>
<th>Lat. femoral</th>
<th>Med. tibial</th>
<th>Lat. tibial</th>
<th>Whole joint</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL75 w</td>
<td>8.50 ± 4.00</td>
<td>5.25 ± 3.20</td>
<td>6.78 ± 7.22</td>
<td>6.78 ± 7.22</td>
<td>6.78 ± 7.22</td>
<td>6.78 ± 7.22</td>
<td>5.25 ± 3.20</td>
</tr>
<tr>
<td>BL25 w</td>
<td>8.50 ± 4.00</td>
<td>5.25 ± 3.20</td>
<td>6.78 ± 7.22</td>
<td>6.78 ± 7.22</td>
<td>6.78 ± 7.22</td>
<td>6.78 ± 7.22</td>
<td>5.25 ± 3.20</td>
</tr>
</tbody>
</table>

Conclusions: This study demonstrates the functional impact of mtDNA variation in the process of joint deterioration associated to ageing, leading to consider the mtDNA as a potential therapeutic target in osteoarthritis associated to ageing.

REFERENCES:

Disclosure of Interest: None declared

SAT0562  
HIP SHAPE PREDICTS KNEE OSTEOARTHRITIS OUTCOMES OVER A DECade IN OLDER-ADULTS
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Background: Various hip shapes may be important as a risk factor for development and progression of knee osteoarthritis, due to the biomechanical link between the two joints.

Objectives: This study aims to identify the relationship between hip morphology and structural and clinical osteoarthritis outcomes in the knee over 10.7 years, in older-adults.

Methods: 377 community-dwelling older-adults aged 50–80 years were studied. At baseline, dual-energy X-ray absorptiometry images of the left hip were obtained and hip shapes were described using mode scores from an 85-point statistical shape model. MRI scans were conducted at baseline and a mean follow-up of 10.7 (SD:0.67) years later, to assess right knee tibial cartilage volume and bone-marrow lesions (BMLs). Knee pain was assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Knee replacement (KR) data were obtained by data linkage to the Australian Orthopaedic Association National Joint Replacement Registry. Linear mixed-effects, log-binomal models

Disclosure of Interest: None declared

SAT0561  
MITOCHONDRIAL BACKGROUND INFLUENCES THE JOINT EVOLUTION IN A CONPLASTIC MOUSE MODEL OF AGING
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Background: Several studies showed interesting associations between mtDNA haplogroups and different OA-related features, including prevalence, incidence or progression of the disease.1,2,3 The use of conplastic animals-individuals with the same nuclear genome but different mtDNA variants-provides an accurate tool to study the influence of the mitochondrial background in the ageing process.2,3

Objectives: To study the influence of mtDNA variation in the degree of joint deterioration of the knees of aged animals using a conplastic mouse model of ageing

Methods: mtDNAs from C57BL/6 and NZB/OLA/Hsd mice were used. These mtDNAs differ by 12 missense mutations, 4 tRNAs mutations and 5 rRNAs-coding region mutations. Then, a conplastic mice strain was developed with the C57BL/6 nuclear genome and the NZB/Ola/Hsd mtDNA (BL6/26-37) to compare with the original C57BL6 strain (BL6/26) in animals of 25 and 75 weeks. A total of 38 limbs from 19 mice were processed to perform histologic analyses: 8 BL6/26-37 w, 10 BL6/26-26 w, 5 BL6/26-25 w and 10 BL6/26-25 w.

Results: Mankin score data showed significantly increased values in all knees from both strains at 75 w compared with 25 w (p<0.001), confirming the ageing of the joint. When 75 w mice were selected (table 1), the BL6/26-37 strain showed a significantly increased score in whole joint (p=0.038), femoral condyles (p=0.021) and medial femoral condyle (p=0.015) than BL6/26 strain. Safranin-O-Fast-green ratio value at 75 w was higher in the medial compartment of BL6/26 compared with BL6/26-37 (both tibial plateau and femoral condyle); however, only the differences detected in the medial compartment of the tibial plateau reached the statistical significance (p<0.001), whilst the differences detected in the femoral condyle borderline the statistical significance (p=0.091).

The width of the epiphyseal plate was analysed in both tibia and femur bones. The results showed significantly decreased values in BL6/26-25 w compared with the same strain at 25 w in tibial plateau (p=0.001) and femoral condyle (p=0.049); however, these differences were not observed in animals belonging to BL6/26-25 strain. In addition, the BL6/26-37 should also significantly lowered values in tibial plateau than BL6/26-37 strain at the same age (p=0.032)

Disclosure of Interest: None declared