portions of deep hip and thigh musculature may experience an adaptive compensation in patients with chronic knee osteoarthritis.

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424 DIETARY FATTY ACIDS DIFFERENTIALLY AFFECT THE DEVELOPMENT OF INJURY-INDUCED OSTEOARTHRITIS WITH DIET-INDUCED OBESITY IN MICE


Purpose: Obesity and joint injury are major risk factors for osteoarthritis (OA) that potentially involve alterations in the biomechanical and inflammatory environments of the joint. Recent studies have shown that high-fat diet-induced obesity increases the severity of post-traumatic arthritis; however, the link between OA and biochemical factors, such as dietary fatty acids, remains largely unknown. We hypothesized that diets supplemented with pro-inflammatory fatty acids, such as saturated fatty acids (SFA) and ω-6 polyunsaturated fatty acid (PUFA), would accelerate injury-induced OA, while anti-inflammatory fatty acids such as ω-3 PUFA would mitigate joint degeneration.

Methods: From 4 to 28 weeks of age, male C57BL/6j mice were fed a control low-fat diet (10% kcal fat) or one of the three high fat diets (60% kcal fat): SFA-rich, ω-6 rich, or ω-3 rich diet. At 16 weeks of age, mice underwent surgery for destabilization of the medial meniscus (DMM) to induce knee OA in the left hind limb. Serum biomarkers and behavioral measurements were evaluated at various time points. Upon euthanasia, synovial fluid and knee joints were harvested. MicroCT and histological scores averaged from three independent, blinded graders were used to quantify the extent of bone changes, OA severity, and synovitis. Bivariable and multivariable analyses were performed to evaluate the associations among diets, weight gain and OA severity.

Results: At the time of euthanasia, mice fed ω-6 and SFA diets were significantly heavier than the mice fed control and ω-3 diets. MicroCT analysis revealed that mice fed ω-6 and SFA diets had increased heterotopic bone formation in the operated joint as compared to the mice fed control and ω-3 diets (Fig 1). The ω-6 and SFA diets significantly increased OA severity (Fig 2) and synovitis (Fig 3), but they did not influence spontaneous locomotion of the mice. Multivariable linear regression showed that OA severity was significantly associated with diet, but not weight gain.

Figure 1. Representative microCT 3D reconstructions of mouse limbs at 28 weeks: (A) non-operated (right) hind limb from SFA mice (F – femur, T – tibia, P – patella; black arrows indicate partially calcified menisci) (B) Operated (left) joints of ω-6 and SFA mice had increased heterotopic bone formation in the joint space (white arrows), as compared to the operated joints of Control and ω-3 mice. Scale bar is 1 mm.
Figure 2. Assessment of OA severity. (A) Representative joint histology of the medial tibiofemoral contact region in left (DMM surgery) hind limbs (F = femur, M = meniscus, T = tibia). Severe cartilage cleft and loss were found in the joints of ω6 and SFA mice. Scale bar is 500 μm. (B) Modified Mankin scores representative of OA severity. Data was analyzed by two-factor (diet and surgery) repeated measures ANOVA. Both factors and their interaction were significant (p < 0.01). Tukey’s HSD post-hoc test on diet showed that the joints from ω3 diet had significantly lower score compared to the joints from ω6 and SFA diet (p < 0.05). All operated limbs had significantly higher score than their corresponding control non-operated (right) joints (p < 0.01) and the operated joints of ω6 and SFA mice also had worse OA as compared to the operated joints of Control and ω3 mice (* p < 0.05). n ≥ 11 mice per diet group. Data shown as mean ± standard error.

Figure 3. Assessment of joint synovitis. (A) Representative joint histology of the medial femoral condyle of left (DMM surgery) hind limbs (F = femur, M = meniscus, T = tibia, S = synovium). Thickened synovium from ω6 and SFA diet with a high number of infiltrated cells was observed (indicated by black arrows). Scale bar is 500 μm. (B) Total joint synovitis scores are representative of the degree of synovial inflammation. Data was analyzed by two-factor (diet and surgery) repeated measures ANOVA. Both factors but not their interaction were significant (p < 0.01). Tukey’s HSD post-hoc test on diet showed that the joints from ω3 diet had significantly lower synovial inflammation compared to the joints from SFA and ω6 diet (* p < 0.05). n ≥ 11 mice per diet group. Data shown as mean ± standard error.

Conclusions: Our results indicate that dietary fatty acids differentially influence the risk for development of OA following joint injury, with ω6 and SFA diets significantly increasing OA severity following DMM. Despite the fact that mice fed pro-inflammatory high-fat diets showed worse OA, they had similar locomotor activity levels as the control mice, indicating that changes in voluntary exercise did not significantly contribute to OA in obese mice. The significant association between the different diets and OA severity further suggests a role of fatty acids and their lipid mediators in OA development and OA-related joint inflammation.

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SECRETED 14-3-3ε: DISCOVERY BY PROTEOMICS OF A NOVEL BIOMARKER AND/OR THERAPEUTICAL TARGET IN OSTEOARTHRITIS
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Purpose: Several experiments suggest that subchondral bone remodeling triggered by overload could initiate and/or contribute to cartilage loss in osteoarthritis (OA) through a bone/cartilage interplay. In order to find novel biomarkers and/or therapeutic targets, we used a secretomic approach in a novel and unique bone/cartilage communication model.

Methods: Murine experiments: Thanks to a three dimensional (3D) culture model, murine osteoblasts were submitted to compression in