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SAT0541 INHIBITING αVβ3 INTEGRIN AND CD47 SIGNALING AMELIORATES THE PROGRESSION OF OSTEOARTHRITIS

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Background: Osteoarthritis is leading cause of disability, and its prevalence is rising due to the aging population and obesity epidemic[1]. Despite the substantial morbidity and health costs attributed to osteoarthritis, no treatment has been approved to prevent or slow disease progression, largely because the underlying pathogenic mechanism remains elusive. Both integrin αVβ3 and the integrin-associated receptor CD47 are considered important therapeutic targets for a number of diseases, but the potential involvement of these receptors in osteoarthritis remains unclear[2].
Objectives: Our study aimed at assessing the role of integrin αVβ3 and the integrin-associated receptor CD47 signaling pathways in the pathogenesis of osteoarthritis, and identifying potential targets for disease-modifying therapy.
Methods: We performed transcriptomic and proteomic analyses of human and murine osteoarthritic tissues to examine the involvement of integrin αVβ3 and CD47 with osteoarthritis. Further, we evaluated the effects of genetic deficiency in and pharmacological modulations of integrin αVβ3 subunits, CD47, and their downstream signaling molecules Fyn and FAK on the destabilization of the medial meniscus (DMM) mouse model. Additionally, we used microPET/CT imaging of the DMM mouse model to assess the ligand-binding capacities of integrin αVβ3 and CD47 in osteoarthritic joints. Finally, we carried out multiple *in vitro* assays to determine how integrin αVβ3 and CD47 signaling might become activated in osteoarthritis, and what the molecular consequences of such activation might be.
Results: Our transcriptomic and proteomic analyses revealed the involvement of dysregulated integrin αVβ3 and CD47 signaling in osteoarthritis. Data from investigations of genetically deficient mice and pharmacological modulations showed that αVβ3, CD47, Fyn, and FAK are crucial to the pathogenesis of arthritis. We detected elevated ligand-binding capacities of integrin αVβ3 and CD47 in osteoarthritic joints by microPET/CT imaging of mice subjected to DMM. Our *in vitro* studies demonstrated that chondrocyte breakdown products, derived from the articular cartilage of individuals with osteoarthritis, induced αVβ3/CD47-dependent expression of inflammatory and degradative mediators, and revealed that the signaling network involved the Ras-CRAF-MEK-ERK pathways.
Conclusions: Our findings identify a central role of deregulated αVβ3 and CD47 signaling in the pathogenesis of osteoarthritis, and provide a rationale for targeting these signaling pathways as a disease-modifying therapy.
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SAT0542 SUBCLINICAL CRYSTAL ARTHROPATHY MIGHT INFLUENCE FUNCTIONAL DISABILITY IN PATIENTS WITH KNEE OSTEOARTHRITIS? AN EGYPTIAN CROSS SECTIONAL STUDY

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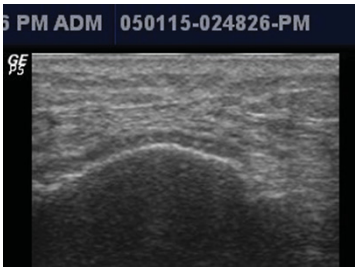
Background: Osteoarthritis is a complex slowly progressive degenerative disease that affects joint components.Concomittant articular crystal deposits are able to stimulate an inflammatory response in OA through stimulation of the innate immune system.
Objectives: Assess the contribution of sonographically detected crystal deposits to pain severity and functional disability in patients with knee OA (WOMAC score)
Methods: Single-center cross sectional study. Adult patients diagnosed with knee OA diagnosed in accordance with ACR criteria from the Department of Rheumatology and Rehabilitation, Kasr Alainy School of Medicine, Cairo University were recruited. Clinical assessment of pain and functional status in patients with knee osteoarthritis was measured using: Western Ontario and McMaster Universities Arthritis Index score. The Logic p5 ultrasound machine (GE) with linear array probe (8–13 MHz). Examination of the articular and periarticular structures was performed by a trained rheumatologist according to the standard EULAR guidelines for exam of the knee. Serum uric acid was investigated. Plain radiography was done for comparison.
Results: 53 patients (44 females 83% & 9 males 17%) were included, mean age 53.5 years ± 8.3 SD, disease duration 42.5 months ± 49.5 SD, body mass index mean 34.9±6.3 SD. Crystal deposits were sono-graphically diagnosed in 73 knees (68.9%), Monosodium urate deposits found in 33 knees (31.1%) and Calcium Pyrophosphate Dihydrate deposits were diagnosed in 67 knees (63.2%). Pain, stiffness and disability scores were significantly higher in OA knees with crystal deposition as compared to those without ($p<0.05$) that was in fact resistant to conventional analgesics, chondro-protectives and physiotherapy demanding the ongoing use of NSAIDs.

Table 1. WOMAC pain, stiffness and disability scores in the studied Patients with knee OA showing sonographic evidences of CDDs versus those without

WOMAC score	OA with CDDs (Mean ± SD)	OA without CDD (Mean ± SD)	Mann-Whitney U- test r	P-value (significance)
WOMAC pain score	15. 6±3.6 (8–20)	12.0 ±3.8 (5–20)	596	0.00*
WOMAC stiffness score	5. 5 ±2.0 (0–8)	3.8 ±1.8 (0–8)	643	0.00*
WOMAC disability score	53.4 ±11.6 (25–67)	41.5±12.8 (14–67)	606	0.00*

WOMAC = Western Ontario and McMaster Universities Arthritis Index score. *Significant difference ($p\leq0.05$).



Conclusions: Crystal deposition was associated with significantly increased pain intensity, knee joint stiffness and functional disability as measured by WOMAC in patients with knee OA.
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SAT0543 CLINICAL PREDICTORS AND RADIOGRAPHIC EVIDENCES OF OCCULT CRYSTAL DEPOSITION DISEASE WITH KNEE OSTEOARTHRITIS

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Background: Osteoarthritis is a slowly progressive degenerative disorder that affects joint components from cartilage to meniscus, subchondral bones and might even lead to synovial inflammation.
Objectives: To investigate the clinical and radiographic findings associated with asymptomatic crystal deposition disease in patients with knee osteoarthritis.
Methods: A single-center cross sectional study, sixty adult patients with knee OA diagnosed according to the ACR criteria were enrolled. Participants were all subjected to history taking, general as well as musculoskeletal clinical examination, serum uric acid, and plain radiography. Examination of the knee joints for intraarticular/periarticular crystal deposits was done using a Logic p5 ultrasound machine (GE) with linear array probe (8–13 MHz) according to the standard EULAR guidelines.
Results: A total of sixty adult patients were enrolled, fifty three patients satisfied the inclusion criteria, 44 females (83%) & 9 males (17%), mean values for; ages