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SAT0541 INHIBITING α V β 3 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 epidemic¹. 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 α V β 3 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 unclear².

Objectives: Our study aimed at assessing the role of integrin α V β 3 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 α V β 3 and CD47 with osteoarthritis. Further, we evaluated the effects of genetic deficiency in and pharmacological modulations of integrin α V β 3 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 α V β 3 and CD47 in osteoarthritic joints. Finally, we carried out multiple *in vitro* assays to determine how integrin α V β 3 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 α V β 3 and CD47 signaling in osteoarthritis. Data from investigations of genetically deficient mice and pharmacological modulations showed that α V β 3, CD47, Fyn, and FAK are crucial to the pathogenesis of arthritis. We detected elevated ligand-binding capacities of integrin α V β 3 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 α V β 3/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 α V β 3 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. Concomitant 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 periarthritic 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 $\pm$ 8.3 SD, disease duration 42.5 months $\pm$ 49.5 SD, body mass index mean 34.9 $\pm$ 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 $\pm$ SD)	OA without CDD (Mean $\pm$ SD)	Mann-Whitney U- test r	P-value (significance)
WOMAC pain score	15.6 $\pm$ 3.6 (8–20)	12.0 $\pm$ 3.8 (5–20)	596	0.00*
WOMAC stiffness score	5.5 $\pm$ 2.0 (0–8)	3.8 $\pm$ 1.8 (0–8)	643	0.00*
WOMAC disability score	53.4 $\pm$ 11.6 (25–67)	41.5 $\pm$ 12.8 (14–67)	606	0.00*

WOMAC = Western Ontario and McMaster Universities Arthritis Index score. *Significant difference ($p \leq 0.05$).

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

Abstract SAT0543 – Table 1. Odds ratio and Forest plot analysis

Risk factors	Knees with sonographic crystals (Total: 73 knees) r	Knees without sonographic crystals (Total: 33 knees)	Odds ratio	95% CI	p value (significance)
Male Gender	15	3	2.6	0.7 to 9.6	0.16
Female Gender	58	30	0.4	0.1 to 1.4	0.16
Dyslipidemia	38	16	1.2	0.5 to 2.6	0.73
Chronic medical illness as Diabetes mellitus and hypertension	20	10	0.9	0.4 to 2.1	0.76
Clinically detected knee effusion	7	2	1.6	0.3 to 8.4	0.55
Limitation in ROM	36	10	2.2	0.9 to 5.4	0.07
Bursitis by sonography	35	6	4.1	1.5 to 11.2	0.01*
Effusion by sonography	47	12	3.2	1.3 to 7.4	0.01*
Total (fixed effects)	430/1022	156/462	1.9	1.4 to 2.6	0.23
Total (random effects)	430/1022	156/462	1.9	1.3 to 2.8	

53.5 years $\pm$ 8.3 SD, disease duration 42.5 months $\pm$ 49.5 SD. Crystal deposits were sono-graphically diagnosed in 73 knees with normal serum uric acid values (68.9% > MSU in 31.1%, CPPD in 63.2%, a picture of mixed deposits in 5.7%). Plain radiography revealed chondrocalcinosis in 3 patients only. Regression analysis models and Forest Plot test revealed a 4.1 fold incidence of crystal deposition in patients with sonographic bursitis than those without (OR=4.13, CI=1.5–11.2, $p=0.01$) and a 3.2 fold incidence of crystal deposition in patients with sonographic effusion than those without (OR=3.16, CI=1.34–7.44, $p=0.01$).

Conclusions: The study concluded a number of clinical as well as radiographic associates that might be considered as predictors of silent CDD in patients with knee OA as diagnosed by ultrasonography, the most commonly reported clinical associates were bursitis and effusion.

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SAT0544 SUBGROUPS IN RADIOGRAPHIC FEATURES IN PATIENTS WITH HIP OSTEOARTHRITIS: RESULTS OF THE AMS-OA COHORT

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Background: Radiographic features are important in diagnosing hip osteoarthritis (OA)^{1,2}. In daily practice, only the anterior-posterior view is visualized but not the false profile view. Since we assessed radiographic features in both types of radiographic hip images in the AMS-OA cohort, we were able to examine the differences in radiographic features in two regions of the hip (superior-lateral and central-axial region).

Objectives: (i) To describe the presence of radiographic features in patients with hip OA; and (ii) to determine whether radiographic features differ between the superior-lateral and central-axial region of the hip.

Methods: Data from 97 patients with bilateral hip pain and a Kellgren and Lawrence score of ≥ 1 of the Amsterdam Osteoarthritis (AMS-OA) cohort of patients with knee and/or hip OA were used. Standard radiographic images were examined of patients in an erect position, both with an anterior posterior view and with a false profile view, which is an oblique lateral view of the hip. Radiographic images were scored by an experienced radiologist (DR) and an independent researcher (ME). Consensus between two raters was achieved for each score. Four radiographic features were scored: presence of joint space narrowing, osteophytes, sclerosis and cysts. All joint features were scored separately for the superior-lateral and the central-axial region of the hip. A Fisher's exact test was performed for testing the significance of the differences between the two regions of the hip.

Results: Table 1 shows the frequencies of radiographic features (joint space narrowing, osteophytes, sclerosis and cysts) in the superior-lateral and the central-axial region of the left and right hip joint of patients with hip OA. Significant differences between the two regions were found for osteophytes, sclerosis and cysts with the highest frequency of these features in the superior-lateral region of the hip.

Conclusions: In our cohort we found as expected, that joint space narrowing of the hips was the most frequent feature (>80% in both the superior-lateral and central-axial region). Moreover, osteophytes, sclerosis and cysts were more frequently present in the superior-lateral region. Our findings indicate that hip OA may exist of two subgroups with differences in radiographic features (i.e., superior-lateral and central-axial). Future research should confirm these results

Radiographic feature	Superior Lateral part				Central Axial part				Fisher's exact test	
	Left		Right		Left		Right		Left	Right
	N	%	N	%	N	%	N	%	P-value	P-value
JSN	77	79.4	78	80.4	81	84.4	83	85.6	NS	NS
Osteophytes	68	70.1	65	67.0	49	51.0	45	46.9	0.014*	0.003*
Sclerosis	43	44.8	44	45.8	15	15.6	11	11.5	0.023*	0.021*
Cysts	28	29.2	30	31.3	3	3.1	2	2.1	<0.001**	<0.001**

TABLE 1: presence of radiographic features in patients with bilateral hip pain. (* $p<0.05$) (** $p<0.001$)

and focus on possible associations with biomechanical and physical function variables.

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SAT0545 PREDICTIVE FACTORS FOR RESPONSE TO ULTRASOUND-GUIDED INTRA-ARTICULAR GLUCOCORTICOIDS IN KNEE OSTEOARTHRITIS

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Objectives: To investigate predictive factors for good outcome of ultrasound intra-articular glucocorticoids in knee osteoarthritis (OA).

Methods: We conducted a prospective monocenter cohort study including 116 patients with knee OA, after failure to standard treatments, with pain >4 (numerical rating scale NRS 0–10). Patients received an ultrasound-guided injection of 40 mg triamcinolone acetonide in their most painful knee. We exhaustively collected demographic and clinical data at inclusion, as well as lab, radiographs and ultrasound parameters of the included knees. WOMAC score was calculated at inclusion and after 4 weeks. Responders were defined as patients with at least 40% improvement of their WOMAC score. Univariate analysis was performed in order to select possible predictive factors, and stepwise multiple logistic regression analyses were conducted to identify predictors of response.

Results: Among the 116 patients, 101 were females. Median age was 64 years (40–85) and mean duration of the disease was 14.1 $\pm$ 14.8 years. Mean BMI was 29.9 $\pm$ 3.8 Kg/m². Mean NRS of pain was 8.4 $\pm$ 1.2 and mean WOMAC was 73.3 $\pm$ 11.8 at inclusion. 70.0% of the knees were grade 3 or 4 of Kellgren-Lawrence. 98% of knees expressed ultrasound synovial effusion and/or hypertrophy at inclusion. After 4 weeks, 61.2% of patients were responders. Regression analysis showed that patients with a BMI <30 Kg/m² (OR=0.38, 95% CI 0.16–0.89) and an ESR <20 mm (OR=0.27, 95% CI 0.08–0.90) were more likely to respond to ultrasound-guided glucocorticoids injection. Having both predictive factors of good response increases the response rate to 73.5%, whereas having no predictive factor decreases the response rate to 25.0%.

Conclusions: Our study is the largest study evaluating predictive factors of response for intra-articular glucocorticoids injections in knee OA. Also, it is the first study of predictive factors for ultrasound-guided injections. Patients with high BMIs and high ESR seem less likely to respond to intra-articular injections.

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