Results: Altogether, 129 patients (12 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2017. Out of these patients, 72 had erosive disease. The disease duration ($p<0.01$) was significantly higher in patients with erosive compared with non-erosive disease. Pain ($p<0.05$) and the number of clinically swollen joints ($p<0.05$) were significantly higher in patients with erosive compared with non-erosive disease at baseline. There were significant progression of pain ($p<0.05$) and the number of clinically swollen joints ($p<0.01$) at the two years follow up. The progression in clinically swollen joint count was about 21% higher in patients with erosive disease.

According to the AUCAN, patients with erosive compared with non-erosive disease had more pain ($p<0.05$) and stiffness ($p<0.01$) at baseline. Pain and stiffness, but not function, got worse ($p<0.01$) in patients with erosive compared with non-erosive disease at the two years follow up.

US-detected pathologies such as gray-scale synovitis total score ($p<0.001$), intensity of PDS ($p<0.01$) and number of osteophytes ($p<0.01$) were significantly higher in patients with erosive compared with non-erosive disease at baseline. There were improvements in gray-scale synovitis total score and intensity of PDS in patients with non-erosive disease while patients with erosive disease worsened at the two years follow up. On the other hand, the progression of US-determined osteophyte formation was observed in both groups.

Conclusions: The findings of this study show that pain and number of clinically swollen joints associated with US-detected synovial hypertrophy inflammatory signs and osteophyte formation is more severe in patients with erosive HOA than in patients with non-erosive disease. In addition, osteophyte formation is more likely to progress independent of synovial inflammation.

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SAT0539 DIFFERENTIAL PROFILE OF ENDOGENOUS PEPTIDES DETECTED BY TARGETED PROTEOMICS IN HIP AND KNEE CARTILAGE SECRETOMES FROM OSTEOARTHRITIS PATIENTS

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Background: Peptidomics can be defined as the comprehensive, qualitative and quantitative study of all native peptides in a sample in a defined space at a defined time under defined biological conditions. LC-MS/MS targeted proteomics have been used to identify and quantify candidate molecular biomarkers in diverse range of samples, including cells, tissues, serum/plasma, and other types of body fluids.

Objectives: In the present work, we have developed a targeted method to detect a panel of endogenous peptides that were identified as released from human healthy (N) and/or osteoarthritic (OA) hip and knee cartilage. Secretomes were obtained separately from the wounded (WZ) and unwounded (UZ) zones of OA cartilage. The enrichment of endogenous peptides was achieved by ultrafiltration and solid phase extraction (SPE). After peptide extraction, the different peptide profiles of these secretomes were relative quantified by target proteomics.

Methods: Proteins secreted from human articular cartilage (secretomes) were obtained by culture of tissue explants [1]. The enrichment of endogenous peptides was standardized using ultrafiltration procedures and solid phase extraction with reversed phase (C18) resins. A method for the targeted identification and relative quantitation of endogenous peptides by Multiple Reaction Monitoring (MRM)-mass spectrometry was developed employing cartilage secretome samples, and then applied on synovial fluid and serum. The peptides were separated by nano-LC coupled to a 5500 QTRAP mass spectrometer using stable isotope-labeled (SI) peptides as an internal control. Peptide identifications were searched using the ProteinPilot program. Data analysis was performed using the Skyline software.

Results: 23 endogenous peptides belonging to 9 proteins related with OA, as Cartilage Oligomeric Matrix Protein (COMP), Cartilage Intermediate Layer Protein (CILP), Prolargin (PRELP), Dermcidin (DCD), Fibronectin (FNC) and Glia Derived Nexin (GDN) among others, were differentially detected and relatively quantified in the cartilage secretomes. Some of the endogenous peptides belonging to COMP, FNC and GDN were found with a significant high release in the UZ of hip cartilage, however in knee cartilage the release is higher in the WZ. On the other hand, certain peptides belonging to proteins like CILP or PRELP were found to be mostly increased in the UZ of both hip and knee OA cartilages when compared to healthy tissue.

Conclusions: A panel of endogenous peptides has been identified in articular cartilage, which are differentially released between OA and healthy patients, as well as between knee and hip OA patients. These endogenous peptides may be potential biomarkers to differentiate osteoarthritis from hip and knee. Our targeted proteomics approach would be widely applicable to quantify low abundant peptides of interest in complex biological samples as synovial fluid and serum in order to unravel their putative biomarker value for osteoarthritis.

References:

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SAT0540 THE REDUCTION IN ADRENERGIC AND INFLAMMATORY SERUM MARKERS IN OSTEOARTHRITIS PATIENTS AFTER TREATMENT WITH CHONDROITIN SULFATE/GLUCOSAMINE HYDROCHLORIDE AND CELECOXIB IS DIFFERENT ACCORDING TO THE PRESENCE OF BACTERIAL DNA IN BLOOD

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Background: Inflammation in osteoarthritis (OA) has been characterized by infiltration of immune cells and secretion of cytokines into synovial tissues. Synovial macrophages production of IL-1 β and TNF- α is increased in response to lipopolysaccharide (LPS) suggesting a potential role of pathogen-associated molecular patterns (PAMPs) in OA development and/or evolution. Adrenergic activity have been associated with subchondral bone loss and increased osteoclast activity. Also, adrenergic activity is a main modulator of immune response to PAMPs in different settings. However, the relationship between activation of adrenergic and immune system with OA progression and treatment response remains still unknown.

Objectives: To assess the adrenergic and immune activation in OA patients according to the presence of bacterial DNA (bDNA) fragments in blood before and after Chondroitin Sulfate/Glucosamine Hydrochloride (CS/GH) or Celecoxib (CE) treatment.

Methods: Serum samples from patients participants in a 6-month controlled, double blind and randomized clinical trial comparing the analgesic efficacy of CS/GH and CE were analyzed to determine cytokines (IL-2, IL-4, IL-6, IL-10, IL-8, IL-1 β), catecholamines (noradrenaline, adrenaline and dopamine) and the presence of endotoxin or LPS and bDNA. Results are shown as mean $\pm$ sd or median with ranges (Q25-Q75).

Results: Samples from 100 OA patients (age: 62 $\pm$ 8yr.; BMI: 31 $\pm$ 6kg/m² 86 females; VAS: 73 $\pm$ 15; WOMAC: 369 $\pm$ 43) treated with CS/GH (50) or CE (50) were analyzed. There were no baseline significant differences between the two treatment groups regarding demographics, clinical and experimental variables. Thirty-four patients (17-CS/GH and 17-CE) showing bDNA in blood had significantly higher levels of noradrenaline compared with patients without bDNA (1993 [1354–3183] vs. 1324 [738–1899]; $p=0.0002$). After 6 months, both groups of treatment showed a similar reduction in VAS and WOMAC score (pain assessment) and serum adrenaline levels independent of presence or absence of bDNA (Table 1). Thirty-three patients showed bDNA presence at the end of the study (23 negative and 10 positive at baseline). Patients with bDNA at 6 months after treatment showed reduced serum noradrenaline levels compared with those observed in patients with bDNA at baseline (1993 [1354–3183] vs. 1561 [1174–2193]; $p=0.0325$). IL-8 was significantly reduced after 6 months of treatment only in patients without bDNA. There were no significant differences between baseline and 6 months samples in the other experimental variables.

Table 1

	Baseline				6 months			
	No bDNA		bDNA		No bDNA		bDNA	
	CS/GH	CE	CS/GH	CE	CS/GH	CE	CS/GH	CE
Adrenaline (pg/mL)	98 (88-127)	100 (77-118)	92 (78-114)	98 (75-115)	78* (65-92)	81* (62-92)	76* (58-97)	77* (66-105)
Noradrenaline (pg/mL)	1357 (790-1693)	1228 (738-1967)	1723# (1385-2381)	2765# (1232-3250)	1050 (811-1600)	1588 (882-2133)	1563 (1209-2180)	1528 (1174-2229)
IL-8 (pg/mL)	5.5 (1.3-9.4)	5.6 (1.7-14)	4.8 (3.9-5.7)	11 (1.9-15)	3.3* (0.0-11)	0.0* (0.0-5.9)	6.1 (3.7-14)	5.6 (1.5-16)
VAS score (0-100)	72 (66-82)	75 (65-81)	79 (67-90)	76 (70-80)	32* (22-45)	20* (10-60)	37* (27-50)	52* (24-60)
WOMAC score	364 (341-389)	354 (321-389)	382 (372-407)	360 (340-400)	150* (87-217)	135* (64-238)	180* (84-218)	282* (139-318)

* $p<0.05$ vs baseline values (Mann-Whitney-Wilcoxon Test, # $p<0.05$ vs No bDNA values

Conclusions: OA patients show bDNA fragments in blood associated to higher serum noradrenaline levels. Six month treatment with CS/GH or CE reduces significantly and in a similar fashion the pain intensity and adrenaline levels. IL-8 levels were reduced with the treatment except in patients with presence of bDNA fragments in blood. Systemic adrenergic and inflammatory activity in OA patients is influenced by the presence of PAMPs as bDNA in blood and this may be a factor to take into consideration to evaluate the severity, evolution and response to treatments.