Table 1. ***Multivariate logistic regression model: factors associated with response to treatment (CD + intensive rehabilitation)***

	Univariate analyses		Multivariate analyses	
	Crude HR 95% CI	**p**	**Adjusted HR 95% CI**	**p**
Age	1.07 [0.99-1.15]	0.06	1.04 [0.99-1.11]	0.14
Male gender	0.31 [0.09-1.05]	0.06	0.94 [0.37-2.35]	0.89
Currently working	1.31 [0.49-3.48]	0.60	1.62 [0.82-3.65]	0.24
Initial traumatism	0.51 [0.15-1.72]	0.28	0.86 [0.33-2.23]	0.75
Disease duration < 9 months	**3.85 [1.35-11.10]**	**0.01**	**2.27 [1.00-5.26]**	**0.05**
DASH score at baseline	**0.95 [0.92-0.98]**	**0.01**	**0.96 [0.93-0.98]**	**0.03**
NAS maximal pain in daily activities at baseline	0.98 [0.81-1.18]	0.81	0.96 [0.82-1.12]	0.63
MRI thickness of rotator interval (mm)	**1.80 [1.02-3.17]**	**0.04**	**1.65 1.04-2.62]**	**0.04**

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Disclosure of Interests: None Declared.
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AB1394

INTRADISCAL CUTIBACTERIUM ACNES DECIDE ON INNATE AND ADAPTIVE IMMUNE PATHWAYS IN MODIC TYPE 1 CHANGES

Keywords: Adaptive immunity, Innate immunity, -omics

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Background: Modic type 1 changes (MC1) are painful vertebral bone marrow (BM) edema of unclear etiology. Besides mechanical aspects, animal studies show the plausibility for two biological etiologies. In the bacterial etiology, *Cutibacterium acnes* (*C. acnes*) invades damaged intervertebral discs (IVDs) resulting in IVD infection and endplate damage. IVD-derived pro-inflammatory cytokines and virulence factors can consequently drain into the adjacent BM and induce an inflammatory response. In the autoimmune etiology, IVD and endplate damage expose immune privileged IVD cells and matrix to BM leukocytes, which react with an autoimmune response.
Objectives: To show that intradiscal *C. acnes* load is decisive for the pathomechnisms in MC1 bone marrow.
Methods: In a first study population, degenerated IVDs adjacent to a MC1 and not adjacent to a MC1 lesion were collected and *C. acnes* copy numbers/gram tissue (CCN) were quantified. The upper 99 % confidence interval (CI) limit in the control group was defined as threshold that distinguishes the two etiologies. From a second study population of MC1 patients, a MC1 and an intra-patient control BM aspirate, and the MC1 adjacent IVD was obtained from each patient. IVD CCN were determined, the etiology was assigned, and bulk RNA sequencing from total BM cells was performed. MC1 gene expression was normalized to intra-patient control and then compared between etiologies. Differentially expressed genes (DEGs) ($p < 0.01$, log2 fold-change > |0.5|) were identified and gene set enrichment analysis (GSEA) was performed. From a third study population, BM aspirates and IVDs were obtained. IVD CCN were quantified, ten pro- and anti-inflammatory and pro-fibrotic BM plasma proteins were quantified with ELISA, and RNA sequencing of $CD45^+CD66b^+$ sorted BM neutrophils was performed. BM plasma protein concentrations were clustered and compared between cluster with Mann-Whitney test, and overrepresentation analysis (ORA) of DEGs between MC1 and intra-patient control BM neutrophils was determined.
Results: Of the first study population, the median CCN of control IVDs (n = 10) was 388 (interquartile range (IQR): 118-685)) and the upper 99 % CI limit was 870. MC1 IVDs (n = 30) had similar median CCN overall (Mann-Whitney: p = 0.29, 464 (229-1614)), but eleven samples (36 %) had > 870 CCN (2659, (899-12900)), which was unique to MC1 IVDs and indicated a bacterial etiology (**Fig. 1a**). From a second study population, three MC1 patients from the bacterial (the three with the lowest CCN) and three from the autoimmune (the three with highest CCN) etiology were selected. Bulk RNA sequencing revealed 222 DEGs between the bacterial and the autoimmune etiology. GSEA showed enriched "neutrophil mediated immunity" and "granulocyte activation" in the bacterial and "adaptive immune response", "B- and T-cell activation" in the autoinflammatory etiology, pointing towards innate immune system contribution in the bacterial, and adaptive immunity in the autoimmune MC1 etiology (**Fig. 1b**). In the third population, MC1 to intra-patient control normalized BM plasma protein concentrations of the ten measured proteins were visualized using UMAP dimensionality reduction technique. Thereby, two patient clusters could clearly be distinguished (**Fig. 1c**). To identify whether clusters represented patients of different etiologies, CCN were compared between clusters and found to differ strongly (cluster 1: 351, (325, 387) vs. cluster 2: 2848, (1355, 3339)). Cytokine analysis between clusters showed upregulated neutrophil associated cytokines in cluster 1 vs. cluster 2 (IL-8: 16 pg/ml, (1, 54) vs. -15 pg/ml, (-21, -11), p = 0.004; ENA-78: 91 pg/ml (-5, 456) vs. -25 pg/ml, (-137, -21), p = 0.048), and a BM neutrophil "defense response to bacterium" in cluster 1, but not in cluster 2, further supporting that clusters represent different etiologies.

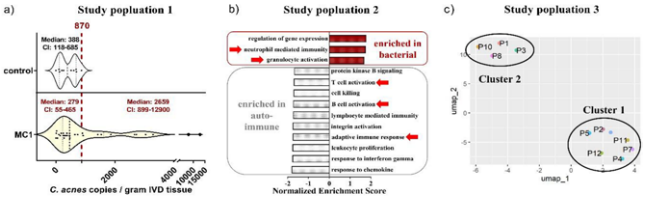

Figure 1: a) *C. acnes* copy number distribution. b) GSEA between etiologies of total cells. c) Cytokine clustering.

Conclusion: We show that IVD *C. acnes* load is decisive for the etiology-specific MC1 pathomechanisms. This has important clinical implications, as different MC1 etiologies might require different treatment strategies.
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AB1395

UROLITHIN A AND B ACCELERATE MYOCYTE FUSION INTO MYOTUBES

Keywords: -omics, Sarcopenia, Cell biology

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Background: Urolithins are intestinal bacterial metabolites of ellagic acid, from pomegranate and nuts. They modulate oxidative-regulated pathways and display anti-inflammatory, antioxidative properties. Several studies indicate that they could be inducers of muscle strengthening.
Objectives: The aim of this in vitro study was to investigate their mechanisms of action at plasma concentrations on primary human myotubes.
Methods: Urolithin A and B (UA and UB) were evaluated separately on primary human muscle CD56+ cells, isolated from the vastus lateralis of 6 men and 3 women (aged range 55 to 96-y) and differentiated in myotubes. 24h-treatment mRNA-sequencing of these 9 patients was studied by DESeq2 analysis (R software). Modulation of several target genes was then validated in several concentrations (1-5 or 10 µM) by RT-qPCR and ELISA on 4 different patients. Organelles and cell morphology changes were observed by NanoLive CX-A live cell imaging during 72h.
Results: After 24h of treatment at 5 µM, UA and UB significantly modified the expression of 1779 and 319 genes, respectively (adjusted p-value of 0.01 and Log2FoldChange |>0.32|). Among the most regulated genes, we found genes involved in myoblasts to myotubes differentiation. UA increased the expression of MYMX (+70%), PANX1 (+50%), MSTN (+64%), MYH2 (+28%) and conversely decreased FGF9 (-75%), MRLN (-33%), ICAM5 (-52%) and TGFBI (-55%). Regarding UB, it decreased IGFN1 (-75%), TGFBI (-60%) and increased MYH2 (+34%) and TGM2 (+59%). However, UA, but not UB, decreased DMD gene expression (-86%), a key factor in muscle strength, and MEF2C (-45%), a regulator of skeletal myogenesis. We also have observed the modulation of genes involved in the inflammatory process. They both induced a important decrease

of CYP1B1 expression (-95%). Further, LIF was increased by 80% by UA and PTGS1 was decreased by 41% by UA and 43% by UB. UA and UB had the opposite effect on IL17B, a cytokine involved in tissue repair but its role in muscle is still to be defined. IL17B was decreased by 49% by UA and conversely upregulated by 45% by UB. In a second step, we confirmed the modulation of MYMX, PANX1, FGF9, ICAM5, PTGS1-PGE2, IL17B and TGFBI following UA and/or UB treatment at 1, 5 and 10 µM by RT-qPCR and ELISA. Finally, we also observed with live cell imaging that UA and UB increased myocyte fusion in myotubes, already after 6h of treatment.

Conclusion: UA and UB promote the differentiation process of myoblasts to myotubes. In parallel, urolithins present anti-inflammatory properties, mainly by reducing CYP1B1 expression and the PGE2 synthesis via PTGS1, but also for UA by increasing LIF. Our data provide a better understanding of urolithin activities and highlight their potential in the treatment of muscle disorders such as sarcopenia.

References: NA.

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Disclosure of Interests: Yves Henrotin Consultant of: Artialis SA Nestlé Expanscience Tilman Allegro Immubio, Cécile Lambert: None declared, Antoine Florin: None declared, Jérémie Zappia: None declared, Prescilia Centonze: None declared, christelle sanchez: None declared.

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AB1396 FUTURE OF HIP CARTILAGE PRESERVATION: A ANGLE ENDPOINTS OPTIMIZE INDICATIONS FOR CONSERVATIVE CARE

Keywords: Cartilage, Prognostic factors, Imaging

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Background: In the context of osteoarthritis (OA) prevention, great attention is given to hip preservation surgery [1]. Patients with femoroacetabular impingement (FAI), a highly prevalent painful condition, are at increased risk of developing OA [2]. However, an undefined fraction of these patients manage to get rid of clinically significant OA with conservative care [3]. Recently, we realized that α angle can be a key to define which patients would benefit from conservative care and which of these should undergo surgery to prevent clinically significant OA.

Objectives: This meta-analysis aimed to answer: i) "does α angle predict the degree of hip chondral health in FAI?" and ii) "what are the α angle endpoints that correspond to each group of degree of chondral health?."

Methods: We followed the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA). Two independent reviewers performed the study selection and data extraction steps. Databases were screened: Embase, MEDLINE/PubMed, SCOPUS, SPORTDiscuss and The Cochrane Library. Good quality primary studies that, by using regressions and other similar statistical tests, assessed the capability of α angle values in predicting the degree of hip chondral health for patients with FAI were considered eligible. Risk of bias was assessed through the QUIPS tool. We conducted a pooled linear regression in order to establish α angle endpoints correlated to each chondral health group.

Results: Twelve studies were considered eligible for bias assessment. We found a high risk of bias due to misreporting and the presence of confounders in 2 studies, which were then excluded from analysis. A summary of the included studies' reported findings is in the Table 1. All 10 included studies demonstrated that α angle predicts the degree of chondral health, with good to excellent effect sizes. For the pooled analysis, 447 patients were enrolled. As the severity of chondral deterioration increases from 1 to 4 in an Outerbridge scale, the corresponding α angle endpoints are 56°, 61°, 65° and 72°- respectively (R^2 = 0,987; p <.001) (Figure 1).

Conclusion: The α angle is a good tool to identify FAI patients who are at higher risk of developing clinically significant OA without surgical intervention. In order to prevent clinically significant OA, we recommend that patients with an α angle greater than 65° should undergo surgery - since they are at high risk of developing significant chondral damage associated with OA progression.

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Table 1.

Author	Mean Age	N	α Angle Measurement	Chondral Health Scale	Findings
Bisciotti	39	41	45°-Dunn view (DV)	Outerbridge	**Logistic regression, ROC curve:** predictive value of the α angle for severe cartilage damage was 81° p < 0.05
Grace	36	46	DV	Beck	**Spearman:** increasing α angles correlated with less hip chondral health r: 0.61; p <.001
Heyworth	30	118	Tomography	ALAD	**Kendall Tau:** increasing α angles correlated with less hip chondral health r: 0.37; p <.001
Kapron	37	100	DV	Beck	**Logistic regression:** adjusted odds of severe chondral damage increased with greater alpha angle values OR = 1.06; p = 0.02
Ishøi	35	1511	Undefined	Beck	**Logistic regression:** OR = 2.2 between severe chondral damage and an 55°< α <78°, with an OR = 4.8 when α ≥78°
Martínez	37	155	DV	MAHORN	**Logistic regression:** Patients with severe chondral damage had greater α angle RR = 5.2; p <.001
Ortiz	37	2701	DV	Outerbridge	**2-tailed Student:** More severe chondral damage for the α angle ≥78° group 39% vs 16%; p <.001
Beaulé	38	180	DV	Beck	**Pearson:** greater α angle was independently associated with increased odds of having severe chondral damage OR = 1.04; p = 0.01
Shapira	37	1485	DV	Outerbridge	**Logistic regression:** every additional degree in α angle was associated with a 6% increase in the odds of severe chondral damage OR = 1.06; p = 0.02
Tang	33	71	AP view	MAHORN	**Logistic regression:** α angle > 70° was a significant risk factor for severe chondral damage OR = 8.84; p = 0.049

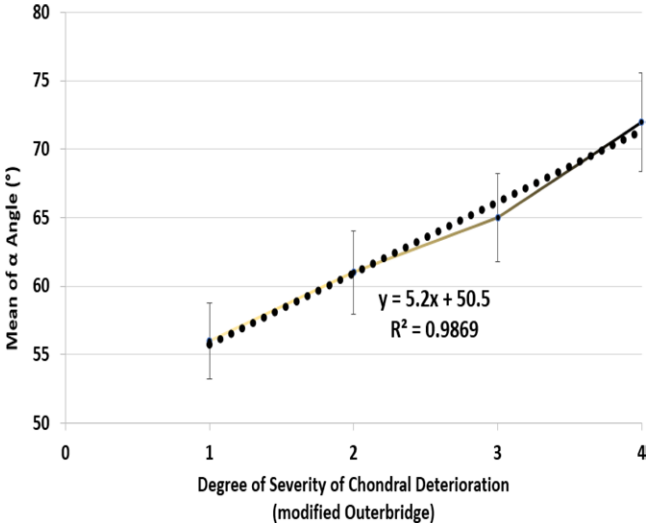

Figure 1.

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Disclosure of Interests: None Declared.

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AB1397 SERUM MASS SPECTROMETRY IDENTIFIES APOLIPOPROTEIN D AS POTENTIAL BIOMARKER FOR MODIC TYPE I CHANGES

Keywords: Pain, Diagnostic Tests, Biomarkers