joint pain and RA symptoms in the group. The groups were adjusted for age ($p > 0.05$) and showed no statistically significant differences.

We measured serum Adiponectin levels ($\mu\text{g/ml}$) using Human Adiponectin ELISA commercial test systems (BioVendor, Czech Republic, cat N^o RD195023100). We used spectrophotometer with wavelength of 450 nm to detect the test results («Multiskan» immunoenzyme analyzer, Finland). We plotted a curve using computer software. We diagnosed OP using dual-energy X-ray absorptiometry with LUNAR DPX PRO (GE, USA).

Results: Serum adiponectin levels in the control group were $12.5 \pm 0.9 \mu\text{g/ml}$ ($M \pm m$). Adiponectin levels in healthy subjects measured as $M \pm 2\delta$, ranged between 0.44 and $24.56 \mu\text{g/ml}$. Patients with OP and RA had significantly higher levels of serum Adiponectin ($p < 0.001$). Mean serum Adiponectin levels in RA patients who had normal bone density and had no OP were $35.21 \pm 0.6 \mu\text{g/ml}$. Mean serum Adiponectin levels in RA/OP patients with low bone mineral density were $52.42 \pm 0.69 \mu\text{g/ml}$. Adiponectin levels of $44 \mu\text{g/ml}$ and higher were associated with osteoporosis. Adiponectin levels of $43.9 \mu\text{g/ml}$ and lower were associated with normal bone density.

Conclusion: Thus, we revealed that Adiponectin levels depend on osteoporosis presence in RA patients. We suppose that Adiponectin determination may be useful laboratory marker for OP diagnosis. The test may be used to reduce the risk of low-energy fractures and to improve the quality of life in RA.

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FRI0515

HSP90AA1, A CHAPERONE-MEDIATED AUTOPHAGY, IS A BIOMARKER ASSOCIATED WITH DEFECTIVE AUTOPHAGY IN OSTEOARTHRITIS

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Background: In osteoarthritis (OA), defects in cellular homeostasis, such as autophagy, are evident and precede joint damage (1). We have shown that there is a defect in autophagy in OA human chondrocytes and cartilage (2). Indeed, pharmacological activation of autophagy protects against joint damage (3). Our working hypothesis is that joint damage in OA could be due to a failure of autophagy that can be detected in the blood and tissue of patients.

Objectives: The objective of this study is to identify biomarkers associated with autophagy defects that could facilitate the development of personalized therapeutic strategies to prevent OA progression.

Methods: A comparative analysis of 35 autophagy genes was performed in blood from a Prospective OA Cohort of A Coruña (PROCOAC) of Non-OA and knee OA patients. Non-OA patients (Age: 61.44 ± 1.16 years; BMI: 25.25 ± 0.52 ; Females, $n=18$) and Knee OA patients (Age: 65.50 ± 1.05 years; BMI: 29.55 ± 0.67 ; Females, $n=18$, OA grade III-IV) were profiled using PrimePCR autophagy human panel array (Bio-Rad). Confirmatory studies of the candidate genes were performed in blood from Non-OA patients (Age: 60.13 ± 1.12 years; BMI: 24.85 ± 0.59 ; Females, $n=30$) and Knee-OA patients (Age: 68.4 ± 1.11 years; BMI: 29.65 ± 0.55 ; Females, $n=30$, OA grade III-IV) by Taqman Technology. A quantitative proteomic analysis of defective autophagy genes regulated upon deletion of Atg5 in human OA chondrocytes was performed by iTRAQ analysis. Moreover, the candidate gene was evaluated as a potential biomarker in human cartilage from Normal ($n=19$) and Knee-OA ($n=20$) patients and in both spontaneous aging (6, 12, 18, and 30 months old, $n=3$) and surgically-induced OA (10 weeks after surgery, $n=4$) in mice by immunohistochemistry. Remarkably, the consequences of candidate gene silencing on autophagy, FOXO signaling, inflammation, senescence and cell death by apoptosis was investigated by gene expression and flow cytometry.

Results: 15 autophagy-related genes were downregulated in blood from knee OA patients compared to non-OA patients ($p < 0.05$). Importantly, key autophagy-related genes, including ATG16L2, ATG12, ATG4B and MAP1LC3B, involved in relevant process including initiating autophagy, phagophore extension and autophagosome formation, were significant downregulated in knee OA patients ($p < 0.05$). Interestingly, HSP90AA1 and HSPA8, chaperone-mediated autophagy genes involved in stress response and protein folding, were significant downregulated ($p < 0.001$). In addition, several regulators of autophagy and apoptosis, such as BNIP3, BCL-2 and BCL2L1 were downregulated ($p < 0.01$). Confirmatory studies for MAP1LC3B and HSP90AA1, showed a significant downregulation ($p < 0.001$) in blood from knee OA patients. Remarkably, total proteome screening of human OA chondrocytes with defective autophagy, showed a significant reduction of HSP90AA1 ($p < 0.05$). Remarkably, HSP90AA1 expression was reduced in OA cartilage ($p < 0.01$) and in spontaneous aging and surgically-induced OA in mice ($p < 0.05$). Interestingly, HSP90AA1 silencing increased LC3 and FOXO1 expression ($p > 0.01$), might be as a protective response, and increased NF κ B and p16 expression ($p < 0.05$) at 48 hours. In addition, genetic deletion of HSP90AA1 increased cell death by apoptosis ($p < 0.05$). These data indicate that HSP90 might be a potential biomarker associated with defective autophagy in OA.

Conclusion: We identified biomarkers of defective autophagy as a mechanism of central homeostasis, which gives us a general vision of the disease mechanisms linked to OA clinical reality.

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FRI0516

CHONDROGENIC EFFECT OF KARTOGENIN ON AN IMMORTALIZED CELL LINE DERIVED FROM MESENCHYMAL STROMAL CELLS ISOLATED FROM HUMAN BONE MARROW

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Background: Mesenchymal stromal cells (MSCs) currently tested in regenerative medicine approaches for osteoarthritis (OA) present limitations in obtaining stable hyaline-like cartilage phenotype. Kartogenin (KGN) has been recently described to promote both reparative and protective effects hampering the hypertrophic effects of chondrogenesis.¹

Objectives: The aim of this study is to evaluate the chondrogenic effect of kartogenin on an immortalized cell line (3a6), using a conventional cell pellet model and gold-standard chondroinductor transforming growth factor 3 (TGF- β 3), as positive reference.

Methods: 3a6 cells, originally obtained from a 61-year old Asian woman bone marrow, was cultured under pellet culture system with basal (DMEM, low glucose) or commercial chondrogenic medium, supplemented with 10 ng/ml TGF- β 3 or 100nM KGN for 3, 7, 14 and 21 days. Total RNA was isolated and real-time quantitative reverse transcription-polymerase chain reaction (RT-qPCR) was performed, using custom-made primers for runt-related transcription factor 1 (RUNX1), proteoglycan 4 (PRG4), cartilage intermediate layer protein (CILP), collagens type-II (COL2A1), -X (COL10A1) and -I (COL1A1), using RPL13A as housekeeping. Proteoglycans and zonal markers protein synthesis was evaluated by safranin-O (SO) staining and lubricin/PRG4 and CILP immunohistochemical analysis (both 1:500), respectively. The experiment was performed in triplicate and differences judged using one-way ANOVA with Bonferroni's corrections, considering $p < 0.05$ significantly different.