taking into account that as yet we do not know whether the two definitions correlate.
The analysis of follow up data in GARP may reveal whether genetic predisposition for a higher baseline serum CRP is causally contributing to the development of hand OA.

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PREVALENCE AND VIRAL LOAD OF PARVOVIRUS B19, VARICELLA-ZOSTER VIRUS, AND HUMAN HERPESVIRUS-6 IN MESENCHYMAL STEM CELLS OF PATIENTS WITH OSTEOARTHRITIS

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Purpose: Viruses have long been suspected to be involved in the pathogenesis of rheumatic diseases. In the last years, an increasing number of studies of viral DNA prevalences in blood, serum and synovial fluid suggest the involvement of the viruses in these diseases. Less numerous, but not less important, are the studies carried out in bone marrow. In addition, total bone marrow transplantation has been used for repairing of damaged tissues in different pathological situations (i.e. osteogenesis imperfecta) and mesenchymal stem cells (MSCs) seem to be the best candidates for cell therapy for regeneration of injured tissue. Thus, the risk of viral transmission in bone marrow transplantation or autologous MSCs transplantation could be a serious problem.
The purpose of this study was to evaluate the importance of viral infections in osteoarthritis (OA) through the measurement of the prevalence and viral load of Parvovirus B19 (B19), Varicella-zoster virus (VZV), and Human Herpesvirus-6 (HHV-6), in MSCs from bone marrow of patients with OA and healthy donors.
Methods: A total of 18 patients with OA (mean age 74.7 years, range 61-89) and 10 healthy donors with no known history of joint disease (mean age 66.6, range 44-90) were recruited from the Service of Orthopaedic Surgery of Hospital Clinico San Carlos. Fresh bone marrow aspirates were obtained from the distal femur of the patients with OA after total knee replacement surgery and from healthy donors during tissue harvest in the process of multiorganic donation (n=3) or from proximal femur in the surgery for the subcapital fracture of the hip (n=7). MSCs were established from bone marrow aspirates of OA patients and healthy donors. DNA was extracted from primary MSCs culture established from these cells and quantitative real time polymerase chain reaction was performed to analyse the prevalence and viral load of B19, VZV and HHV-6. Differences between groups were analyzed using the two-tailed Student's t test and the Mann-Whitney U test for normal and non-normal quantitative variables respectively. The Chi-square test was used to compare categorical variables. A two-sided P value of 0.05 was the criterion for statistical significance in all cases.
Results: We found a total viral DNA prevalence of 16.7% (3/18) among OA patients: 1/18 was positive for B19, 2/18 for VZV, and 0/18 for HHV-6. In the control group, we found a total viral DNA prevalence of 20% (2/10); the two positives belonged to B19. We did not find any statistical significant difference.
Conclusions: This first approach to the viral prevalence in MSCs of bone marrow in OA patients seem do not support the possible involvement of the viruses in the pathophysiology of OA, and show a very low risk of viral reactivation in a possible MSCs transplantation.

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CIS- AND TRANS-ACTING GENE REGULATION IS ASSOCIATED WITH OSTEOARTHRITIS

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Purpose: Osteoarthritis (OA) is a complex disease of the skeleton and is associated with ageing. Both environmental and genetic factors contribute to the pathogenesis. We here set out to identify novel genes associated with OA, concentrating on regulatory polymorphisms allowing for differential expression.
Methods: Our strategy included an initial transcriptome analysis of the PBMC of 6 OA patients and 6 age-matched healthy controls in order to identify differentially expressed genes. These were screened for allelic expression imbalances and potentially regulatory SNPs in the 5'regions of the genes. To establish disease association, disparate promoter SNP distributions correlating with the differential expression were tested on larger cohorts.
Results: Our approach yielded 26 candidate genes differentially expressed between patients and controls. While BLP2 and CIAS1 seem to be trans-regulated as suggested by the absence of allelic expression imbalances, the presence of allelic imbalances confirms cis-regulatory mechanisms for RHOB and TXNDC3. Interestingly, on/off switching suggests additional trans-regulation for TXNDC3. Moreover, we demonstrate statistically significant associations between 5' SNPs and the disease for RHOB and TXNDC3, hinting at regulatory functions.
Conclusions: Investigating the respective genes functionally will not only shed light on the disease association but will also add to the understanding of the pathogenic processes involved in OA and may point out novel therapeutic approaches.

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NONSYNONYMOUS POLYMORPHISMS OF THE MAIN IN VIVO AGGRECANASE, A DISINTEGRIN AND METALLOPROTEINASE WITH THROMBOSPONDIN MOTIFS 5, IN SUSCEPTIBILITY TO OSTEOARTHRITIS

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Purpose: To explore the possibility that non-synonymous SNPs altering conserved aminoacids of the main in vivo aggrecanase could play a role in OA susceptibility. That ADAMTS5 (a disintegrin and metalloproteinase with thrombospondin motifs 5) is the main aggrecasnase has been shown in knockout mouse models of OA and of inflammatory arthritis where cartilage degradation was prevented.
Methods: A case-control study has been done with samples from Spain, the UK and Greece. Three groups of Spanish OA patients were studied: with total joint replacement for primary OA in the hip, THR (n = 310), or the knee, TKR (n = 277) or with hand OA, HOA (n = 242). Samples form TKR patients from the