Conclusion: Hsa_circ_0012732, hsa_circ_0008961, hsa_circ_0405239 and hsa_circ_0088784 may be related to the pathogenesis of AS. Among them, hsa_circ_0012732 may be involved in AS inflammation and has the potential to participate in the judgment of disease activity.

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SLE, Sjögren's and APS - aetiology, pathogenesis and animal models.

AB0077

ASSOCIATION BETWEEN VITAMIN D RECEPTOR GENE POLYMORPHISMS AND SYSTEMIC LUPUS ERYTHEMATOSUS IN MALTESE PATIENTS

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Background: Vitamin D deficiency is highly prevalent in patients with systemic lupus erythematosus (SLE). Vitamin D acts through the vitamin D receptor (VDR) that is present in most cells, and it can regulate the transcription of over 200 genes. The expression of vitamin D receptors by a variety of cells belonging to the innate and adaptive immune systems has created interest with regards to the role of vitamin D in the pathogenesis of SLE. Several polymorphisms of the VDR gene have been described, namely BsmI, ApaI, TaqI and FokI. A number of VDR gene polymorphism genotypes have been associated with increased risk of SLE mostly in Asians and Africans.

Objectives: The aim of this study was to establish whether an association was present between VDR gene polymorphisms and SLE susceptibility in a cohort of SLE patients living in Malta. A further aim was to assess the relationship between these VDR gene polymorphisms and SLE disease characteristics.

Methods: 59 SLE patients living in Malta and attending Rheumatology clinic at Mater Dei Hospital were recruited for the study after providing informed consent. The patients were over the age of 18 years and fulfilled the SLICC classification criteria for SLE. The patients were interviewed and blood samples were taken. RNA extraction was performed from whole blood. QuantGene Plex technology was used to measure the expression of 12 interferon (IFN) signature genes in the extracted RNA. 63 SLE samples obtained from individuals living in Malta who were used as a control. DNA extraction was carried out from the blood samples obtained from the patients and controls. The VDR gene was screened and the regions containing the VDR polymorphisms were amplified for each patient. The amplified regions were then digested with their respective restriction enzymes in order to view the patient’s genotype via restriction fragment length polymorphism. Statistical analysis, including odds ratio (OR), was carried out to gauge the significance in the association of these polymorphisms with SLE.

Results: 94.9% of SLE patients were female and they had a mean age of 44.5 years. All the patients were of Caucasian ethnicity. 13.6% had vitamin D deficiency (serum 25-hydroxyvitamin D <20ng/ml) and 25.4% were vitamin D insufficient (serum 25-hydroxyvitamin D 20-29ng/ml). The results showed that when ApaI polymorphism was present, a significant decrease in SLE prevalence (OR=0.39, CI 0.17-0.87, p=0.02). The results were also analysed by placing the polymorphs into haplotypes. The haplotype containing all wild-type alleles with the variant allele for FokI are associated with a significant increase in the prevalence of SLE (OR=1.13, CI 0.12-11.00, p=0.02 respectively). The patients who were homozygous for the variant allele for BsmI had a significantly higher SLE disease activity index-2K (SLEDAI-2K) (mean 5.00) compared to those that were heterozygous (mean 2.66; p=0.010). No significant difference was noted in damage, IFN signature gene expression, organ manifestation and autoantibody profile between the different genotypes for the 4 VDR polymorphisms. SLE patients who were homozygous for the Apal or TaqI polymorphisms had an increased prevalence of fibromyalgia (OR=1.38, 1.47-38.16, p=0.02 and OR=12.00, CI 1.80-80.05, p=0.02 respectively).

Conclusion: The study showed that in the Maltese population the presence of the VDR gene polymorphism haplotype containing all wild-type alleles and the haplotype containing all wild-type alleles with the variant allele for FokI are associated with an increased risk of SLE. Moreover the homozygous variant genotype for BsmI was associated with a higher SLE disease activity. The homozygous
variant genotype for Apal and TaqI was associated with a higher risk of fibromyalgia in SLE patients.

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Objectives: Objective of the study is to research the effect of emulsion polymerization on active sites of cardiolipin antigen determinant in antiphospholipid syndrome (APS) in patients with systemic lupus erythematosus (SLE).

Methods: Having integrated antigen nanoobjects we developed magnetically controllable antigen nanosystems and put them to an evaluation test. The nanosystems are polyacrylamide granules with a built in antigen. To obtain stable immobilized multi–use biopharmaceuticals with targeted properties (shape, particle diameter, pore size, density) we used a modified version of emulsion polymerization method using polyacrylamide carrier gel. This method permitted a greater sorptive capacity, preserving the antigen in maximum native state, and opened up the possibility of controllable modification of nanoobjects.

Cardiolipin was used as the antigen in question.

Results: Following the method described above we performed sorption of anti-cardiolipin antibodies from blood plasma of SLE patients who showed clinical presentations of antiphospholipid syndrome. Blood serum from 10 apparently healthy individuals served as control. The level of cardiolipin antibodies was determined before and after sorption by indirect solid phase immunoenzyme method. In the eluate we estimated total protein by Lowry method. In vitro testing showed that the obtained antigen nanosystems based on immobilized cardiolipin could effectively remove cardiolipin antibodies from whole blood of SLE patients with clinical presentations of APS to achieve the values of healthy individuals (before sorption cardiolipin antibodies 0.328 ± 0.028; after sorption 0.059 ± 0.017; p<0.001; sorption capacity 8.60 ± 0.390 mg/ml).

Conclusion: The method of emulsion polymerization with consideration to hydrophobic and hydrophilic properties of lipid molecules permits obtaining and modifying biomolecules with certain properties, in a controlled fashion.

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Background: As widely demonstrated, circulating endothelial progenitor cells (EPCs) could be considered biomarkers of endothelial dysfunction. Their frequency and function varied in systemic lupus erythematosus (SLE) patients, with a significant association with subclinical atherosclerosis1. Cardiolipin, one of the most widely consumed products in the world, seems to interact with multiple components of the immune system by acting as a non-specific phosphodiesterase inhibitor1. In terms of cardiovascular disease (CVD), data from the literature showed a U-shaped association between habitual coffee intake and CVD in patients4. Finally, caffeine seems to play a role in endothelial cells and EPCs migration in relation to coffee consumption in coronary artery disease5. Spyridopoulos et al. demonstrated a significant improvement in mature endothelial function in SLE patients, by evaluating its effect on circulating EPCs.

Methods: We performed a cross-sectional study enrolling SLE patients, fulfilling the revised 1997 ACR criteria. According with the protocol study, we excluded patients with history of smoking, CVD, chronic kidney failure, dyslipidaemia, and/or diabetes. At recruitment, the clinical and laboratory data were collected and disease activity was assessed using the SLEDAI-2k. Caffeine intake was evaluated using a 7-day food frequency questionnaire, previously employed in SLE cohort7. At the end of questionnaire filling, blood samples were collected. EPCs were isolated from peripheral blood mononuclear cells (PBMC) by a flow cytometry analysis and they were defined as early EPCs CD34+KDR+CD133+ cells and late EPCs CD34+KDR+CD133-, expressed as a percentage within the lymphocyte gate.

Results: We enrolled 19 patients (F:M 18:1, median age 45 years, IQR 15; median disease duration 240 months, IQR 168). In this cohort, we observed a mean±SD SLEDAI-2k value of 13.3±3.3 and the most frequent disease-related feature was joint involvement (73.7%). Concerning treatment at the time of enrolment, the majority of patients were receiving treatment with hydroxychloroquine (78.9%) and seven with glucocorticoids (36.8%). The mean intake of caffeine was 163 mg/day (IQR 138) and we used this value as cut-off to categorize SLE patients in 2 groups: group 1 (N=10, caffeine intake ≤ 163 mg/day) and group 2 (N=9, caffeine intake > 163 mg/day). Patients with less intake of caffeine showed a significantly more frequent history of lupus nephritis (p=0.03), haematological manifestations (p=0.0003) and anti-dsDNA positivity (p=0.0003). Moving on EPCs, a positive correlation between caffeine intake and EPCs percentage was observed (p=0.04. r=0.4) (Figure 1A). Moreover, patients with more caffeine intake showed higher levels of early EPCs (p=0.02) (Figure 1B).

Conclusion: This is the first report analysing the impact of caffeine on EPCs frequency in SLE patients. We found a positive correlation between its intake and both early and late EPCs percentage, suggesting a caffeine influence on endothelial function in SLE patients. Nonetheless, these results support the possible impact of dietary habits on autoimmune diseases.

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Background: Large extracellular vesicles (EVs) are involved in various thrombotic disorders [1], including APS [3, 4], and therefore may influence the prothrombotic status of patients with APS. Small extracellular vesicles (sEVs) are involved in the interactions with leukocytes and platelets. The method of emulsion polymerization with consideration to hydrophobic and hydrophilic properties of lipid molecules permits obtaining and modifying biomolecules with certain properties, in a controlled fashion.

Methods: Whole blood was collected from 4 APS patients and 3 healthy blood donors (HBDs) and processed to obtain platelet-depleted plasma. The size and concentration of sEVs were determined using ExoView platform (NanoView Biotechnology). Cardiolipin was used as the antigen in question. Having integrated antigen nanoobjects we developed immobilized magnetocontrollable antigen nanosystems and put them to an evaluation test. The nanosystems are polyacrylamide granules with a built in antigen. To obtain stable immobilized multi–use biopharmaceuticals with targeted properties (shape, particle diameter, pore size, density) we used a modified version of emulsion polymerization method using polyacrylamide carrier gel. This method permitted a greater sorptive capacity, preserving the antigen in maximum native state, and opened up the possibility of controllable modification of nanoobjects.

Cardiolipin was used as the antigen in question.

Results: Following the method described above we performed sorption of anti-cardiolipin antibodies from blood plasma of SLE patients who showed clinical presentations of APS to achieve the values of healthy individuals (before sorption cardiolipin antibodies 0.328 ± 0.028; after sorption 0.059 ± 0.017; p<0.001; sorption capacity 8.60 ± 0.390 mg/ml).

Conclusion: The method of emulsion polymerization with consideration to hydrophobic and hydrophilic properties of lipid molecules permits obtaining and modifying biomolecules with certain properties, in a controlled fashion.

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