Genomics, genetic basis of disease and functional genomics

AB0001

PLASMA miRNA PROFILE IN PATIENTS WITH HAND OSTEOARTHRITIS

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Background: MicroRNAs (miRNA) are short non-coding RNAs that can be involved in diverse physiological processes¹. Aberrant miRNA profiles have been shown in various diseases including osteoarthritis (OA)²; for instance, miR-21-5p or miR-140 are known for their altered expression in osteoarthritic cartilage^{3,4}. However, no screening of circulating miRNAs has been done in patients with hand OA (HOA) so far.

Objectives: Our aim was to profile circulating miRNAs in plasma of patients with HOA in screening and validation cohort.

Methods: We screened the expression of miRNA profiles in 4 patients with erosive (3 females, mean age=63.7±7 yrs) and 4 patients with non-erosive (3 females, mean age=62.4±6 yrs) HOA, and 4 control subjects (3 females, mean age=63.5±7 yrs). The validation cohort included 10 patients with erosive (7 females, mean age=67.5±7 yrs) and 10 patients with non-erosive (6 females, mean age=67.6±8 yrs) HOA, and 10 control subjects (8 females, mean age=64.3±8 yrs). Circulating miRNA screening were performed using TLDA and selected miRNAs were validated by qRT-PCR.

Results: Profiling circulating plasma discovered 42 miRNAs from 754 analysed miRNAs with different concentration among subjects, including miR-23a-3p (1.7 fold), -222-3p (2.0 fold), and -30e-3p (13.0 fold) to be elevated in patients with HOA compared to control subjects. In addition, six miRNAs were distinctive between erosive and non-erosive HOA, e.g. hsa-miR-24-3p was 2.3 times lower and hsa-miR-576-5p was 3.4 times higher in erosive compared to non-erosive disease.

Out of these selected miRNAs, qRT-PCR validated 42 miRNAs and confirmed 11 miRNAs (e.g., miR-23a-3p or -222-3p) with different concentration between patients and controls. However, no miRNAs distinguished between erosive and non-erosive HOA, although miR-101-3p (4.5 fold) and -320b (13.7 fold) almost reached statistical significance.

Conclusion: Based on our study, we identified 11 miRNAs that may have a potential as biomarkers of HOA. However, further studies on larger cohorts are needed.

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AB0002

CONGENITAL DEFECTS IN A COHORT OF PREGNANT WOMEN FROM A CLINIC OF RHEUMATIC DISEASES AND PREGNANCY

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Background: Some studies have suggested an increased risk of adverse health outcomes for the child of patients with Rheumatic Diseases (RD), including neurodevelopmental disorders, congenital heart defects, hematological malignancies and autoimmune diseases. It is well known that 2 to 3% of

live births have a congenital defect. About 7 % of all newborn deaths are due to birth defects.

Objectives: Describe Genetical Evaluation in a cohort of pregnant patients with RD

Methods: We included 22 women from February to December 2019 from a Clinic of Pregnancy and Rheumatic Diseases in Hospital Universitario in Monterrey, Mexico. All spontaneous pregnancies (21 singletons, 1 double twin), with adequate prenatal control. Ten Rheumatoid Arthritis, Antiphospholipid Syndrome in 4 cases; 5 Systemic Lupus Erythematosus, 2 Sjögren's Syndrome and a case of Dermatomyositis. In the perinatal genetics approach, medical and familial history was obtained, and pedigree was developed; ultrasound information of 12 and 22 weeks of gestation was integrated, risks for aneuploidies were adjusted according to maternal age. At birth, the dysmorphological description was made, somatometry is performed, and the newborn screening were evaluated (metabolic, hearing, cardiac). Thus, giving genetic counseling for each case.

Results: Two patients were excluded, so 20 women with follow-up, 12 (60%) were born without complications or birth defects; in 3(15%) there were adverse events (a spontaneous abortion at 12 weeks-of-gestation [wg]; a fetal death in the case of twin pregnancy, at 34.1 wg, with facial asymmetry, intrauterine growth restriction; and a premature delivery, at 36.5 wg; no defects; there were 5(25%) congenital defects: a preauricular appendix, with normal renal ultrasound. A congenital heart disease (transposition of large vessels, tricuspid stenosis). A case of macrosomia (diabetic fetopathy); a heart block with perinatal pacemaker placement (mom with lupus). And in the latter case, Krabbe disease, even without confirming it. Table 1.

Table 1.

Maternal diagnosis	Effects on fetus/neonate	N (%)
Congenital Defects		5 (25%)
Antiphospholipid syndrome	Congenital Heart Disease	
Lupus erythematosus systemic	Heart Block with Perinatal Pacemaker Placement	
Rheumatoid arthritis	Krabbe Disease	
Rheumatoid arthritis	Preauricular appendix	
Sjögren Disease	Diabetic Fetopathy	
Adverse events		3 (15%)
Rheumatoid arthritis	Spontaneous Abortion	
Antiphospholipid syndrome	Fetal death	
Rheumatoid arthritis	Premature delivery	

Conclusion: One out of every 4 pregnancies of women with rheumatic diseases presented a congenital defect, of which, the heart diseases (CHD) have been described as of greater presentation in these groups.

It is very important that women with rheumatic diseases are well attached to a comprehensive clinic in which, in addition to receiving proper attention of their rheumatic disease, they have adequate preconception and prenatal control of their pregnancies, since there is a greater risk of congenital alterations and of perinatal adverse events, as shown by this cohort. Further research is needed to fully elucidate the potential disease-related factors that might lead to the increased risk of adverse health outcomes in offspring, as well as to improve the monitoring and control of their rheumatic diseases.

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AB0003

SINGLE-NUCLEOTIDE POLYMORPHISMS (RS28493229 AND RS2290692) IN ITPKC GENE IN CHILDREN WITH KAWASAKI DISEASE

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Background: Kawasaki disease (KD) is an acute medium vessel vasculitis manifesting with mucocutaneous lesions and cardiac complications especially coronary artery lesions (CALs). Inositol 1,4,5-triphosphate 3-kinase C (ITPKC) gene polymorphisms are have been shown to be associated with susceptibility to KD and CAL.

Objectives: This study was designed to investigate the association of single nucleotide polymorphisms (SNPs) of the ITPKC gene with KD and CAL in Indian children.

Methods: Two SNPs of the ITPKC gene (rs28493229 and rs2290692) were studied in 50 cases of KD and 50 healthy controls. The Deoxyribonucleic acid

(DNA) samples from test subjects and controls were analysed for the two polymorphisms by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP). The allele, genotype, and haplotype frequencies were compared in different groups. A meta-analysis was also performed for the CC and GG genotype of both SNPs of interest.

Results: No significant differences were found in frequencies of C allele, CC genotype and C carriers of rs28493229 and rs2290692. Combined CG+GG genotype frequency of rs2290692 was found to be significantly associated with susceptibility of KD (95% Confidence interval (CI) = 1.38-13.83, $p = 0.015$). A meta-analysis did not show a significant association of SNP rs28493229 (Odds ratio = 1.46, CI = 0.96-2.23) and rs2290692 (OR = 1.07, 95% CI = 0.663-1.731) of *ITPKC* and susceptibility to KD.

Conclusion: Combined CG+GG genotype of SNP rs2290692 at 3' UTR of the *ITPKC* gene was found to be significantly associated with susceptibility to KD. Our study did not show a significant association of any allele or genotype with susceptibility to KD. The meta-analysis combining our study with previous studies on these 2 SNPs also failed to show a significant association of different genotypes and susceptibility of KD.

Table:

Table 1. Allele, genotype and carrier frequencies of single nucleotide polymorphisms of rs28493229 and rs2290692

Allele, genotype and carrier frequencies of SNP rs28493229 of <i>ITPKC</i> (n = 100)	KD patients (n = 50) n (%)	Controls (n = 50) n (%)	Odds ratio (95% C.I.)	P value
Allele/ Genotype				
G allele	89 (89%)	92 (92%)	-	-
C allele	11 (11%)	8 (8%)	1.42 (0.49-4.26)	0.468
GG genotype	39 (78%)	42 (84%)	-	-
CG genotype	11 (22%)	8 (16%)	1.48 (0.54-4.19)	0.446
CC genotype	0 (0%)	0 (0%)	-	-
Frequencies of allele and genotype of rs2290692 SNPs in KD patients and controls (n = 100)				
Allele/ Genotype				
G allele	63 (63%)	56 (56%)	-	-
C allele	37 (37%)	44 (44%)	0.747 (0.41-1.36)	0.313
GG genotype	19 (38%)	20 (40%)	-	-
CG genotype	25 (50%)	16 (32%)	1.64 (0.68-4.04)	0.272
CC genotype	6 (12%)	14 (28%)	0.45 (0.14-1.37)	0.173

C.I. Confidence interval, KD- Kawasaki disease

Figure:

Figure 1. Forest plot for the association between (A) CC genotype of rs28493229 and risk of having KD (B) GG genotype of rs2290692 and risk of having KD (C) CG genotype of rs2290692 and risk of having KD

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AB0004

TLR10 SINGLE NUCLEOTIDE POLYMORPHISMS ARE ASSOCIATED WITH HIDRADENITIS SUPPURATIVA IN A CAUCASIAN SPANISH POPULATION (NORTHERN SPAIN)

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Background: Hidradenitis suppurativa (HS) is a chronic, relapsing inflammatory cutaneous disease affecting terminal hair follicles in apocrine-gland bearing skin. The pathogenesis of HS is still unknown, although increasing evidence suggests that the immune system plays an important role. In order to study the role of innate immunity we analyzed several Toll Like Receptors (TLRs) functional single nucleotide polymorphisms (SNPs). To date, only one previous study focused about the role of TLR4 SNPs in HS showing no association with this disease.

Objectives: The main goal of this study was to analyze the role of several TLRs functional SNPs in HS patients and healthy controls, in a Caucasian population from Cantabria (northern Spain).

Methods: Through a case-control study, we analyzed the allele and genotype distribution of the SNPs in 106 patients with HS and 278 age and sex matched healthy control subjects for the following SNPs (TLR1 rs5743611 and rs4833095, TLR2 rs5743704 and rs5743708, TLR6 rs5743810, and TLR10 rs11096955, rs11096957 and rs4129009, by Real-Time PCR using a TaqMan assay.

Results: We did not find any significant difference in the allelic distribution of the different SNPs between HS patients and controls. Regarding genotypes, only TLR10 rs11096955 (dominant, codominant and overdominant), rs11096957 (dominant, codominant and overdominant) and rs4129009 (codominant and overdominant) showed significant differences between HS patients and controls. However, no association was found when we analyzed the different TLR10 haplotypes.

Conclusion: To the best of our knowledge, this is the first study showing an association of TLR10 SNPs with HS.

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AB0005

HLA CLASS II CONFERS RESISTANCE OR SUSCEPTIBILITY TO HIDRADENITIS SUPPURATIVA IN A CAUCASIAN SPANISH POPULATION (NORTHERN SPAIN)

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Background: Hidradenitis suppurativa (HS) is a chronic inflammatory cutaneous disease affecting terminal hair follicles in apocrine glands bearing skin. The pathogenesis of HS remains unknown, although increasing evidence suggests that the immune system plays an important role. To date, two previous studies, did not find any association between HLA and HS.