Disease-Modifying Antirheumatic Drug and TNF-α inhibitor use was higher in the group with MEFV mutation.
Conclusion: This study showed that the incidence of MEFV gene mutation in AS patients was higher than the incidence of mutations in health population in our country. This relationship was stronger particularly with M694V mutation. On the other hand, based on the findings of this study and our clinical experience, it can be said that the clinical progression of AS patients with MEFV gene mutations is more severe, and this suggests that MEFV gene mutations may be contributive to AS pathogenesis.

THEMATIC STREAM: SYSTEMIC AUTOIMMUNE DISEASE

BPP4. FOUR NOVEL MEFV GENE MUTATIONS IN A POPULATION WHERE THE PREVALENCE OF CRIMEAN-CONGO HEMORRHAGIC FEVER AND MEFV GENE CARRIER STATUS IS VERY HIGH

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Purpose: Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne disease caused by an arbovirus in the family Bunyaviridae, which is associated with high mortality. CCHF is common in mid Anatolia where FMF is also very prevalent (1.2%), thus MEFV gene carrier status is very high (44%).To test our hypothesis that a selective biological advantage obtained by a carrier state for MEFV mutations may enhance the host's ability to withstand CCHF, we studied the distribution of MEFV gene mutations in patients with CCHF.
Methods: MEFV gene mutations of exon 2 and 10 were detected with polymerase chain reaction (PCR) and direct sequencing in 100 patients with CCHF with a definite diagnosis of CCHF followed in Cumhuriyet University, Sivas / Turkey, (mean age 45.6 ± 17, 58 M: 42 F) and in 91 healthy blood donors (HC) living in the same area. All CCHF patients were classified into two groups in terms of disease severity (mild and severe), according to the predictive factors for fatal outcome reported by Swanepoel et al. (1).
Results: Four new mutations were found on exon 10 of 7 CCHF patients and none of the healthy controls. A database search for these novel mutations was negative. The loci of these new MEVF gene mutations on exon 10 are as follows: Q778L, R717Q, P754A and R737K. Q778L mutation was found in four patients, one had a mild whereas the remaining 3 had severe disease. Carrier of R717Q had a severe disease and died, however the carriers of P754A and R737K had mild disease course. All of these patients except the one who died were reevaluated for co-existence of FMF but none had any personal or familial history of FMF.
Conclusion: Here we describe 4 novel MEFV gene mutations in patients with CCHF from a geographical area where MEFV gene carriership is very high. We do not yet know whether these mutations have any effect on the host's ability to withstand an infection.
Reference:
1. Swanepoel R, Gill DE, Shepherd AJ, Leman PA, Mynhardt JH, Harvey S. The clinical pathology of Crimean-Congo hemorrhagic fever. Rev Infect Dis 1989. May-Jun;11 Suppl 4:S794-800.

BPP5. EPISTATIC INTERACTION BETWEEN THE IRF5 AND STAT4 GENES IN SUSCEPTIBILITY TO SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Activation of the type-I interferon (IFN) pathway has been observed in the patients with systemic lupus erythematosus (SLE), and susceptibility to SLE has also associated with *IRAK1*, *IRF5*, and *STAT4*, which play crucial roles in the IFN pathway. This study aimed to examine epistatic interactions among the SLE-associated polymorphisms in *IRF5*, *IRAK1*, and *STAT4*.
Methods: For this study, we retrieved the genotype information of SLE-associated polymorphisms in the three genes from our previous studies using 796 Korean SLE patients and 1,129 unrelated controls. Epistatic interaction analyses for all possible variation pairs were performed by the PLINK '–epistasis' option using multiplicative logistic regression that took the affected status as a dependent factor, two SNPs from each gene as main factors, and the two-SNP interaction term.
Results: Significant non-additive effects were found only in four pairs between the polymorphisms in *IRF5* and *STAT4*, as their interaction terms were significantly associated with SLE development ($0.015 \leq P \leq 0.043$). Additionally, effects of the risk alleles in *STAT4* on the susceptibility were stronger in the group having no risk alleles of *IRF5* ($1.60 \leq$ OR ≤ 1.78, $7.2 \times 10^{-8} \leq P \leq 2.7 \times 10^{-6}$) than in the heterozygote group ($1.37 \leq$ OR ≤ 1.62, $1.7 \times 10^{-5} \leq P \leq 0.063$) or in the risk-allele homozygote group ($0.71 \leq$ OR ≤ 1.19, $0.28 \leq P \leq 0.72$). However, no evidence was found for inter-gene dependency between *IRAK1* and *IRF5* or between *IRAK1* and *STAT4*.
Conclusions: Risk alleles in *IRF5* increase IFN-α production and those in *STAT4* increase sensitivity against IFN-α, but the effect of a risk allele in one gene is reduced in a group having a risk allele in the other gene. The results suggest that risk variants in either *IRF5* or *STAT4* alone may be enough to activate IFN-α pathway for enhancing SLE susceptibility.

BPP6. CYTOTOXIC T LYMPHOCYTE ACTIVITY IN THE PATHOGENESIS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Activated cytotoxic T lymphocyte (CTL) mediated target cell death has been implicated in the development of systemic autoimmune disease like SLE. CTL induced target cell death by secretion of perforin and granzyme B however, relation of soluble granzyme B in the CTL activity and their together role in the pathogenesis of SLE remain to elucidate. In this study, we evaluated the levels of soluble granzyme B and cytotoxic activity in SLE patients.
Method: The soluble granzyme B was measured in the serum by an enzyme-linked immunosorbent assay (ELISA). The cytotoxic T lymphocyte activity was measured by evaluation of the expression of perforin and granzyme B positive cells in $CD8^+$ T cells. The disease activity was determined by using SLE Disease Activity Index (SLEDAI) score.
Results: The soluble granzyme B levels were higher in SLE patients and associated with various clinical features like reduced complement components; C3 & C4 and skin lesion. The cytotoxic T lymphocyte activity was also found to increase in SLE patients. The levels of soluble granzyme B and cytotoxic T activity were also sturdily related with severity of disease.
Conclusion: The findings of this study suggest that excessive secretion of soluble granzyme B and enhanced activity if cytotoxic T lymphocyte may play a vital role in the pathogenesis of SLE and organ damage. Also, evaluation of soluble granzyme B may be helpful in monitoring the clinical features associated with activated CTL in SLE.

THEMATIC STREAM: CO-MORBIDITY

BPP7. EFFECT OF ANTI TNF-ALPHA THERAPIES ON INSULIN RESISTANCE, BODY COMPOSITION AND ADIPOKINES IN RHEUMATOID ARTHRITIS PATIENTS

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