DQB1*0301/4, in Malay SLE patients, DRB1*13, DRB3*0301, in Chinese SLE patients, DRB3*0201.

Conclusion These results differ from those obtained in other ethnic groups, i.e. suggesting a different disease pathogenesis.

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THU0008 TNF- α GENE POLYMORPHISM IN SEVERE AND MILD RHEUMATOID ARTHRITIS

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Background TNF- α is thought to be the key driving cytokine in Rheumatoid Arthritis (RA) and recently became a therapeutic target for treatment of patients particularly resistant to conventional therapy. In our study we looked for a genetic background that should indicate some criteria to address RA patients towards more aggressive treatments with anti-TNF- α agents.

Objectives We assessed the role of the -238 and +489 TNF- α gene polymorphisms in a series of patients with severe aggressive disease who were treated with anti-TNF- α therapy because of their poor response to a DMARDs combination strategy. The phenotypes of these patients were compared to those of a cohort of patients who had a good response to Methotrexate (MTX), thus revealing a mild/moderate disease.

Methods One hundred and thirty-eight (138) RA patients and sixty-four (64) controls (Healthy Blood Donors, HBD) entered the study. RA patients were divided into 2 subgroups. Group A: 72 rheumatoids, called MTX-responders (MTX-R), who were in stable partial remission since at least six months after MTX treatment (15 mg/w weekly, range 10–25 mg/w). Stable partial remission was defined when patients had less than 3 swollen joints and a morning stiffness of less than 20'. Group B: 68 rheumatoids with still active disease (more than 6 swollen joints and a morning stiffness of at least 60') despite 6 months of combination therapy (MTX + Sulphasalazine + Hydroxychloroquine or MTX + Cyclosporine, including low doses of prednisone, 5 mg/day). This group subsequently received anti-TNF- α therapy and was labelled as anti-TNF-treated, (TNF-T). Genotyping for -238 and +489 TNF- α polymorphisms was made according to Weiss *et al.*¹ Statistical analyses (Odds Ratio, 95% Confidence Interval) were performed using Prism Software (Graph-Pad, S. Diego, CA 92121-USA).

Results MTX-R had an overall frequency of GG homozygosity for the -238 polymorphism of 91.6% vs 92.2% in HBD, while in TNF-T subgroup the GG genotype had a frequency of 100% (OR = 13, CI = 0.7–240, $p = 0.008$ vs MTX-R). The comparison between TNF-T and HBD is similarly striking (POR = 12, CI = 0.7–230, $p = 0.01$). The major finding concerning the +489 polymorphism is the lower frequency of the AA genotype in RA in general (OR = 4.2, CI = 1–18, $p = 0.01$) and in TNF-T in particular.

Conclusion The GG genotype for the -238 TNF- α polymorphism marks all patients who received anti-TNF- α therapy. This group of patients also showed a significant reduction of the AA genotype of the +489 polymorphism. This latter finding supports the hypothesis that the A allele of the +489 TNF- α

intronic polymorphism is linked to a genetic setting that offers a less aggressive phenotype in RA.

REFERENCE

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THU0009 FIBRONECTIN GENE POLYMORPHISM IN SEVERE AND MILD RHEUMATOID ARTHRITIS

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Background The importance of Fibronectin (Fn) in RA chronic synovial inflammation is increasing. There are at least 6 restriction fragment length polymorphisms (RFLPs) described so far in the Fn gene, but very few is known about their possible functional relevance.

Objectives In this study we assessed the role of the Msp-I Fn gene polymorphism in a series of patients with severe aggressive disease who were treated with anti-TNF- α therapy because of their poor response to a DMARDs combination strategy. The phenotype of these patients were compared to those of a cohort of patients who had a good response to Methotrexate (MTX), thus revealing a mild/moderate disease.

Methods Seventy-nine (79) RA patients and sixty-one (61) controls (Healthy Blood Donors, HBD) entered the study. RA patients were split into 2 subgroups: 57 rheumatoids in stable partial remission (less than 3 swollen joints and a morning stiffness of less than 20') since at least six months after MTX treatment (15 mg/w weekly, range 10–25 mg/w), thus called MTX-responders (MTX-R) and 22 rheumatoids with still active disease (more than 6 swollen joints and a morning stiffness of at least 60') despite 6 months of combination therapy (MTX + Sulphasalazine + Hydroxychloroquine or MTX + Cyclosporine, including low doses of prednisone, 5 mg/day). This latter group received anti-TNF- α therapy and was then labelled anti-TNF-treated (TNF-T). Genotyping for the Msp-I Fn gene polymorphism was made according to Avila *et al.*,¹ who named C the allele resistant to enzyme's digestion and D the variant susceptible. Statistical analyses (Odds Ratio, 95% Confidence Interval) were performed using Prism software (Graph-Pad, S. Diego, CA 92121-USA).

Results MTX-R had an overall frequency of DD homozygosity of 56.1% vs 52.5% in HBD, while in TNF-T subgroup the DD genotype had a frequency of 81.8% (OR = 4.1, CI = 1.2–13, $p = 0.008$ vs HBD). The comparison between TNF-T and MTX-R is similarly striking (OR = 3.5, CI = 1.1–12, $p = 0.01$).

Conclusion The DD genotype for Msp-I Fn gene polymorphism marks the patients who received anti-TNF- α therapy and may lead to a more aggressive phenotype in RA.

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THU0010 VITAMIN D AND OESTROGEN RECEPTOR POLYMORPHISM IN RHEUMATOID ARTHRITIS

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