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Genetic Effects on Leukotriene Production in Aspirin Exacerbated Respiratory Disease

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Background: It is widely known that there have been strong genetic associations with aspirin exacerbated respiratory disease (AERD) development. Leukotriene overproduction is the major feature of AERD. Genetic polymorphisms of CysLTR1 and HLA-DPB1*0301 were associated with the phenotypes of AERD. **Objective:** To investigate the genetic effects on leukotriene production in AERD. **Subjects and Methods:** A total of 95 AERD and 94 aspirin tolerant asthma (ATA) patients were enrolled. Serum samples were collected from all of the study subjects whereas urine samples were collected from 45 AERD and 44 ATA patients when the asthma was stable. The metabolites of LTE4 were analyzed using liquid chromatography with mass spectrometry. HLA-DPB1 high-resolution genotyping wasobtained from direct sequencing method and polymorphism of CysLTR1 was genotyped using SNaP shot ddNTP primer extension kit. **Results:** The frequency of HLA-DPB1*0301 allele was significantly higher in AERD compared with ATA ($p=0.004$, OR=4.178). The TT genotype frequency at CysLTR1 -634C>T is significantly higher in AERD compared to ATA ($p=0.006$, OR=2.891). Serum and urine LTE4 levels were significantly higher in AERD than in ATA (19.10 ± 14.14 pg/mL vs. 13.59 ± 10.10 pg/mL, $p=0.002$; 7.36 ±13.19 pmol/mg creatinine vs. 2.69 ±3.62 pmol/mg creatinine, $p=0.047$, respectively). The levels of urine LTE4 were significantly higher in patients carrying HLA-DPB1*0301 ($p=0.041$), while no differences were found in serum LTE4. The asthmatic patients with the TTgenotype at -634C>T had a significantly higher levels of urine LTE4 ($p=0.015$), but no differences were found in serum LTE4 levels. The levels of urine LTE4 correlated significantly with fall of FEV1% after lysine aspirin bronchoprovocation test (r=0.463, $p=0.008$). **Conclusions:** HLA-DPB1*0301 and genetic polymorphisms of CysLTR1 -634C>T affect cysteinyl leukotriene overproduction which can contribute to develop the phenotypes of AERD.

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Increased basophil activation in adult patients with anaphylaxis

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Introduction: Anaphylaxis is a life-threatening allergic reaction mediated by IgE antibodies that interact with basophils and mast cells to release vasoactive and proinflammatory mediators. We evaluated basophil activation status using CD203c and CD63 expressions in adult patients with anaphylaxis. **Methods:** 41 patients with asthma/rhinitis, chronic urticaria and anaphylaxis and 23 normal controls were recruited and divided into three groups; anaphylaxis (n=13), non-anaphylaxis (n=28) and normal control groups. Basophil CD203c and CD63 expressions were measured by flow cytometry. The whole blood samples were collected and red blood cells (RBCs) were lysed with a RBC lysis buffer. Basophils wereincubated with anti-IgE antibody or calcium ionophore. The resuspended cells were stained with anti-human CD203c or CD63, anti-human CD123, and anti-human human leukocyte antigen-DR, or isotype-matched controls on ice in the dark. **Results:** Baseline expression levels of CD203c and CD63 were higher in the anaphylaxis group than NC group (30.28±23.10 vs 13.76±14.60, $p=0.036$; 17.67±20.48 vs 3.31±3.73, $p=0.028$, respectively) and tended to be higher in anaphylaxis group than in non-anaphylaxis group ($p=0.320$, $p=0.922$, respectively). The positive BAT rates tended to be higher in anaphylaxis group than in non-anaphylaxis group (38.46% vs 17.85%, $p=0.20$), while no differences were noted in CD63 expression levels. **Conclusions:** These findings suggest that increased basal activation status of basophils may contribute to the development of anaphylaxis in adult patients.

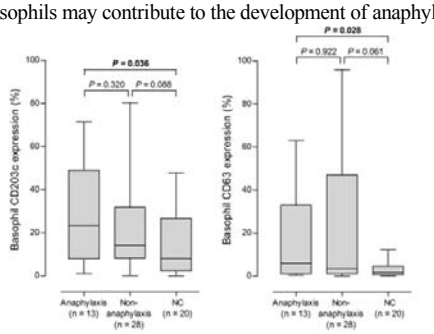

Figure1. Mean percentages of basophil CD203c and CD63 expression (%) at baseline in the anaphylaxis and non-anaphylaxis groups compared to the NC group. *P* values were determined using the Mann-Whitney *U* test.