

Topic 06: Immunogenetic Factors

P06.05

IL-4, IL-10 and TNF- α Promotor Gene Polymorphism in North-Eastern Ukrainian HIV-1 Infected Individuals

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Background: The objective of the research was to study distribution character of the allele variants of IL-4 promoter gene area in position -590, IL-10 in position -592, TNF- α in position -308 in HIV-1 infected Ukrainians of North-Eastern region.

Methods: Data for the study were DNA samples, received from peripheral blood leukocytes of 200 inhabitants of North-Eastern region of Ukraine: 78 HIV-infected, 22-HIV-negative individuals from the group of high risk of contamination, 100 healthy blood donors. Gene polymorphism detection was made with PCR-RLFP method.

Results: IL-4 (rs 2243250), IL-10 (rs 1800872) and TNF- α (rs 1800629) gene polymorphism has been studied for the first time in the population of HIV-infected Ukrainians. By analysis of frequency of IL-4 gene allele variants it has been discovered that homozygotes by the main allele were the dominant variant. It has been found out that among people with HIV there were 9.0 % of T/T minor gene carriers and were 4.5 more often met in comparison with control group ($p < 0.05$) that can prove the tendency to association of the mentioned genotype with infection. Distribution of allele variants of IL-10 gene promoter region in position -592 is characterized by homozygote dominance by the main gene. It has been established that among the individuals with HIV A/A minor allele carriers were 3.4 more often met in comparison with control group ($p < 0.05$). The occurrence of the homozygous combination of the allele variant G/G of the promoter of TNF- α has been shown to prevail almost twofold over the occurrence of the variant G/A among all groups. High frequency of heterozygote by the main allele has been recorded among the individuals with HIV.

Conclusion: Our data suggest that IL-4, IL-10, TNF- α variations may contribute to the acquisition of HIV infection and encourages carrying out of further populations studies in this sphere of HIV-infection immunogenetics.

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Predictors of HVTN 503 MRK AD5 HIV-1 Gag/Pol/Nef Vaccine-Induced Immune Response

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Background: Phambili, the HVTN 503Phase IIb efficacy study of MRK-Ad5 HIV-1 clade B vaccine conducted in South Africa, neither prevented HIV-1 infection nor lowered viral load setpoint. However, immune responses recognizing Clades B and C HIV-1 subtypes were elicited. We investigated predictors of vaccine-induced HIV-1 specific T cell immune responses.

Methods: An analysis of vaccine-induced immunogenicity by interferon- γ ELISPOT assays was conducted on the first 186 enrolled vaccine and placebo recipients four weeks post second vaccination. Descriptive and frequency analysis stratified by study arm and gender were performed on baseline demographics (gender, age, BMI, study site, Ad5 titre, HSV2, circumcision status) and risk behaviours. Multivariate logistic regression determined predictors of immune response to any Clade B or C antigens in the vaccine arm using backward selection. Each analysis was two-sided with 5% level of significance.

Results: Of the 186 participants, 53.7% (n=100) were female, median age was 23 years [IQR:21-27], median BMI was 22.5 [IQR:20.4-27.0], 53.7% (n=100) were from Soweto, 85.5% (n=159) were Ad5-seropositive, 18.8% (n=35) were heavy drinkers; 31.7% (n=59) reported drinking/drug use with sex, 61.3% (n=114) had unprotected vaginal sex and 79% (n=147) reported a main partner. All participants in the vaccine arm (n=93, 50%) developed T cell responses to either Clade B (n=87, 47%) and/or Clade C antigens (n=74, 40%), $p=0.17$. In multivariate analysis, normal/underweight BMI [AOR: 5.926, CI: 1.069-32.84, $p = 0.0417$], female gender [AOR: 0.172, CI: 0.033-0.883, $p=0.0350$], and one-log increase of Ad5 titre [AOR: 0.374, CI: 0.164-0.850, $p=0.0189$] significantly predicted immune response to any Clade C antigens. Heavy drinking [AOR: 0.224, CI: 0.056-0.891, $p=0.0336$] inhibited immune response.

Conclusion: Gender, BMI, Ad5 titre and heavy drinking affected vaccine-induced HIV-1 specific immune responses to Clade C antigens. The role of BMI in blunting these immune responses requires elucidation. Whether these factors affect HIV vaccine efficacy remain to be determined.