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Abstract Topic: - Clinical Genetics

Abstract Title: - In-silico approach to characterise the VDR variants and assess their association with tuberculosis susceptibility in global populations.

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Aims: - To check selection patterns and linkage disequilibrium among four VDR variants in different human populations and to test their association with pulmonary tuberculosis

Methods: - We have characterised the four most potent VDR SNPs in global populations and correlated their frequency with the average number of tuberculosis cases in those populations. The global allele distribution of the four SNPs was created. Linkage disequilibrium maps were made to understand the relation between the SNPs and positive/balancing selection of the SNPs if any. Next median joining networks were synthesised to understand the haplotype diversity of the SNPs in samples of different populations. The minor allele frequency and genotype frequency was calculated for each population and correlated with the average number of tuberculosis cases for the same.

Results: - The linkage disequilibrium pattern is very different in South Asia than West and East Eurasian population. The later populations show high degree of recombination. BsmI (rs1544410), ApaI (rs7975232), TaqI (rs731236), Tru9I(rs757343) gives rise to haplotypes with West Eurasian predominance while the haplotypes without these SNPs are mainly found in East Eurasian populations. Highest 'within population' differences is seen in South Asians whereas least in East Eurasians suggesting higher homozygosity. South Asians share most similarity with West Eurasians and highest dissimilarity with East Eurasians. This is reflected both in Nei's distance and pairwise differences between populations. A negative Tajima's D value for West and East Eurasia indicates a selective sweep but still not conclusive. Only FokI (rs2228570) shows a negative value in South Asian populations. Further, correlation analysis shows no association between the MAF of SNPs and the number of average cases in populations contrary to most studies yet.

Conclusions: - The four SNPs of VDR behave differently in South Asian populations as compared to West and East Eurasian populations but no significant association was found with the incidence of tuberculosis in global populations.

Keywords: - The linkage disequilibrium pattern is very different in South Asia than West and East Eurasian population. The later populations show high degree of recombination. BsmI (rs1544410), ApaI (rs7975232), TaqI (rs731236), Tru9I(rs757343) gives rise to haplotypes with West Eurasian predominance while the haplotypes without these SNPs are mainly found in East Eurasian populations. Highest 'within population' differences is seen in South Asians whereas least in East Eurasians suggesting higher homozygosity. South Asians share most similarity with West Eurasians and highest dissimilarity with East Eurasians. This is reflected both in Nei's distance and pairwise differences between populations. A negative Tajima's D value for West and East Eurasia indicates a selective sweep but still not conclusive. Only FokI (rs2228570) shows a

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