Genetics and biomarkers of headache disorders

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POTENTIAL CANDIDATE GENES FOR CLUSTER HEADACHE INVOLVED IN CA2+ SIGNALING AND T-CELL DIFFERENTIATION

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Introduction: Genetic variants in PCDHB6, PLCE1, ANO3 and ITGAL have been suggested to associate with a positive response to verapamil in migraine patients. Verapamil is a voltage-dependent calcium channel blocker and a potent vasodilating agent commonly used as a preventive treatment also for cluster headache (CH).

Objectives: We are currently investigating these four genes as potential new candidate genes for CH.

Methods: We used TaqMan SNP genotyping to screen four genetic variants in a Swedish CH case-control material consisting of 630 CH patients and 586 controls. 31,9 % of the CH patients were female, the average age of CH patients was 52 years and 10,6 % had a chronic version of the disorder. Around 30% of the patients used Verapamil as a prophylactic treatment. Most of the controls were anonymous blood donors, 39,4% were female. Genotyping was performed on an Applied Biosystems 7500 Fast system, using the recommended TaqMan reagents and genotyping SNP assays: C__32960006_10 for rs17844444, C___1946626_10 for rs10882386, C___1616984_10 for rs1531394 and C__11789692_10 for rs2230433.

Results: Preliminary data indicates that rs1531394 in ANO3 and rs2230433 in ITGAL might be associated with CH in Sweden. The less common genotype of rs1531394 (AA) is more common in the disease group. This difference in genotype distribution is more pronounced when only patients using verapamil are analyzed. The rs1531394 variant is located in the 5'UTR of ANO3 and constitutes an eQTL according to the gtex portal (http://www.gtexportal.org). Also rs2230433, a missense mutation in ITGAL, potentially affects gene expression. rs17844444 which is located in the PCDHB6 gene and rs10882386 in PLCE1 are not associated with CH in the Swedish cohort.

Conclusion: Our data points to ANO3 and ITGAL as two new candidate genes for CH, these genes might provide new insight to the pathophysiological mechanisms of the disorder. ANO3 encodes a Ca2+ activated Cl− channel and ITGAL is membrane protein involved in T-cell differentiation and signaling. We are currently performing more genotyping experiments to verify these data in the entire case-control material. In a later stage we will analyze at the expression of these genes in patient and control derived cell lines and test gene expression correlation with disease and/ or genotype.

Disclosure of Interest: None Declared

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