IDENTIFICATION OF GENETIC PROTECTIVE FACTORS IN CJD AND HEALTHY CARRIERS OF THE E200K PRNP MUTATION

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Introduction: The Glu to Lys change at codon 200 (E200K) of the PRNP gene is a dominant mutation responsible for Creutzfeldt-Jakob disease (CJD), with highly variable expressivity and incomplete penetrance as shown by healthy mutation carriers who do not develop CJD during their lifespan, suggesting the existence of other modulating genetic factors.

Aim: In order to identify possible genetic factors other than PRNP mutations or polymorphisms conferring susceptibility to or modulating the disease, we performed GWAS analyses on E200K CJD patients and healthy relatives from the high risk isolated population of the Calabria cluster.

Methods: GWA assay was performed on 42 E200K mutation carriers (23 CJD patients and 19 healthy relatives) and 32 non-carriers relatives from 15 unrelated pedigrees. Association analyses using Cox regression and logistic regression models were applied.

Results: We identified four SNPs (rs6692559, rs1064395, rs9793471, rs2057680) as candidate modifiers of the phenotypic expression or risk factors for the development of disease.

Conclusions: Our results indicate that genetic factors, other than PRNP gene, may modulate the onset and the progression of disease. Such variants may help to better understand the metabolic pathway regulating the onset and the progression of these disorders and may be the basis for new strategies to modulate CJD onset (if not to prevent it).