COMPLEMENT REGULATOR FACTOR H (FH) LEVELS IN CSF OF MCI CASES DEPEND ON THE Y402H POLYMORPHISM

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Introduction: Age-related macular degeneration (AMD) and Alzheimer's disease (AD) both are age-related and associated with amyloid deposits and complement activation. The Y402H polymorphism in complement regulator factor H (fH) is strongly associated with AMD.

Aim: To determine if fH polymorphisms are a risk factor for AD.

Methods: Probable AD (N=111), MCI (N=53), and age matched control cases (N=34) were recruited at the Alzheimer center of VUmc and clinically diagnosed according to NINCDS-ADRDA (AD) and Peterson (MCI) criteria. The concentration of total fH and the fH-Y402H status in plasma and CSF samples were determined by ELISA (Hakobyan et al, 2008).

Results: Median concentrations of total fH in EDTA-plasma (180, 188 and 172 µg/ml) and CSF (0.70, 0.65 and 0.69 µg/ml in CTL, MCI and AD, respectively) did not differ between groups. Also when separate fH genotypes were compared, no differences in plasma fH values were observed. However, in CSF significant differences between diagnostic groups were observed in the cases with YY402 genotype (p=0.004). No such effect was seen for the HH402 (p=0.706), and HY402 (p= 0.502) genotypes. MCI cases with the YY402 genotype had lower CSF median fH levels (0.46 µg/ml) than CTL (0.72 µg/ml; p=0.005) and AD cases (0.69 µg/ml; p=0.013).

Conclusions: Decreased CSF levels of fH are seen in MCI with the YY402 genotype, not with other genotypes. This may mirror binding of especially the Y402 variant of fH in amyloid deposits, as the fH H402 variant was found to have reduced binding capacity in other studies.