

CD33 and TREM2 peripheral gene expression in relation to cortical thickness

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Background and Hypothesis: Genome-wide association and whole genome sequencing studies have uncovered over 20 novel Alzheimer's Disease (AD) risk genes. Many of these genes are involved with neuroinflammation. Neuroinflammation plays a pivotal role in disease development. *CD33* and *TREM2* are two immune pathway genes implicated in AD. We studied the association between peripheral blood expression of *CD33* and *TREM2*, with cortical thickness – a marker of neurodegeneration in AD. We hypothesized that expression of some these genes would correlate with cortical atrophy in our pooled sample.

Experimental Design or Project Methods: Data from 155 subjects (50 NC and 105 MCI) were gathered from the UCLA ImaGene study. The imaging data was processed using the FreeSurfer 6.0 longitudinal pipeline and cortical anatomy was standardized for all subjects. A GLM analysis using Surfstat investigated the association of gene expression levels in peripheral blood and cortical thickness controlling for age, gender, education, and diagnosis and generated 3D visualization maps of these associations. Statistical significance was determined with p set at 0.05.

Results: *CD33* expression showed a positive correlation with cortical thickness in the right medial, inferior and lateral temporal, lateral parietal, posterior cingulate and inferior lateral frontal cortices. *TREM2* did not show statistically significant association with cortical atrophy.

Conclusion and Potential Impact: Peripheral blood *CD33* expression level seems to be lower in individuals with greater cortical atrophy in AD-relevant areas. This contributes to a growing body of research that indicates a role for the immune system and *CD33* in particular in the pathology of AD and may contribute to future mechanism and biomarker studies.