Immunosuppression in humans with AD

https://neurodegenerationresearch.eu/survey/immunosuppression-in-humans-with-ad/

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Research Abstract

? DESCRIPTION (provided by applicant): Microglial activation is considered to be a primary pathophysiology of Alzheimer’s disease. While the exact outcomes of a microglial response during the disease process remain unclear in humans with AD, it is now evident from genome wide gene association studies as well as other studies that inflammation is a primary factor in neurodegeneration. Data from our mouse model of AD that presents characteristic pathological features of AD including amyloid deposition, disease progression to phosphorylated, aggregated

tau, behavioral changes, and neuronal loss show a complex immune phenotype. Using flow cytometry we have isolated a sub type of CD11c+ microglia associated with areas of neuronal loss from our mouse model. We have used gene screening to identify genes expressed by this cell type and these data clearly indicate an immunosuppressive characteristic reminiscent of monocyte derived suppressor cells (MDSCs). The close regional association of these CD11c+ immunosuppressive microglia and AD pathology in our model suggest a causative role of immunosuppression in AD. A primary mechanism for tissue damage under these conditions is amino acid starvation of surrounding cells caused by the increased consumption of specific amino acids, primarily arginine, methionine and tryptophan. Data from our mouse model supports this hypothesis. In humans with AD, “”activated-disease”” microglia exhibit similar characteristic antigens used to identify immune “”activated-disease”” microglia in mouse brain including CD11c, major histocompatibility complex class 1 and 2 antigens and St6gal1 antigen. Using our mouse model data as a guide and brain autopsied tissue from normal, mild cognitive impairment (MCI), mild and severe AD we will determine if a population of immunosuppressive microglia is found in humans with MCI and if this immuno-phenotype gene expression differs with disease progression. Experiments will be carried out using laser capture microscopy and unbiased gene analysis . If true, this finding will provide a broader understanding of the complexity and timing of immune phenotypes during disease progression in humans with AD and provide insight into novel disease mechanisms. These data may also impact the design and application of anti-inflammatory therapeutics as treatment for individuals with AD

Further information available at:

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