In silico Transcriptomic Analysis of Microglial Cells: Towards a Global Understanding of Immune Activation in Alzheimer's Disease

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Alzheimer's Disease (AD) is a progressive neurodegenerative disease. Patients suffering from this condition exhibit a neuroinflammatory response mediated by microglial cells; this response has been shown to be a major determinant in the pathogenesis and progression of AD. However, the molecular mechanisms underlying immune dysregulation—and the phenotypic activation of microglial cells—remain unclear. The purpose of this research project was to assess how microglial cells change at the transcriptomic level throughout aging under physiological and pathological conditions. Using standardized algorithms, computational analyses were performed on RNA-Seq data retrieved from the Gene Expression Omnibus. The data analyzed corresponded to the microglial transcriptome of WT mice (control samples) and APP/PS1 mice (murine models of AD). Through these analyses, sets of differentially expressed genes were identified. These genes were either differentially expressed throughout physiological or pathological aging, or between healthy and unhealthy aged samples. Further, using computational tools such as STRING and Cytoscape, analyses were performed to evaluate how the proteins encoded by these differentially expressed genes interact with each other, and to determine whether any of these proteins may play a key role in the adoption of a microglial proinflammatory phenotype. An integrative mechanism involving the identified proteins of interest was proposed, and pathways were suggested from which this mechanism could lead to the development of the neuroinflammatory response present in AD. Multiple pathways were implicated in the recruitment of T lymphocytes, therefore suggesting an important role of the peripheral immune system in the neuroinflammatory response present in AD.

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