The Cross-Application of Oxidative Stress Conceptualizations to Inflammatory Microglia's Role in Neurological Diseases for Candidate Drug Discovery

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According to the United Nations, about 1 in 6 of the world’s population suffers from neurological conditions. Microglia within the brain, aggravated by amyloidosis, serve as reactive oxidative species (ROS) generators, perpetuating a state of oxidative stress (OS) and damaging neurological functions, leading to conditions like dementia. Disease-associated microglia (DAM) and (OS) are pathological hallmarks of several neurodegenerative diseases; however, they haven’t been clinically proven to be effective drug targets as the molecular mechanisms haven’t been well-defined. Pharmaceutical discovery in Alzheimer’s focuses on amyloid and tau pathology when finding the proximity of drug targets and the genes associated with amyloid and tau. However, drugs that otherwise would not have been identified as possible treatments because of the focus on amyloid and tau can now be considered as candidates by creating disease modules based on DAM and OS pathology, where drugs associated with other neurological diseases, like glioma, can be considered for Alzheimer’s as they share the trait of OS. First, a human interactome is selected for the disease module. A list of genes associated with DAM and OS is created through the NCBI database, then cross-checked with the interactome. A permutation test is conducted for the significance of the module to the interactome. Then, a list of possible drug candidates associated with Alzheimer’s is selected and processed through R for proximity analysis and statistical significance.

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