The role of cellular senescence in the pathology of Alzheimer's disease

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Introduction

One possible mechanism that may be common to all age-related diseases in general and neurodegenerative diseases specifically is cellular senescence (CS). CS (from Latin: senescere, meaning "to grow old") is a state in which cells cease to divide and undergo many morphological and functional changes[1]. Among the changes is the senescence associated secretory phenotype (SASP) which includes pro-inflammatory cytokines[1]. Senescent cells have been shown to accumulate with age[1] and to disrupt tissue morphology and function and clearance of senescent cells was found to attenuate age-related diseases[2]. Alzheimer's disease (AD) is the most common type of dementia and its most common risk factor is aging[5]. It is characterized by the accumulation of extra and intracellular amyloid beta (Aβ) depositions and neurofibrillary-tangles (NFTs)[5]. Moreover, there is a gradual decline in the number of neurons[5]. The role of CS has been shown in many age-related diseases, such as cancer and type 2 diabetes[1], but there is little data regarding cellular senescence and its role in neurodegenerative diseases, such as AD.

Working hypothesis

We postulate that CS accelerate neurodegeneration, Aβ pathology and cognitive deficits and that inhibition of cellular senescence will attenuate disease progression. We aim to assess the changes in CS levels during the progression of AD and to identify specific cellular mechanism that affiliated with CS. Our results will increase the knowledge in the etiology of AD and may suggest a new target for therapeutic intervention.

References

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