

Health & Physiology

The power of our adaptive immunity against Alzheimer's Disease

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One of the fears that arise with ageing is being afflicted with dementia. [Alzheimer's disease](#) (simply "Alzheimer" from now onwards) is the most common type of dementia worldwide, representing up to 60% of total cases of dementia in western countries. Alzheimer is a serious world-health threat that involves 5.2 million of patients only in the United States. Furthermore, due to the increasing average age within modern societies, the number is predicted to rise in the future. Since multiple causes lead to the onset of the disease, Alzheimer is called multifactorial disease. The scientific community considers the involvement of our [innate immune system](#) as part of such multiple causes. As a matter of fact, during the early stage of the disease, the chronic activation of [microglia cells](#) causes neuronal cell damage that, in turn, leads to dementia. Microglia are innate immune cells important for the clearance of pathogens, defending the brain environment. In Alzheimer's patients, microglia cells are not able to perform their job properly, promoting the accumulation of a misfolded protein known to be the sadly-famous marker of this disease: the beta-amyloid protein. Due to that, the chronic inflammation that follows within the brain, leads to neuronal damage that culminates with the shrinking of the brain.

Innate immunity rarely works independently of adaptive immune response. [Adaptive immunity](#) represents the second line of defence and its special power resides in the ability to memorise different types of pathogens. Such "memory" activates a more potent immune response during the second encounter with the same pathogen. The so-called "memory cells" are the main players of this mechanism - which

is the basis of vaccines. In order to test whether or not adaptive immunity is also involved in the onset of Alzheimer, Marsh and colleagues generated a mouse strain affected by Alzheimer, called Rag-5xfAD, lacking the key cells involved in adaptive immune response (natural killer (NK), B and T cells). When the researchers compared Rag-5xfAD with another mouse strain that equally shows Alzheimer but possesses all immune cells (WT-5xfAD), they observed an increment in the total amount of beta-amyloid plaques. Moreover, the researchers found that this increase in beta-amyloid plaques was due to a defect in their clearance instead of an increment in their production. Indeed, they showed that the absence of adaptive immune cells leads to an even more impaired ability of microglia in maintaining the level of beta-amyloid plaques low. Interestingly, Marsh and collaborators prove that this more pronounced inability of microglia was caused by the absence of immunoglobulin G (IgG) in the brain. IgG is a molecule, produced by microglia cells, that recognises foreign particles, dead cells and misfolded protein to help their removal from our organism. In this study, the researchers found that IgG helps microglia in the clearance of beta-amyloid plaques. In fact, the injection in the brain of non-specific IgG molecules efficiently reduces the number and the size of beta-amyloid plaques in Rag-5xfAD mice. Furthermore, the reacquisition of the adaptive immune cells, by bone marrow transplantation, improves beta-amyloid clearance in Rag-5xfAD mice.

Marsh et al. added a new piece to the puzzle of the Alzheimer's picture. The researchers proposed a role for the adaptive

immune cells in the clearance of beta-amyloid, whose accumulation causes brain damage. These peripheral immune cells can produce IgG molecules, which then accumulate in the brain through a still unknown mechanism, and improve microglia activity. The use of IgG in the clinic to cure Alzheimer has already been tested in humans, with a reported decrease in number and size of beta-amyloid plaques, but without any improvement in cognitive functions, meaning that further studies are still needed to further understand the molecular mechanism behind this disease.