GSC Advanced Research and Reviews

eISSN: 2582-4597 CODEN (USA): GARRC2

Cross Ref DOI: 10.30574/gscarr

Journal homepage: https://gsconlinepress.com/journals/gscarr/

(REVIEW ARTICLE)

Check for updates

Immune Modulation in Alzheimer's Disease via Allergy-Cascade Activation

Michael John Dochniak *

Alleamit™ Corporation, Minnesota, United States of America.

GSC Advanced Research and Reviews, 2026, 26(01), 162-165

Publication history: Received on 08 December 2025; revised on 12 January 2026; accepted on 15 January 2026

Article DOI: https://doi.org/10.30574/gscarr.2026.26.1.0017

Abstract

Alzheimer's disease is increasingly recognized as a disorder of chronic, maladaptive neuroinflammation driven by persistent microglial activation, Th1/Th17 immune polarization, and blood–brain barrier dysfunction. Therapeutic strategies targeting amyloid-β or tau alone have yielded limited clinical success, suggesting that downstream immune dysregulation plays a central role in disease progression. This review proposes a theoretical immunotherapeutic framework in which the Alleamit™ Immune Modulation Platform leverages-controlled activation of the allergy cascade to redirect immune polarity from neurotoxic Th1/Th17 pathways toward reparative Th2 and regulatory immune states. Recent breakthroughs in protein structure prediction enable the design of highly specific antigens, enabling patient-specific allergens to be engineered based on individual biomarker profiles while minimizing autoimmune risk. The review outlines how immunoglobulin-E-mediated mast cell activation, Th2 cytokine signaling (IL-4, IL-13), and Treg induction may promote microglial repolarization, enhance amyloid clearance, and suppress neuroinflammatory feedback loops. This speculative framework integrates established immunology and neuroinflammation biology with advances in computational protein folding to present a testable hypothesis for personalized immune redirection in Alzheimer's Disease.

Keywords: Allergy cascade; Alzheimer's disease; Immune modulation; Microglia; Precision antigens; Th2 polarization

1. Introduction

Alzheimer's disease (AD) is the leading cause of dementia worldwide and remains without a disease-modifying therapy. While amyloid-β (Aβ) plaques and tau neurofibrillary tangles have long been recognized as pathological hallmarks of AD, accumulating evidence now implicates chronic neuroinflammation as a central driver of neurodegeneration [1-3]. Activated microglia, infiltrating T cells, and sustained cytokine production converge to drive synaptic loss, neuronal injury, and progressive cognitive decline [4-6].

Immune profiling of AD patients and animal models reveals a predominance of Th1 and Th17 responses, characterized by elevated levels of IFN-γ, IL-17, and TNF-α [7–9]. These pro-inflammatory pathways promote an M1-like microglial phenotype that exacerbates both amyloid deposition and tau pathology [10]. In contrast, Th2 cytokines such as IL-4 and IL-13 induce a reparative, phagocytic microglial state and significantly improve cognitive outcomes in preclinical models [11,12].

This review advances the hypothesis that AD is, in part, a disease of immune polarity misalignment, and that deliberate immune redirection—rather than broad immune suppression—may represent a transformative therapeutic paradigm. It is proposed that the Alleamit™ IM Platform, augmented by AI-driven protein-folding technologies, could enable precision induction of the allergy cascade to reprogram neuroimmune dynamics and alter the disease trajectory in AD.

* Corresponding author: Michael John Dochniak.

2. Neuroimmune Pathophysiology of Alzheimer's Disease

2.1. Th1/Th17 Dominance and Neurotoxicity

Multiple studies demonstrate that Aβ-specific Th1 cells exacerbate microglial activation and plaque burden via IFN-γ signaling [9]. Th17 cells further contribute to neuronal injury through IL-17–mediated oxidative stress and apoptosis [8]. These adaptive immune responses amplify innate neuroinflammation, creating a self-reinforcing degenerative loop.

2.2. Microglial Priming and Plasticity

Microglia in the aging and AD brain exhibits a primed state, responding to stimuli with exaggerated inflammatory output [4]. Importantly, microglial phenotypes are plastic. IL-4 and IL-13 signaling through STAT6 promotes an alternative (M2-like) phenotype associated with debris clearance, neurotrophic support, and resolution of inflammation [11,13].

2.3. Mast Cells and Immune Gateways to the CNS

Mast cells reside in meningeal and perivascular regions of the CNS and act as immune sentinels at the blood–brain interface [14]. While excessive mast cell activation may worsen neuroinflammation, controlled activation can produce cytokines and regulatory mediators that skew Th2 responses [15]. This duality positions mast cells as potential modulators rather than purely pathogenic actors.

3. The Allergy Cascade as an Immune Redirection Strategy

3.1. Canonical Features of the Allergy Cascade

The allergy cascade is defined by IgE class switching, mast cell and basophil activation, and Th2 cytokine production (IL-4, IL-5, IL-13). Importantly, Th2 responses exert antagonistic control over Th1/Th17 differentiation [16]. This immune competition suggests a mechanism by which allergic signaling could suppress neurotoxic immunity.

3.2. Evidence for Th2-Mediated Neuroprotection

Direct administration of IL-4 and IL-13 into AD mouse models reduces Aβ accumulation and improves cognitive performance by inducing $Arg1^+$ microglia [11]. Additionally, regulatory T cells expanded under Th2-biased conditions suppress microglial inflammation and restore immune homeostasis [17].

4. Immune Modulation Platform

4.1. Conceptual Overview

Alleamit's IM Platform [21] is based on controlled induction of atopy to redirect immune metabolism and signaling. Rather than suppressing immunity, the platform seeks to outcompete pathogenic immune programs by activating the allergy cascade through antigen-specific activation.

4.2. Precision Antigen Design via Protein Folding Breakthroughs

Recent advances in protein structure prediction (e.g., AlphaFold) enable high-confidence modeling of antigen–antibody and T-cell receptor interactions [18,19]. In this framework, patient-specific biomarkers—such as cytokine profiles, HLA type, autoantibody repertoires, and inflammatory signatures—inform the design of custom antigens that preferentially induce IgE-mediated Th2 responses while minimizing Th1 activation. Such precision design reduces the risk of epitope spreading or autoimmune exacerbation and allows immune modulation to be tailored to individual disease endophenotypes.

5. Therapeutic Strategy

5.1. Step 1: Cytokine evaluation and treatment to promote Th2 expression

• Administration of cytokine treatment includes intravenous (IV) infusion and subcutaneous (SC) injection. The specific administration method, frequency, and dosage depend heavily on the type of cytokine (or cytokine inhibitor) being used and the patient's individual health status.

5.2. Step 2: Sensitization phase

- Topical or transdermal hyperallergenic composition applied over a period to initiate Type-1 hypersensitivity.
- Monitor IgE titers specific to chosen allergens to safely maintain a Type l hypersensitivity.

6. Proposed Mechanism of Action in Alzheimer's Disease

It is hypothesized that Alleamit-designed antigens would:

- · Induce IgE-mediated mast cell activation, generating IL-4 and IL-13.
- · Shift adaptive immunity toward Th2 and Treg phenotypes, suppressing Th1/Th17 signaling.
- · Repolarize microglia from an M1-like inflammatory state to an M2-like reparative state.
- · Enhance amyloid clearance and synaptic preservation, reducing neurodegenerative momentum.

This mechanism represents immune redirection, not immune suppression.

7. Biomarker-Guided Personalization

AD is immunologically heterogeneous. Stratification based on inflammatory biomarkers (e.g., IL-17/IL-10 ratios, microglial activation markers, genetic risk variants) would enable selection of appropriate antigen constructs and dosing regimens. Such personalization aligns with precision medicine paradigms already employed in immunotherapy [20].

8. Challenges and Considerations

Potential challenges include excessive mast cell activation, blood–brain barrier disruption, and systemic allergic reactions. These challenges underscore the necessity of controlled dosing, rigorous antigen design, and preclinical validation. Importantly, this review does not propose immediate clinical application but rather a testable theoretical framework.

9. Conclusion

Alzheimer's disease may be amenable to immune polarity reprogramming through controlled activation of the allergy cascade. By integrating Alleamit's IM Platform with AI-driven protein folding for precision antigen design, it may be possible to redirect neuroimmune signaling toward repair rather than degeneration. While speculative, this framework is grounded in established immunology and neuroinflammation research and warrants systematic experimental investigation.

Compliance with ethical standards

Acknowledgments

Michael John Dochniak (Co-Founder) of Alleamit Corporation, Minnesota, and the United States of America.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Author Profile

Michael John Dochniak has authored several books on Alzheimer's disease, Artificial Intelligence, Autism Spectrum Disorders, and Climate Change through Cambridge Scholars Publishing and Nova Science Publishers.

References

[1] Heneka MT, Carson MJ, El Khoury J, Landreth GE, Brosseron F, Feinstein DL, Jacobs AH, Wyss-Coray T, Vitorica J, Ransohoff RM, Herrup K, Frautschy SA, Finsen B, Brown GC, Verkhratsky A, Yamanaka K, Koistinaho J, Latz E, Halle A, Petzold GC, Town T, Morgan D, Shinohara ML, Perry VH, Holmes C, Bazan NG, Brooks DJ, Hunot S, Joseph

B, Deigendesch N, Garaschuk O, Boddeke E, Dinarello CA, Breitner JC, Cole GM, Golenbock DT, Kummer MP. Neuroinflammation in Alzheimer's disease. Lancet Neurology. 2015;14(4):388-405.

[2] Ransohoff RM. How neuroinflammation contributes to neurodegeneration. Science. 2016; 353(6301):777-83.

[3] Leng F, Edison P. Neuroinflammation and microglial activation in Alzheimer disease: where do we go from here? Nature Reviews Neurology. 2021;17(3):157-172.

[4] Li Q, Barres BA. Microglia and macrophages in brain homeostasis and disease. Nature Reviews Immunology. 2018;18(4):225-242.

[5] Heppner FL, Ransohoff RM, Becher B. Immune attack: the role of inflammation in Alzheimer disease. Nature Reviews Neuroscience. 2015;16(6):358-72.

[6] Hansen DV, Hanson JE, Sheng M. Microglia in Alzheimer's disease. Journal of Cell Biology. 2018; 217(2):459-472.

[7] Zhang J, Ke KF, Liu Z, Qiu YH, Peng YP. Th17 cell-mediated neuroinflammation is involved in neurodegeneration of aβ1-42-induced Alzheimer's disease model rats. PLoS One. 2013; 8(10): e75786.

[8] Browne TC, McQuillan K, McManus RM, O'Reilly JA, Mills KH, Lynch MA. IFN-γ Production by amyloid β-specific Th1 cells promotes microglial activation and increases plaque burden in a mouse model of Alzheimer's disease. Journal of Immunology. 2013;190(5):2241-51.

[9] McManus RM, Heneka MT. Role of neuroinflammation in neurodegeneration: new insights. Alzheimer's Research and Therapy. 2017;9(1):14.

[10] Keren-Shaul H, Spinrad A, Weiner A, Matcovitch-Natan O, Dvir-Szternfeld R, Ulland TK, David E, Baruch K, Lara-Astaiso D, Toth B, Itzkovitz S, Colonna M, Schwartz M, Amit I. A Unique Microglia Type Associated with Restricting Development of Alzheimer's Disease. Cell. 2017;169(7):1276-1290.e17.

[11] Kawahara K, Suenobu M, Yoshida A, Koga K, Hyodo A, Ohtsuka H, Kuniyasu A, Tamamaki N, Sugimoto Y, Nakayama H. Intracerebral microinjection of interleukin-4/interleukin-13 reduces β-amyloid accumulation in the ipsilateral side and improves cognitive deficits in young amyloid precursor protein 23 mice. Neuroscience. 2012; 207:243-60.

[12] Town, T., Tan, J., Flavell, R.A. *et al.* T-cells in Alzheimer's disease. NeuroMolecular Medicine. 2005;7, 255–264.

[13] Cherry, J.D., Olschowka, J.A. & O'Banion, M.K. Neuroinflammation and M2 microglia: the good, the bad, and the inflamed. 2014. Journal of Neuroinflammation. 11, 98.

[14] Dong H, Zhang X, Qian Y. Mast cells and neuroinflammation. Medical Science Monitor Basic Research. 2014; 20:200-6.

[15] Sayed BA, Christy A, Quirion MR, Brown MA. The master switch: the role of mast cells in autoimmunity and tolerance. Annual Review of Immunology. 2008; 26:705-39.

[16] Abbas AK, Lichtman AH, Pillai S, Henrickson S. Cellular and Molecular Immunology*.* 11th ed. Elsevier; 2025.

[17] Faridar A, Thome AD, Zhao W, Thonhoff JR, Beers DR, Pascual B, Masdeu JC, Appel SH. Restoring regulatory T-cell dysfunction in Alzheimer's disease through *ex vivo* expansion. Brain Communication. 2020; 2(2): fcaa112.

[18] Jumper J, Evans R, Pritzel A, Green T, Figurnov M, Ronneberger O, Tunyasuvunakool K, Bates R, Žídek A, Potapenko A, Bridgland A, Meyer C, Kohl SAA, Ballard AJ, Cowie A, Romera-Paredes B, Nikolov S, Jain R, Adler J, Back T, Petersen S, Reiman D, Clancy E, Zielinski M, Steinegger M, Pacholska M, Berghammer T, Bodenstein S, Silver D, Vinyals O, Senior AW, Kavukcuoglu K, Kohli P, Hassabis D. Highly accurate protein structure prediction with AlphaFold. Nature. 2021;596(7873):583-589.

[19] BioRxIV [Internet] Protein complex prediction with AlphaFold-Multimer. Available from https://www.biorxiv.org/bioRxiv.

[20] Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. Nature Medicine. 2019;25(1):44-56.

[21] Dochniak MJ. Topical hyper-allergenic composition and method of treating using the same. USPTO 11,911,463. 02/27/2024.