Advances in APOE-Targeted Therapies for Alzheimer's Disease: A Comprehensive Review of Current Research

Xuanhui Quan
Suzhou Foreign Language School, Suzhou, Jiangsu, China

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Abstract: Alzheimer's disease (AD), the leading cause of dementia, is characterized by amyloid-beta (Aβ) plaques, tau tangles, neuroinflammation, and lipid imbalances, with the APOE4 allele being a major genetic risk factor. Recent therapeutic advances include APOE4-targeted strategies such as small molecules, CRISPR-Cas9 gene editing, and immunotherapies, alongside monoclonal antibodies that reduce Aβ plaques but pose safety risks. Lipid nanoparticles (LNPs) enhance drug delivery, while anti-inflammatory approaches and lipid regulators address multiple pathways. However, no therapy fully cures AD, and challenges like low gene-editing efficiency limit clinical translation. This review analyzes APOE4's role in AD pathology and evaluates therapies targeting Aβ, tau, inflammation, and lipid metabolism. Findings reveal monoclonal antibodies offer short-term cognitive benefits with safety trade-offs, lipid regulators show broader mechanistic potential, and neuroinflammation strategies integrate drug and lifestyle interventions. Combined approaches, such as Aβ clearance with lipid restoration, demonstrate cooperative promise. This article emphasizes APOE4's centrality and advocates for personalized therapies based on genetic profiles. Future research could prioritize optimizing gene-editing systems, refining the delivery efficiency of LNPs, and investigating synergistic interactions between neuroinflammation and lipid metabolism. These directions can advance multi-target therapeutic strategies, offering innovative approaches to address fundamental mechanisms in AD.

1 INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the most common cause of dementia worldwide, accounting for approximately 60 to 80 percent of all dementia cases associated with aging (Pires & Rego, 2023). It is characterized by neurodegeneration, neural loss, neurofibrillary tangles (NFTs) and amyloid-beta (Aβ) plaques accumulation(Srivastava, et al., 2021). Among the growing number of genetic risk factors for AD discovered, the apolipoprotein E (APOE) gene including ε2 allele, ε3 allele and ε4 allele has been the most predominant, as the cause of over half of AD patients. People with the ε4 allele of the APOE gene have a higher likelihood of being susceptible to AD, whereas the ε2 allele reduces the risk of AD, and the ε3 allele has no significant influence on AD (Pires & Rego, 2023).

Researchers have developed innovative small molecules and peptides to target APOE4's detrimental effects in AD. For instance, CBA2 as a small molecule has been shown to modulate lipid metabolism and enhance APOE-mediated Aβ clearance, reducing amyloid plaque formation and improving cognitive function in preclinical models (Balasubramaniam, et al., 2024). Similarly, APOE-mimetic peptides have demonstrated potential in reducing Aβ aggregation and tau pathology in animal models. APOE-mimetic peptides similarly reduce Aβ aggregation and tau tangles, confirming APOE4's role in driving AD progression (Ahmed, et al., 2022).

Researchers used CRISPR-Cas9 delivered via Synthetic Exosomes (SEs) to edit ApoE4 to ApoE3 in an AD mouse model, achieving 0.14% editing in the brain and confirming functional ApoE3 mRNA expression (Teter, et al., 2024; Hanafy, et al., 2020). This proof-of-concept demonstrates the feasibility of gene editing for APOE4-related risk reduction, though higher efficiency is needed for clinical translation.

Immunotherapy targeting APOE4 has shown promise in AD treatment. For example, HAE-4, an APOE4-specific antibody, reduces Aβ plaques and tau pathology in preclinical models by blocking

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APOE4's harmful interactions (Lemprière, 2021). These findings validate APOE4 as a druggable target for slowing AD progression.

Lipid nanoparticles (LNPs) have emerged as a promising drug delivery system for targeting AD pathology, particularly due to their ability to cross the blood-brain barrier (BBB) without requiring functionalization. Their small size and lipid-based nature make them highly biocompatible and efficient for delivering therapeutic agents to the brain. LNPs, including liposomes, niosomes, and nanostructured lipid carriers (NLCs), can be produced at scale, offering a practical solution for large-scale therapeutic applications (Chakraborty, et al., 2024). LNPs efficiently transport drugs like CRISPR components or lipid regulators to the brain, with scalable production methods supporting future clinical use (Lu, et al., 2021).

This article aims to review the pathological mechanisms of AD related to the APOE4 allele, including its role in A β aggregation, tau pathology, neuroinflammation, and lipid metabolism disruption. It evaluates the efficacy of APOE-targeted therapies, aiming to identify more promising strategies. The study not only highlights innovative therapeutic approaches but also deepens the understanding of APOE's role in neurodegeneration, offering hope for millions of patients worldwide.

2 MECHANISM

2.1 Amyloid Hypothesis

Amyloid precursor protein (APP) as a transmembrane protein is located in the cell membrane of neurons in the brain, and its function is to help repair damaged neurons. It is usually cleaved by the beta site APP cleaving enzyme 1 (BACE1) and γ -secretase. Under physiological conditions, BACE1 cleaves APP at the extracellular N-terminal domain, releasing a soluble fragment (sAPP β) and leaving a 99-amino acid membrane-bound C-terminal fragment (CTF) C99. This process is followed by γ -secretase, which is a multi-subunit protease complex containing presenilin, nicastrin, PEN-2, and APH-1. This secretase cleaves C99 to different-length A β peptides, primarily A β 40 and A β 42, within its transmembrane region. With a long term, the aggregation of A β leads to A β plaques forming. These plaques clump around neurons and can block neuron communication. Hence, brain cells gradually cannot send signals, leading to AD (Hampel, et al., 2021; Neaţu, et al., 2024).

2.2 Tau Protein Hypothesis

Tau hypothesis explains how changes in Tau protein in the brain lead to AD. Normally, Tau helps keep brain cells healthy by supporting microtubules, which help transport nutrients and signals, inside nerve cells. Tau protein attaches to these microtubules, and a process controlled by chemical changes like adding or removing phosphate groups after the protein is made. However, in AD, too many phosphate groups are added to Tau, resulting in hyperphosphorylation. This happens when enzymes that add phosphates (like GSK-3 β) become overactive, while enzymes that remove phosphates do not work well. The extra phosphate groups change the shape of Tau protein and charge, making it separate from microtubules. Without the support of Tau, the microtubules break down, disrupting nutrient transport in nerve cells. Freed Tau proteins then clump together, and then first form oligomers that damage connections between brain cells and mitochondria. Over time, these clumps grow into twisted fibers and finally form NFTs inside brain cells. These NFTs are a key sign of AD and are linked to brain cell death and memory loss (Wegmann, et al., 2021; Zhang, et al., 2024).

2.3 Neuroinflammation Hypothesis

The neuroinflammation hypothesis explains how long-term brain inflammation causes AD. Microglia, the brain's immune cells, normally protect the brain by cleaning up harmful proteins like A β . However, when people age, these cells become less efficient and start releasing harmful chemicals like IL-1 β and ROS that damage brain cells. A β proteins activate a dangerous protein complex called NLRP3, which makes A β clump together faster and harms connections between nerve cells. Aging also weakens microglia's ability to clean up waste, making inflammation worse. In addition, there are other factors that exacerbate inflammation. Genes like APOE4 increase A β accumulation and inflammation, and senescent cells release toxic chemicals that keep inflammation active. Hence, this creates a cycle that inflammation damages neurons, which releases more toxins, causing more inflammation. The neuroinflammation gradually causes neuron damage and synaptic loss (Maylin, et al., 2023; Zhang, et al., 2024).

2.4 Lipid Metabolism Hypothesis

The lipid metabolism hypothesis explains how imbalances in brain fats contribute to AD. The blood-brain barrier (BBB) typically blocks large lipoproteins like LDL and VLDL, as well as free fatty acids (FFAs), from entering the brain. However, aging, genetic factors (e.g., APOE4), and environmental stressors such as hypertension and trauma can weaken the BBB. When they are compromised, the BBB allows lipoproteins containing ApoB and FFAs to infiltrate the brain, disrupting normal lipid regulation by astrocytes. Excess cholesterol from peripheral lipoproteins interferes with neuronal cholesterol balance. While astrocytes usually provide cholesterol through HDL-like particles, an overload of LDL triggers β- and γ-secretase activity, increasing Aβ production. This cholesterol buildup can also encourage Aβ aggregation and tau hyperphosphorylation, leading to NFT formation (Estes, et al., 2021). Additionally, FFAs enter the brain as monomers through a weakened BBB and overstimulate TLR4 and extrasynaptic GABAA receptors, contributing to neuroinflammation, memory impairment, and oxidative stress. APOE4 further worsens lipid accumulation and promotes BBB damage, intensifying neurodegeneration (Rudge, 2023).

These four hypotheses collectively explain AD through interconnected mechanisms. While amyloid plaques and tau tangles directly damage neurons, chronic neuroinflammation and lipid imbalances accelerate neurodegeneration. Although these hypotheses focus on different pathways, they likely interact synergistically – Aβ and tau abnormalities may trigger inflammation, while lipid disorders worsen amyloid and tau pathologies. Understanding these connections helps develop multi-target therapies, such as reducing Aβ production, blocking tau phosphorylation, controlling microglial activation, and restoring lipid balance to protect brain function.

3 TREATMENT

3.1 Protein Regulation

Current therapeutic approaches for AD focus on modulating enzymatic activity to reduce Aβ accumulation. Key targets include BACE1 and γ-secretase, enzymes critical for Aβ generation. BACE1 inhibitors were designed to block the initial cleavage step in Aβ formation. For instance, LY2886721 demonstrated efficacy in lowering Aβ levels in cerebrospinal fluid (CSF) but was withdrawn due to hepatotoxicity. Subsequent candidates, including atabecestat, elenbecestat, and umibecestat, faced challenges in clinical trials with limited BBB permeability and off-target interactions caused by structural similarities between BACE1 and other aspartyl proteases. These issues hindered their therapeutic potential. Similarly, γ-secretase inhibitors (GSIs) aimed to suppress Aβ production but exhibited adverse effects by disrupting Notch signaling, a pathway vital for cellular homeostasis. Although avagacestat selectively reduced Aβ without Notch interference, trial discontinuation occurred due to toxicity in gastrointestinal and skin tissues. To address this, γ-secretase modulators (GSMs) emerged as an alternative strategy, adjusting enzyme activity to decrease toxic Aβ42 isoforms while maintaining physiological functions. Promising GSM candidates such as SGSM-36 and EVP-0962 showed selective Aβ42 reduction but did not advance to clinical use. Despite extensive research, no protein-targeted therapy has achieved regulatory approval for AD (Zhang, et al., 2023).

3.2 Monoclonal Antibodies (mAbs)

MAbs represent a promising therapeutic approach for AD, focusing on neutralizing pathological Aβ aggregates to slow disease progression. Two notable examples, lecanemab and donanemab, demonstrate distinct mechanisms of action, pharmacokinetic profiles, and clinical outcomes. Lecanemab (BAN2401) is a humanized monoclonal antibody that selectively binds soluble Aβ species, including oligomers and protofibrils, while sparing monomeric and insoluble fibrillar forms. By interacting with the N-terminal region (amino acids 1–16) of Aβ, it facilitates the removal of protofibrils from the brain and cerebrospinal fluid (CSF). Unlike many mAbs, lecanemab does not exhibit target-mediated drug disposition (TMDD), likely because its primary targets are localized within the brain. Pharmacokinetic studies report a half-life of approximately 9.5 days, shorter than typical antibodies. In clinical trials, lecanemab slowed cognitive decline and reduced amyloid plaques, leading to its accelerated FDA approval in January 2023 for mild cognitive impairment (MCI) and early-stage AD. Donanemab (LY3002813) distinguishes

itself by targeting the N-terminal pyroglutamate-modified Aβ epitope, a structural feature exclusive to aggregated amyloid plaques. This specificity allows it to effectively clear existing plaque deposits and delay functional and cognitive deterioration. Pharmacokinetic analyses indicate a half-life of about 11.8 days, with drug clearance influenced by body weight—higher elimination rates occur in individuals with greater body mass. Additionally, donanemab reduces plasma levels of phosphorylated tau (P-tau217), a biomarker strongly associated with AD pathology. However, its use carries an elevated risk of amyloid-related imaging abnormalities (ARIA), particularly in patients with the APOE ε4 genetic variant, necessitating careful clinical monitoring. Both antibodies demonstrate efficacy in reducing amyloid burden and slowing disease progression in early AD. Lecanemab's action on soluble aggregates contrasts with donanemab's focus on plaque removal, offering complementary strategies for Aβ clearance. Key differences in pharmacokinetics—such as half-life and weight-based clearance patterns—highlight the importance of individualized dosing. Safety remains a critical concern, as both therapies are linked to ARIA, a side effect involving brain swelling or microhemorrhages. Risk factors, including APOE ε4 carrier status, must guide patient selection and monitoring protocols (Neaţu, et al., 2024).

3.3 Lipid Metabolism Regulation

Recent therapeutic strategies targeting lipid metabolism show potential in AD management. Dietary approaches, particularly omega-3 fatty acids like DHA and EPA, may reduce AD-related cognitive decline by supporting brain function. Statins, which is commonly used to lower cholesterol, demonstrate additional benefits in AD models by reducing brain inflammation and improving cognitive performance. For instance, atorvastatin was found to enhance memory in AD mice by influencing TLR4 signaling pathways, which interact with TREM2—a protein critical for lipid processing in brain immune cells. Research highlights abnormal cholesterol storage in microglia lacking functional TREM2, a genetic risk factor in some AD cases. Inhibiting acetyl-CoA acetyl transferase 1 effectively reduces these cholesterol deposits, suggesting a treatment avenue for TREM2-related dysfunction. While TREM2 mutations are rare, its activity is interconnected with other AD-associated genes like APOE and TYROBP, implying broader relevance for lipid-focused therapies. Notably, correcting lipid imbalances through TREM2-related pathways could benefit AD patients regardless of specific genetic mutations. Combining cholesterol regulation with anti-inflammatory interventions may address multiple AD mechanisms simultaneously (Estes, et al., 2021). These findings emphasize lipid metabolism as a key area for developing targeted AD treatments, offering hope for both genetic and sporadic forms of the disease.

3.4 Control of Neuroinflammation

Emerging therapies targeting neuroinflammation offer new hope for AD treatment. Recent failures of anti-amyloid and anti-tau therapies highlight the urgency for alternative approaches. Modulating microglia—the brain's immune cells—has shown particular promise. Depleting dysfunctional microglia with CSF1R inhibitors reduces amyloid plaques, protects neural connections, and improves memory in AD mice. Conversely, boosting microglial activity using TREM2-activating antibodies like AL002a enhances plaque clearance and cognitive outcomes. Suppressing harmful inflammation pathways represents another strategy. Natural substances such as pterostilbene and sulforaphane block NLRP3 inflammasome activation, reducing brain inflammation and cognitive decline. Similarly, β-hydroxybutyrate, a ketone metabolite, combats oxidative stress by activating Nrf2 while inhibiting NLRP3 and NF-κB. Targeting the P2X7 receptor, which drives amyloid-induced NLRP3 activation, has also proven effective. Experimental drugs like brilliant blue G disrupt Aβ-triggered inflammation and memory loss in animal studies, though better brain penetration is needed for clinical use. Dietary interventions complement pharmacological efforts. Vitamin D, plant-based foods, and culturally diverse diets like the Multicultural Healthy Diet correlate with slower cognitive decline. These combined strategies underscore the dual potential of drug-based and lifestyle interventions to control neuroinflammation in AD (Liu, et al., 2023). While challenges remain in optimizing drug delivery, focusing on inflammatory mechanisms provides a multifaceted framework for tackling this complex disease.

4 EVALUATION

Current approaches for AD management exhibit distinct advantages and limitations based on their mechanisms and clinical applicability. MAbs, such as lecanemab and donanemab, represent the most advanced strategies with demonstrated efficacy in early-stage AD. Lecanemab selectively neutralizes soluble Aβ oligomers, slowing cognitive decline by 27% over 18 months, while donanemab accelerates plaque clearance by targeting pyroglutamate-modified Aβ. However, both therapies carry significant risks, including amyloid-related imaging abnormalities (ARIA) in up to 35% of APOE ε4 carriers, necessitating rigorous safety monitoring. Their short half-lives (9.5–11.8 days) and high costs further limit accessibility, and neither halts neurodegeneration in advanced disease stages (Neaţu, et al., 2024).

In contrast, protein regulation therapies targeting Aβ production through BACE1 or γ-secretase inhibition face persistent challenges. Early BACE1 inhibitors reduced Aβ levels but were discontinued due to hepatotoxicity and poor blood-brain barrier penetration. GSMs showed selectivity in reducing toxic Aβ42 isoforms but failed to achieve clinical relevance due to modest efficacy and unresolved safety concerns (Zhang, et al., 2023). While these approaches directly address Aβ overproduction—a core AD pathology—their lack of specificity disrupts vital pathways like Notch signaling, leading to systemic toxicity.

Strategies focusing on lipid metabolism regulation offer broader mechanistic benefits. Omega-3 fatty acids (DHA/EPA) and statins like atorvastatin improve synaptic function and reduce neuroinflammation via TLR4/TREM2 pathways. Inhibiting acetyl-CoA acetyltransferase 1 resolves cholesterol accumulation in TREM2-deficient microglia, presenting a targeted repair mechanism. However, lipid therapies face variability in patient responses; statins may induce muscle toxicity or cognitive side effects in elderly populations, and TREM2-focused interventions remain experimental for non-mutation carriers (Estes, et al., 2021).

Neuroinflammation control approaches, including microglial modulation and inflammasome suppression, address multiple AD pathways. Depleting dysfunctional microglia with CSF1R inhibitors restores cognition in preclinical models, but risks over-suppressing brain immunity. Natural NLRP3 inhibitors (e.g., sulforaphane) and P2X7R antagonists reduce inflammation yet struggle with bioavailability. Dietary interventions, though safer, lack standardized protocols for consistent cognitive benefits (Liu, et al., 2023). While these methods synergistically target plaques, oxidative stress, and inflammation, long-term microglial manipulation may impair neural repair, and inflammasome drugs require enhanced brain delivery systems (Liu, et al., 2023).

Overall, mAbs provide the clearest short-term clinical benefits but with safety trade-offs. Protein regulation therapies, despite their conceptual appeal, are hampered by toxicity and specificity issues. Lipid and neuroinflammation strategies, though mechanistically versatile, demand refinement for reliability. Future advancements may lie in combining Aβ-targeting agents with metabolic and anti-inflammatory interventions, tailored to genetic profiles (e.g., APOE ε4 or TREM2 status) to optimize efficacy and minimize risks. Such integrated approaches could address AD's multifactorial nature more comprehensively than single-target therapies.

5 CONCLUSION

AD is a complex neurodegenerative disorder driven by interconnected mechanisms, including Aβ plaque accumulation, tau protein hyperphosphorylation, neuroinflammation, and lipid metabolism disruption. The APOE4 allele plays a central role in exacerbating these pathologies, as a critical therapeutic target. Current strategies, such as mAbs, show clinical promise by reducing Aβ burden and slowing cognitive decline in early-stage AD, but have safety risks like amyloid-related imaging abnormalities and limited accessibility due to high costs. Other approaches, including protein regulation and lipid metabolism interventions, face issues such as toxicity, poor specificity, or variable patient responses. Neuroinflammation control through microglial modulation or NLRP3 suppression offers multi-target benefits but requires optimization for brain delivery and long-term safety.

The findings underscore the importance of APOE4 in AD progression and validate innovative therapies like CRISPR-Cas9 gene editing, APOE-specific antibodies, and LNPs for targeting APOE4-related pathways. These advancements focus on understanding APOE4's multifaceted role and developing multi-mechanism treatments. By addressing the four hypotheses, these strategies

provide a foundation for future research to explore synergistic interactions between AD pathways and refine personalized therapeutic approaches.

Despite progress, current research has limitations. Most studies rely on preclinical models that may not fully replicate human AD complexity, particularly regarding genetic diversity and disease progression. MAbs, while effective, are restricted to early-stage AD and pose safety risks for APOE4 carriers. Protein-targeting drugs often lack specificity, leading to systemic side effects. Lipid and neuroinflammation therapies, though mechanistically versatile, lack standardized protocols and long-term efficacy data. Additionally, the interplay between AD hypotheses, such as how lipid imbalances influence tau phosphorylation or neuroinflammation, remains underexplored. Few studies test combination therapies, which could address AD's multifactorial nature more effectively.

Moving forward, research should prioritize enhancing drug delivery systems, such as optimizing LNPs for brain penetration or improving CRISPR-Cas9 editing efficiency in vivo. Personalized therapies based on APOE or TREM2 genotypes could improve efficacy while minimizing side effects. Investigating combination therapies, like pairing A β -targeting antibodies with anti-inflammatory agents or lipid regulators, may yield synergistic effects. Further exploration of lipid metabolism's role in neuroinflammation and tau pathology could uncover novel therapeutic targets. Clinical trials should adopt diverse cohorts and long-term follow-ups to assess real-world outcomes. By integrating genetic, molecular, and lifestyle factors, future studies may unlock transformative AD treatments that halt or reverse neurodegeneration.

REFERENCES

Ahmed, S., Pande, A. H., & Sharma, S. S. 2022. Therapeutic potential of ApoE-mimetic peptides in CNS disorders: Current perspective. Experimental Neurology, 353, 114051.

Balasubramaniam, M., Jagadeesh Narasimhappagari, Liu, L., Akshatha Ganne, Srinivas Ayyadevara, At-luri, R., Haarika Ayyadevara, Caldwell, G., Shmookler, R. J., Barger, S. W., & Griffin, S. T. 2024. Rescue of ApoE4-related lysosomal autophagic failure in Alzheimer's disease by targeted small molecules. Communications Biology, 7(1).

Chakraborty, B., Patel, G., Bandana Padhan, Das, J., & Patel, M. 2024. Evolution of lipid nanoparticles as charioteers of Alzheimer's disease therapeutics. Applied Materials Today, 41, 102442–102442.

Estes, R. E., Lin, B., Khera, A., & Davis, M. Y. 2021. Lipid Metabolism Influence on Neurodegenerative Disease Progression: Is the Vehicle as Important as the Cargo? Frontiers in Molecular Neuroscience, 14.

Hampel, H., Hardy, J., Blennow, K., Chen, C., Perry, G., Kim, S. H., Villemagne, V. L., Aisen, P., Vendruscolo, M., Iwatsubo, T., Masters, C. L., Cho, M., Lannfelt, L., Cummings, J. L., & Vergallo, A. 2021. The Amyloid-β Pathway in Alzheimer's Disease. Molecular Psychiatry, 26(10).

Hanafy, A. S., Schoch, S., & Lamprecht, A. 2020. CRISPR/Cas9 Delivery Potentials in Alzheimer's Disease Management: A Mini Review. Pharmaceutics, 12(9), 801.

Lemprière, S. 2021. Antibody targets apolipoprotein E to remove amyloid-β deposits. Nature Reviews Neurology, 17(4), 194–194.

Liu, Y., Si, Z.-Z., Zou, C.-J., Mei, X., Li, X.-F., Luo, H., Shen, Y., Hu, J., Li, X.-X., & Wu, L. 2023. Targeting neuroinflammation in Alzheimer's disease: from mechanisms to clinical applications. Neural Regeneration Research, 18(4), 708.

Maylin Wong-Guerra, Calfío, C., Maccioni, R. B., & Rojo, L. E. 2023. Revisiting the neuroinflammation hypothesis in Alzheimer's disease: a focus on the druggability of current targets. Frontiers in Pharmacology, 14.

Neațu, M., Covaliu, A., Ioniță, I., Jugurt, A., Davidescu, E. I., & Popescu, B. O. 2024. Monoclonal Antibody Therapy in Alzheimer's Disease. Pharmaceutics, 16(1), 60.

Pires, M., & Rego, A. C. 2023. Apoe4 and Alzheimer's Disease Pathogenesis-Mitochondrial Deregulation and Targeted Therapeutic Strategies. International Journal of Molecular Sciences, 24(1), 778.

Rudge, J. 2023. The Lipid Invasion Model: Growing Evidence for This New Explanation of Alzheimer's Disease. Journal of Alzheimer's Disease, 94(2), 457–470.

Srivastava, S., Ahmad, R., & Khare, S. K. 2021. Alzheimer's disease and its treatment by different approaches: A review. European Journal of Medicinal Chemistry, 216, 113320.

Teter, B., Campagna, J., Zhu, C., McCauley, G. E., Spilman, P., Kohn, D. B., & John, V. 2024. Successful Gene Editing of Apolipoprotein E4 to E3 in Brain of Alzheimer Model Mice After a Single IV Dose of Synthetic Exosome-Delivered CRISPR. BioRxiv (Cold Spring Harbor Laboratory).

Wegmann, S., Biernat, J., & Mandelkow, E. 2021. A current view on Tau protein phosphorylation in Alzheimer's disease. Current Opinion in Neurobiology, 69, 131–138.

Zhang, J., Zhang, Y., Wang, J., Xia, Y., Zhang, J., & Chen, L. 2024. Recent advances in Alzheimer's disease: Mechanisms, clinical trials and new drug development

strategies. Signal Transduction and Targeted Therapy, 9(1).

Zhang, Y., Chen, H., Li, R., Sterling, K., & Song, W. 2023. Amyloid β-based therapy for Alzheimer's disease: challenges, successes and future. Signal Transduction and Targeted Therapy, 8(1), 1–26.