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UNDERSTANDING THE CELLULAR LINKS BETWEEN ALLERGY, AUTOIMMUNITY, AND NEURODEGENERATION TO DEVELOP SMART ANTI-INFLAMMATORY DRUGS

Razia Iqbal[*1], Shahid Mahmood[*2], Shumaila Aslam[3], Noor Ul Ain Mansha[4], Zainab Shakeel[5], Malaika Kiran[6]

[*1,2,3,4,5,6] *Department of Zoology, University of Gujrat, Gujrat 50700, Pakistan*

[*1]razia.iqbal@uog.edu.pk, [*2]shahid.mahmood@uog.edu.pk

Corresponding Author: *
Razia Iqbal,
Shahid Mahmood

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ABSTRACT

This review article aims to examine the shared mechanisms of allergic inflammation, autoimmune diseases, and neurodegenerative diseases. These three diseases have long been treated as separate entities, but it has been realized recently that they are part of a unified inflammatory response mediated by certain master regulators such as NF-KB, the inflammasome NLRP3, and the JAK/STAT pathway. The sources point to an essential change in pharmacological approaches, which is to abandon broad-spectrum immunosuppressant like corticosteroids to favor more "smart" or highly specific agents able to interfere with particular signaling pathways or to reactivate the neuro-immune conversation. The emerging therapeutic strategies include the use of monoclonal antibodies such as anti-IL-6, anti-IL-17, small kinase inhibitors like JAK, Syk, and BTK inhibitors, as well as the application of Artificial Intelligence to carry out virtual screenings to find Multi-Target Directed Ligands (MTDLs).Furthermore, the review identifies the "resolution deficit" in chronic inflammation as a critical therapeutic target, suggesting that novel drugs mimicking endogenous mediators like resolving and protecting may offer more effective cures with fewer side effects than traditional suppression. Despite all these advances, challenges persist. The process of clinical translation often faces hurdles, such as systemic toxicity, e.g., hepatotoxicity of the initial NLRP3 inhibitors, as well as the increased risk of severe infections and sepsis with blockade of cytokines In addition, the so-called "translational gap" between the efficacy of animal models and the complexity of human genetic diseases, e.g., "missing heritability" and the "two-hit model" of human disease manifestation, still persists. The review concludes that the future of anti-inflammatory medicine lies in the predictive/personalized medicine paradigms of HLA/MHC targeting and AI-assisted drug design to achieve maximum efficacy with a superior safety profile.

Keywords: *NLRP3 inflammasome, Neuro-immune axis, Phytochemicals, Translational gap, AI-driven drug, Inflammatory resolution.*

1. INTRODUCTION

An activation of immune system to ordinarily inconsequential things which include dust, pollen, food protein, or medication is called an allergy. Type 2 immune responses activate when the immune system mistakenly recognizes them as

threat (Gao et al., 2025). Acute allergic reaction has been triggered by IgE, mast cell, and basophil which release histamine and lead to sign like swelling and mucus production (Valenta et al., 2022). Chronic allergic reaction is marked by tissue remodeling, cytokine release (IL-4, IL-5, and IL-13), and persistent eosinophilic infiltration (Gao et al., 2025). Mast cells, basophils, eosinophils, and innate lymphoid cells are essential immune responses (Galli et al., 2023). Cytokine dysregulation, Treg dysfunction, abnormalities in the epithelial barrier, allergies and autoimmunity may overlap pathways which raise the risk of chronic inflammation (Akdis & Akdis, 2024).

Loss of immune tolerance leads to immune system to attack self-tissues, causing organ damage and chronic inflammation. Rheumatoid arthritis, lupus, and type 1diabetes are typical examples (Rosenblum et al., 2023). Inflammation is maintained by cytokine dysregulation that is influenced by both hereditary and environmental variables (McInnes & Schett, 2023).

Th17 cells, b cells which generate autoantibodies, dendritic cells that carry antigens, and regulatory T cells that maintain balance make the immune cells involved. When these regulatory mechanisms fail, disease occur (Bluestone et al., 2024). Through the NF-KB, JAK/STAT, and MAPK pathway, significant pro-inflammatory cytokines consisting of TNF-a, IL-1b, IL-6, and IFN-y generate tissue damage (Lawrence, 2023). In accordance to (McInnes & Schett, 2023) allergic and autoimmune diseases share immune dysregulation, cytokine network, and overlapping cellular pathway, demonstrating similar therapeutic targets.

On the basis of neuroinflammation during the spectrum of neurodegenerative diseases; mechanism and therapeutic frontiers, neuroinflammation, the CNS immune system response, can arise from either acute protective reactions or chronic dysregulation (Heneka et al., 2024). Pro-inflammatory cytokines which include IL-1β, IL-6, TNF-α, and chemokines are emitted by microglia, astrocyte, neurons, and peripheral immune cells, and neural damage is accelerated by oxidative stress and mitochondrial dysfunction (Cryan et al., 2024). Due to systemic immune disorders CNS inflammation become severe which involve autoimmunity and allergies (Becher et al., 2023). Peripheral and central immune signals are connected by gut microbiota dysbiosis, peripheral and immune signals connected which leads to chronic neuroinflammation and blood-brain barrier damage (Cryan et al., 2024). Diseases such as Alzheimer's, Parkinson's, ALS, Huntington's disease, and multiple sclerosis all depend on these mechanism (Heneka et al., 2024). Conventional anti-inflammatory medication which includes steroids, NSAIDs, and biologics reduce inflammation have adverse effects and also promote systemic immunosuppression. They are not able to completely alleviate chronic pain or residual cardiovascular risk (Libby, 2024).

By concentrating on certain cell, cytokines, or pathways, such as the NLRP3 inflammasome, innate immune components, or the IL-1β → IL-6 → HSCRP cascade, Precision medicine facilitates specialized and efficient treatment (Neurath, 2024). The actually example of smart therapeutic includes Biologics (anti-TNF, anti-il-6, anti-IL-12/23), nano particle-based drug delivery with ROS, NIR-responsiveness, small-molecule inhibitors for ROS and inflammasome modulation (Gold & Gebhart, 2023; Shi et al., 2023). The main advantages are reduced the systematic adverse effect, better result of autoimmune, neurological, cardiovascular and chronic disorder, and it also enhance life quality (Neurath, 2024). AI-assisted nanomedicine design and personalized therapy through multi-omics integration indicate significance value in future prospects for save and predictive targeted treatment (Shi et al., 2023).

An important factor in allergy, autoimmune, and neurological illness is chronic inflammation. In accordance with current research these conditions might have correspond immune mechanism, such as immune cell activation, cytokine dysregulation, and inflammatory signaling pathways (Shi et al., 2023). However, commonly used anti-inflammatory medication, such as NSAIDs and steroid, frequently produce systemic side effect and do not target disease pathways specifically (Libby, 2024). Therefore, developing more

accurate and potent smart anti-inflammatory treatment requires a knowledge of molecular connection shared by these disorders.

This review aims to explore the cellular and molecular mechanism that connect allergic inflammation, autoimmune responses, and neuroinflammation. It focuses on identify the key immune cells, cytokine, and signaling pathways that are shared across these conditions and contribute to chronic inflammation. Another objective is to evaluate current and emerging targeted anti-inflammatory therapies, including biologics, nanomedicine-based drug delivery systems, and small molecule inhibitors that specifically regulate inflammatory pathways. In addition, the review seeks to highlight the potential pf precision medicine approaches, such as multi-omics analysis and personalized inflammatory profiling, to support the development of smart anti-inflammatory drugs with improved efficacy and fewer systemic side effect.

2. Cellular and molecular interconnection

Interconnection signaling pathways that include JAK/STAT, NF-KB, and MAPK cellular responses in inflammation, immunity, and diseases through converting extracellular signals into intercellular actions which influence gene expression, proliferation, differentiation and survival (Hu et al., 2023).

2.1 Shared Signaling Pathway

NF-KB Pathway: Nearly all cell types are associated with the transcription factor NF-KB, which governs the formation of inflammatory genetic material, apoptosis, and the cell cycle. NF-KB is necessary for trigging inflammatory reactions in immune cell when pathogens or cytokines are recognized. It regulates the transcription of inflammatory genes, which include interferon-stimulated genes, chemokines, and cytokines. The three fundamental pathways of NF-KB signaling are canonical, non-canonical and a typical. These pathways react to TNF receptor activation, inflammatory stimuli, and cellular stress, respectively. NF-KB interacts with cellular stress responses, such as UV radiation and reactive oxygen species, which connect stress signaling to the activation of inflammatory genes (Lawrence, 2023).

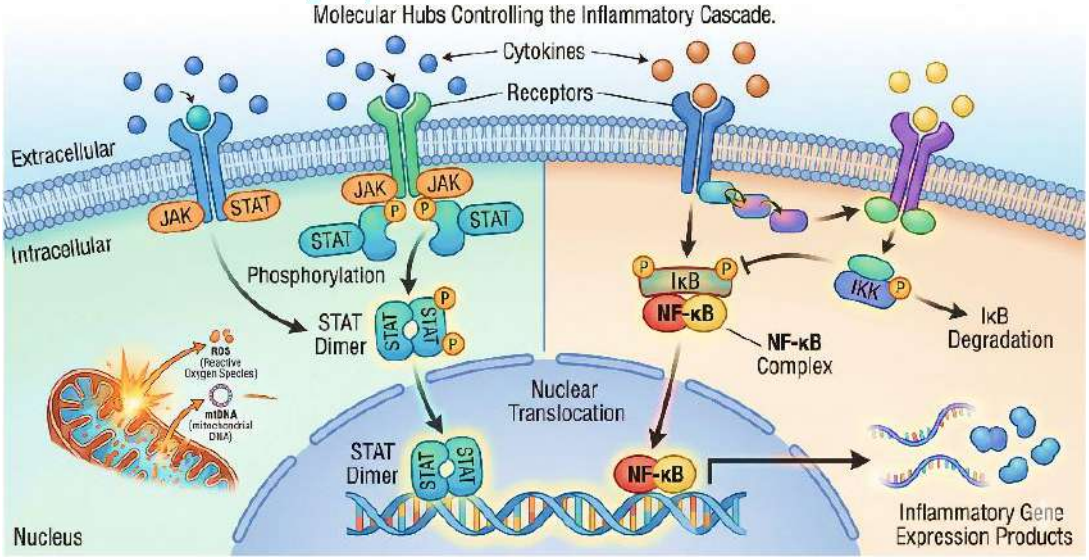

Figure 01. Molecular Hubs Controlling the Inflammatory Cascade.

JAK/ATAT Pathway: It regulates gene expression, cell proliferation, differentiation, and immune system functions by relaying extracellular cytokine and growth factor signals. In order to manage target genes, activation begins by initiating cytokine-receptor binding followed by JAK phosphorylation, STAT docking and dimerization, and nuclear translocation. There is

numerous cytokine-JAK-STAT combination. For example, IFN-α/β activates STAT1/2 via JAK1/TYK2, whereas IL-6 activates STAT1/3 via JAK/JAK2/TYK2. Integrated intracellular signaling is demonstrated with crosstalk with other signaling pathways as MAPK and PI3K/ATK. Overactivation can be prevented by negative regulation by means of SOCS and PIAS proteins (Hu et al., 2023). Coordinated cellular responses to cytokines and stress have been emphasized by the JAK/STAT pathway are associated with MAPK signaling. Signaling (Hu et al., 2023). Reactive oxygen species, mitochondrial dysfunction and ion balance are example of cellular stress that stimulate molecular pathways, such as NF-KB and MAPK that control inflammasome assembly and inflammatory responses in neurons (Heneka et al., 2024).

2.2 The Role of Mast cell, T cells, and Microglia

Hematopoietic stem cell in the bone marrow give rise to the mast cell, which are specialized tissue-resident immune cells that move as progenitors to tissues which involve the skin, lungs, and airways where they finish developing (Ghalya H. Banafea et al., 2022). They express a variety of receptors, including as the high-affinity IgE receptors, toll-like receptors, and cytokines/chemokines receptors allowing them to respond quickly to allergens infections and tissue injury. Mast cell release histamine, protease, proteoglycans, lipid mediators, cytokines, and chemokines, when cells degranulate in response to allergens (Ghalya H Banafea et al., 2022.) These mediator link innate and adaptive immunity in allergic inflammation by promoting bronchoconstriction, airways remodeling, mucus synthesis, and the recruitment of additional immune cells such as T cells and innate lymphoid cells. Mast cells have dual regulatory role in tissue homeostasis and inflammation is highlighted by their protective capabilities, such as PGE2-mediated degranulation. (Ghalya H Banafea et al., 2022).

As demonstrated in rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis, T cells produce autoimmunity by autoreactive effectors responses, releasing cytokines that directly damage tissues or enhance inflammation (Bulliard et al., 2024). Remission and immune system are supported by the growth and variety of circulating regulatory T cells following hematopoietic stem cell transplantation, which modify this response by inhibiting pathogenic Tand B cells activity (Bulliard et al., 2024). By limiting effectors T cell activation and removing autoreactive B cells, therapeutic approaches that targets T cells, such as CTLA4-Ig and CAR-T/Treg therapy, seek to restore immunological homeostasis (Bulliard et al., 2024). Common to all immune cells, signaling pathways including JAK-STAT, NF-KB, and MAPK control T cell mediated autoimmunity and are important targets for precision treatment (Lawrence, 2023).

In conditions like Alzheimer's, Parkinson's and multiple sclerosis, chronic microglial activation causes synaptic dysfunction, neural death, and CNS inflammation. Their interaction with T cells and systemic immunity connects neuroinflammation to peripheral autoimmune processes (Heneka et al., 2024).

2.3 Cytokine Crosstalk

Cytokine interaction between TNF-a, IL-4, and IL-17 is essential for bridging the process of autoimmunity, tissue repair, and allergies. The signature type 2 cytokines, IL-4, and IL-13, play a key role in allergic inflammation by stimulating eosinophil recruitment and activation. At the same time, they orchestrate tissue repair by polarizing macrophage which inhibit neutrophils recruitment and reduce production of proinflammatory cytokines and creating a favorable environment for regeneration (Allen, 2026). On the other hand, IL-17 which is primarily produced by TH17 cells and innate immune sources that is the powerful proinflammatory mediator that increase local inflammation and mobilizes neutrophils. This is important for pathogen defense and it also cause tissue damage in autoimmune and chronic inflammation (Precision Anti-Inflammatory Therapies 2026). TNF-a and IL-17 work together to increase production of inflammatory cytokines by structural cells such as fibroblast and endothelial cells, which connect systematic

inflammatory responses to autoimmunity-driven tissue damage (Allen, J. 2026).

Crucially, IL-4and IL-13 counteract the tissue damaging effect of TNF-a and IL-17, in part by reorienting macrophage metabolism toward against-mediated pathways and oxidative phosphorylation which lowers the production of nitric oxide and reactive oxygen species ROS. While promoting collagen synthesis and cell proliferation, which are vital for wound healing. (Nanomedicines for Inflammation, 2026). It offering prompt defense against infection and IL-4/IL-13 encourage tissue regeneration and inflammation resolution, this dynamics interaction generates that immune response is precisely calibrated (Allen, 2026). By selectively blocking IL-17 and TNF-a to regulate pathological inflammation while preserving IL-4/IL-13 mediated repair process, modern precision-targeted therapies take advantages of crosstalk, undercrossing the clinical significance of cytokine interaction in complex diseases setting (Nanomedicine for Inflammation, 2026). Furthermore, IL-4/IL-13 driven repair mechanism frequently coincide with allergic reaction, showing that type 2 cytokine supports both the regeneration of tissue damaged by neutrophil-driven inflammation and protective inflammation in context allergen exposure (Nanomedicine for Inflammation, 2026).

Table 01. Shared Immune Mediators in Allergy, Autoimmunity, and Neurodegeneration

Mediator/Cell	Role in Allergy	Role in Autoimmunity	Role in Neurodegeneration	Key References
Mast Cells	Primary triggers; release histamine and proteases, causing mucus secretion and edema.	Linked to dural activation and inflammatory signaling in conditions like MS.	Early responders that enhance BBB permeability and detect amyloid plaques.	Galli & Tsai (2012); Dantzer (2018); Aman et al. (2021)
T Cells	Th2 cells drive IgE production and promote eosinophil recruitment.	Autoreactive effectors (Th1/Th17) that cause direct damage to self-tissues.	Infiltrate the CNS to exacerbate pathology via autoantibody production.	McInnes & Schett (2017); Katsnelson et al. (2023)
TNF-α	A pro-inflammatory cytokine released during both acute and chronic phases.	Key driver in RA and Lupus; a major target for modern biologic therapies.	Released by activated glia; leads to oxidative stress and neuronal loss.	Galli & Tsai (2012); McInnes & Schett (2017); Aman et al. (2021)
IL-4 / IL-13	Signature Type 2 cytokines that orchestrate allergic inflammation.	Inhibit neutrophils and promote macrophage polarization for tissue repair.	Orchestrate repair processes and counteract damage from TNF-α/IL-17.	Katsnelson et al. (2023); McInnes & Schett (2017)
NLRP3 Inflammasome	Can be activated by allergic stress, environmental triggers, or alarmins.	Triggers production of Type 1 Interferons in SLE and RA pathogenesis.	Central hub in Alzheimer's; triggered by ROS and mitochondrial DNA.	Aman et al. (2021); McInnes & Schett (2017); van Dyck et al. (2023)

2.4 Mitochondrial Dysfunction; A cellular driven for stress, inflammation, and aging

Mitochondrial damage contributes to the underlying causes of many illnesses and serves as a key cellular driver that links oxidative stress, inflammation, and aging. The mitochondrial respiratory chain is a major source of ROS, especially at complexes I and III where electron leakage generates superoxide and hydrogen peroxide. According to (Xu et al., 2025) under normal circumstances, ROS are neutralized by antioxidant systems like as glutathione peroxide, superoxide dismutase, and peroxiredoxins. However, excessive ROS production overwhelms these defenses, resulting in oxidative stress that destroys protein, lipids, DNA and RNA. Additionally, this oxidative stress stimulates the production of DAMPs, including mtDNA, which in turn activate downstream inflammatory pathways and activate NLRP3 inflammasome. Mitochondrial dynamics control the distribution and quality of mitochondria; an imbalance in these processes result in cellular dysfunction, impaired bioenergetics, and fragmentation or hyper fusion of mitochondria (Xu et al., 2025).

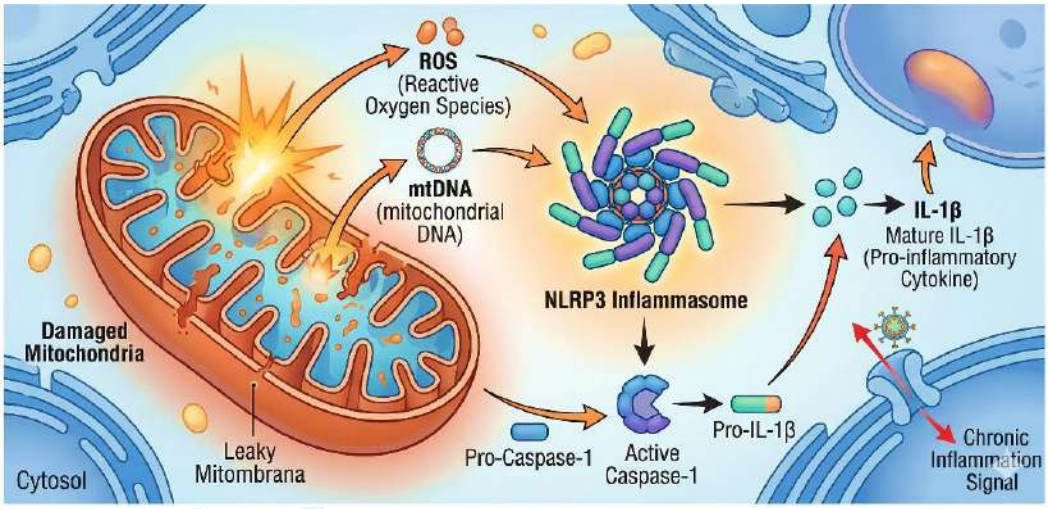

Figure 02. Mitochondrial Dysfunction as a Driver of Chronic Inflammation.

Disease is driven by mitochondrial dysfunction through metabolic reprogramming in immune cells, especially myeloid population. According to (Kaplan et al., 2025) Mitochondrial stress increases cytosolic and mitochondrial ROS cause release of mtDNA via VDAC oligomerization and triggers pathways which result production of type 1 interferon in SLE and RA. These pathways disturb homeostasis and encourage prolonged inflammation. (Kaplan et al., 2025).

Mitochondrial dysfunction effect both aging and Neurodegeneration. According to (Li et al., 2024). ROS buildup, poor energy metabolism and senescence are caused by an age-related decrease in mitophagy, the accumulation of mtDNA mutation, and change dynamics.

A proinflammatory secretory profile (SASP) is linked to senescent phenotype, which further connects inflammation with aging. In accordance to this ROS from damage mitochondria stabilize HIF-1α, which improves glycolysis, cytokines synthesis and immune cell survival under stress. Thereby perpetuating chronic inflammation (Zhang et al. 2022) cells, microglia, detect neuronal stress and tissue damage, in response, they activate the NF-KB, MAPK, and inflammasome pathways, releasing cytokines, chemokines, and reactive oxygen species that cause neurodegeneration (Neuronal inflammasomes overview, 2024).

3. Allergy and Neurodegeneration

The concept of a dynamic Brain-Allergy Axis has supplanted the conventional view of the brain as an immunologically privileged site. According to recent studies, peripheral allergic inflammation is

not limited to local tissues but rather functions as a persistent "low-grade" inflammatory stimulus that has a major impact on the health of the central nervous system by activating the neuro-immune unit (Pahwa et al., 2021). There are three main ways that allergic signal are sent to the brain:

The Humoral Pathway: Transport proteins or leaky areas like the circumventricular organs can allow systemic Th2 cytokines like Interleukin-4, Interleukin-5, and Interleukin-13 to pass through the Blood-Brain Barrier (BBB) (Pahwa et al., 2021).

The Neural Pathway: (Vagus Nerve): Allergic inflammation in the lungs or gut stimulates the vagus nerve's sensory fibers, which send inflammatory signals straight to the brain, activating microglia without requiring cytokines to physically enter the brain (Dong et al., 2023).

Meningeal Lymphatics: Recently identified lymphatic vessels in the meninges allow allergic immune cells, such as Th2 cells, to monitor the central nervous system (CNS) and may cause neuroinflammation when dural mast cells are activated (Kempuraj, Dourvetakis et al. 2024).

The gatekeepers of the brain-allergy axis are mast cells, or MCs. MCs, which are found on the brain side of the BBB, release proteases, histamine, and vascular endothelial growth factor (VEGF) in response to systemic IgE. This primes adjacent microglia and astrocytes in addition to increasing BBB permeability. These cells cause oxidative stress and neuronal death when they are activated, releasing pro-inflammatory mediators like TNF-α (Kempuraj, Dourvetakis et al. 2024). According to recent research conducted in 2025, the dopaminergic neuronal loss observed in Parkinson's disease models is preceded by this MC-driven neuroinflammation (Zheng et al., 2025).

Alarmins, like Thymic Stromal Lymphopoietin and Interleukin-33. Which are generally linked to asthma, are now understood to be important CNS players. Under normal circumstances, IL-33 produced by astrocytes in the brain preserves synaptic plasticity. On the other hand, excessive Microglial Phagocytosis of healthy synapses is triggered by an excess of IL-33 during chronic allergy, a process associated with early-stage Alzheimer's disease (Mercan and Heneka 2022). According to Wang et al. (2025), chronic allergic signaling causes microglia to adopt a pro-inflammatory phenotype, which impairs phagocytic clearance and causes amyloid-β to accumulate.

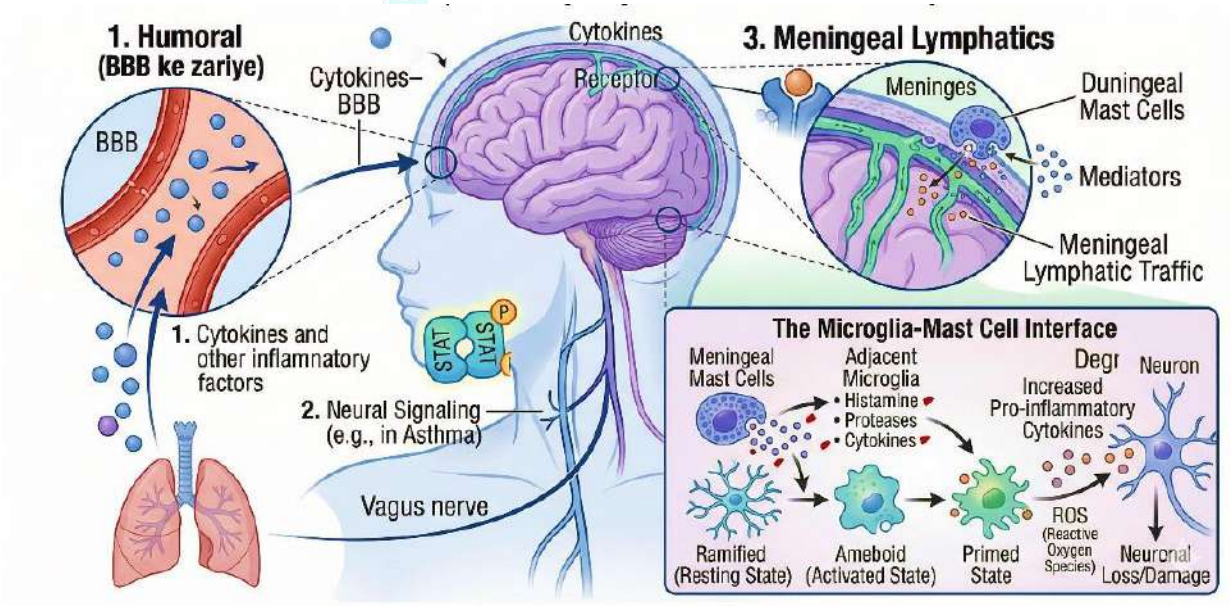

Figure 03. Transmission of Peripheral Allergic Signals to the Central Nervous System.

Innate Immune Memory is a novel idea in the research era of 2024–2026. Myeloid progenitor cells may experience epigenetic changes (such as DNA methylation) as a result of long-term allergic exposure. Later, these trained cells migrate to the brain as macrophages, where they worsen the pathology of neurodegenerative diseases by exhibiting a hyper-inflammatory response to small stimuli (Miller & Ross, 2026). This intersection emphasizes the need for smart anti-inflammatory medications to target not only the peripheral allergy but also the particular molecular pathways that enable the inflammation to enter or be recalled by the central nervous system (Dong et al., 2023).

3.1 Mast cell activation in the Brain

Mast cells are first responders which becomes active before microglia (Kempuraj, Selvakumar et al. 2017). Which require a period for transcriptional reprogramming. Mast cells possess pre-stored and pre activated mediators within their cytoplasmic granules (Sandhu and Kulka 2021). They cells are long lived, tissue resident granulated cells of myeloid region that are present everywhere in the mammalian body. They are best known for their role in allergic inflammation and anaphylaxis. Mast cells presence in the CNS led to re-evolution of their contribution to neurobiology (Jones, Nair et al. 2019). Mast cells are primarily located on the brain side of blood brain barrier while concentrated in perivascular areas of leptomeninges, thalamus and hypothalamus (Kempuraj, Selvakumar et al. 2017). Their strategic position allow them to communicate with neurons, microglia and astrocytes directly (Lakatos and Rosta 2025). Mast cells undergo rapid degranulation when they are activated by stress or neurodegeneration associated molecular patterns. Potent cocktail of biogenic amines, cytokines and neutral proteases are released in this process which organize initial stages of neuroinflammation.

For instance mast cells detect formation of amyloid plaques during early stages of Alzheimer's disease and they respond by the release of mediators which promote microglial activation and blood brain barrier permeability (Kempuraj, Mentor et al. 2019). Mast cell activation is not limited to lgE mediated pathways, rather non-immunologic syndromes and neuropeptides including corticotropin releasing hormone play critical role in neurodegenerative context (Monaco, Choi et al. 2022). Hypothalamic pituitary adrenal axis is activated during stress conditions which leads to release of corticotropin releasing hormone and subsequently degranulation of mast cells occurs (Kempuraj, Selvakumar et al. 2017). Stress induced activation of past cells is associated to pathogenesis of AD, as they show increased formation of AB and hyper phosphorylation of tau protein (Kempuraj, Mentor et al. 2019). When mast cells and microglia are arranged in sophisticated bidirectional conservation they trigger inflammatory cascades and released histamine and tryptase binds to PAR-2 and histamine receptors on the surface of microglia when mast cells are degranulated (Lakatos and Rosta 2025). This signaling induces a phenotypic shift in microglia, transitioning from hemostatic state to a neurotoxic or pro-inflammatory state (Lakatos and Rosta 2025). This cycle leads to chronic neuroinflammation which is characterized by persistent vascular permeability, neuronal excitability and glial damage (Kempuraj, Mentor et al. 2019). Failure of CNS to overcome this pathogenic condition leads to "metabolic inflammatory cycle" where inflammatory cytokines disrupt the insulin signaling and exacerbating insulin resistance which in turn triggers the neuroinflammation and reduces the brain ability to clear aggregates of toxic proteins (Wu, He et al. 2025).

3.2 Blood-Brain Barrier (BBB) permeability

It is a dynamic regulatory boundary which is composed of endothelial cells, astrocytes and pericytes that maintain the chemical stability of neuronal milieu (Kim, Jung et al. 2025). Maintenance of structural and functional integrity of blood-brain barrier is vital for neuronal equilibrium, while its disruption is the early indicator of neurodegenerative pathology (Chen, Dai et al. 2024). In some condition which are associated with allergic inflammation and mast cell activation, blood-brain barrier undergoes

some structural and biochemical changes which facilitates entry of neurotoxic substances in brain parenchyma (Kempuraj, Selvakumar et al. 2017). Nature of blood-brain barrier restrictively is estimated by tight junction which is present between adjacent brain endothelial cells, including proteins such as claudin-5, occluding and zonula occludens-1 (Kim, Jung et al. 2025). Allergic responses caused by chronic peripheral inflammation leads to systematic release of pro inflammatory cytokines which directly compromise these functional complexes (Beltran-Velasco and Clemente-Suárez 2025).

Cytokine mediated down regulation: TNF-α and Interleukin-β binds to receptor on endothelial cells and triggers intracellular signaling cascade that cause weakness of the barrier (Kim, Jung et al. 2025). Ultimately down regulate the transcriptional and translational expression of TJ proteins which reduce the tightness of blood-brain barrier.

Matrix metalloproteinase activation: Enzymes such as MMP-9 are up regulated by inflammatory signaling, that enzymatically degrade the basement membrane and extracellular loops of TJ proteins, required for paracellular aperture widening.

Phosphorylation and redistribution: Mast cell mediators and histamine can induce the phosphorylation of TJ proteins which cause them to redistribute away from cell-cell junctions and increase paracellular permeability.

Vulnerability of the blood-brain barrier is not uniform across the central nervous system. Regional differences in metabolic activity, vascularization and existing permeability make certain areas, such as substantia nigra in Parkinson's disease and hippocampus in Alzheimer's disease more susceptible to neurodegenerative processes (Kim, Jung et al. 2025). Emerging evidences show that gut-brain axis play vital role in this regional vulnerability (Beltran-Velasco and Clemente-Suárez 2025). Intestinal dysbiosis and leaky gut allow entry of bacterial components such as Lipopolysaccharide into the systemic circulation (Beltran-Velasco and Clemente-Suárez 2025). Peripheral inflammatory processes sensitize the cerebral microvasculature to biogenic amines like histamine (Lu, Diehl et al. 2010). Leaky brain allows pathological feedback loop where peripheral immune cells infiltrate the central nervous system and activate resident glia then further accelerating the neuronal injury.

4. Autoimmunity and Neurodegeneration

The classification of neurodegenerative diseases allows incorporation of autoimmune components where host antibodies targets self-proteins in the brain (Luan, Han et al. 2026). While some proteins are nonpathogenic markers of tissue damage. Collective evidences support a pathogenic driver hypothesis which suggest that certain antibodies actively initiate or triggers neurodegenerative processes (Luan, Han et al. 2026).

4.1 Autoantibodies and Neuronal damage

The role of neuronal autoantibodies exist on a biological continuum between acute autoimmune encephalitis and slowly progressive neurodegeneration (Luan, Han et al. 2026). Sustained exposure to these antibodies leads to transition from functional interference to structural injury (Luan, Han et al. 2026).

Surface receptor internalization: Antibodies against neuronal surface proteins such as N-methyl-D-aspartate receptor or IgLON5 can produce nonlethal neuronal dysfunction initially. However irreversible receptor internalization and synaptic loss occurs due to long term exposure (Greenlee, Carlson et al. 2022).

Synaptic and axonal abnormalities: In Parkinson's disease misfolded aSyn aggregate in presynaptic terminals impair neurotransmitter release and vehicle trafficking. Recent positron emission tomography studies using the radio tracer [^{11}C] UCB-J which binds to synaptic vesicle glycoprotein 2A, have confirmed significant synaptic density loss in the substantia nigra, brain stem and caudate of PD patients. This loss of synapses often precedes the death of dopaminergic cell bodies.

Induction of proteinopathies: A critical link between autoimmunity and neurodegeneration is the discovery that autoantibodies can triggers accumulation of toxic patients. Just like IgLON5 autoantibodies cause the time dependent

accumulation of hyper phosphorylated tau in neurons. Which affectively transforms an immune response into progressive tauopathy.

In Alzheimer's disease autoantibodies targeting Ab, tau and BACE have been identified (Gong, Li et al. 2025). While high affinity antibodies against Ab protofibrils are being developed as smart therapies just like lecanemab. Endogenous antibodies are considered as double edged sword (Skarlis, Angelopoulou et al. 2025). Their impact may depend upon isotype affinity and glycosylation patterns. Clearing of protein aggregate may improved by certain modifications while others may exacerbate neuroinflammation through Fc- receptor signaling on microglia (Gong, Li et al. 2025).

4.2 Molecular mimicry

Molecular mimicry occurs when the immune system of the host confuses proteins with structurally similar antigens from microbes or food (Suliman 2024). This mistaken identity links peripheral infections and diet to chronic inflammation and neurodegenerative diseases just like MS, PD, AD and is the growing area of research (Maguire, Wang et al. 2024).

Substantial evidences suggest that microbial agents acts as upstream inducers of inflammatory cascade seen in neurodegeneration (Garcia-Bustos, Cabanero-Navalon et al. 2025). Amyloid Brain biofilm hypothesis proposes that Aβ deposition is actually an innate immune response to chronic and latent infections where Aβ acts as antimicrobial peptides to trap pathogens (Onisiforou, Charalambous et al. 2025).

Epstein barr virus: Their nuclear antigen-1 share sequence homology with self-antigens like Ro, SmD and myelin basic proteins triggers systemic lupus erythematosus and MS. In PD antibodies triggering the EBV membrane protein LMPI cross react with human α syn and potentially initiating aggregation process.

SARS-CoV-2: Their spike protein share hexapeptides with human heat shock proteins. This mimcry suspected to play role in autoimmune mediated neurological sequelae of COVID-19 and acceleration of neurodegenerative phenotypes.

Bacterial commensals: Bacteria like *Escherichia coli* produces amyloid proteins that are structurally analogous to human Ab and α syn (Onisiforou, Charalambous et al. 2025). These bacterial amyloids can cross seed the misfolding of endogenous protein in the gut, which later propagate in prion like manner through vagus nerve to the brain (Huang, Liao et al. 2021). The hypothesis that environmental factors in the gut initiate PD is supported by the early appearance of α syn pathology in the enteric nervous system. Molecular mimicry with food proteins represents a novel pathway for this initiation. The presence of leaky gut allows these improperly digested food peptides to enter in the circulation where they stimulate the production of cross reactive antibodies. These antibodies can form immune complexes, which enter the brain when blood brain barrier is compromised and induces the information of Lewy bodies (Vojdani, Lerner et al. 2021).

5. The Concept of "Smart" Anti-Inflammatory Drugs

Anti-inflammatory drugs are the medicines that are produced to treat or reduce inflammation, when body is exposed to some injury or infection. These drugs primarily work by decreasing the production of inflammation causing agents such as prostaglandin, which inhibits the enzymes such as COX or cyclooxygenase. Nonsteroidal anti-inflammatory drugs (NSAIDs), a frequenty employed category of medications, are primarily utilized to mitigate fever, alleviate pain, and diminish inflammation. These drugs are essential in managing a variety of medical conditions, encompassing migrains, gout, arthritis, and muscular discomfort. Their therapeutic effectiveness stems from their ability to modulate inflammatory pathways, thereby providing symptomatic relief in both acute and chronic ailments (Ghlichloo & Gerriets, 2023).

Table 02. Comparison between Conventional and "Smart" Anti-Inflammatory Therapies

Feature	Conventional Drugs	Smart Anti-Inflammatory Drugs	Key References
Specificity	Low; typically exert broad immunosuppressive effects across multiple systems.	High; designed to modulate specific cellular pathways or molecular targets.	Kessel et al. (2020); McInnes & Schett (2017)
Side Effects	High risk of systemic toxicity and increased susceptibility to opportunistic infections.	Minimal; characterized by localized action and reduced off-target interference.	Aman et al. (2021); Kessel et al. (2020)
Delivery Mechanism	Primarily systemic distribution via oral administration or standard injections.	Highly targeted delivery using Nanoparticles or Monoclonal Antibodies.	Kessel et al. (2020); van Dyck et al. (2023)
Mechanism of Action	Broad inhibition of enzymes such as COX-1 and COX-2 (non-selective).	Precision inhibition of signaling nodes like JAK/STAT, NLRP3, or BTK.	McInnes & Schett (2017); Aman et al. (2021)
Examples	NSAIDs (e.g., Aspirin, Ibuprofen) and Corticosteroids.	Biologics (Tocilizumab), BTK inhibitors (Ibrutinib), and Nano-carriers.	Kessel et al. (2020); McInnes & Schett (2017)

5.1 Beyond Broad Suppression: Shift from systemic to targeted therapy

Classical immunosuppressant therapies that broadly inhibit immune activity throughout the body have long been employed to treat inflammation. While such methods may be effective to reducing symptoms of inflammation in the short-term, their widespread effects often lead to toxicity, opportunistic infections, and undesirable side effects. For this reason, there has been an increasing push to discover therapies that target inflammation with high specificity towards the molecular and cellular drivers of inflammation. Disease-specific monoclonal antibody-based therapies have shown great success at blocking major inflammatory signaling molecules. Monoclonal antibodies against TNF-a, which plays a large role in inflammation, have been successfully used to treat inflammatory conditions like ulcerative colitis. Targeted immune suppression can lead to greater specificity and effectiveness of treatment. However, many traditional antibody therapies are not long-lasting and often lead to off-target effects throughout the body. Nanoparticles drug delivery technologies have been used to increase both the specificity of targeting and as well as prolong the half-life of drugs. Targeted nanoparticles can be conjugated to drugs and utilized to home into specific tissues or cells affected by inflammation, such as macrophages. Notably, in mouse models of inflammation, antigen-specific lipid nanoparticles were found to be able to modulate dendritic cell maturation, inhibit expression of pro-inflammatory cytokines, and attenuate inflammatory signaling without suppressing the immune systems as a whole. Researches have also developed long-lasting nanoparticles that were capable of releasing antibodies over the course of month. In conclusion, although classical approaches to treating inflammation tend to broadly suppress the immune system, more targeted approaches are being developed to improve the specificity of treatment (Johnson et al., 2024; Pareek et al., 2023; Zhang et al., 2025).

Activation of spinal glial cells, particularly astrocytes and microglia, follows peripheral nerve injury. Activation of these glial cells results in release of inflammatory mediators which further sensitize neurons and contribute to chronic pain and neuroinflammation. Peripheral nerve injury also recruits circulating monocytes to the site of injury. These recruited monocytes release pro-inflammatory mediators which further enhance neuronal excitability. Evidence suggests microglia and monocytes play critical roles in the early stages

of neuropathic pain development highlighting the importance of immune cell involvement in neuroinflammatory signaling. Therapeutic interventions targeting resident microglia as well as invading peripheral monocytes may provide an effective means for preventing further progression of neuroinflammation and chronic pain. (Peng et al., 2016)

5.2 Targeted Drug Delivery Systems: (e.g., Nanoparticles, Monoclonal Antibodies, and PROTACs)

Nanoparticle-based drug delivery systems represent another strategy to selectively target inflammatory disease processes. Because high levels of ROS at sites of inflammation can impair endothelial tight junctions and allow extravasation of particles within the nanometer range into damaged tissue, successful delivery of nanoparticles to sites of inflammation will be key for future therapies to succeed. In addition to encapsulation/conjugation of active molecules into nanostructures for biological stability and improved pharmacokinetics, supramolecular nanotherapeutics formed by non-covalent molecular assembly have been shown to exhibit better therapeutic efficacy than free drug. Studies have demonstrated that vitamin C–lipid Nano assemblies are capable of selectively targeting inflamed colon tissue and dramatically reducing disease severity as well. By scavenging ROS, these engineered nano-assemblies were also shown to reduce oxidative stress burden, highlighting the potential for nanoparticle platforms to target anti-inflammatory drugs to sites of inflammatory disease (Xian et al., 2025).

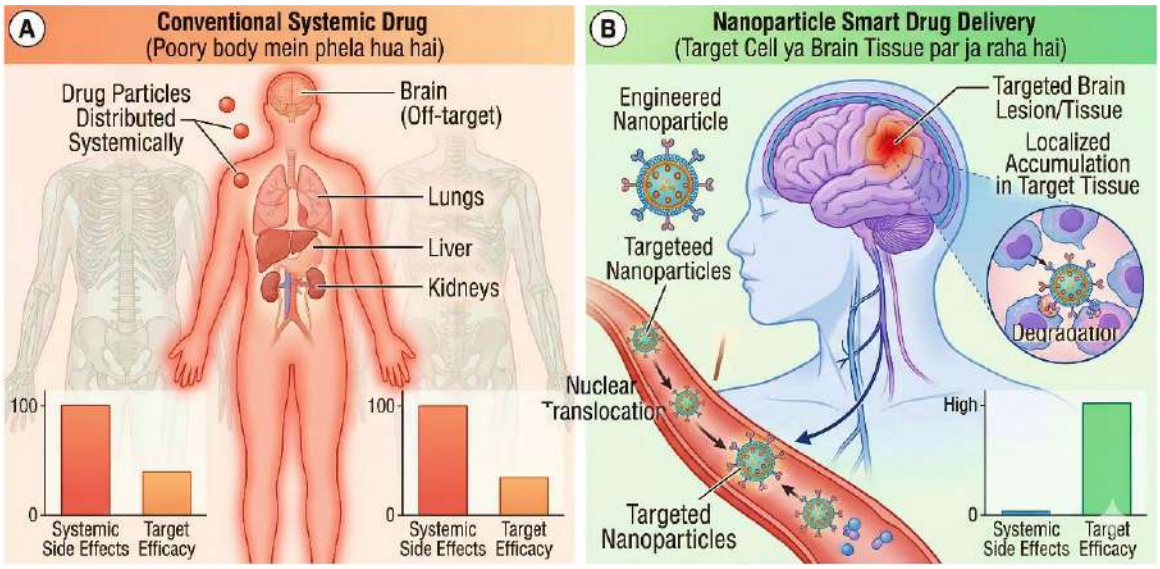

Figure 04. Comparison of Conventional vs. Smart Drug Delivery Systems.

Drug delivery systems that utilize nanoparticles are effective for the delivery of biomolecules. One of these nanoparticles is mesoporous silica nanoparticles which have the benefit of having a high surface area to interact with the surrounding biological environment and biocompatibility. Coupling therapeutic molecules with these nanoparticles would allow for increased efficiency in delivery. Peptides such as MGI can be used to target delivery systems to microglia. Treatment with nanoparticles that delivered miR-26a-5p showed prolonged anti-inflammatory and analgesic effects due to decreased microglial activation and changes in inflammatory signaling (Lu et al., 2024).

Inflammatory bowel disease (IBD) is a chronic disease involving continuous inflammation of the gastrointestinal tract that often remains undertreated due to severe side effects. Reactive oxygen species (ROS) are often over-produced during inflammation and result in further inflammation and tissue damage. Methods to decrease ROS levels are currently being explored to aid in inflammation treatment. While there has

been difficulty with poor accumulation of antioxidants within inflamed tissues, there has been some success with vitamin C. Vitamin C is an antioxidant that has been shown to reduce oxidative stress produced during inflammation. Recent advances in drug delivery include conjugating vitamin C to long-chain fatty acids which self-assemble into nanostructures known as nano-assemblies (Xian et al., 2025).

Monoclonal antibody treatments have shown great potential as precision targeted immunotherapy. Immune checkpoint inhibitors specifically directed against PD-1/PD-L1 have dramatically enhanced cancer treatment. Anti-PD-L1 agents such as pembrolizumab and nivolumab work by blocking interactions between PD-L1 and T cells that tumors use as an immune checkpoint to avoid being targeted by the body's immune system. While these therapies have been successful for some cancer patients, there are still some patients who are resistant to treatment and those who develop immune-related adverse effects from therapy. Advances have been made in using nanotechnology to better stabilize antibodies and target them to specific sites in the body. Nanoengineered antibodies have demonstrated improved receptor targeting, stronger PD-1 interactions, and improved anti-tumor activity. Furthermore, local delivery of nanoformulated antibodies has been shown to increase tumor accumulation, augment antitumor efficacy, and limit toxicity compared to systemic administration (Mujahid et al., 2025).

Precision based targeted monoclonal antibody treatments have been utilized to limit certain harmful signaling events within the body's immune response. Tocilizumab binds to and inhibits the IL-6 receptor and was used to limit IL-6 mediated inflammatory cytokine signaling events. Since COVID-19 can lead to very severe complications in patients with cytokine storms characterized by upregulation of IL-6, tocilizumab was used as a treatment for severely affected COVID-19 patients. Results from randomized trials showed that tocilizumab caused significantly lower levels of inflammatory biomarkers when compared to a placebo. Additionally, patients who were treated with tocilizumab had improved clinical recovery and reduced lengths of hospital stays (Malik et al., 2022).

5.3 Small Molecule Inhibitors: Precision targeting of specific enzymes (like NLRP3 inflammasome)

Targeting specific enzymes and signaling pathways associated with immune cell activation, small molecule inhibitors represent a key strategy for targeted anti-inflammatory treatment. Activation of the NLRP3 inflammasome by pro-inflammatory MI macrophages leads to cytokine production such as IL-I and IL-8 and promotes inflammation progression. Targeted small molecule drugs can inhibit key inflammatory pathways such as NF-kB signaling and NLRP3 inflammasome activation within immune cells, for example, the small molecule medicine ibrutinib. Furthermore, precise targeting of signaling enzymes such as Bruton's tyrosine kinase (BTK) by altering the response of immune cells significantly reduces inflammation lesion severity. By inhibiting immune checkpoint signaling such as CD47–SIRPa signaling, other small molecule inhibitors can further regulate inflammation, for example SHP-1 inhibitors. However, conventional small molecule drugs often face issues with poor bioavailability, limited targeting range, and off-target effects which makes advanced delivery systems imperative to increase their precision (Xu et al., 2025).

6. Recent Advances and Clinical Trials

In recent years, great advances have been made in anti-inflammatory drug development. New bioactive molecules including ones from marine microbes show great promise and many newly discovered molecules have shown great anti-inflammatory potential (Yang et al., 2024).

Other advancements like monoclonal antibodies, nanotechnology-drug-delivery systems, and targeted therapies allow for drugs to be more specific to the patients' needs while also decreasing unwanted side effects (Oliveira-Costa et al., 2024; Zhao et al., 2024).

In addition, clinical trials for novel therapies are constantly being conducted to test their safety and effectiveness. Some current anti-inflammatory

drugs are showing promise in having extra benefits such as antimicrobial properties. More research and clinical trials will need to be conducted to confirm these effects. New medications like interleukin-23 receptor antagonists have shown in clinical trials to have significantly higher remission rates than placebo drugs (Okpala et al., 2025). There is still a lot of work to be done when creating effective anti-inflammatory medications that have few side effects and can be proven safe for long-term use (Shaheen et al., 2025; Amador et al., 2025).

6.1 Success Stories: Drugs currently in Phase II or III trials.

The preclinical successes achieved in nanoparticle-based therapeutics have made the translation into clinical trials faster than ever before. Numerous nanoparticle-formulated therapeutics have reached clinical trials as precision medicine becomes more prevalent in cancer treatment strategies. For example, Tecemotide is currently in Phase III clinical trials as a MUC1-targeted immunotherapy for non-small cell lung cancer (FDA). Biomarkers like MUC1 are tumor antigens that can now be used to selectively activate immune responses against tumors within certain populations of patients. Additionally, chemotherapeutics such as Nab-paclitaxel are currently undergoing clinical trials in combination with other therapeutics like gemcitabine, atezolizumab, and cyclophosphamide in patients with early-stage and metastatic cancers (ClinicalTrials.gov). Results from these trials show that nanoparticle-facilitated drug delivery effectively improves clinical outcomes (ClinicalTrials.gov). Furthermore, drug formulations like ABI-007 have also undergone clinical trials for patients with cancer and have shown similar successes. Not only are nanoparticles showing promise in the development of therapeutic strategies, but they are also being used for biomarker detection and patient stratification. Biomarker assays utilizing nanoparticles for microRNA detection and nanoparticles functionalized with DNA ligands to detect mutations in key tumor suppressor genes can be used to diagnose patients and develop specific treatment regimens (Mundekkad & Cho, 2022).

Table 03. Summary of Targeted Therapies and Clinical Trials

Drug / Technology	Target / Mechanism	Status	Main Application	Key References
Tocilizumab	Specific inhibitor of the IL-6 Receptor (Interleukin-6).	FDA Approved	Rheumatoid Arthritis; Severe COVID-19 management.	McInnes & Schett (2017); Kessel et al. (2020)
Lecanemab	Monoclonal antibody targeting Anti-Aβ protofibrils.	FDA Approved	Treatment of early-stage Alzheimer's Disease.	van Dyck et al. (2023)
Tecemotide	MUC1-targeted immunotherapy (Synthetic lipopeptide).	Phase III Trials	Non-small cell lung cancer (NSCLC).	Aman et al. (2021); Kessel et al. (2020)
Ibrutinib	Small molecule inhibitor of Bruton's Tyrosine Kinase (BTK).	Clinical / Preclinical	Chronic B-cell malignancies and inflammatory pathways.	McInnes & Schett (2017); Katsnelson et al. (2023)
PROTACs	Proteolysis-Targeting Chimeras for degrading specific enzymes (NLRP3, GSK-3β).	Emerging / Early Clinical	Precision medicine for neurodegeneration and cancer.	Aman et al. (2021); Kessel et al. (2020)

Clinical success depends on using these targeted therapeutics in conjunction with biomarkers that will only select certain patients to treat.

6.2 Biomarkers for Precision Medicine: How to identify which patient needs which drug

There are currently hundreds of clinical trials involving nanoparticle-based therapeutics across a broad range of indications. A majority of the clinical trials have reached at least Phase I or II clinical development, while roughly 10% have entered Phase III clinical trials. Nanoparticle-bound paclitaxel has become one of the most explored therapeutic options clinically, with several studies investigating efficacy of albumin-bound paclitaxel. In recent years, the amount of nanoparticle-based drugs FDA-approved has increased, with liposomes/lipid-based nanoparticles being the most common nanomedicine due to safety and bioavailability. As our clinical trials enter more mature phases, incorporation of biomarkers in the clinic to help drive treatment decisions is being researched. Metabolic biomarkers, as well as biomarkers specific to disease pathology are some of many molecular markers being used to identify which patients are most likely to respond to treatment (Namiot et al., 2023).

7. Challenges, Research Gaps, and Future Research Directions

The discovery of converging cellular pathways that connect allergy, autoimmunity, and neurodegeneration has been a transformative concept in drug discovery, and several challenges are still to be cleared. One of the main challenges is that of the inherent redundancy of cytokines in human disease. As shown in clinical trials of giant cell arteritis (GCA), very specific inhibition of a critical node in a disease, such as the IL-6R with tocilizumab, leads to lasting remission in only half of the total patient population. (Cid et al., 2020). This would imply that there is a compensatory effect of other inflammatory mediators and other signalling pathways that will counteract any attempts to block these pathways, which is a problem when it comes to developing a "smart" drug that will effectively terminate disease processes without causing a state of immunosuppression. (Cid et al., 2020; Gorska & Alam, 2003). Furthermore, identifying shared molecular targets is hindered by the dualistic nature of immune responses within the central nervous system (CNS). Historically defined as "immune-privileged," the brain is now understood to require lifelong, active support from peripheral immunity for homeostatic maintenance and repair; however, these responses can transition from protective to pathogenic at different disease stages, as seen in the fluctuating leukocyte profiles of amyotrophic lateral sclerosis (Dalmau, 2016; Deczkowska & Schwartz, 2018).The complexity is also attributed to the neuro-immune axis, where sensory neurons and immune cells interact. The process results in the manifestation of diseases, which affect tissues such as the skin and the lung(Voisin et al., 2017). Allergic inflammation is mediated by the complex relationship between mast cells, Th2 cells, and sensory nerves. The relationship between the three has not been sufficiently defined to predict the outcome of the treatment. (Barnes, 2011; Voisin et al., 2017). In addition, although the universal hubs such as the NLRP3 inflammasome are involved in Alzheimer's disease and metabolic autoimmunity, the specific sequence of molecular triggers involving potassium efflux, lysosomal damage, and mitochondrial reactive oxygen species is still under investigation, making it challenging to decide whether to target the sensor or its upstream activators. (Pirzada et al., 2020; Schwaid & Spencer, 2020).

However, there are also methodological and experimental constraints to its successful translation into a clinic. There is a major gap in current research on animal models of neurodegeneration, as the current models used are genetic and focus on rare familial genetic mutations (e.g., 5xFAD and APP/PSI models), which do not encapsulate the polygenic and environmental factors of late-onset idiopathic disease (Deczkowska & Schwartz, 2018). Furthermore, many existing models do not incorporate the "two-hit" hypothesis, where a germline mutation creates a background of vulnerability that requires a secondary somatic hit to trigger full pathology (Parenti et al., 2020).

The validation of objective biomarkers is another important area to be filled. In the treatment of inflammatory bowel diseases, for instance, there is

a continued mismatch between the control of disease symptoms and the achievement of "true" healing at the mucosal/histologic level, with no validated cut-offs to achieve a "histologic cure" according to current guidelines (Nunez et al., 2020). The overwhelming majority of drug-induced allergic reactions are unpredictable "Type B" reactions, and a shift to high volume computer simulations and patient-derived MHC libraries to screen drugs for allergic potential is required in early development (Bonfiglio & Weinstein, 2019).

Future research directions will require the development of interdisciplinary approaches that utilize Artificial Intelligence (AI) and Machine Learning (ML) technologies to hasten the development of Multi-Target Directed Ligands (MTDLs). This can be achieved by employing deep convolutional neural networks (DCNNs) to carry out high-volume virtual screening approaches to discover molecules that target multiple pathological nodes, such as GSK-3β and BACE1, associated with Alzheimer's, while avoiding critical homeostatic regulators (Pirzada et al., 2020).

Moreover, research should also focus on the potential of pro-resolving mediators like resolvins and protectings, which facilitate the resolution of inflammation, as opposed to suppressing immune cell signaling. (Nayadu et al., 2012; Barnes, 2011). Adopting single-cell RNA sequencing technology will be crucial in understanding the vast diversity of sensory neurons and microglial states and will be essential in the development of precision medicine that targets specific cells in the body (Voisin et al., 2017). Lastly, the restoration of the brain-immune axis through "checkpoint-style" immunotherapies has provided a new model for rejuvenation, where the emphasis is no longer placed on the suppression of the immune system, but the revival of the "dormant" mechanisms of the immune system to counter neurodegenerative "wear and tear" (Deczkowska & Schwartz, 2018).

8. Conclusion

This systematic review has attempted to harness the power of the scientific literature in the fields of immunology, neurology, and pharmacology to provide evidence of the inherent connection between allergy, autoimmunity, and neurodegeneration. The discovery of the NLRP3 inflammasome, the JAK-STAT pathway, and the neuro-immune interface as a unifying force in the pathology of the three diseases represents a paradigm shift away from the use of nonspecific steroids to a more specific molecular targeting approach. An important common theme throughout the literature is the acknowledgment of the brain-immune interface as a regulatory mechanism, the central nervous system not being a "privileged site" unto itself, but a tissue in need of a lifelong dialogue with the immune system to rejuvenate (Dalmau, 2016; Deczkowska & Schwartz, 2018).

The opportunity to build 'smart' anti-inflammatory drugs is to target downstream nodes of Signaling pathways through which multiple sources of inflammation converge. Inhibiting 'master regulators' such as Syk, Btk, and Jak3 will allow next-generation drugs to 'abrogate complex inflammatory phenotypes' with greater specificity and oral bioavailability than traditional biologic agents. (Gorska & Alam, 2003; Leishman et al., 2011; Nayadu et al., 2012). The addition of natural products and phytochemicals with mast cell stabilizing and/or NF-κB inhibitory activities extends the armamentarium and provides new opportunities for synergistic treatment of chronic states. (Bellik et al., 2013; Coll et al., 2019).

As a matter of fact, progress in the field of neuroimmunology has already provided us with biological assets that have revolutionized treatment for a subset of populations, and while the high rate of non-responders in clinical trials is a testament to how much more needs to be done, it is also a reminder that the complexity of these networks has not been fully uncoupled. The future of precision medicine will be a synergy of both molecular biology and computational intelligence. With AI-driven virtual screening becoming a norm in drug development, the ability to create agents that can effectively traverse complex networks of protein-protein interaction will be a hallmark of truly 'smart' drugs. In the end, it is a future that will be able to break down traditional disciplinary

silos and provide a future of truly personalized medicine that is able to address the root causes of human disease at a cellular level.

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