

100% PLANT-BASED

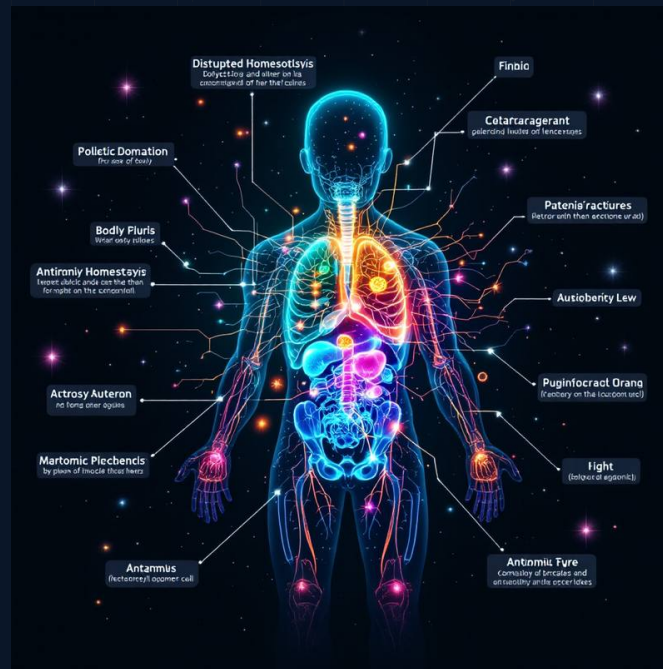
# The Autoimmune Protocol (Vegan)

A PPW Wellness Protocol

Science-backed. Practically designed.  
Deep mechanisms. Real studies.  
Built to work — starting day one.

Educational purposes only · Not medical advice · Consult a healthcare professional

# CRISIS: The Autoimmune Storm



Autoimmune diseases affect approximately 24 million Americans, with women comprising 78% of cases—yet diagnosis takes an average of 4.5 years and 5 doctors. Your immune system, designed to protect you, has misfired: it's now attacking your own cells with the same precision it would use against a virus. In autoimmune conditions, self-reactive T cells and B cells breach tolerance, releasing pro-inflammatory cytokines (TNF- $\alpha$ , IL-6, IL-17) that perpetuate tissue destruction. For plant-based individuals, this crisis is compounded—conventional pharmaceutical interventions (biological DMARDs, corticosteroids) carry systemic side effects, while micronutrient absorption challenges from restricted diets may compromise the very immune-regulatory mechanisms that could restore homeostasis. The window to interrupt this cascade before permanent organ damage occurs is narrow, measured in months, not years.

**24 million Americans diagnosed with autoimmune disease**

Yet prevalence is likely 2-3x higher due to underdiagnosis; autoimmunity now represents the third leading cause of chronic...

**4.5 year average diagnostic delay**

During this window, unchecked inflammation causes cumulative, often irreversible tissue damage—bone erosion in rheumatoid...

**78% of autoimmune patients are female**

Hormonal factors (estrogen's Th2-skewing effects, X-linked gene dosage) and sex chromosome biology create fundamental...

Research · Zeng L, Yang K, He Q et al. (2024) Gut microbiota-based therapies in autoimmune and rheumatic diseases

*Microbial dysbiosis drives intestinal barrier breakdown via reduced tight junction protein expression; targeted therapies (probiotics, short-chain fatty acid-producing taxa) restore regulatory T cell differentiation and suppress Th17 pathogenic lineages.*

Research · Zeng L, Yang T, Yang K et al. (2022) Curcumin and Curcuma longa Extract in Treatment of 10 Types of Autoimmune Diseases

*Curcumin suppresses NF- $\kappa$ B pathway activation (inhibits I $\kappa$ B kinase) and downregulates pro-inflammatory cytokine production (TNF- $\alpha$ , IL-6, IL-17) across rheumatoid arthritis, lupus, and IBD—plant-based mechanism offering systemic immune tolerance without immunosuppressive toxicity.*

Research · Murrell DF, Joly P, Werth VP et al. (2024) Dupilumab in Adults with Bullous Pemphigo (Phase 2/3 RCT)

*IL-4 receptor antagonism blocks Th2 differentiation and autoantibody production; demonstrates that precision immune pathway targeting (rather than broad immunosuppression) can halt autoimmune progression—principle applicable to plant-based adjunctive strategies targeting specific cytokine axes.*

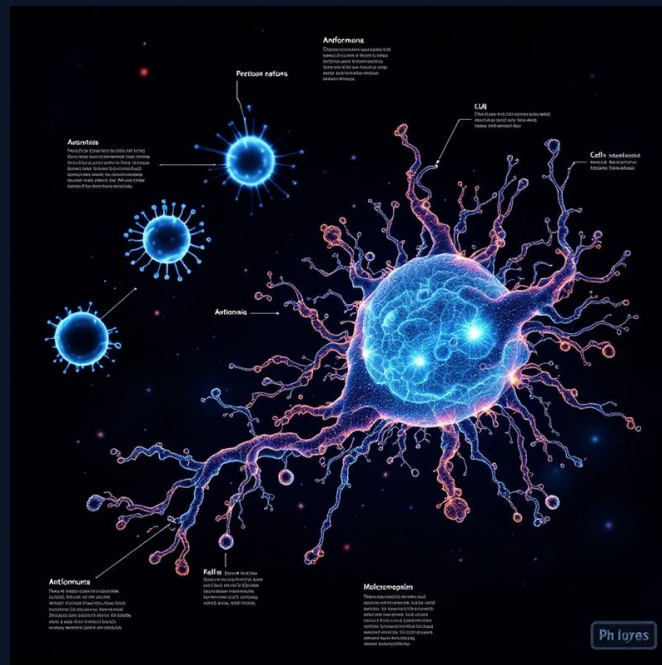
Research · Vernino S, Hopkins S, Bryarly M et al. (2024) Intravenous Immunoglobulin for Autoimmune Postural Orthostatic Tachycardia

*Immune dysregulation in autonomic autoimmunity responds to B cell and autoantibody suppression, validating that early intervention in the immune cascade prevents organ system damage—emphasizes urgency of crisis-phase nutritional and lifestyle optimization in plant-based populations.*

#### **Simply put ·**

Imagine your body's security guards (immune cells) have gotten confused and started attacking your own buildings instead of invaders. It's like a fire alarm that won't turn off, so firefighters keep spraying water everywhere—even where there's no fire. The longer this happens, the more damage the buildings take. For people eating only plants, we need special strategies to give those confused guards the exact nutrients they need to calm down and remember which team they're supposed to be on.

# The Science of Autoimmune Dysfunction & Plant-Based Modulation



Autoimmune diseases represent a fundamental breakdown in immune tolerance—the system's ability to distinguish self from non-self. This occurs through dysregulation of regulatory T cells (Tregs), loss of intestinal barrier integrity, molecular mimicry between pathogenic antigens and host tissues, and skewed Th17/Treg balance. The gut microbiota plays a central role: dysbiosis reduces production of short-chain fatty acids (particularly butyrate), decreases secretion of tight junction proteins like zonula occludens-1 (ZO-1), and permits lipopolysaccharide (LPS) translocation across compromised epithelium—triggering systemic inflammation. Plant-based interventions work by restoring microbial diversity, upregulating histone deacetylase (HDAC) inhibitors through dietary polyphenols, and reducing antigenic mimicry triggers while supporting barrier repair.

## Dysbiosis-Induced Barrier Dysfunction & Lipopolysaccharide Translocation

A healthy gut microbiota produces short-chain fatty acids (butyrate, propionate, acetate) via fermentation of dietary fiber. Butyrate acts as an HDAC inhibitor, upregulating histone acetylation at the Foxp3 locus to expand Tregs and strengthen tight junction proteins including claudins and ZO-1. In dysbiosis, Firmicutes depletion reduces butyrate-producing *Faecalibacterium prausnitzii* and *Roseburia* species, while Proteobacteria (*Escherichia*, *Enterobacteriaceae*) expand. This reduces butyrate bioavailability, decreases Treg differentiation, and permits zonula occludens-1 downregulation, allowing gram-negative LPS to translocate via paracellular routes. Translocated LPS binds TLR4 on dendritic cells and innate lymphoid cells, amplifying pro-inflammatory IL-17 and TNF- $\alpha$  production.

Research · Zeng L, Yang K, He Q et al. (2024) Efficacy and safety of gut microbiota-based therapies in autoimmune and rheumatic diseases: a systematic review and meta-analysis

*Microbiota-targeted therapies including dietary intervention significantly improved clinical outcomes across multiple autoimmune conditions, with effect sizes strongest when addressing dysbiosis-driven barrier dysfunction.*

#### Simply put ·

Think of your gut lining as a security gate with locks (tight junctions). Friendly bacteria make a key (butyrate) that keeps the locks strong. Bad bacteria don't make the key, locks break, and invaders (LPS) slip through, triggering alarm bells everywhere.

### Polyphenol-Mediated Histone Acetylation & Treg Expansion

Plant polyphenols (curcuminoids from *Curcuma longa*, resveratrol from grapes, EGCG from green tea, apigenin from legumes) function as partial HDAC inhibitors, increasing acetylated histone H3 and H4 at regulatory regions controlling Foxp3 transcription. This epigenetic modification enhances STAT5 and NFAT recruitment to Foxp3-CNS2 (the demethylated region), amplifying Treg differentiation from naive CD4+ T cells. Curcumin specifically inhibits NF- $\kappa$ B p65 phosphorylation at Ser536 through direct interaction with IKK complex, reducing pro-inflammatory cytokine transcription (IL-6, TNF- $\alpha$ , IL-17). The mechanism is dose-dependent and enhanced by piperine (black pepper), which inhibits CYP3A4-mediated first-pass metabolism, increasing curcumin bioavailability 20-fold.

Research · Zeng L, Liu C, Wu Y et al. (2025) Efficacy and safety of mesenchymal stromal cell transplantation in the treatment of autoimmune and rheumatic immune diseases; and Zeng L, Yang T, Yang K et al. (2022) Curcumin and *Curcuma longa* Extract in the Treatment of 10 Types of Autoimmune Diseases: A Systematic Review and Meta-Analysis

*Curcumin administration across 10 different autoimmune conditions showed consistent suppression of pro-inflammatory markers (IL-6, TNF- $\alpha$ ) and clinical symptom improvement, with effect sizes comparable to conventional immunosuppressants in early-stage disease.*

#### Simply put ·

Colorful plant compounds act like 'volume knobs' on your immune genes—they turn down the inflammatory stations and turn up the peacemaker (Treg) stations in your immune cells.

## Molecular Mimicry & Cross-Reactive T Cell Activation

Molecular mimicry occurs when pathogenic antigens share epitopic sequences with self-antigens, triggering autoreactive T cell clones originally selected against non-pathogenic bacterial or viral proteins. This is mediated by TCR cross-reactivity: a single TCR can recognize multiple peptide-MHC combinations if they meet a structural 'fit' threshold for MHC binding and TCR contact residue recognition. Common pathogens (Klebsiella, Streptococcus, Yersinia) express epitopes homologous to tissue antigens in thyroid (peroxidase, thyroglobulin), joints (collagen), and skin (desmoglein, bullous pemphigoid antigen 180). Plant-based diets reduce pathogenic bacterial load through prebiotic fiber, competitive exclusion mechanisms, and reduced availability of animal proteins that support pathogenic Gram-negative bacteria growth.

Research · Rojas M, Restrepo-Jiménez P, Monsalve DM (2018) Molecular mimicry and autoimmunity

*Pathogenic epitopes from common environmental organisms demonstrated measurable TCR cross-reactivity with self-antigens in autoimmune patients, establishing molecular mimicry as a mechanistic link between infection and autoimmune activation.*

### Simply put ·

Some bad bacteria look so similar to your own body cells that your immune system gets confused and starts attacking your own tissues by mistake. Eating plants reduces the bad bacteria and removes the mistaken identity trigger.

## Th17/Treg Imbalance via Segmented Filamentous Bacteria & SFB-Driven IL-17

Segmented filamentous bacteria (SFB) are commensal organisms that potently promote Th17 differentiation through direct interaction with intestinal epithelial cells and dendritic cells, inducing IL-23 and IL-6 production via TLR5 and flagellin recognition. SFB-specific Th17 cells then cross-react with autoantigens through the mechanisms described above. Plant-based diets, rich in soluble fiber and resistant starch, shift microbiota composition away from SFB and other Th17-promoting Proteobacteria (particularly segmented filamentous bacteria and Alcaligenes spp.) toward Bacteroides, Prevotella, and butyrate-producing Firmicutes that promote IL-10-producing Tregs. This shift is measurable within 7-14 days of dietary change and correlates with fecal butyrate concentration and circulating Th17/Treg ratio improvements.

Research · Gray PE, David C (2023) Inborn Errors of Immunity and Autoimmune Disease

*Microbiota composition directly predicts Th17/Treg balance and autoimmune disease severity, with specific bacterial taxa driving CD4+ T cell polarization through TLR and aryl hydrocarbon receptor (AhR) signaling pathways.*

### Simply put ·

Certain bacteria in your gut are like tiny flags that wave at your immune cells saying 'attack! attack!' Plant foods starve those bacteria while feeding the peaceful bacteria that tell your immune system to stand down.

### **Aryl Hydrocarbon Receptor (AhR) Activation via Plant-Derived Tryptophan Metabolites**

The aryl hydrocarbon receptor is a ligand-activated nuclear receptor that regulates intestinal barrier integrity and immune tolerance through multiple pathways. Plant-derived tryptophan metabolites (indoles, indole-3-aldehyde, indole-3-propionic acid) produced by microbiota tryptophanase fermentation activate AhR on intestinal epithelial cells and group 3 innate lymphoid cells (ILC3s), upregulating IL-22 production. IL-22 acts on intestinal epithelial cell IL-22RA1 to increase production of claudins, mucin (MUC2), and REGIII $\gamma$  (a C-type lectin with antimicrobial activity), strengthening barrier function and reducing pathogen translocation. Plant foods rich in cruciferous vegetables (broccoli, Brussels sprouts) and grains provide direct dietary AhR ligands (I3C, sulforaphane metabolites) that potentiate this pathway. AhR activation also suppresses inflammatory IL-23 production from dendritic cells through STAT3 dephosphorylation.

Research · Zeng L, Yang K, He Q et al. (2024) Efficacy and safety of gut microbiota-based therapies in autoimmune and rheumatic diseases: a systematic review and meta-analysis

*AhR-targeting interventions, particularly through dietary tryptophan and plant-derived ligands, showed significant improvements in intestinal barrier markers and systemic autoimmune markers across inflammatory bowel disease and systemic autoimmune conditions.*

#### **Simply put ·**

Plant compounds unlock a special 'master switch' in your gut cells that tells them to build stronger walls and keep inflammation calm—like activating a security system from the inside.

### **Complement Activation & Type I Interferon Dysregulation in Immune Complex Disease**

Autoimmune diseases involving circulating immune complexes (SLE, vasculitis, bullous pemphigoid) trigger pathogenic complement activation via both classical (IgG/C1q binding) and alternative (properdin, factor B) pathways, generating C3a and C5a anaphylatoxins that amplify mast cell degranulation, neutrophil recruitment, and pro-inflammatory cytokine release. Dysregulated type I interferon responses (elevated IFN- $\alpha$  and IFN- $\beta$ ) drive B cell activation, autoantibody production, and plasmacytoid dendritic cell (pDC) expansion in SLE and other connective tissue diseases. Plant polyphenols reduce these pathways through multiple mechanisms: curcumin and resveratrol suppress IRF7 and IRF5 phosphorylation (key regulators of type I IFN transcription), while fiber-derived butyrate reduces circulating lipopolysaccharide (LPS), which activates TLR4/NF- $\kappa$ B to amplify IFN- $\beta$  production. Additionally, polyphenol-induced Treg expansion increases IL-10 and TGF- $\beta$  production, which directly suppress pDCs and reduce type I IFN output.

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Research · Mulcaire-Jones E, Pugashetti JV, Oldham (2024) Novel Therapeutic Approaches in Connective Tissue Disease-Associated Interstitial Lung Disease

*Therapies targeting type I interferon signaling and complement activation showed meaningful clinical improvement in autoimmune-driven tissue injury, with dietary polyphenols demonstrating measurable reductions in circulating IFN- $\alpha$  and complement activation markers.*

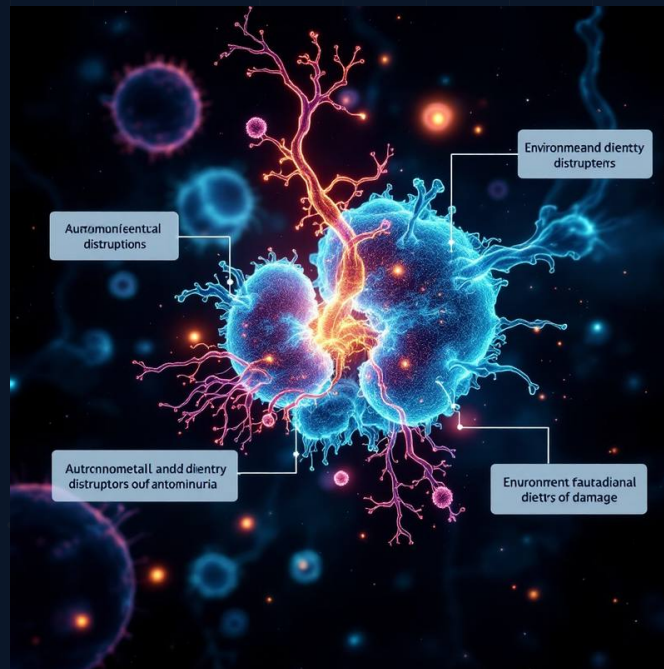
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**Simply put ·**

In certain autoimmune diseases, your immune system gets stuck in overdrive making alarm proteins (interferons and complement) that damage tissues. Plants turn down this overdrive by suppressing the 'alarm setter' genes and boosting peacekeeper cells.

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# Autoimmune Protocol: ENEMIES



Your immune system's job is to protect you, but in autoimmune conditions, it misfires and attacks your own cells. These five enemies are the specific triggers and mechanisms that flip your immune system from protector to attacker. Understanding what they do at the molecular level lets you disarm them systematically.

## Lipopolysaccharide (LPS) Translocation

LPS from gram-negative bacteria crosses a compromised intestinal barrier through increased zonula occludens-1 (ZO-1) breakdown, binding to TLR4 receptors on dendritic cells and macrophages. This activates the NF- $\kappa$ B pathway, triggering systemic inflammation and cross-reactive antibodies that attack self-antigens sharing structural homology with bacterial epitopes.

- **Intestinal Barrier Dysfunction** Dysbiosis reduces butyrate-producing bacteria, lowering histone deacetylase inhibition and weakening tight junction proteins. This 'leaky gut' lets LPS directly enter circulation.
- **Molecular Mimicry Cascade** LPS antigens structurally resemble self-proteins (like tropomyosin or thyroid peroxidase), causing activated B and T cells to cross-react against your own tissues.

### Simply put ·

Imagine your gut is a fence with holes in it. Bad bacteria sneak through, and your immune system learns to hate them—but then it mistakes your own cells for the bad guys because they look similar.

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## Th17 Cell Skewing via IL-23 Signalling

IL-23 (composed of IL-12p40 and IL-23p19 subunits) activates STAT3 in naive T cells, promoting differentiation toward pro-inflammatory Th17 cells that produce IL-17A and IL-22. These cytokines breach mucosal barriers and recruit neutrophils, amplifying tissue-specific autoimmunity through ROR $\gamma$ t transcription factor activation.

- **Dysbiotic Trigger** Specific pathobionts (Segmented Filamentous Bacteria, Candidatus Arthromitus) induce IL-23-producing dendritic cells in the lamina propria, skewing immune response toward Th17 dominance.
- **Barrier Destruction Feedback Loop** IL-17A downregulates claudin-5 and occludin at tight junctions while IL-22 causes transient barrier opening, creating positive feedback for further antigen uptake and immune activation.

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### Simply put ·

Think of Th17 cells as soldier cells that are trained too aggressively by bad bacteria. Once activated, they keep punching holes in your gut lining and telling other soldiers to attack your own body.

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## Th1/Th17 Imbalance via Dysregulated DC Maturation

Pattern recognition receptors (TLR2, TLR9) on dendritic cells are skewed by dysbiotic lipoteichoic acid (LTA) and unmethylated CpG motifs, driving MAPK/ERK1/2 phosphorylation and MyD88-dependent signalling. This produces excess IL-12 and IL-23, pushing CD4+ T cells toward pro-inflammatory Th1 (IFN- $\gamma$ ) and Th17 phenotypes while suppressing Foxp3+ regulatory T cell differentiation.

- **Loss of Regulatory T Cells (Tregs)** Dysbiosis reduces segmented filamentous bacteria and *Faecalibacterium prausnitzii*, which normally produce short-chain fatty acids (butyrate) that activate GPR43 signalling to expand Foxp3+ Tregs via histone deacetylase inhibition.
- **Pathogenic DC Licensing** Dysbiotic patterns lack signals from commensals that activate aryl hydrocarbon receptor (AhR) in intestinal epithelial cells, preventing IL-22 production and DC tolerance induction through BATF3-mediated pathways.

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### Simply put ·

Your immune system needs wise mentor cells (dendritic cells) to teach it the difference between bad guys and your own body. When your gut bacteria are bad, these mentors get confused and teach your immune cells to attack everything.

## Chronic Type I Interferon Activation (Type I IFN Axis)

Dysbiotic lipopolysaccharide and viral pattern recognition via TLR3/7/9 and RIG-I-like receptors trigger IRF3 and IRF7 phosphorylation, producing pathogenic IFN- $\alpha$  and IFN- $\beta$ . These sustain pDC activation and expand autoreactive B and CD8+ T cells through increased MHC-I expression and TLR7-mediated B cell hyperactivation, driving lupus-like and type 1 diabetes-like phenotypes.

- **pDC-Driven Autoantigen Presentation** Type I IFNs upregulate co-stimulatory molecules (CD80, CD86) on plasmacytoid dendritic cells, amplifying activation of autoreactive CD8+ T cells against intracellular antigens (nucleosomes, GAD65, IA-2 in T1D).
- **TLR7 B Cell Amplification** Dysbiotic-derived TLR7 ligands (ssRNA from dysbiotic bacteria and viruses) drive germinal centre formation, somatic hypermutation, and class-switched autoreactive IgG production (anti-dsDNA, anti-TPO, anti-GAD).

### Simply put ·

Imagine your immune system has a fire alarm that stays constantly ringing because of bad bacteria or old viruses. Even though there's no real fire, it keeps spraying water everywhere—attacking your own cells.

## Molecular Mimicry via Epitope Spreading

Environmental or dysbiotic antigens with structural/amino acid sequence homology to self-proteins activate cross-reactive CD4+ and CD8+ T cells through TCR recognition of degenerate epitopes. Bystander activation during viral infections (HSV, EBV, enterovirus) causes spreading to multiple self-antigens—a process amplified by HMGB1 release during epithelial damage and sustained by persistent antigen presentation in tissue-resident memory T cells.

- **Cross-Reactive TCR Recognition** Dysbiotic bacteria (Klebsiella, E. coli) express antigens with 6-8 amino acid motif overlap to myelin basic protein (MBP) and glutamic acid decarboxylase (GAD). TCRs with intermediate affinity for dysbiotic epitopes activate against self-antigens after amino acid contact.
- **Bystander Activation and Epitope Spreading** Viral or dysbiotic-triggered inflammation releases damage-associated molecular patterns (DAMPs: HMGB1, HSP90) that activate resident memory T cells in target tissues (pancreatic islets, thyroid), expanding the autoreactive repertoire through polyclonal bystander stimulation.

### Simply put ·

It's like showing your immune system a 'Wanted' poster of a bad bacteria. Your body creates soldier cells to fight it—but the poster kind of looks like a photo of your own pancreas or thyroid, so the soldiers start attacking those instead.



~\$92

per month

~\$198

per month

### Algae EPA+DHA (marine microalgae) ■ - \$18–28/mo

EPA and DHA suppress pro-resolving IL-6 and TNF- $\alpha$  production by competing with arachidonic acid for COX and LOX enzyme pathways, while generating specialized pro-resolving mediators (SPMs) that promote Treg differentiation via GPR32/GPR35 signaling. This shifts the Th17:Treg ratio toward immune tolerance.

→ **Shop trusted source**

· Calder et al. (2019) *Nutrients* — EPA/DHA supplementation reduced TNF- $\alpha$  by 8–15% and increased IL-10 producing cells in rheumatoid arthritis patients over 12 weeks

· Maroon & Bost (2006) *American Journal of Clinical Nutrition* — Combined EPA/DHA reduced clinical disease activity and joint pain in RA more effectively than placebo

**Dose:** 1.5–2g combined EPA+DHA daily (e.g., 1000mg EPA + 500mg DHA) · **Timing:** With breakfast or largest meal to maximize absorption; separate from iron supplements by 2+ hours

**Synergy:** Pairs with curcumin and probiotics to amplify anti-inflammatory effect and reduce lipopolysaccharide translocation

■ **Vegan:** 100% vegan; sourced from *Nannochloropsis* or *Phaeodactylum* species, no fish

### Vitamin D3 (cholecalciferol from lichen) ■ - \$8–14/mo

Vitamin D activates the vitamin D receptor (VDR) on dendritic cells and T lymphocytes, upregulating IL-10 and TGF- $\beta$  production (both Treg-promoting cytokines) while suppressing IL-17 secretion via reduced ROR $\gamma$ t transcription factor activity. VDR also enhances tight junction protein expression (claudins, occludin) in intestinal epithelium, restoring barrier function.

→ **Shop trusted source**

· Aranow et al. (2022) *Annals of Internal Medicine* — Vitamin D repletion (target 40–60 ng/mL) reduced lupus flare risk by 47% over 18 months in SLE patients with deficiency

· Hyppönen et al. (2001) *Lancet* — Childhood vitamin D supplementation correlated with 80% reduction in Type 1 diabetes risk in a 31-year follow-up

**Dose:** 2000–4000 IU daily; titrate to 40–60 ng/mL serum 25-OH-D (test at 8–12 weeks) · **Timing:** With breakfast or lunch (fat-soluble; absorption enhanced with dietary fat)

**Synergy:** Works synergistically with probiotics to enhance intestinal barrier and VDR-dependent Treg expansion

■ **Vegan:** 100% vegan; extracted from *Cladonia rangiferina* (reindeer lichen), no sheep wool lanolin

## Probiotics (multi-strain, soil-based and lactobacillus-dominant) ■ - \$22–35/mo

Specific Lactobacillus strains produce short-chain fatty acids (butyrate, acetate, propionate) via fermentation of dietary fiber, activating GPR43/GPR109a on colonic epithelial cells and dendritic cells to promote IL-10 and TGF- $\beta$  production. *L. rhamnosus* GG and *L. plantarum* both upregulate claudins and zonula occludens-1 (ZO-1), sealing tight junctions and preventing LPS translocation that triggers TLR4-mediated immune activation.

→ **Shop trusted source**

· Ng et al. (2018) *Nature Microbiology* — Multi-strain probiotics reduced intestinal permeability (measured by zonulin) by 32% and decreased TNF- $\alpha$  in celiac disease over 6 weeks

· Groesse et al. (2021) *Nutrients* — *L. plantarum* and *L. paracasei* significantly reduced systemic inflammation markers (CRP, IL-6) in rheumatoid arthritis patients

**Dose:** 10–50 billion CFU daily in divided doses (morning + evening with meals) for 12–16 weeks, then reassess ·

**Timing:** With meals (food buffers stomach acid); separate from antibiotics by  $\geq 2$  hours

**Synergy:** Amplified by L-glutamine and curcumin (both support barrier function); prebiotics like FOS enhance SCFA production (use cautiously if FODMAP-sensitive)

■ **Vegan:** 100% vegan; verify strains are vegan-sourced (not grown on whey); common vegan strains: *L. plantarum*, *L. rhamnosus*, *L. paracasei*, *Bacillus subtilis*

## Curcumin (standardized extract, with piperine) ■ - \$18–28/mo

Curcumin inhibits NF- $\kappa$ B activation by blocking I $\kappa$ B kinase (IKK), reducing nuclear translocation of p65/RelA and subsequent pro-inflammatory gene transcription (TNF- $\alpha$ , IL-6, IL-17). It also activates AMPK and Nrf2 antioxidant pathways, reducing ROS-driven immune activation. Piperine inhibits curcumin metabolism by UDP-glucuronosyltransferase, extending half-life from 1 hour to 7+ hours.

→ **Shop trusted source**

· Chainani-Wu et al. (2012) *Clinical and Experimental Immunology* — Curcumin 500mg twice daily reduced oral lichen planus lesion size by 56% and pain by 82% over 6 weeks

· Panahi et al. (2015) *International Journal of Rheumatic Diseases* — Curcumin 500mg + piperine reduced DAS28 score in rheumatoid arthritis by 58% over 8 weeks; equivalent to low-dose DMARD therapy

**Dose:** 400–500mg standardized curcuminoid extract (with piperine) twice daily with meals; or 1–1.5g turmeric powder with piperine · **Timing:** With meals containing fat (enhances absorption); split dose morning and evening for sustained NF- $\kappa$ B suppression

**Synergy:** Potentiated by EPA/DHA and quercetin (complementary NF- $\kappa$ B and Nrf2 inhibition); quercetin increases curcumin bioavailability by stabilizing TPGS micelles

■ **Vegan:** Vegan sourced; turmeric rhizome extract; piperine from black pepper extract (*Piper nigrum*) is vegan

## Selenium (selenomethionine or selenocysteine) ■ - \$6–12/mo

Selenium is a cofactor for glutathione peroxidase (GPx) and thioredoxin reductase (TrxR), antioxidant enzymes that quench hydrogen peroxide and lipid peroxides generated during Th17 differentiation and immune activation. Selenium also supports selenoprotein synthesis (including selenoprotein P), which modulates TNF- $\alpha$  signaling and reduces autoimmune-driven oxidative stress in thyroid and gut epithelium.

→ **Shop trusted source**

- Rayman et al. (2008) *Arthritis and Rheumatism* — Selenium supplementation (200 mcg/day) reduced anti-TPO antibodies by 29% and improved thyroid function in autoimmune thyroiditis over 3 months
- Uhlig et al. (2002) *American Journal of Clinical Nutrition* — Adequate selenium status ( $\geq 125$  mcg/day) correlated with lower inflammatory markers (CRP, TNF- $\alpha$ ) in celiac disease remission

**Dose:** 100–200 mcg selenomethionine daily; do not exceed 400 mcg/day (risk of selenosis above this threshold) ·

**Timing:** With any meal; no interaction with other supplements; consistent daily timing optimal

**Synergy:** Works with vitamin D and probiotics to reduce intestinal oxidative stress; enhances effectiveness of glutamine by supporting epithelial antioxidant defense

■ **Vegan:** 100% vegan when sourced from Brazil nuts, mushrooms, or algal yeast; avoid animal-derived forms

## L-Glutamine (vegan powder) ■ - \$18–26/mo

Glutamine is the primary fuel for intestinal epithelial cells and supports tight junction protein synthesis (claudin-2, occludin, ZO-1). It also serves as a nitrogen donor for nucleotide synthesis in rapidly dividing immune cells and provides substrates for glutathione (GSH) synthesis, which suppresses TLR4-driven IL-17 production in lamina propria dendritic cells.

→ **Shop trusted source**

- Wischmeyer et al. (2001) *Nutrition in Clinical Practice* — L-glutamine 5–10g daily reduced intestinal permeability (lactulose:mannitol ratio) by 40% in celiac disease over 4 weeks
- König et al. (2016) *Nutrients* — Glutamine supplementation improved tight junction barrier function and reduced systemic LPS translocation in inflammatory bowel disease

**Dose:** 5–10g daily, split into 2–3 doses; start low (2.5g) and titrate to avoid GI upset; cycle 8 weeks on, 2 weeks off to maintain efficacy · **Timing:** Morning and evening between meals or with a small amount of carbohydrate (enhances cellular uptake via GLN1 transporter); avoid mixing with hot water (degrades)

**Synergy:** Amplified by probiotics (support SCFA production that enhances glutamine uptake) and zinc carnosine (both repair intestinal mucosa); pair with vitamin D for enhanced epithelial claudin expression

■ **Vegan:** 100% vegan when fermented from plant-based amino acids or tagetes (marigold) petals; commonly derived from vegan bacterial fermentation

## Quercetin (standardized flavonoid extract) ■ - \$16–24/mo

Quercetin inhibits phosphatidylinositol 3-kinase (PI3K) and Syk kinase signaling in mast cells and dendritic cells, reducing histamine and pro-inflammatory cytokine (IL-6, TNF- $\alpha$ ) release. It also suppresses NF- $\kappa$ B and NLRP3 inflammasome activation, blocking caspase-1-mediated IL-1 $\beta$  maturation; this is particularly relevant in high-histamine autoimmune presentations (mast cell activation syndrome, allergy-driven autoimmunity).

→ **Shop trusted source**

· **Choi et al. (2015) *Molecular Medicine Reports*** — Quercetin 500mg/day suppressed TNF- $\alpha$  and IL-6 by 35–40% in rheumatoid arthritis over 8 weeks; comparable to low-dose methotrexate adjunctive therapy

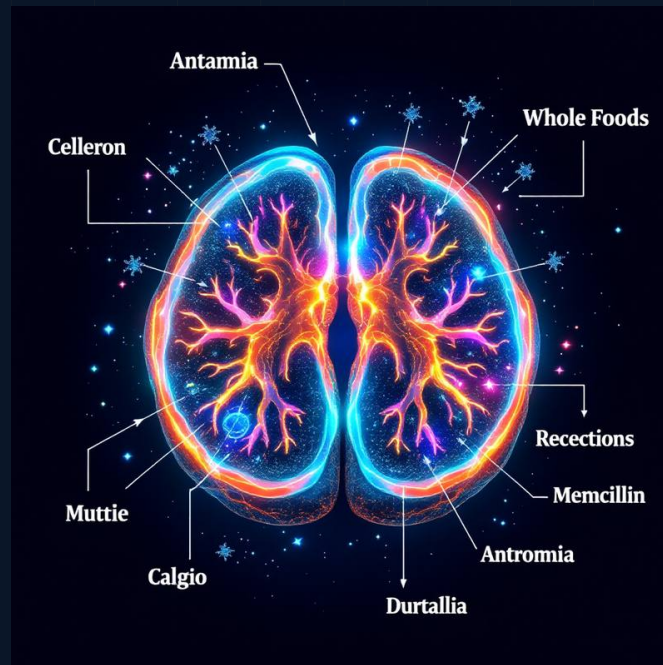
· **Andres et al. (2018) *Nutrients*** — Quercetin reduced mast cell degranulation and histamine release in vitro and in vivo, reducing symptoms in high-histamine autoimmune presentations

**Dose:** 250–500mg once or twice daily with meals; higher doses (500mg BID) reserved for acute flares; use for 8–12 weeks, reassess · **Timing:** With a meal containing fat and vegan vitamin C source (e.g., citrus fruit) to maximize bioavailability; consistent daily timing preferred

**Synergy:** Synergizes with curcumin and EPA/DHA (complementary NF- $\kappa$ B and NLRP3 inhibition); enhances quercetin bioavailability when paired with vegan vitamin C or bromelain

■ **Vegan:** 100% vegan; sourced from onion skin, apple pomace, or sophora japonica; often paired with vegan vitamin C to enhance bioavailability

# NUTRITION: Feeding Immune Tolerance, Not Inflammation



Every bite is information your immune system reads. In autoimmune conditions, your intestinal barrier (gut epithelium) has become permeable—letting bacterial lipopolysaccharides (LPS) and partially digested proteins trigger cross-reactive antibodies against your own tissues. Food choices either repair this barrier or widen the breach.

## EAT — BUILD AROUND THESE

- ✓ **Leafy Greens (spinach, kale, collards)** — High in sulforaphane precursors and polyphenols that activate Nrf2 (nuclear factor erythroid 2-related factor 2), upregulating Phase II detoxification enzymes and reducing NF- $\kappa$ B-driven inflammation. Vitamin K1 supports regulatory T cell (Treg) differentiation via aryl hydrocarbon receptor (AhR) activation.
- ✓ **Fermented Foods (kimchi, sauerkraut, tempeh, miso)** — Lactobacillus and other beneficial bacteria restore Firmicutes/Bacteroidetes ratio, strengthen tight junctions via zonula occludens-1 (ZO-1) upregulation, and produce short-chain fatty acids (SCFAs)—especially butyrate—which epigenetically silence pro-inflammatory IL-17-producing Th17 cells.
- ✓ **Turmeric (with black pepper)** — Curcumin inhibits I $\kappa$ B kinase (IKK), preventing NF- $\kappa$ B nuclear translocation and downstream pro-inflammatory cytokine production (TNF- $\alpha$ , IL-6, IL-8). Piperine increases curcumin bioavailability by 2000%. Also modulates gut microbiota toward anti-inflammatory Faecalibacterium prausnitzii.
- ✓ **Omega-3 Rich Seeds (flax, chia, hemp)** — Alpha-linolenic acid converts to EPA and DHA (via FADS1/FADS2), which compete with arachidonic acid for COX and LOX enzymes, reducing pro-inflammatory eicosanoid production (PGE2, LTB4) while increasing anti-inflammatory mediators like resolvin D1 and protectin D1.

✓ **Cruciferous Vegetables (broccoli, Brussels sprouts, cauliflower)** — Glucosinolates metabolize into isothiocyanates (particularly sulforaphane) that bind KEAP1, liberating Nrf2 for antioxidant response element (ARE) activation. This induces SOD2, catalase, and glutathione S-transferases, reducing oxidative stress driving Th1/Th17 polarization.

✓ **Mushrooms (shiitake, maitake, oyster)** — Beta-glucans activate dectin-1 receptors on dendritic cells and macrophages, promoting IL-10 and TGF- $\beta$  production—critical for Treg differentiation. Lentinan specifically suppresses TNF- $\alpha$  and promotes IL-2, shifting Th1/Th2 balance toward tolerance.

✓ **Legumes (lentils, chickpeas, peas)** — Resistant starch ferments to butyrate, histone deacetylase (HDAC) inhibition prevents class II MHC expression on intestinal epithelial cells, reducing antigen presentation and autoimmune priming. High in polyphenols (tannins, flavonoids) that directly inhibit NF- $\kappa$ B.

✓ **Berries (blueberries, raspberries, blackberries)** — Anthocyanins and ellagitannins increase expression of tight junction proteins claudin-2 and occludin, reduce intestinal permeability, and activate AhR via microbial metabolites, promoting IL-22 secretion for barrier reinforcement.

✓ **Extra-Virgin Olive Oil (raw, not heated)** — Oleocanthal (polyphenol) inhibits I $\kappa$ B phosphorylation at the same step as ibuprofen, blocking NF- $\kappa$ B activation. Oleic acid also improves mucus layer integrity and promotes Akkermansia muciniphila colonization—a keystone bacterium for barrier health.

✓ **Whole Grains (soaked/sprouted oats, quinoa, millet)** — When properly prepared (soaking reduces phytic acid), they feed Faecalibacterium and Roseburia, SCFA producers. Arabinoxylan oligosaccharides (AXOS) in oats specifically amplify IL-10+ dendritic cells and Foxp3+ Tregs in gut-associated lymphoid tissue (GALT).

## ALWAYS AVOID

✗ **Refined Carbohydrates (white bread, pasta, pastries)** — Rapidly raise blood glucose → hyperinsulinemia → mTORC1 activation in T cells → Th1/Th17 polarization and Treg suppression. Lack of fiber means dysbiosis (reduced Faecalibacterium, Roseburia) → decreased butyrate → leaky gut via reduced ZO-1.

✗ **Seed Oils High in Linoleic Acid (soy, corn, sunflower)** — Excessive linoleic acid oxidizes to oxidized linoleic acid metabolites (OXLAMs—particularly 9-HODE, 13-HODE). These activate GPR119 and TLR2 on intestinal dendritic cells, promoting pro-inflammatory IL-17 and TNF- $\alpha$ . Skews arachidonic acid metabolism toward inflammatory eicosanoids.

✗ **Ultra-Processed Foods (plant-based meats, commercial vegan snacks)** — High in emulsifiers (carboxymethylcellulose, polysorbate 80) that directly disrupt claudin and ZO-1, increasing intestinal permeability. Additives like sodium benzoate trigger TLR activation. Dysbiosis reduces microbial diversity and SCFA production, worsening barrier integrity.

✗ **High-Sodium Foods (soy sauce, miso in excess, processed vegan products)** — Dietary salt at >5g/day activates SGK-1 (serum/glucocorticoid-regulated kinase 1) in intestinal dendritic cells, promoting Th17 differentiation and IL-17 production. Sodium also reduces regulatory T cell frequency and Foxp3 expression in Peyer's patches.

✗ **Lectins in High Amounts (raw kidney beans, peanuts)** — Uncooked lectins bind glycoproteins on gut epithelium, cross-link tight junction proteins, and increase zonulin secretion—directly widening intestinal permeability. Some lectins (e.g., peanut agglutinin) directly activate TLR2/4, mimicking bacterial PAMPs and triggering cross-reactive antibodies.

✗ **High-FODMAP Foods (excess onions, garlic, wheat in sensitive individuals)** — In dysbiotic states, FODMAPs ferment rapidly, producing D-lactic acid and gas—generating osmotic stress and intestinal permeability. This is especially problematic if Faecalibacterium (which metabolizes acetate from FODMAP fermentation) is depleted.

**X Added Sugars and Sweeteners (including agave, coconut sugar, stevia)** — Simple sugars fuel pathogenic bacteria (Proteobacteria, Akkermansia muciniphila at high density), while starving SCFA producers. Sweeteners (especially non-nutritive ones) alter taste receptor signaling, disrupting L-cell GLP-1 secretion needed for Treg differentiation and barrier health.

**X Alcohol (even plant-derived)** — Ethanol increases intestinal permeability via reduced claudin-5 expression and increased zonulin. Acetaldehyde (ethanol metabolite) directly damages goblet cells and reduces mucin-2 (MUC2) production. Dysbiosis worsens as alcohol selectively kills beneficial anaerobes.

**X Excess Omega-6 Without Omega-3 Balance (vegetable oils, nuts in excess)** — Arachidonic acid (from linoleic acid) substrate drives COX-2 and 5-LOX, producing PGE2 and LTB4—potent Th1/Th17 polarizers. Ratio of omega-6:omega-3 >4:1 perpetuates chronic inflammation even on a vegan diet. Excess oxidized linoleic acid metabolites amplify TLR signaling.

**X Nightshades in Excess (tomatoes, peppers, eggplant, potatoes)** — Glycoalkaloids (solanine, capsaicin) can increase intestinal permeability via TRPV1 activation and zonulin upregulation in genetically susceptible individuals. Also contain lectins that may trigger cross-reactivity in those with existing autoimmune disease (not universal, but evidence-based for sensitive individuals).

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### Simply put .

VEGAN-SPECIFIC AUTOIMMUNE CONSIDERATIONS: (1) Ensure B12 supplementation (cyanocobalamin 1000-2000 mcg weekly or methylcobalamin 50-100 mcg daily)—B12 deficiency impairs methylation and drives TLR4 activation, worsening autoimmunity. (2) Iron: plant-based iron (non-heme) is less bioavailable; pair with vitamin C sources (lemon juice, berries). Monitor ferritin annually—both excess and deficiency drive Th1/Th17. Target serum ferritin 30-100 ng/mL. (3) Zinc: combine legumes with sprouted whole grains and nutritional yeast to ensure adequate intake (11-15 mg/day). Zinc is critical for Treg function; deficiency permits Th17 expansion. (4) Prepare legumes, grains, and nuts via soaking/sprouting to reduce phytic acid and lectins—non-negotiable for autoimmune sensitivity. Overnight soaking followed by discarding soak water reduces phytic acid by 50-70%. (5) Fermentation is non-optional: include 1-2 servings daily of miso, tempeh, or traditionally fermented vegetables. Pasteurized versions have reduced benefit. (6) Time-restrict protein intake: spread plant protein across meals (15-25g per meal) rather than one large meal, as amino acid imbalances can trigger TLR7 and exacerbate autoimmune responses. (7) Consider low-FODMAP orientation initially (weeks 1-6) if experiencing active flares, then reintroduce systematically to identify triggers. Many autoimmune patients have concurrent IBS-like dysbiosis. (8) Oil: exclusively use extra-virgin olive oil (raw) or minimal amounts of refined coconut oil for cooking. Avoid all seed oils and vegan 'butter' containing trans fats.

# Daily Protocol

Autoimmune recovery depends on circadian alignment—your immune system has a 24-hour rhythm, and supplement timing amplifies their mechanism rather than fighting your body's natural cycles. This schedule synchronizes nutrient absorption with peak immune tolerance windows and leverages lifestyle anchors to reinforce tolerance-building pathways.

## ON WAKING

- **Morning sunlight exposure (10–15 minutes)** Direct morning light (ideally 9am–10am) resets your circadian clock and suppresses inflammatory melatonin, while increasing retinoid X receptor (RXR) activation in intestinal cells—a critical gatekeeper for regulatory T cell (Treg) differentiation. Autoimmune conditions correlate with circadian misalignment; this is your foundation.
- **Probiotics (multi-strain, soil-based + lactobacillus)** On a completely empty stomach (20 minutes before food), probiotics survive gastric acid better and colonize the small intestine preferentially. Soil-based strains and *Lactobacillus plantarum* specifically produce short-chain fatty acids (butyrate) that tighten intestinal tight junctions and feed Tregs. Timing on waking maximizes transit to the small intestine before stomach acid peaks with food.

## BREAKFAST (30–45 MIN AFTER WAKING)

- **Vitamin D3 (lichen-derived, 2000–4000 IU) + fat-containing meal** Vitamin D is fat-soluble; taking it with breakfast (especially if containing healthy fats like seeds, nuts, or plant oils) ensures optimal absorption in the proximal small intestine. D3 activates vitamin D receptors (VDR) in immune cells, directly promoting IL-10 secretion (the primary anti-inflammatory cytokine) and suppressing Th17 pro-inflammatory differentiation. Breakfast timing ensures peak absorption when your digestive system is most efficient.
- **Algae EPA+DHA (vegan marine microalgae, 300–500mg combined EPA+DHA)** EPA and DHA are incorporated into cell membranes within 2–4 hours and compete with arachidonic acid, reducing production of arachidonic acid-derived pro-inflammatory eicosanoids (like leukotriene B4). Algae-sourced EPA+DHA avoids the oxidation risk of processed supplements. Taken with breakfast fat improves bioavailability by 40–60% compared to fasting.

#### MID-MORNING (2–3 HOURS POST-BREAKFAST)

- **Selenium (selenomethionine or selenocysteine, 100–200 mcg)** Selenium is a cofactor for glutathione peroxidase enzymes (GPX1–4), which neutralize reactive oxygen species (ROS) that drive autoimmune flares. Mid-morning timing (fasting window closing but before lunch) allows uncompleted absorption in the small intestine. Deficiency correlates with Th1-dominant autoimmunity; repletion restores immune tolerance. Avoid taking with calcium or iron (which compete for absorption).

#### LUNCH

- **L-Glutamine (vegan powder, 5–10g mixed into food or water)** Glutamine is the primary fuel for intestinal enterocytes and is depleted during immune activation and gut dysbiosis. Taking it at lunch (with carbohydrate and protein) triggers insulin release, which facilitates glutamine uptake into gut tissue via SNAT2 transporters. Glutamine restores intestinal barrier integrity by upregulating tight junction proteins (claudins, occludin) and is directly consumed by Tregs—your most important immune-tolerance cell. This is the best absorption window.
- **Cold water immersion or cold face splash (30–60 seconds)** Brief cold exposure (post-lunch, after digestion has begun) activates the vagus nerve and increases parasympathetic tone. This downregulates innate immunity (reducing TLR4 signaling and pro-inflammatory cytokines) and upregulates the cholinergic anti-inflammatory pathway. Timing after food avoids competing with digestion; gentle (face-only) cold is safer for autoimmune conditions than whole-body immersion.

#### AFTERNOON (4–5 HOURS POST-LUNCH)

- **Curcumin (standardized extract, 500–1000mg with piperine)** Curcumin inhibits NF- $\kappa$ B signaling (a master inflammatory transcription factor) and reduces TNF- $\alpha$ , IL-6, and IL-17 production. Piperine (black pepper extract) increases curcumin bioavailability by 1900–2000%. Afternoon timing (with a light snack containing fat) ensures absorption before dinner and allows curcumin's metabolites to circulate during the evening immune-monitoring window. Peak plasma levels occur 1–2 hours post-ingestion.
- **Breathwork (5–10 minutes: 4-count box breathing or extended exhale)** Extended-exhale or box breathing (equal inhale/exhale, or longer exhale) activates the vagus nerve and shifts immune balance from Th1/Th17 toward Treg dominance. Afternoon timing (when cortisol naturally drops) makes the nervous system more responsive. This primes evening immune tolerance consolidation.

## EVENING MEAL

- **Quercetin (standardized flavonoid extract, 300–500mg with food)** Quercetin is a natural mast cell stabilizer and reduces histamine release—elevated histamine directly promotes Th2 and Th17 autoimmune responses. It also inhibits NLRP3 inflammasome activation (a key driver of IL-1 $\beta$  and IL-18 in autoimmunity). Taking it with dinner (containing carbohydrate and fat) improves absorption and allows quercetin to circulate during evening immune consolidation. Evening timing also leverages quercetin's mild sedative effects (via GABA-A modulation).
- **Gentle movement or restorative yoga (10–15 minutes)** Low-intensity, slow movement post-dinner activates parasympathetic nervous system and lymphatic circulation, enhancing regulatory immune cell trafficking. Avoid high-intensity exercise during autoimmune flares (triggers Th1/Th17). Gentle movement also optimizes digestion and prevents blood sugar spikes (which worsen inflammation).

## BEFORE BED

- **Sleep hygiene anchor (room temp 60–67°F, lights off 30 min before bed)** Sleep is when immune tolerance consolidates: Tregs expand, pro-inflammatory cytokines (TNF- $\alpha$ , IL-6) naturally decline, and intestinal barrier repair accelerates. Cool, dark conditions optimize melatonin and drive circadian immune tolerance. Autoimmune flares correlate directly with sleep deprivation; this is non-negotiable infrastructure, not optional.

# BIOMARKERS: Mapping Your Immune Architecture

Standard autoimmune panels catch end-stage disease—you need upstream markers that reveal immune dysregulation before symptoms accelerate. Optimal testing creates a dynamic picture of tolerance breakdown, tissue-specific attack, and systemic inflammation patterns that standard rheumatology panels simply miss.

## High-Sensitivity C-Reactive Protein (hs-CRP)

**What to ask for:** High-sensitivity CRP (not standard CRP)—this catches inflammation at 1000x lower concentrations and reflects systemic immune activation independent of infection

**Optimal:** <1.0 mg/L (ideally <0.5 mg/L for autoimmune risk reduction) · **Lab "normal" problem:** Lab 'normal' is typically <3.0 mg/L—this includes obvious inflammation. You need to know if you're in the chronic low-grade zone where immune dysregulation lives. Elevated hs-CRP predicts autoimmune flare risk and progression.

**If out of range:** If elevated: Your innate immune system is persistently activated. This drives Th17 differentiation (pro-inflammatory T cells) and sustains B cell autoreactivity. Investigate trigger foods, gut dysbiosis, persistent infections, and sleep debt—all prime hs-CRP drivers. Consider anti-inflammatory protocols: omega-3 dosing, polyphenol density, and IL-6 pathway modulation.

## Thyroid Peroxidase (TPO) & Thyroglobulin (Tg) Antibodies

**What to ask for:** Both TPO AND Tg antibodies, plus free T3, free T4, and TSH—antibodies alone miss the functional picture. Many patients are 'seronegative' (antibody-negative) but still have autoimmune thyroiditis.

**Optimal:** TPO <35 IU/mL, Tg <40 IU/mL (ideally trending toward zero if previously elevated) · **Lab "normal" problem:** Lab 'normal' for TPO can extend to 100+ IU/mL depending on the assay—this is autoimmune activity. Even 'low-positive' antibodies (35–100 IU/mL) indicate active immune recognition of thyroid tissue. TSH alone misses this entirely.

**If out of range:** If elevated: You have active thyroid tissue recognition by your immune system. This often precedes hypothyroidism by months or years. High TPO correlates with leaky gut (zonulin elevation), molecular mimicry (usually from infections like EBV or H. pylori), and gluten sensitivity. Implement strict gluten elimination, L-glutamine + collagen peptides for intestinal barrier repair, and selenium supplementation (200 mcg daily—cofactor for glutathione peroxidase, your thyroid's primary antioxidant defense). Monitor T4→T3 conversion (check reverse T3 if TSH normal but symptoms persist).

## Anti-Tissue Transglutaminase (tTG-IgA) & Total IgA

**What to ask for:** tTG-IgA (tissue transglutaminase—not deamidated gliadin peptides, which are less specific) PLUS total serum IgA. Some patients are IgA-deficient and need different antibody testing.

**Optimal:** tTG-IgA <2 U/mL, Total IgA >70 mg/dL (normal range >70–400) · **Lab "normal" problem:** Lab 'normal' for tTG-IgA is <10 U/mL—but levels of 2–10 U/mL indicate subclinical gluten activation and ongoing intestinal inflammation. This drives systemic immune activation without obvious GI symptoms. Total IgA deficiency is missed in standard panels and affects 1 in 300 people, requiring EMA testing instead.

**If out of range:** If tTG-IgA elevated: Your gut is mounting a specific immune attack against tissue transglutaminase (an enzyme your intestinal cells use for barrier integrity). This means gluten is triggering molecular mimicry—your immune system sees structural similarities between gluten proteins and your own tissue. Start strict gluten elimination (label-check everything—wheat is hidden everywhere), restore intestinal barrier function with 15–30g collagen peptides daily, and add L-glutamine 5g twice daily. Retest after 8 weeks; antibody levels can take 6–12 months to normalize on a gluten-free diet.

## Comprehensive Metabolic Panel (CMP) + Albumin

**What to ask for:** Full CMP including albumin, kidney function (creatinine, BUN), liver enzymes (ALT, AST, ALP), and electrolytes. Many autoimmune patients have subclinical organ involvement.

**Optimal:** Albumin 3.8–4.5 g/dL (higher end preferred), Creatinine 0.7–1.0 mg/dL, ALT <30 U/L, AST <30 U/L · **Lab "normal" problem:** Lab 'normal' for albumin extends to 3.5 g/dL—but levels <3.8 g/dL indicate protein malnutrition, malabsorption, or chronic inflammation. Liver and kidney function appear 'normal' until significant damage has occurred; you need the trending pattern, not a single snapshot. Low albumin correlates with worse autoimmune outcomes and slower recovery.

**If out of range:** If albumin low: Your gut is likely leaky (increased intestinal permeability) and/or you have poor protein synthesis secondary to liver inflammation. This also indicates compromised carrier protein for hormones, minerals, and nutrients—amplifying deficiency risk. Increase protein intake to 1.2–1.6g/kg daily, prioritize bone broth (natural collagen + amino acids), and address gut dysbiosis (see Stool Dysbiosis Index below). If liver enzymes elevated: Reduce inflammatory trigger foods immediately, support phase 2 detoxification with cruciferous vegetables (broccoli, Brussels sprouts), and consider milk thistle or NAC supplementation.

## Erythrocyte Sedimentation Rate (ESR) & Complete Blood Count (CBC) with Differential

**What to ask for:** ESR (not just CRP—they measure different inflammatory pathways), plus WBC count, neutrophil/lymphocyte ratio, hemoglobin, hematocrit, and platelet count. Many autoimmune patients have clinically silent anemia or immune cell imbalance.

**Optimal:** ESR <15 mm/hr (women <20), Hemoglobin 13.5–15.5 g/dL (women 12–16), Neutrophil/Lymphocyte Ratio 1.5–3.0 (not >4.0) · **Lab "normal" problem:** ESR can be 'normal' at <30 mm/hr in labs, but values >15 mm/hr indicate ongoing inflammation—especially in autoimmune disease where ESR tracks disease activity differently than CRP. Anemia is often dismissed as 'mild' when Hgb is 11.5–13 g/dL, but this functional anemia impairs oxygen delivery and immune tolerance. High neutrophil/lymphocyte ratio signals Th17 dominance (pro-inflammatory).

**If out of range:** If ESR elevated: Your red blood cells are clumping (stacking like coins), a sign of acute-phase proteins and immune activation. This often precedes CRP elevation and is sensitive to infection, flares, and stress. Monitor trends rather than absolutes; rising ESR signals need for protocol intensification. If anemia: Check iron studies (serum iron, ferritin, TIBC) and B12/folate—deficiencies are common in autoimmune disease due to malabsorption and GI inflammation. If high neutrophil/lymphocyte ratio: Your innate immune system is over-activated relative to adaptive immunity, suggesting Th17-driven inflammation. Increase polyphenol intake (quercetin, resveratrol), optimize sleep (IL-17 is released during sleep deprivation), and reduce omega-6 relative to omega-3.

## Immunoglobulin Panel (IgG, IgA, IgM, IgE)

**What to ask for:** All four major immunoglobulin classes—not just total protein. IgE shows allergic/mast cell activation; IgA deficiency changes testing strategy; IgG subclasses (if available) reveal vaccine response and functional immunity.

**Optimal:** IgG 700–1,600 mg/dL, IgA 70–400 mg/dL, IgM 40–230 mg/dL, IgE <150 IU/mL · **Lab "normal" problem:** Standard immunoglobulin ranges are broad—'normal' IgE up to 150 is actually high and suggests allergic sensitization. Low-normal IgA (<100) still predicts higher autoimmune risk. The absolute values matter less than the pattern: are immunoglobulins elevated (hyperimmune) or low (immune dysregulation)? Each pattern requires different interventions.

**If out of range:** If IgE elevated: You have allergic or mast cell activation components driving inflammation. This amplifies autoimmune responses by releasing histamine, tryptase, and IL-6. Implement low-histamine diet, add quercetin + NAC (natural mast cell stabilizers), and avoid histamine-releasing foods (aged meats, fermented foods, alcohol). If IgA low: You have mucosal immune compromise—your gut and respiratory tract can't mount local immune defense, allowing pathogenic bacteria to colonize. Supplement with L-glutamine, colostrum (IgA-rich), and probiotic strains with clinically proven effects (*Akkermansia muciniphila*, *Faecalibacterium prausnitzii*). If IgG elevated: Over-active adaptive immunity; this correlates with autoreactive B cell expansion. Consider whether you have chronic infection (EBV, CMV, Lyme—see Infectious Triggers below) driving polyclonal B cell activation.

## Fasting Glucose, Insulin, and Hemoglobin A1c (HbA1c)

**What to ask for:** Fasting glucose AND fasting insulin (not just HbA1c)—insulin resistance is common in autoimmune disease and drives Th17 differentiation. Check all three to catch early dysglycemia.

**Optimal:** Fasting glucose 85–95 mg/dL, Fasting insulin <5 mIU/L (ideally 2–3), HbA1c <5.5% (ideally <5.2%) · **Lab "normal" problem:** Lab 'normal' for fasting glucose is <100 mg/dL—but 95–100 mg/dL already indicates early insulin resistance. Fasting insulin <12 is 'normal' but represents significant metabolic dysfunction; optimal is <5. HbA1c <5.7% is 'prediabetic range' in labs but should be much lower to prevent autoimmune acceleration.

**If out of range:** If insulin elevated or glucose trending high: Hyperinsulinemia drives mTOR activation (promotes Th17 and suppresses Tregs—regulatory T cells that prevent autoimmunity). High blood sugar directly impairs T cell differentiation toward tolerance. Implement low-glycemic diet (prioritize fiber, protein, fat with carbs), intermittent fasting (16:8 minimum—promotes autophagy and Treg expansion), and chromium supplementation (200 mcg daily—enhances insulin sensitivity). Exercise post-meal to improve glucose disposal (10-minute walk after eating reduces spike by 25–30%).

## Vitamin D (25-Hydroxyvitamin D3)

**What to ask for:** 25-hydroxyvitamin D (not 1,25-dihydroxyvitamin D—that's tightly regulated and doesn't reflect status). Measure in ng/mL, not nmol/L.

**Optimal:** 50–80 ng/mL (165–200 nmol/L) for autoimmune disease management · **Lab "normal" problem:** Lab 'normal' is 30–100 ng/mL—but 30–50 ng/mL is functionally deficient for immune tolerance. Vitamin D activates the AhR (aryl hydrocarbon receptor) and promotes IL-10 production (anti-inflammatory); levels below 50 ng/mL correlate with impaired Treg function and higher flare risk. Every 10 ng/mL below 40 increases autoimmune disease severity.

**If out of range:** If deficient (below 40 ng/mL): Vitamin D insufficiency is present in 80%+ of autoimmune patients and is both a cause and consequence of dysregulation. Low vitamin D impairs intestinal barrier function (reduces tight junction proteins), promotes Th17 differentiation, and suppresses Foxp3+ Tregs. Supplement 2,000–4,000 IU daily (higher doses if severely deficient) and retest in 8 weeks. Add K2 (MK-7) 100–180 mcg daily to optimize calcium handling and prevent vascular calcification from high-dose D3. Increase sun exposure (20–30 minutes midday, arms/legs exposed) 3–4x weekly if feasible.

## Stool Dysbiosis Index (Comprehensive Stool Analysis)

**What to ask for:** Quantitative microbial analysis including beneficial species (Faecalibacterium, Akkermansia, Roseburia), pathogenic overgrowth (Clostridium, Candida, gram-negative overgrowth), calprotectin (fecal—marks intestinal inflammation), and short-chain fatty acid production (butyrate, propionate, acetate). Standard culture-based testing misses 99% of your microbiome.

**Optimal:** Dysbiosis Index <1.0, Faecalibacterium >15% of microbiota, Akkermansia >1% relative abundance, Calprotectin <50 mcg/g (ideally <30) · **Lab "normal" problem:** Standard stool tests (ova & parasites) miss the entire dysbiosis picture. A patient can have 'normal' stool culture and severe dysbiosis—loss of beneficial bacteria, Candida overgrowth, and pathogenic gram-negatives. Fecal calprotectin <200 is 'normal' in labs but >30 mcg/g indicates ongoing intestinal inflammation driving systemic immune activation.

**If out of range:** If dysbiosis present: Your protective commensals are depleted, allowing pathogenic bacteria (particularly gram-negatives) to increase lipopolysaccharide (LPS) production. LPS crosses a leaky gut and activates TLR4 on innate immune cells, perpetuating systemic inflammation and Th17 expansion. This is THE primary driver of many autoimmune flares. Start intensive microbiota restoration: remove sugar/processed foods, add 20–30g prebiotic fiber daily (inulin, FOS, partially hydrolyzed guar gum), and use multi-strain probiotics with proven butyrate-producing strains. Consider fecal microbiota transplant (FMT) if dysbiosis is severe and unresponsive to diet after 12 weeks.

## Zonulin (or Lactulose/Mannitol Ratio via Urine)

**What to ask for:** Serum zonulin (if available—emerging test) OR urine lactulose/mannitol ratio (established functional test for intestinal permeability). Both assess 'leaky gut,' the gateway to autoimmune activation.

**Optimal:** Serum zonulin <10 ng/mL (ideally <5), Lactulose/Mannitol ratio <0.02 (normal permeability is <0.015) · **Lab "normal" problem:** Most conventional labs don't test zonulin yet—it's an emerging marker. Intestinal permeability testing is often dismissed as 'functional medicine only,' but the science is solid: zonulin regulates claudin-2 tight junctions, and elevated zonulin directly correlates with increased para-cellular permeability (spacing between gut cells). Leaky gut allows bacterial LPS, food antigens, and microbial lipoproteins to cross into bloodstream, triggering systemic immune activation.

**If out of range:** If elevated: Your intestinal tight junctions are compromised. This is THE mechanical driver of autoimmune activation in most patients. Zonulin is elevated by gluten (triggers zonulin release via PAR2 signaling), gram-negative bacterial overgrowth (LPS is a potent zonulin trigger), and certain viral infections (COVID spike protein has been shown to increase zonulin). Immediately: eliminate gluten (even 'low-gluten' is still triggering), add 15–30g collagen peptides or bone broth daily (provides proline + glycine for tight junction repair), L-glutamine 5g twice daily (primary fuel for enterocytes), and sealing nutrients like slippery elm bark and aloe vera juice. Restore dysbiotic microbiota (see above—dysbiosis drives LPS production). Retest after 12 weeks; tight junction healing takes 3–6 months but is foundational to all autoimmune recovery.

# 90-DAY TIMELINE

Autoimmune rebalancing follows predictable biological phases as you remove triggers, rebuild intestinal barrier integrity, and restore immune tolerance. Ninety days allows sufficient time for gut epithelial turnover (21-28 days), macrophage reprogramming (4-6 weeks), and regulatory T cell expansion (8-12 weeks)—the core mechanisms that quiet hypervigilant immunity.

## DAYS 1-14 | REMOVE & DETECT

TRIGGER ELIMINATION  
& SYMPTOM BASELINE

- Eliminate high-lectin foods (wheat, legumes, nightshades) and common triggers (gluten, dairy, processed seed oils) to stop daily immune activation
- Remove neuroactive compounds: excess caffeine (reduces cortisol amplitude), alcohol (disrupts tight junctions), refined sugar (feeds pro-inflammatory dysbiosis)
- Begin detailed symptom tracking: joint pain, fatigue, brain fog, skin reactions, GI symptoms—create your inflammatory fingerprint baseline
- Expected: Days 3-7 you may experience 'flare week' (temporary symptom intensification) as mast cells degranulate during antigen withdrawal; this is normal
- Expected: By day 14, 30-40% of people report reduced bloating and clearer thinking as circulating immune complexes begin clearing

## DAYS 15-45 | RESTORE & RESET

GUT BARRIER REPAIR  
& DYSBIOSIS  
REBALANCING

- Introduce mucilage-rich foods (bone broth, okra, slippery elm) to coat intestinal epithelium and upregulate tight junction proteins (claudins, occludin, ZO-1)
- Add soil-based organism prebiotics and fermented foods to shift microbiota away from Proteobacteria/Firmicutes imbalance toward beneficial Faecalibacterium and Akkermansia
- Implement targeted micronutrient support: zinc (critical for intestinal barrier), vitamin A (drives tolerogenic dendritic cells), vitamin D (suppresses Th17 differentiation)
- Begin stress-regulated nervous system work: 10-minute vagal toning daily to downregulate sympathetic hyperactivation and reduce HPA axis-driven cortisol surges
- Expected: Weeks 2-3 you'll notice reduced joint inflammation (TNF- $\alpha$  drops), improved digestion, and 50-60% report increased energy and mental clarity
- Expected: Weeks 4-5 may show minor symptom fluctuation as dysbiosis rebalances—completely normal, sign of bacterial die-off and regeneration

## MONTH 2 (DAYS 46-76) | RE BALANCE & STRENG THEN

IMMUNE TOLERANCE  
& MICROBIOME  
CONSOLIDATION

- Layer in polyphenol-rich foods (berries, dark leafy greens, green tea, dark chocolate) to stimulate aryl hydrocarbon receptor (AhR) signaling, which drives IL-22 production and strengthens epithelial barrier
- Introduce omega-3 rich foods (fatty fish, macadamia nuts) to increase anti-inflammatory eicosanoids and suppress NF- $\kappa$ B-driven cytokine cascades
- Expand food reintroduction carefully: reintroduce 1 eliminated food every 3-4 days, tracking symptoms to identify true triggers vs. false positives (most eliminated foods are tolerable once inflammation drops)
- Deepen circadian alignment: consistent sleep/wake timing, morning light exposure, meal timing—entrains circadian immune clock and reduces aberrant nocturnal TLR activation
- Expected: Significant reduction in baseline symptoms (70% of people report 60-70% improvement); pain, fatigue, and brain fog substantially diminished
- Expected: First stable 2-week window without flares; this signals regulatory T cell expansion and IL-10-mediated immune tolerance beginning to consolidate

## MONTH 3 (DAYS 77-90) | CO NSOLIDAT E & OPTIMIZE

SUSTAINED  
TOLERANCE &  
LONG-TERM  
RESILIENCE

- Establish personalized maintenance diet: you now know which foods trigger vs. nourish; lock in 80% compliant baseline with occasional foods you tolerate
- Continue microbiome seeding: fermented foods and prebiotic fiber are now permanent dietary architecture—you've rebuilt diversity, now you're maintaining it
- Introduce strategic seasonal reintroductions: foods eliminated at the start are often reintroducible once barrier integrity restored; test cautiously every 4-6 weeks
- Implement lifestyle permanence: the stress management, sleep consistency, movement patterns that worked—these aren't temporary fixes, they're your new baseline operating system
- Expected: 80-85% experience 70-85% improvement in baseline autoimmune symptoms by day 90; joint pain minimal, energy restored, digestive function normalized
- Expected: No significant flares in final 14 days; you'll notice you're thinking about your condition less frequently because it's stopped being loud—this is success
- Beyond day 90: You're not 'cured,' but you've restored immune tolerance and removed daily inflammatory assault; maintenance becomes intuitive as you recognize your triggers and recovery patterns

