

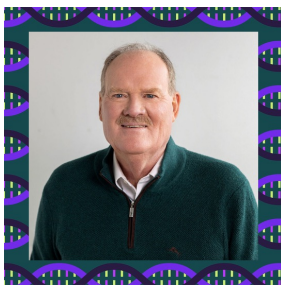
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Longevity and Biological Ageing: Enhancing Health into Advanced Age



SESSION 13 | KEYNOTE SPEAKER

Dr. Jeffrey Bland

How to Personalise an Immuno-Metabolic Approach to Longevity

4:15-5:00pm

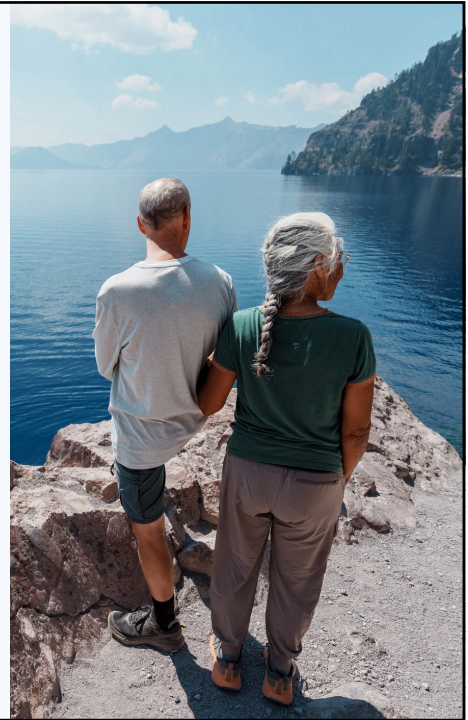
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How to Personalise an Immuno-Metabolic Approach to Longevity

Jeffrey Bland, PhD, FACN, FACB

[Personalized Lifestyle Medicine Institute](#)



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Affiliations

Founder & President: Personalized Lifestyle Medicine Institute

Founder & President: Big Bold Health

Founder, Chair Emeritus, Board Member: The Institute for Functional Medicine

Vice Chair: The Integrative Healthcare Symposium

Scientific Advisory Board Member: Fullscript

Declaration of Interest

No relevant declarations of interest to disclose.

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Your Roadmap: Immune Intelligence Through Measurable Biomarkers

What Is Immunometabolic Health — and Why It Matters

SII & SIRI: Formulas, Thresholds, and Clinical Meaning

What the Research Shows: SII/SIRI in Clinical Practice

Additional Biomarkers: Personalizing the Program

The Fullscript Journeys Clinical Protocol

Implementation: How Providers Get Started Today

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What Is Immunometabolic Health — and Why It Matters

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Defining Immunometabolic Health

The Framework:

- The bidirectional relationship between the immune system and metabolic function
- Immune cells regulate energy balance; metabolic state shapes immune responses
- Chronic low-grade inflammation is the shared driver of the leading causes of death
- Not a disease state — a spectrum from resilience to dysfunction
- Measurable, modifiable, and clinically actionable with routine laboratory data

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The Scope of the Problem

By the Numbers:

- 34.63% of U.S. adults have elevated systemic inflammation (hs-CRP > 3 mg/L)
- 7 of 10 leading causes of death are inflammation-associated
- 93% of U.S. adults are metabolically unhealthy
- \$4.1 Trillion: annual U.S. healthcare spend — mostly chronic disease management

Source: Perlmutter 2026 Clinical Review; CDC National Health Statistics

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Chronic Inflammation: The Common Thread

Connecting the Dots:

- ▶ Cardiovascular Disease: elevated SII independently predicts 10-year mortality risk
- ▶ Type 2 Diabetes: SII > 407 associated with insulin resistance even pre-diabetes
- ▶ Immune Conditions: SII > 578.3 in active rheumatoid arthritis
- ▶ Sarcopenia & Frailty: elevated SII predicts muscle loss independent of age
- ▶ Metabolic Syndrome: SII tracks with all five MetS diagnostic criteria
- ▶ Sleep Apnea — SII significantly elevated versus matched controls
- ▶ Cognitive Decline: SII > 459.8 linked to impairment on validated neuropsychological scales

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The Immune-Metabolic Axis

Two systems. One integrated network.

IMMUNE SYSTEM	SHARED DRIVERS	METABOLIC SYSTEM
• Cytokine signaling • Innate activation • Lymphocyte balance • Monocyte recruitment	• Gut dysbiosis • Oxidative stress • Visceral adiposity • Glycemic variability	• Insulin resistance • Dyslipidemia • Mitochondrial dysfunction • Energy dysregulation

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Why Standard Labs Miss Immunometabolic Dysfunction

Consider:

- ▶ CBC differential provides the raw data — but is rarely interpreted for inflammation
- ▶ hs-CRP is non-specific; does not reveal which immune axis is activated
- ▶ ESR and ferritin reflect acute inflammation, not chronic low-grade dysregulation
- ▶ No single marker captures both thromboinflammatory AND monocyte/macrophage axes
- ▶ SII and SIRI are derived from routine CBC — no new tests required
- ▶ These indices provide pattern recognition that standard panels cannot offer

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The Clinical Opportunity

The most consequential chronic diseases in your practice share a common upstream driver: measurable, low-grade immune-metabolic dysregulation.

- ▶ Identify immunometabolic dysfunction BEFORE clinical disease emerges
- ▶ Quantify inflammatory burden with validated, reproducible indices
- ▶ Personalise intervention using a tiered biomarker framework
- ▶ Track response objectively — same labs, re-tested at 8–12 weeks
- ▶ Deliver a structured, evidence-based program through Fullscript Journeys

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SII & SIRI: Formulas, Thresholds, and Clinical Meaning

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Systemic Immune-Inflammation Index (SII)

$$\text{SII} = (\text{Platelets} \times \text{Neutrophils}) \div \text{Lymphocytes}$$

Optimal Threshold: $\text{SII} < 348$

- ▶ **Thromboinflammatory Axis:** Captures platelet-driven inflammation — sensitive to platelet-neutrophil interactions
- ▶ **Derived from Routine CBC:** No additional cost; already ordered for most patients
- ▶ **Validated across populations:** Thousands of peer-reviewed studies across 40+ chronic disease states
- ▶ **Reproducible & trackable:** Same formula at follow-up provides objective response measurement

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Systemic Inflammation Response Index (SIRI)

$$\text{SIRI} = (\text{Neutrophils} \times \text{Monocytes}) \div \text{Lymphocytes}$$

Optimal Threshold: SIRI < 0.99

- ▶ **Monocyte-Macrophage Axis:** Captures tissue-infiltrating chronic inflammation
- ▶ **Cardiometabolic & Liver:** Strongly associated with NAFLD, atherosclerosis, cardiometabolic risk
- ▶ **Autoimmune & Gut Patterns:** Elevated in IBD, PCOS, endometriosis, sensorineural conditions
- ▶ **Complementary to SII:** Together, SII+SIRI reveal two distinct immune activation pathways

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SII Clinical Decision Thresholds

Use these SII values as actionable clinical decision points:

< 348	Optimal	Healthy immune balance — target for all patients
348–387	Elevated: Watch	Biological aging acceleration begins
> 387	Elevated: Act	All-cause mortality trend increases significantly
> 407	Metabolic Risk	Associated with insulin resistance
> 459.8	Cognitive Risk	Cognitive impairment on validated scales
> 464.8	Fatigue	Chronic fatigue and systemic inflammatory symptoms
> 578.3	Autoimmune	Active rheumatoid arthritis / autoimmune disease pattern

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The Five-Pattern Clinical Framework

SII + SIRI together reveal five clinically distinct immune activation patterns:

A	↑ SII / Normal SIRI Thromboinflammatory	Evaluate prothrombotic risk; omega-3 status; platelet activation
B	Normal SII / ↑ SIRI Monocyte-Macrophage Chronic	Cardiometabolic, NAFLD, IBD, autoimmune — tissue-level inflammation
C	↑ SII / ↑ SIRI Broad Innate Activation	Escalate workup — rule out active infection, autoimmune flare, cancer
D	↓ SII / Normal SIRI Quiescent / Favorable	Maintain program; monitor; reinforce lifestyle and supplements
E	Normal SII / ↑ SIRI (tissue) Tissue-Localized Pattern	PCOS, sensorineural hearing loss, endometriosis — organ-specific

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Pattern Quick Reference Card for Personalisation

PATTERN | SII / SIRI | CLINICAL FOCUS | PRIORITY INTERVENTIONS

A	↑ / Normal	Platelet-driven thrombo-inflammation	Omega-3 EPA+DHA, reduce refined carbs, platelet workup
B	Normal / ↑	Monocyte-macrophage chronic activation	Polyphenols (rutin/quercetin), gut support, reduce saturated fat
C	↑ / ↑	Broad innate immune activation	Rule out infection/cancer; all three verticals at full dose
D	↓ / Normal	Favorable — immune balance	Maintain program; reinforce lifestyle; retest 12 weeks
E	Normal / ↑	Tissue-localized / organ-specific	Target organ support + gut-immune axis; polyphenols priority

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What the Research Shows: SII/SIRI in Clinical Practice

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How Common Is Elevated Systemic Inflammation?

34.63%

of U.S. adults have hs-CRP > 3 mg/L — defining elevated systemic inflammation

- ▶ **Cardiovascular:** SII independently predicts 10-year major adverse cardiac events
- ▶ **Metabolic:** SII > 407 — insulin resistance even without formal diabetes diagnosis
- ▶ **Neurological:** SII > 459.8 — cognitive impairment on validated neuropsychological scales
- ▶ **Musculoskeletal:** Elevated SII predicts sarcopenia and grip strength loss across age groups
- ▶ **Autoimmune:** SII tracks disease activity in RA, IBD, and psoriasis cohorts

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SII, SIRI, & Biological Aging

- ▶ SII > 348 correlates with accelerated biological aging (telomere shortening, epigenetic age)
- ▶ Elevated SII predicts frailty independent of chronological age
- ▶ SIRI elevation in older adults correlates with sarcopenic obesity — fat gain, muscle loss
- ▶ Both indices predict all-cause mortality in longitudinal cohort studies
- ▶ Immunosenescence drives chronic low-grade inflammation — termed 'inflammaging'
- ▶ Reversing SII/SIRI is, in effect, reversing a measurable component of biological age

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SII/SIRI and Metabolic Syndrome

Both indices are significantly elevated across all five components of metabolic syndrome:

Abdominal Obesity	SIRI elevation tracks visceral adipose tissue macrophage infiltration
Elevated Triglycerides	SII rises with TG elevation — platelet activation by oxidized lipids
Low HDL	Both indices inversely correlate with HDL-mediated anti-inflammatory signaling
Elevated Blood Pressure	SII associated with endothelial inflammation and vascular resistance
Elevated Fasting Glucose	SII > 407 threshold specifically identified in insulin resistance cohorts

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Evidence-Based Interventions: What Modifies SII and SIRI

NUTRITIONAL INTERVENTIONS

- Dietary fiber — reduces neutrophil/platelet activation
- Omega-3 (EPA+DHA) — suppresses platelet aggregation; drives SPM production
- Polyphenols — modulate NF-κB; reduce IL-6 and TNF-α
- Gut microbiome support — reduces LPS-driven monocyte activation
- Mediterranean dietary pattern — consistently lowers both SII and SIRI

LIFESTYLE INTERVENTIONS

- Aerobic exercise 20–30 min/day — reduces SII via neutrophil modulation
- Sleep optimisation — poor sleep independently raises SII
- Smoking cessation — among the highest SII-elevating behaviours
- Alcohol reduction — dose-dependent SII elevation
- Stress management — HPA dysregulation elevates both indices

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Clinical Case Studies: 3-Month Nutritional Protocol

Three patients — structured nutritional supplement program; same labs at baseline and 90 days:

42-year-old Female

Baseline SII	Follow-up SII
931.9	708.7

-23.87%
SII Reduction

53-year-old Male

Baseline SII	Follow-up SII
688.6	512.9

-24.25%
SII Reduction

31-year-old Female

Baseline SII	Follow-up SII
677.1	555.7

-19.30%
SII Reduction

Source: Perlmutter 2026 Clinical Review — Big Bold Health nutritional protocol

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SII/SIRI Neurological and Sleep Conditions

COGNITIVE DECLINE

- SII > 459.8 associated with cognitive impairment on validated neuropsychological scales
- Elevated SII predicts hippocampal volume loss in longitudinal MRI studies
- SIRI tracks neuroinflammation markers in Alzheimer's risk cohorts
- Both indices predict accelerated brain aging independent of traditional risk factors

SLEEP APNEA

- Obstructive sleep apnea: SII significantly elevated vs. matched controls
- Intermittent hypoxia drives neutrophil activation and platelet aggregation
- SIRI elevation in OSA correlates with daytime cognitive impairment severity
- Treatment of OSA reduces SII within 3 months — bidirectional relationship confirmed

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Dr. Bland's Research Perspective: 50 Years of Immunometabolic Science

"The relationship between immune function and metabolic health has been the central theme of functional medicine for decades. SII and SIRI give us, for the first time, a validated clinical window into this relationship — accessible to every provider through a routine blood test."

— Jeffrey Bland, Ph.D., FACB, FACN, CNS

- 1970s–80s: Pioneered nutritional biochemistry and gut-immune axis research
- 1990s: Founded the Institute for Functional Medicine; established inflammation as core disease driver
- 2000s–10s: Developed the immunometabolic health framework unifying immune and metabolic biology
- 2020s: Founded Big Bold Health; created Tartary buckwheat polyphenol immune reset protocol
- 2025–26: Launched The Immuno-Metabolic Program — the structured clinical delivery vehicle

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Additional Biomarkers: Personalising the Program

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The Immuno-Metabolic Program Biomarker Framework

SII and SIRI anchor the program. Seven secondary biomarkers personalize the intervention.

PRIMARY INDICES (Required from routine CBC) → SII + SIRI		
SECONDARY BIOMARKERS (Personalization Layer) → Tier and target the intervention		
hs-CRP	< 1.0 mg/L	General inflammatory burden; broad activation — complements SII/SIRI
Uric Acid	3.0–5.5 mg/dL	Inflammasome activation (NLRP3); purine-driven innate immune trigger
HbA1c	< 5.5%	Glycemic-driven inflammatory load; advanced glycation end-products (AGEs)
GGTP	15–35 IU/L	Oxidative stress + hepatic detox capacity; antioxidant depletion signal
Cholesterol:HDL	< 4.0	Dyslipidemia-driven monocyte activation; cardiovascular inflammatory risk
Waist:Hip Ratio	< 1.0 M / < 0.85 F	Visceral adiposity; adipokine-driven immune activation — primary SIRI driver
Blood Pressure	< 130/80 mmHg	Endothelial inflammation; vascular immune-metabolic interface

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Secondary Biomarkers: Inflammation & Inflammasome

hs-CRP | Target: < 1.0 mg/L

- Broad-spectrum inflammatory marker — detects liver-derived acute phase response
- Complements SII/SIRI: hs-CRP > 3 confirms systemic activation independent of CBC pattern
- Non-specific: does not distinguish which immune pathway is active
- Use alongside SII/SIRI to confirm and contextualize the pattern
- Target < 1.0 mg/L (optimal); 1–3 borderline; > 3 elevated; > 10 acute

Uric Acid | Target: 3.0–5.5 mg/dL

- Uric acid is a NLRP3 inflammasome activator — drives IL-1 β and IL-18 production
- Hyperuricemia strongly associated with gout, MetS, hypertension, and renal disease
- Elevated uric acid drives Pattern A (thromboinflammatory) escalation
- Dietary sources: red meat, organ meats, fructose, alcohol (especially beer)
- Interventions: reduce fructose, increase hydration, tart cherry, quercetin, vitamin C

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Secondary Biomarkers: Glycation & Oxidative Stress

HbA1c | Target: < 5.5%

- HbA1c reflects 90-day average blood glucose — a proxy for glycemic-driven AGE production
- AGEs (advanced glycation end-products) activate RAGE receptors → NF- κ B → sustained inflammation
- SII rises with HbA1c even in pre-diabetic range (5.5–6.4%) — glycemia precedes diagnosis
- Target: < 5.5% optimal; 5.5–6.4% requires carbohydrate intervention; > 6.4% requires escalation
- Interventions: reduce refined carbs, increase fiber, berberine, chromium, cinnamon

GGTP | Target: 15–35 IU/L

- GGTP is the most sensitive early marker of hepatic oxidative stress
- Reflects glutathione turnover — elevated GGTP signals depletion of master antioxidant
- SIRI often co-elevated with high GGTP — liver-gut inflammatory axis
- Alcohol, non-alcoholic fatty liver, and environmental toxin load drive GGTP elevation
- Interventions: N-acetylcysteine, milk thistle, alpha-lipoic acid, reduce alcohol

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Secondary Biomarkers: Cardiometabolic & Body Composition

Cholesterol : HDL Ratio

Target: < 4.0

Dyslipidemia-driven inflammation. Elevated ratio reflects oxidized LDL macrophage uptake — foam cell formation and SII elevation. Omega-3, niacin, polyphenols reduce ratio. Also reflects HDL anti-inflammatory function loss.

Waist : Hip Ratio

Target: < 1.0 (M) / < 0.85 (F)

Single best anthropometric predictor of visceral adiposity. Visceral fat is metabolically active — releases TNF-α, IL-6, and adipokines that directly drive SII elevation. Associated with insulin resistance independent of BMI.

Blood Pressure

Target: < 130/80 mmHg

Endothelial inflammation is both a cause and consequence of elevated SII. Hypertension activates vascular NLRP3 inflammasome. Normalization of SII correlates with measurable blood pressure improvement in intervention studies.

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Extended Immuno-Metabolic Panel: Optional Additional Biomarkers

For deeper personalization — especially in Pattern C or complex metabolic presentations:

Fasting Glucose	75–90 mg/dL	Pre-insulin resistance; glycemic-inflammatory interface
Fasting Insulin	10–30 µIU/mL	Beta-cell compensation; insulin signaling efficiency
HOMA-IR	0.5–1.7	Calculated: Fasting Glucose × Fasting Insulin / 405
Triglycerides	30–80 mg/dL	Platelet-activating lipids; direct SII driver
ALT	10–25 IU/L	Hepatocellular inflammation; NAFLD marker
AST	10–25 IU/L	Mitochondrial stress marker; AST/ALT ratio for liver vs. muscle
Ferritin	30–100 ng/mL	Iron storage + acute phase reactant; elevated in Pattern C

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The Immuno-Metabolic Clinical Protocol

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Protocol Architecture: The Three Verticals

The Immuno-Metabolic Program is built on three mechanistically distinct therapeutic axes:

VERTICAL 1	Polyphenols <i>Tempers Inflammatory Tone</i>	Tartary buckwheat: rutin, quercetin, luteolin, hesperidin Modulates NF-κB; reduces IL-6, TNF-α
VERTICAL 2	Full-Spectrum Omega-3 <i>Drives Inflammation Resolution</i>	30+ omega-3 fatty acids + SPMs (specialized pro-resolving mediators) EPA, DHA, vitamins A & D
VERTICAL 3	Pre/Probiotics <i>Calms Gut-Derived Immune Signaling</i>	Beta-glucan prebiotic + L. rhamnosus CRL 1505 + polyphenols Reduces LPS-driven monocyte/SIRI activation

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Vertical 1: Polyphenols — Tempers Inflammatory Tone

Rutin	~400–500 mg/day	Quercetin-3-rutinoside; capillary integrity, anti-thrombotic, inhibits NLRP3
Quercetin	~200–300 mg/day	Mast cell stabilizer; inhibits histamine release; anti-inflammatory via NF-κB
Luteolin	~150–200 mg/day	Neuroinflammation reduction; crosses blood-brain barrier; Pattern A/E support
Hesperidin	~150–200 mg/day	Cardiovascular anti-inflammatory; endothelial protection; capillary tone

Source: Tartary buckwheat (*Fagopyrum tataricum*) — ~40× the rutin content of common buckwheat

Mechanism: Polyphenols act upstream — modulating the NF-κB master switch that controls inflammatory gene expression. This 'tempers inflammatory tone' without immunosuppression.

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Vertical 2: Full-Spectrum Omega-3 — Drives Resolution

EPA (Eicosapentaenoic Acid):	Suppresses platelet aggregation — directly reduces SII via thromboinflammatory axis
DHA (Docosahexaenoic Acid):	Neuronal membrane integrity; SRI reduction via macrophage polarization (M1→M2 shift)
SPMs (Specialized Pro-Resolving Mediators):	Resolvins, protectins, maresins — actively resolve inflammation; not anti-inflammatory passively
Vitamin A:	Mucosal immune regulation; gut-barrier support; lymphocyte differentiation
Vitamin D:	Immune modulation; Pattern C/D determinant; VDR-mediated NF-κB suppression
Minor omega species:	DPA, SDA, ETA — anti-inflammatory cascade intermediates; full-spectrum provides breadth

Key distinction: Most omega-3 products deliver 2–3 fatty acids. Full-spectrum provides 30+ species — replicating the fatty acid complexity of whole-food marine sources.

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Vertical 3: Pre/Probiotics — Calms Gut-Derived Signaling

Beta-Glucan Prebiotic

Fermentable fiber; increases short-chain fatty acid (SCFA) production — butyrate, propionate; reduces LPS translocation

L. rhamnosus CRL 1505

Clinically studied strain; reduces gut-derived innate immune activation; lowers SIRI in GI inflammatory conditions

Polyphenol Matrix

Synergistic with probiotic; selectively feeds beneficial bacteria; quercetin enhances bifidobacterial growth

Mechanism: 70% of the immune system resides in the gut-associated lymphoid tissue (GALT). Gut dysbiosis is the primary driver of SIRI elevation via LPS-activated monocytes. This vertical addresses the root cause.

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Re-Test Timeline & Expected Response

Same biomarkers, same formula. Objective evidence of clinical response.

Weeks 1–2	Symptom Onset	Early effects: improved energy, sleep quality, reduced bloating (gut vertical active)
Weeks 3–4	Biochemical Shift	hs-CRP begins to decline; early platelet modulation (omega-3 active)
Weeks 6–8	SII/SIRI Movement	First meaningful CBC-derived index changes detectable
Weeks 8–12	Primary Re-Test	Re-order SII, SIRI, and all elevated secondary biomarkers
Week 12+	Personalize & Sustain	Adjust doses based on pattern response; continue for 6–12 months

Case study data: 19–24% SII reduction achieved in 3 months with the nutritional protocol. Providers can expect measurable, documentable improvement at the 8–12 week re-test.

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Lifestyle Integration: The Program Beyond Supplements

- Dietary fiber target: 35–40g/day — each 10g increase reduces SII ~5–8% in intervention studies
- Mediterranean dietary pattern: primary food architecture recommendation for all patterns
- Movement: 150 min/week moderate aerobic activity reduces SII independent of weight change
- Sleep: 7–9 hours/night; sleep restriction of 2 hours raises SII within 72 hours
- Stress: HPA axis activation chronically elevates neutrophil/lymphocyte ratio — a direct SII driver
- Alcohol: each additional drink/week raises SII ~2–3 points — dose-dependent relationship
- Smoking: single largest modifiable SII driver; cessation reduces SII by 20–30% within 6 months

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Implementation

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Why Now? The Convergence Moment

Three forces have aligned to make this program possible and timely:

The Science Is Ready

SII and SIRI are now validated across thousands of peer-reviewed studies. The evidence base for these indices as clinical biomarkers is robust, reproducible, and actionable.

The Platform Is Ready

The Immuno-Metabolic Program provides the infrastructure to deliver a structured, monitored, outcomes-tracked program at scale — without requiring additional systems or staff.

The Need Is Urgent

34.63% of U.S. adults have elevated systemic inflammation. Chronic disease driven by immunometabolic dysfunction is the defining health challenge of our time. The tools now exist to address it.

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The Clinical Promise

Imagine a practice where:

- Every patient with a chronic inflammatory condition receives a measurable, objective inflammation score
- Intervention is guided by two numbers from a test they've already had
- Response is tracked objectively — not by symptoms alone, but by validated biomarker change
- The program is delivered automatically through a platform the patient can access anywhere
- Your outcomes data contributes to a growing body of real-world evidence
- And a 20–24% reduction in systemic inflammation in 90 days becomes the expected standard of care

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Longevity and Biological Ageing: Enhancing Health into Advanced Age

Thank you

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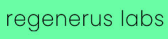
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