CytoDx®

Cytokine Response Profile

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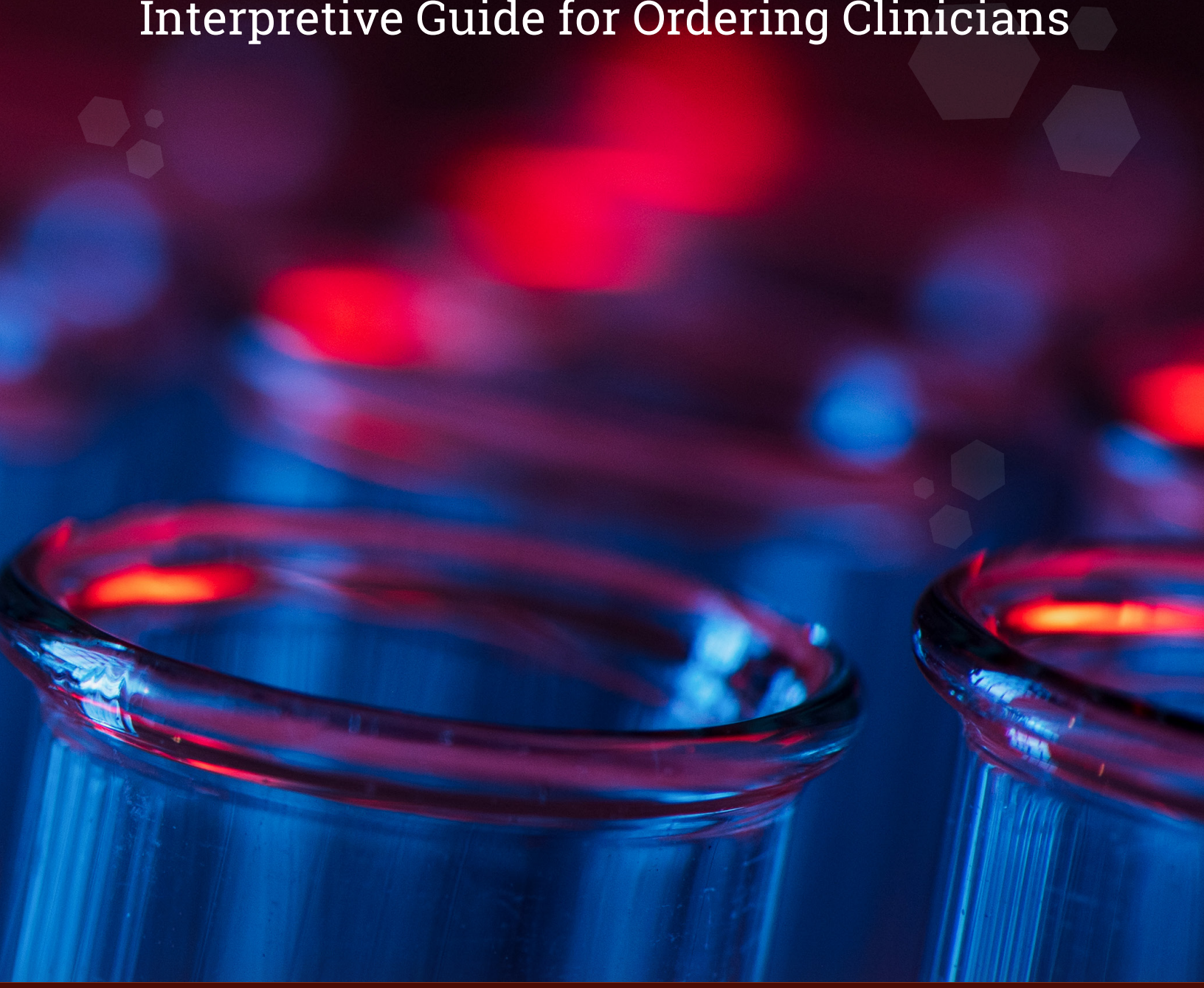
Interpretive Guide for Ordering Clinicians



INTERPRETIVE GUIDE

CytoDx® - Cytokine Response Profile

Our mission: to deliver innovative, accurate and clinically relevant diagnostic testing in a timely and cost-effective manner

Diagnostic Solutions laboratory

RESEARCH. TECHNOLOGY. RESULTS.

INTRODUCTION

The CytoDx® Cytokine Response Profile is a multiplexed serum panel providing quantitative measurement of cytokines, chemokines, inflammatory mediators, angiogenic factors, and vascular markers. Cytokines are signaling proteins produced by immune cells and many other cell types—*including fibroblasts, endothelial cells, hepatocytes, adipocytes, and nerve cells*—that mediate interactions not only among immune cells but across the immune, digestive, nervous, endocrine, and metabolic systems.

Cytokines function primarily at the local tissue level but can be detected in serum—*particularly during an active immune response.* Serum levels are measured in the picogram per milliliter (pg/mL) range. Cytokines that are significantly elevated above normal ranges are flagged as "High" on the CytoDx report, indicating that an immune response is active.

The primary goal of this panel is to answer two questions:

1. **Is the immune system activated?**
2. **And if so, what type of immune response is present?**

Elevated markers signal that immune activity is occurring, but individual markers do not identify a root cause or point to a specific diagnosis, and no single elevated marker implies a specific treatment. Because cytokines operate within highly interconnected signaling networks, clinical value emerges from the **pattern** — the combination of markers that are elevated, the functional categories they fall into, and how those patterns align with the patient's history, symptoms, medications, and other laboratory findings. Imbalances in cytokine signaling have been linked to a wide range of chronic inflammatory, autoimmune, allergic, and metabolic conditions.

Important caveats: immunosuppressive medications, biologics, and corticosteroids frequently suppress cytokine responses and may produce falsely low values. Acute infections and recent illness can cause transient elevations across multiple categories.

1. ACUTE INFLAMMATION

These cytokines are associated with innate immune responses, either acute or chronic. They initiate and amplify the body's earliest response to infection, tissue injury, cellular stress, and metabolic burden. They drive fever, NF-κB activation, neutrophil and macrophage recruitment, and downstream acute-phase protein production (reflected in the Vascular Injury section). Persistent elevation may indicate chronic inflammatory activation or failure of normal inflammatory resolution. A full **innate response** typically presents with co-elevations of IL-1β, IL-6, and TNF-α alongside elevated CRP and SAA.

MARKER	BIOLOGICAL ROLE	CLINICAL RELEVANCE
GM-CSF Granulocyte-Macrophage Colony-Stimulating Factor	Produced by macrophages, T cells, mast cells, NK cells, endothelial cells, and fibroblasts. Drives stem cell maturation into granulocytes (neutrophils, eosinophils, basophils) and monocytes (macrophages, dendritic cells) primarily as part of the host response to infection or injury.	Enhanced myeloid immune activation; autoimmune and chronic inflammatory conditions. Found at high levels in joints during rheumatoid arthritis. May amplify innate inflammatory signaling.
IL-1α Interleukin-1 alpha	Alarmin cytokine released during cellular injury and tissue stress; initiates acute inflammatory signaling at the local tissue level.	Cellular injury or necrosis; tissue stress; early innate immune activation.
IL-1β Interleukin-1 beta	Potent inflammatory cytokine produced by activated macrophages; product of inflammasome immune complex activation. Drives fever (endogenous pyrogen), neutrophil and macrophage recruitment, and NF-κB expression. Critical for host defense following recognition pathogens or endotoxins such as LPS.	Active inflammasome signaling; bacterial and viral infections (LPS-driven); autoimmune conditions; metabolic inflammatory disease.
IL-6 Interleukin-6	Secreted by T cells, macrophages, and monocytes during infection or injury. Critical for induction of the acute-phase response (CRP, SAA) and fever; can cross the blood-brain barrier. Promotes Th17 polarization and inhibits Treg differentiation. Also functions as an anti-inflammatory myokine via inhibition of TNF-α and IL-1 and induction of IL-10.	Systemic inflammatory burden; chronic immune activation; metabolic-inflammatory states. Chronically elevated in diabetes, atherosclerosis, SLE, multiple myeloma, prostate cancer, and rheumatoid arthritis. Acute COVID-19 illness. Expected to co-elevate with CRP and SAA.
TNF-α Tumor Necrosis Factor-alpha	Endogenous pyrogen (fever inducer) produced primarily by activated macrophages in response to microbial infection. Activates NF-κB and MAPK pathways; promotes endothelial activation, leukocyte recruitment, cellular apoptosis, and cachexia. Strong drivers include LPS and *Candida* intestinal overgrowth.	Elevated in a broad range of chronic inflammatory, autoimmune, and infectious conditions including RA, IBD, psoriasis, Alzheimer's disease, Hidradenitis suppurativa, asthma, and cancers, intestinal candida overgrowth. Primary target for biologic therapies.

Results should be interpreted in the context of the patient's full clinical presentation, medications, and additional laboratory findings.

2. ADAPTIVE IMMUNE ACTIVITY

T cell-based adaptive immune responses are organized into three functionally distinct types of immunity, each defined by its target pathogen, immune cell involvement, and cytokine signature.

Type 1 immunity—*mediated by Th1 cells*—coordinates cell-mediated defense against viruses and intracellular bacteria and supports anti-tumor surveillance. Its key effector cytokines are IFN-γ, IL-2, IL-12, IL-15, and TNF-β.

Type 2 immunity—*mediated by Th2 cells*—drives allergic and eosinophilic responses against allergens, helminths, and parasites, characterized by IL-4, IL-5, and IL-13. These cells also promote tissue repair and regeneration after damage.

Type 3 immunity—*mediated by Th17 cells*—governs mucosal defense against fungi (particularly *Candida*) and extracellular bacteria, driven by IL-17A and sustained by the shared IL-12/23p40 subunit. Each axis is counter-regulated by IL-10 and regulatory T cells (Tregs). When chronically overactivated, all three can drive autoimmune and inflammatory disease. The balance across Type 1, 2, and 3 immune activity, together with the regulatory response, provides the interpretive framework for this section of the panel.

IL-7 is included here as a marker of lymphocyte homeostasis and T-cell recruitment supporting all three adaptive immune axes.

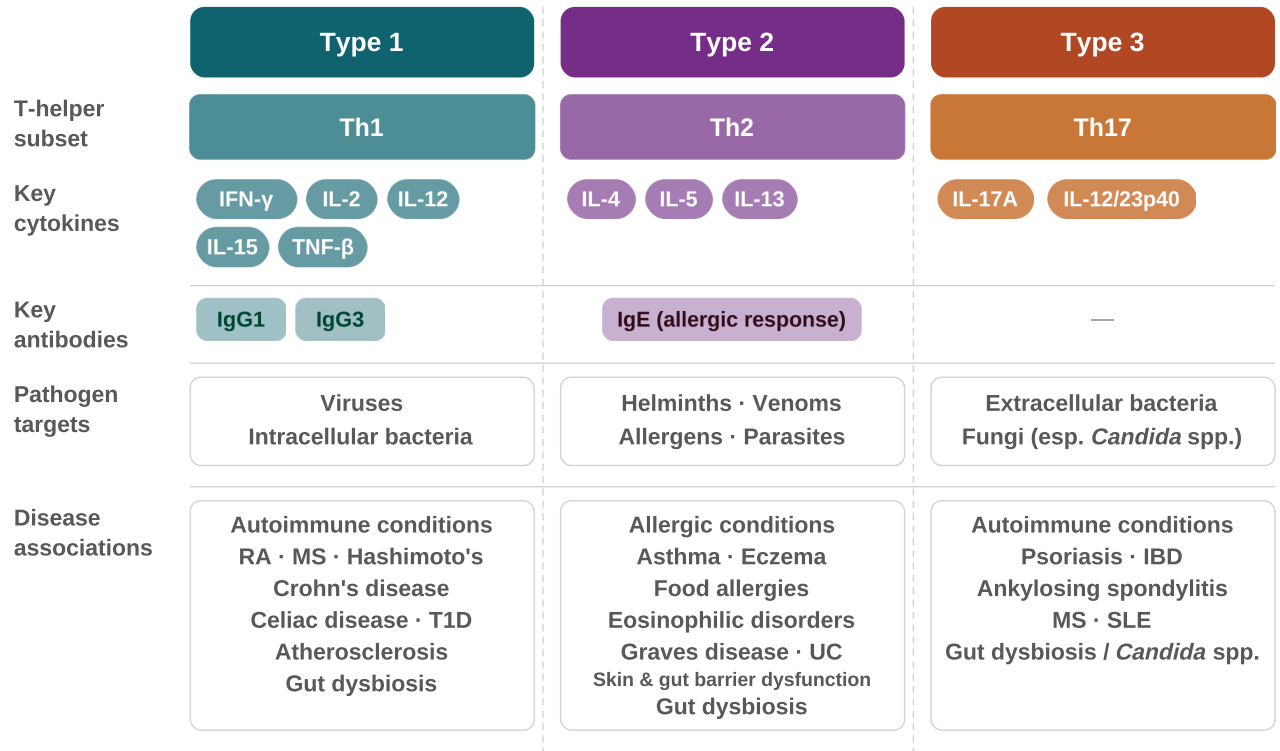


Figure 1. Adaptive Immune Response Types

Th1 — Viral & Bacterial Immune Defense; Autoimmunity

MARKER	BIOLOGICAL ROLE	CLINICAL RELEVANCE
IFN-γ Interferon-gamma	Signature Th1 effector cytokine. Produced primarily by T cells and NK cells in response to viral, bacterial, and protozoal infections. Induces antiviral, immunoregulatory, and anti-tumor activities including NK activation, MHC class I antigen presentation, IgG production from plasma B cells, and other intrinsic defense factor induction.	Viral and intracellular bacterial infections; autoimmune disease; gut dysbiosis and mucosal inflammation. Often co-elevates with IP-10 as a confirmatory Th1 pattern.
IL-2 Interleukin-2	Produced by Th1 cells in response to intracellular pathogens (bacteria, viruses, protozoa). Drives T-cell proliferation and differentiation into regulatory, effector, or memory T cells. Also activates B cells and NK cells. Actively suppresses Th17 differentiation.	Active T-cell-mediated immune response. IL-2 deficiency with concurrent IL-15 elevation is a hallmark pattern in celiac disease. Plays a key regulatory role in Th1/Th2 balance.
IL-15 Interleukin-15	Produced by monocytes, macrophages, dendritic cells, fibroblasts, keratinocytes, and nerve cells. Promotes differentiation, activation, and survival of NK cells; activates cytotoxic T cells and gamma-delta T cells; promotes IFN-γ production.	Elevated in celiac disease (especially alongside IL-2 deficiency), MASLD, SLE, and other organ-specific autoimmune diseases. Staphylococcal infections can amplify the IL-15 cascade. Reflects heightened NK-cell or memory T-cell activity.
TNF-β Lymphotoxin-alpha (LT-α)	Produced by activated T cells; contributes to lymphoid tissue organization and T-cell effector functions. Shares some pro-inflammatory overlap with TNF-α.	Adaptive immune activation; lymphoid tissue inflammatory activity.
IL-12p70 Interleukin-12 (active heterodimer)	Produced by dendritic cells and macrophages in response to bacterial pathogens. Primary driver of Th1 immune response; induces IFN-γ production.	Active innate-to-adaptive immune signaling in response to pathogen or inflammatory stimulus. Elevation without downstream IFN-γ may suggest immune evasion or pathway blockade — seen in some chronic viral infections.
IL-12/23p40 Shared IL-12/IL-23 subunit	Shared subunit of both IL-12 and IL-23; bridges the Th1 and Th17 axes. Interpret alongside IL-12p70 (Th1) and IL-17A (Th17) for pathway context.	Th1 and/or Th17 immune activation. Target of biologic therapies used in IBD and psoriasis.

Th17 — Mucosal & Gut Barrier Defense; Gut and Skin Immune Responses

MARKER	BIOLOGICAL ROLE	CLINICAL RELEVANCE
IL-17A Interleukin-17A	Produced by Th17 cells; plays a pivotal role in bridging innate and adaptive immune responses, particularly recruiting neutrophils to sites of infection. Critical for antifungal defense, especially against *Candida* intestinal overgrowth.	Autoimmune conditions including MS, RA, psoriasis, SLE, and IBD; intestinal *Candida* overgrowth; gut dysbiosis; chronic mucosal inflammatory disease. Excessive IL-17 production is linked to a broad range of chronic inflammatory and autoimmune conditions.

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Th2 — Allergic & Eosinophilic Responses

MARKER	BIOLOGICAL ROLE	CLINICAL RELEVANCE
IL-4 Interleukin-4	Produced by Th2 cells. Induces differentiation of naïve T cells into Th2 cells and B-cell differentiation into plasma cells; drives IgE class switching. Associated with a positive feedback loop promoting chronic inflammation.	Asthma; allergic rhinitis; atopic conditions; food immune reactivity; chronic inflammation. Commonly co-elevates with IL-5.
IL-5 Interleukin-5	Produced by Th2 cells and mast cells. Stimulates B-cell activation, increases immunoglobulin secretion, and is the primary cytokine responsible for eosinophil activation, differentiation, and prolonged survival.	Allergic rhinitis; allergic asthma; eosinophilic esophagitis and other eosinophilic GI disorders. Strong correlation between IL-4 and IL-5 levels; co-elevation represents active Th2/allergic immune activity.
IL-13 Interleukin-13	Produced by Th2 cells, CD4 cells, NK cells, mast cells, basophils, and eosinophils. Drives mucus production, goblet cell hyperplasia, airway smooth muscle hyperreactivity, airway remodeling, and increased epithelial permeability. Regulates IgE synthesis.	Asthma (key pathophysiologic driver); atopic conditions; eosinophilic GI disorders. Elevation alongside IL-4 and IL-5 represents a robust Th2 allergic immune signature.

Other — Chemoattractant Associated With T Cell Recruitment

MARKER	BIOLOGICAL ROLE	CLINICAL RELEVANCE
IL-7 Interleukin-7	Plays a central role in the development and homeostasis of the immune system and in establishing memory T cells.	Higher IL-7 levels are associated with several chronic inflammatory and autoimmune disorders including Type 1 diabetes, multiple sclerosis, ulcerative colitis, and primary biliary cirrhosis. Elevated IL-7 may reflect increased demand for lymphocyte homeostasis or abnormal lymphocyte turnover.

3. ANTI-INFLAMMATORY / REGULATORY / IMMUNE TOLERANCE

These markers reflect the immune system's counter-regulatory capacity. IL-10 is the primary anti-inflammatory cytokine in this panel, with expression triggered by commensal or pathogenic microbial signals. These cytokines should be reviewed in relation to pro-inflammatory findings. Elevated pro-inflammatory markers with low or normal IL-10 may indicate insufficient immune regulation.

MARKER	BIOLOGICAL ROLE	CLINICAL RELEVANCE
IL-10 Interleukin-10	Produced primarily by monocytes and, to a lesser extent, lymphocytes (Th2 cells, mast cells, Tregs, activated T and B cells). Suppresses proliferation and cytokine production of all T cells to prevent overstimulation. Stimulates plasma cells for continued antibody production. Expression is minimal in unstimulated tissues and is triggered by commensal or pathogenic microbes.	Elevated IL-10 may reflect active compensatory immune regulation in the context of concurrent inflammation. Low IL-10 alongside elevated pro-inflammatory markers may indicate insufficient regulatory capacity and failure of normal inflammatory resolution.
IL-16 Interleukin-16	Chemoattractant and immunomodulatory cytokine for CD4+ T cells; recruits CD4+ T cells to sites of immune activity.	Active CD4+ T-cell recruitment; elevated in some chronic inflammatory and autoimmune conditions.

Results should be interpreted in the context of the patient's full clinical presentation, medications, and additional laboratory findings.

4. CHEMOKINES

Chemokines direct immune cell migration and trafficking to sites of infection or inflammation. This panel includes chemokines involved in neutrophil recruitment, monocyte and macrophage trafficking, Th1 immune cell recruitment, and eosinophil and Th2 cell trafficking. Patterns of chemokine elevation can help confirm and characterize the immune polarization suggested by the cytokine findings above.

MARKER	BIOLOGICAL ROLE	CLINICAL RELEVANCE
Eotaxin CCL11	Potent and selective eosinophil chemoattractant; primary driver of eosinophil recruitment to allergic inflammatory sites.	Allergic conditions; atopic disease; eosinophilic inflammation. Elevation strongly suggests active eosinophilic immune activity.
Eotaxin-3 CCL26	Eosinophil chemoattractant with strong associations with eosinophilic esophagitis (EoE) and atopic disease.	Eosinophilic esophagitis; atopic dermatitis; allergic conditions. May be elevated even when peripheral eosinophil counts are borderline. Co-elevation with Eotaxin reinforces an eosinophilic inflammatory picture.
IL-8 CXCL8	Produced by macrophages, epithelial cells, airway smooth muscle cells, and endothelial cells. Primary chemokine for **neutrophil recruitment**. Rapidly produced in response to pathogens, LPS, and inflammatory stimuli.	Bacterial infections; acute inflammatory conditions; mucosal inflammatory disease (IBD); gingivitis; psoriasis; obesity; colorectal cancer; cystic fibrosis. Active neutrophil mobilization.
IP-10 CXCL10	IFN-γ-induced chemokine that recruits activated T cells, NK cells, and monocytes via CXCR3. Closely linked to **Th1 immune cell recruitment**.	Viral infections (hepatitis C, HIV, COVID-19); autoimmune conditions with Th1 involvement. Useful confirmatory marker when co-elevated with IFN-γ.
MCP CCL2 / MCP-1	Primary chemokine for monocyte recruitment and migration into inflamed or infected tissues, where monocytes differentiate into macrophages.	Chronic inflammatory tissue infiltration; macrophage accumulation; metabolic disease; cardiovascular inflammatory activity.
MCP-4 CCL13	Monocyte and macrophage trafficking. Recruits monocytes and eosinophils; active in both innate inflammatory and allergic immune contexts.	Bridges innate monocyte recruitment with allergic eosinophilic activity. Consider alongside both innate and Th2/allergic markers.
MDC CCL22	Recruits Th2 cells and regulatory **T cells (Tregs)**; produced by macrophages and dendritic cells.	Atopic and allergic conditions; Th2 immune polarization. Often co-elevates with TARC in atopic disease.
MIP-1α CCL3	Recruits monocytes and memory T cells; amplifies innate immune responses at sites of infection or tissue injury.	Active innate inflammatory recruitment; infection-associated immune mobilization.
MIP-1β CCL4	Pro-inflammatory chemokine. Monocyte and macrophage trafficking; Functional overlap with MIP-1α in monocyte and T-cell recruitment. Classified as a pro-inflammatory chemokine.	Active macrophage-driven inflammatory recruitment. Co-elevation with MIP-1α suggests significant innate immune cell mobilization.
TARC CCL17	Recruits Th2 cells; one of the most clinically validated biomarkers for atopic dermatitis disease activity and severity.	Atopic dermatitis (established severity biomarker); allergic conditions; Th2 immune activation. Commonly co-elevates with MDC.
RANTES CCL5	Pro-inflammatory chemokine. Recruits T cells, eosinophils, and basophils; bridges innate, Th1, and Th2 immune signaling. Classified as a pro-inflammatory chemokine.	Chronic inflammatory conditions; viral infections; allergic responses. Low RANTES may reflect immune exhaustion or suppression.

5. ANGIOGENESIS

These markers evaluate angiogenesis, lymphangiogenesis, and vascular remodeling. These processes are essential for normal tissue repair but become dysregulated in chronic inflammation, malignancy, and endothelial dysfunction. The balance between pro-angiogenic factors (VEGF-A, PlGF) and the inhibitory decoy receptor sFLT-1 provides more clinical context than any single marker in isolation.

MARKER	BIOLOGICAL ROLE	CLINICAL RELEVANCE
bFGF Basic Fibroblast Growth Factor (FGF-2)	Potent mitogen and angiogenic factor; promotes endothelial cell proliferation, migration, and tissue repair. Contributes to angiogenesis, wound healing, and tissue remodeling.	Active tissue repair; pathological angiogenic activity in chronic inflammation or neoplastic processes.
sFLT-1 VEGFR-1 / Soluble Flt-1	Soluble decoy receptor that sequesters VEGF-A and PlGF, functioning as a natural inhibitor of angiogenesis.	Elevated sFLT-1 relative to VEGF may indicate suppressed angiogenic capacity. Well-established biomarker in preeclampsia. The sFLT-1:PlGF ratio provides context for interpreting angiogenic balance.
PlGF Placental Growth Factor	VEGF family member contributing to pathological angiogenesis and vascular inflammatory signaling; signals through VEGFR-1.	Cardiovascular disease; preeclampsia (obstetric context); active pathological angiogenic or vascular inflammatory activity in non-obstetric patients.
Tie-2 Angiopoietin Receptor (TEK)	Receptor for angiopoietins (Ang-1, Ang-2); central regulator of vascular maturation, endothelial stability, and vessel integrity.	Endothelial dysfunction; vascular inflammatory conditions; sepsis-associated vascular destabilization. Reflects the state of vascular endothelial health.
VEGF-A Vascular Endothelial Growth Factor A	Primary driver of angiogenesis; stimulates endothelial cell proliferation, migration, and new vessel formation. Also increases vascular permeability. Upregulated by hypoxia and inflammation.	Chronic inflammatory tissue remodeling; hypoxic tissue stress; pathological angiogenesis in inflammatory or neoplastic processes.
VEGF-C Vascular Endothelial Growth Factor C	Primarily stimulates lymphangiogenesis — formation of new lymphatic vessels.	Inflammatory lymphatic remodeling; lymphedema-related conditions; tumor lymphangiogenesis.
VEGF-A Vascular Endothelial Growth Factor D	Supports lymphangiogenesis and lymphatic vascular development; functional overlap with VEGF-C.	Active lymphatic remodeling. Co-elevation with VEGF-C may indicate significant lymphatic vascular involvement.

Results should be interpreted in the context of the patient's full clinical presentation, medications, and additional laboratory findings.

6. VASCULAR INJURY

CRP and SAA are hepatic acute-phase proteins produced directly in response to upstream cytokine signaling—*particularly IL-6*—making them important downstream confirmatory markers of systemic inflammatory activity. The soluble adhesion molecules sICAM-1 and sVCAM-1 reflect endothelial activation and vascular inflammatory burden. Co-elevation of all four markers suggests significant systemic inflammation with endothelial involvement.

MARKER	BIOLOGICAL ROLE	CLINICAL RELEVANCE
CRP C-Reactive Protein	Hepatic acute-phase protein; direct downstream product of IL-6 signaling. Rises rapidly during acute inflammation.	Active systemic inflammatory activity; acute infections; autoimmune flares; chronic low-grade inflammation. Co-elevation with IL-6 provides strong confirmatory evidence of active systemic inflammation.
sICAM-1 Soluble ICAM-1	Soluble form of endothelial adhesion molecule ICAM-1; facilitates leukocyte binding and transmigration through vascular walls.	Endothelial activation; vascular inflammation; chronic inflammatory states; cardiometabolic disease.
SAA Serum Amyloid A	Hepatic acute-phase protein; rises in parallel with CRP during inflammatory states. May rise more dramatically than CRP in some conditions.	Sensitive marker of systemic inflammatory activity. Elevated in active infection, autoimmune disease, and chronic inflammatory states.
sVCAM-1 Soluble VCAM-1	Soluble form of endothelial adhesion molecule VCAM-1; mediates immune cell recruitment to inflamed vascular surfaces.	Endothelial activation and vascular inflammatory burden. Co-elevation with sICAM-1 suggests significant endothelial involvement.

SUPPORT INFO

877-485-5336

METHODOLOGY

Serum ELISA

SPECIMEN REQUIREMENTS

Blood serum

Serum cytokines are small molecules that can rapidly degrade at room temperature. Therefore, it is crucial that samples be immediately frozen after collection (freeze overnight, 8-hour minimum) and received frozen upon arrival at the laboratory.

We require shipping these samples on dry ice for best results.

TEST ORDERING OPTIONS

- **CytoDx Cytokine Response Profile®**

Optional Ordering Options

- **GI-MAP® - GI Microbial Assay Plus**
- **IgG Food Explorer™**
- **IgE Allergy Explorer™**

Visit our website for details on any of our test offerings: diagnosticsolutionslab.com.

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