3415A 3 Ave NW, Calgary, Alberta, T2N 0M4, Canada

Patient Name: Patient, Name
Specimen ID (SID): 25-001-0000 **External SID:** 123456789 **Specimen Type:** Plasma
DOB: 01-Jan-2000 **Doctor:** Dr. Doctor **Date/Time Collected:** 01-Jan-2025 / 00:00
PHN: AB 0000000 **Report Date:** 12-Mar-2025 **Specimen Source:** MitogenDx
Reason for Testing: Systemic arthritis/MAS
Relevant Medications: -

Cytokine, Chemokine & Growth Factor Panel

Laboratory Developed Test (LDT)

Report Summary:

Sample Comments:

-

Results Summary:

High Analytes: 6CKine, BCA-1, Eotaxin-2, Granzyme A, I-309, IFN-α2, IFNγ, IL-1β, IL-1RA, IL-2, IL-8, IL-12p40, IL-13, IL-15, IL-17E/IL-25, IL-17F, IL-18, IL-23, IL-27, IL-31, IL-33, IP-10, I-TAC, LIF, Lymphotactin, MCP-3, M-CSF, MIG, MIP-1α, MIP-3α, MIP-3β, Perforin, SDF-1, TGFα, TNFα, TPO, TSLP, VEGF-A
Moderate High Analytes: CCL28, FGF-2, FLT-3L, GROα, IL-4, IL-5, IL-6, IL-9, IL-10, IL-21, MCP-1, MIP-1β, MIP-1δ, sFas, sFasL

Results Interpretation:

The grouping profile indicates significant elevations in group A1, which may reflect innate or autoimmune inflammation, and group A2, suggesting strong pro-inflammatory cytokine activity and active T helper cell-mediated inflammation. Additionally, there is a significant elevation in group B, frequently observed in conditions associated with severe systemic inflammation or cytokine storm, along with moderate elevations in group C, which may suggest moderate cell death/apoptosis, and group D1, indicating possible evidence of moderate lymphocyte activation.

The immune activation profile shows an active type 1 response characterized by initiation/propagation factors (IL-18, IL-27, IL-2), effector cytokines (IFNγ, TNFα), cytotoxic markers (Granzyme A, Perforin), and chemokines (IP-10, MIG, I-TAC). There is also an active type 2 response with initiation/propagation factors (IL-4, IL-17E/IL-25, IL-33, TSLP) and effector cytokines (IL-5, IL-13, IL-9, IL-31), as well as a potential pathogenic type 3 response characterized by initiation/propagation factors (IL-23, IL-1β, IL-6) and effector cytokines (IL-17F, IL-21), indicating a robust immune activation. Furthermore, an active anti-inflammatory profile is noted with moderate high levels of IL-10 and high levels of IL-1RA.

The cytokine profile suggests potential involvement of various immune cells, including B cells (BCA-1, IL-4, IL-6), T cells (IL-15, IL-2), cytotoxic T cells (IL-2, IL-21, Lymphotactin, TNFα), NK cells (IL-15, IL-18, IL-2), basophils (IL-18, IL-33, IL-4, TSLP), and mast cells (IL-33, IL-4, IL-9).

Disclaimer:

The interpretation of these test results should be correlated with clinical findings and other diagnostic tests. Biomarker levels can vary due to many biological, physiological, and diurnal factors; their clinical significance must be assessed by a qualified healthcare professional. This information is not intended to be used as the sole basis for diagnosis or treatment decisions.

Reviewed by: DP
Eve Technologies Corporation is a CLIA certified High Complexity International Laboratory

EVE DIAGNOSTICS
3415A 3 Ave NW, Calgary, Alberta, T2N 0M4, Canada

Patient, Name
PHN: AB 0000000; DOB: 01-Jan-2000; SID: 25-001-0000; External SID: 123456789

Cytokine, Chemokine & Growth Factor Panel

Laboratory Developed Test (LDT)

Analyte	Results (pg/ml)		Reference Interval†
6CKine	1482	**HIGH**	293 - 1243
APRIL	464		52 - 1476
BAFF	1166		285 - 1689
BCA-1	445	**HIGH**	15 - 168
CCL28	520		0 - 574
CTACK	1047		300 - 1415
EGF	13.4		0 - 78.6
ENA-78	290		52 - 1084
Eotaxin	36.9		5.5 - 48.8
Eotaxin-2	1265	**HIGH**	42 - 361
Eotaxin-3	18.6		8.2 - 76.7
FGF-2	215		16 - 225
FLT-3L	24.4		0.7 - 29.0
Fractalkine	235		32 - 305
GCP-2	65.5		5 - 190
G-CSF	48.5		0 - 81.1
GM-CSF	20.1		0 - 62.6
Granzyme A	174	**HIGH**	6 - 109
Granzyme B	8.0		0 - 40.3
GROα	29.8		0.8 - 36.0
HMGB1	1321		0 - 3924
I-309	89.3	**HIGH**	0 - 33.2
IFN-α2	191	**HIGH**	13 - 128
IFNβ	58.6		0 - 99.1
IFNγ	17.3	**HIGH**	0.2 - 8.3
IFNω	40.4		0 - 55.7
IL-1α	32.7		0 - 74.8
IL-1β	517	**HIGH**	0 - 46.2
IL-1RA	57.3	**HIGH**	1.0 - 35.5
IL-2	17.6	**HIGH**	0 - 7.5
IL-3	1.2		0 - 3.5
IL-4	3.3		0 - 3.3
IL-5	14.5		0.5 - 16.9
IL-6	9.1		0.2 - 10.8
IL-7	2.0		0 - 7.5
IL-8	33.9	**HIGH**	0 - 21.2
IL-9	22.7		0 - 22.8
IL-10	17.7		0 - 19.5
IL-11	6.1		0 - 28.3
IL-12p40	419	**HIGH**	7 - 220
IL-12p70	15.1		0 - 21.5
IL-13	311	**HIGH**	5 - 162
IL-15	29.1	**HIGH**	1.2 - 22.3
IL-16	395		25 - 1033
IL-17A	17.1		0 - 24.5
IL-17E/IL-25	24420	**HIGH**	35 - 1545
IL-17F	86.1	**HIGH**	0 - 54.0
IL-18	1816	**HIGH**	3 - 235
IL-20	67.5		5.7 - 99.9
IL-21	19.1		0 - 22.0
IL-22	69.8		0 - 148
IL-23	5455	**HIGH**	0 - 3213
IL-24	182		24 - 1240
IL-27	5991	**HIGH**	324 - 4151
IL-28A	19.6		0 - 42.5
IL-29	21.8		0 - 31.8
IL-31	39.3	**HIGH**	0 - 37.5
IL-33	86.0	**HIGH**	0 - 42.0
IL-34	46.9		4.9 - 82.4
IL-35	118		0 - 362
IP-10	1651	**HIGH**	21 - 281
I-TAC	356	**HIGH**	9 - 289
LIF	21.1	**HIGH**	0 - 17.3
Lymphotactin	227	**HIGH**	0 - 85.7
MCP-1	273		36 - 337
MCP-2	25.2		5.9 - 35.3
MCP-3	59.2	**HIGH**	3.9 - 38.6
MCP-4	32.8		16 - 148
M-CSF	353	**HIGH**	4 - 284
MDC	485		94 - 1213
MIG	10684	**HIGH**	381 - 5907
MIP-1α	118	**HIGH**	12.1 - 93.0
MIP-1β	59.1		9.7 - 65.6
MIP-1δ	3817		862 - 4175
MIP-3α	140	**HIGH**	1.7 - 31.2
MIP-3β	> 1250	**HIGH**	29 - 239
MPIF-1	370		20 - 547
PDGF-AA	96.1		21 - 2962
PDGF-AB/BB	3613		1130 - 16525
Perforin	14703	**HIGH**	1600 - 10826
RANTES	1025		194 - 2150
sCD137	16.6		2.1 - 25.2
sCD40L	510		21 - 1040
SCF	1340		247 - 1820
SDF-1	3424	**HIGH**	849 - 2770
sFas (ng/ml)	24.9		2.4 - 30.6
sFasL	336		28 - 400
TARC	24.8		1 - 106
TGFα	43.4	**HIGH**	0.8 - 18.7
TNFα	112	**HIGH**	11 - 107
TNFβ	1.5		0 - 27.6
TPO	574	**HIGH**	27 - 548
TRAIL	63.6		7.9 - 92.7
TSLP	5.3	**HIGH**	0 - 2.5
VEGF-A	138	**HIGH**	0 - 91.0

† Reference intervals estimated by data-mining ≥2000 PLASMA samples drawn from both healthy and pathological subjects.

Patient, Name

PHN: AB 0000000; DOB: 01-Jan-2000; SID: 25-001-0000; External SID: 123456789

Cytokine Groupings - Immune Signatures

Groupings represent co-expressing cytokines identified by non-biased clustering of >130 clinical plasma-EDTA samples

Analyte	Results (pg/ml)		Reference Interval†
GROUP A1 - INNATE/AUTOIMMUNE INFLAMMATION			
FGF-2	215		16 - 225
IFN-α2	191	**HIGH**	13 - 128
IL-1α	32.7		0 - 74.8
IL-1β	517	**HIGH**	0 - 46.2
IL-1RA	57.3	**HIGH**	1.0 - 35.5
IL-2	17.6	**HIGH**	0 - 7.5
IL-17A	17.1		0 - 24.5
GROUP A2 - PRO-INFLAMMATORY/T CELL BIOMARKERS			
Fractalkine	235		32 - 305
IFNγ	17.3	**HIGH**	0.2 - 8.3
IL-4	3.3		0 - 3.3
IL-5	14.5		0.5 - 16.9
IL-9	22.7		0 - 22.8
IL-12p40	419	**HIGH**	7 - 220
IL-12p70	15.1		0 - 21.5
IL-13	311	**HIGH**	5 - 162
IL-17F	86.1	**HIGH**	0 - 54.0
IL-22	69.8		0 - 148
MCP-3	59.2	**HIGH**	3.9 - 38.6
MIP-1α	118	**HIGH**	12.1 - 93.0
TGFα	43.4	**HIGH**	0.8 - 18.7
TNFα	112	**HIGH**	11 - 107
TNFβ	1.5		0 - 27.6
GROUP A3 - HEMATOPOIETIC GROWTH FACTORS			
GM-CSF	20.1		0 - 62.6
G-CSF	48.5		0 - 81.1
IL-3	1.2		0 - 3.5
IL-7	2.0		0 - 7.5
GROUP B - INNATE INFLAMMATION/CYTOKINE STORM			
BAFF	1166		285 - 1689
FLT-3L	24.4		0.7 - 29.0
IL-27	5991	**HIGH**	324 - 4151
IL-6	9.1		0.2 - 10.8
IL-8	33.9	**HIGH**	0 - 21.2
IP-10	1651	**HIGH**	21 - 281
I-TAC	356	**HIGH**	9 - 289
IL-10	17.7		0 - 19.5
IL-15	29.1	**HIGH**	1.2 - 22.3
IL-18	1816	**HIGH**	3 - 235
MCP-1	273		36 - 337
MCP-2	25.2		5.9 - 35.3
M-CSF	353	**HIGH**	4 - 284
MIG	10684	**HIGH**	381 - 5907
MIP-1β	59.1		9.7 - 65.6
MIP-3α	140	**HIGH**	1.7 - 31.2
MIP-3β	> 1250	**HIGH**	29 - 239
GROUP C - CELL DEATH BIOMARKERS			
Perforin	14703	**HIGH**	1600 - 10826
sFas (ng/ml)	24.9		2.4 - 30.6
TRAIL	63.6		7.9 - 92.7

Analyte	Results (pg/ml)		Reference Interval†
GROUP D1 - LYMPHOCYTE RECRUITMENT/ACTIVATION			
BCA-1	445	**HIGH**	15 - 168
CCL28	520		0 - 574
I-309	89.3	**HIGH**	0 - 33.2
IL-16	395		25 - 1033
IL-23	5455	**HIGH**	0 - 3213
IL-35	118		0 - 362
Lymphotactin	227	**HIGH**	0 - 85.7
sCD137	16.6		2.1 - 25.2
sFasL	336		28 - 400
TPO	574	**HIGH**	27 - 548
GROUP D2 - MUCOSAL INFLAMMATION/DAMAGE			
Eotaxin-3	18.6		8.2 - 76.7
HMGB1	1321		0 - 3924
IFNβ	58.6		0 - 99.1
IFNω	40.4		0 - 55.7
IL-11	6.1		0 - 28.3
IL-17E/IL-25	24420	**HIGH**	35 - 1545
IL-20	67.5		5.7 - 99.9
IL-21	19.1		0 - 22.0
IL-24	182		24 - 1240
IL-28A	19.6		0 - 42.5
IL-29	21.8		0 - 31.8
IL-31	39.3	**HIGH**	0 - 37.5
IL-33	86.0	**HIGH**	0 - 42.0
IL-34	46.9		4.9 - 82.4
LIF	21.1	**HIGH**	0 - 17.3
TSLP	5.3	**HIGH**	0 - 2.5
GROUP E - IMMUNE CELL TRAFFICKING/ACTIVATION			
6CKine	1482	**HIGH**	293 - 1243
CTACK	1047		300 - 1415
Eotaxin	36.9		5.5 - 48.8
Eotaxin-2	1265	**HIGH**	42 - 361
MDC	485		94 - 1213
MIP-1δ	3817		862 - 4175
MPIF-1	370		20 - 547
RANTES	1025		194 - 2150
SCF	1340		247 - 1820
SDF-1	3424	**HIGH**	849 - 2770
GROUP F - PLATELET ACTIVATION/WOUND HEALING			
APRIL	464		52 - 1476
EGF	13.4		0 - 78.6
ENA-78	290		52 - 1084
GCP-2	65.5		5 - 190
GROα	29.8		0.8 - 36.0
MCP-4	32.8		16 - 148
PDGF-AA	96.1		21 - 2962
PDGF-AB/BB	3613		1130 - 16525
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TARC	24.8		1 - 106
VEGF-A	138	**HIGH**	0 - 91.0

† Reference intervals estimated by data-mining ≥2000 PLASMA samples drawn from both healthy and pathological subjects.

Cytokine Groupings Descriptions

GROUP A1 - INNATE / AUTOIMMUNE INFLAMMATION
The analytes in this group are associated with innate immunity (IL-1α/β, IL-17E/IL-25, IFNα2), type 1 (IFNα2, IL-2, MIP-1α), and type 3 (IL-17A, IL-1) immune responses. IL-1, type I interferons, IL-17, MIP-1α, and FGF-2 contribute to autoimmune diseases, while IL-2 and IL-17E/IL-25 can either promote or suppress autoimmunity. IL-17A and FGF-2 synergistically drive inflammation in autoimmune arthritis. IL-1, IL-17, and FGF-2 potentiate Th17-mediated immunity, a key driver of autoimmunity, whereas IL-2 and IL-17E/IL-25 negatively regulate Th17 activity. IFNα2 exacerbates Th17-mediated inflammation, as seen in systemic lupus erythematosus (SLE), where IFNα2 and IL-17A form a pathogenic signaling axis. IL-1α/β also drive innate inflammatory responses and autoinflammatory conditions, and IL-1RA is expressed as a negative regulator of IL-1 signaling.
GROUP A2 - PRO-INFLAMMATORY/T CELL BIOMARKERS
This group of analytes includes pro-inflammatory cytokines involved in initiating innate inflammation and adaptive immune responses. The cytokine profile reflects Th1 (IFNγ, IL-12p70, TNFβ; intracellular pathogens/autoimmunity), Th2 (IL-4, IL-5, IL-13, IL-9; helminths/allergy/tissue repair), Th17 (IL-17F, IL-22; extracellular pathogens/autoimmunity), Th9 (IL-9), and Th22 (IL-22, IL-13) responses, which influence allergy and autoimmunity. Mixed T cell cytokine patterns may indicate diverse inflammatory responses, T cell heterogeneity and plasticity, or hybrid cells expressing multiple cytokines (e.g., IL-4 with IFNγ, IFNγ with IL-17A). These patterns may also reflect regulatory mechanisms, such as type 2 cytokine release following tissue damage from type 1 or type 3 responses.
GROUP A3 - HEMATOPOIETIC GROWTH FACTORS
The analytes in this group are hematopoietic growth factors and could indicate the expansion and activation of lymphocytes (IL-7) and/or leukocytes (GM-CSF, G-CSF, IL-3).
GROUP B - INNATE INFLAMMATION/CYTOKINE STORM
High levels of these analytes may indicate innate immune responses. IL-6 drives acute phase protein release, IL-18 acts as a pro-inflammatory alarmin via inflammasome activation, and Flt-3L supports innate lymphoid cell development. Elevated levels can signify severe systemic inflammation, such as cytokine storm (CRS). Key cytokines involved in CRS include IL-6, IL-10, IL-18, IL-8, MIG, IP-10, MIP-1ß, and MCP-1. IL-10, despite its anti-inflammatory role, is upregulated in CRS, reflecting an insufficient regulatory response. High analyte levels are common in CRS-related conditions like macrophage activation syndrome (MAS), adult-onset Still's disease (AOSD), systemic arthritis, hemophagocytic lymphohistiocytosis (HLH), and lymphocytic leukemia.
GROUP C - CELL DEATH BIOMARKERS
The analytes in this group promote cell death through facilitating (perforin) or directly inducing apoptosis (sFas, TRAIL).
GROUP D1 - LYMPHOCYTE RECRUITMENT/ACTIVATION
Elevated levels of these analytes may reflect the recruitment and activation of NK, T, and B cells. Granzyme A and B are cytotoxic mediators from NK and CD8+ T cells. sCD137 indicates NK and T cell activity, while sFasL regulates apoptosis and is shed by NK and CD8+ T cells. Lymphotactin (CD8+ T cells), CCL28 (NK and T cells), I-309 and IL-16 (CD4+ T cells) recruit lymphocytes to inflammation sites. IL-23 has context-specific pro-inflammatory effects on NK cells, CD4+ and CD8+ T cells, while IL-35 suppresses inflammation and cytotoxic cell function.
GROUP D2 - MUCOSAL INFLAMMATION/DAMAGE
Elevated levels of these analytes may indicate tissue injury and mucosal inflammation. IL-17E/IL-25, TSLP, and IL-33 are epithelial alarmins that activate type 2 immune responses. IFNβ and IFNω (type 1 interferons) and IL-28A and IL-29 (type 3 interferons) are linked to innate antiviral responses and mucosal immunity. HMGB1, released by damaged cells, promotes interferon expression. IL-34 supports mucosal-resident macrophages, while IL-11, IL-20, and IL-21 contribute to epithelial defense and tissue repair.
GROUP E - IMMUNE CELL TRAFFICKING/ACTIVATION
The analytes in this group drive the recruitment, homing and activation of leukocytes and lymphocytes.
GROUP F - PLATELET ACTIVATION/WOUND HEALING
High levels of these analytes suggest platelet activation and wound healing, as they are released by platelets and involved in angiogenesis, tissue remodeling, and inflammation. Elevated levels are seen in conditions linked to vascular injury, angiogenesis, and thrombocytosis, such as AOSD, Kawasaki disease, juvenile arthritis, FMF, COVID-19, and Crohn's disease. Lower levels are associated with thrombocytopenia-related conditions like HLH, lymphocytic leukemia, and hematopoietic stem cell transplantation. Notably, serum samples show significantly higher analyte levels than plasma samples from the same individuals.

Descriptions of the analytes and groupings with citations are available from Eve Diagnostics.
Clusters of co-expressing cytokines were determined with unsupervised clustering analysis of >130 plasma-EDTA specimens, using a similar approach as described in our publication: Polley DJ, et al. (2023) Identification of novel clusters of co-expressing cytokines in a diagnostic cytokine multiplex test. Front. Immunol. 14:1223817. doi: 10.3389/fimmu.2023.1223817. The designations of physiological/pathological significance assigned to each grouping are speculative, based on an analysis of the immune signatures in our database of clinical specimens and on the functional/pathological roles of the analytes in each grouping established in the scientific literature.