Bio-Plex Pro Assays

Bio-Plex Pro Human Immunotherapy 20-Plex Panel

The Bio-Plex Pro Human Immunotherapy 20-Plex Panel detects and quantifies a mix of cytokines, growth factors, macrophage-associated proteins, and valuable markers that provide insight during discovery and development and clinical trial monitoring of immunotherapies.

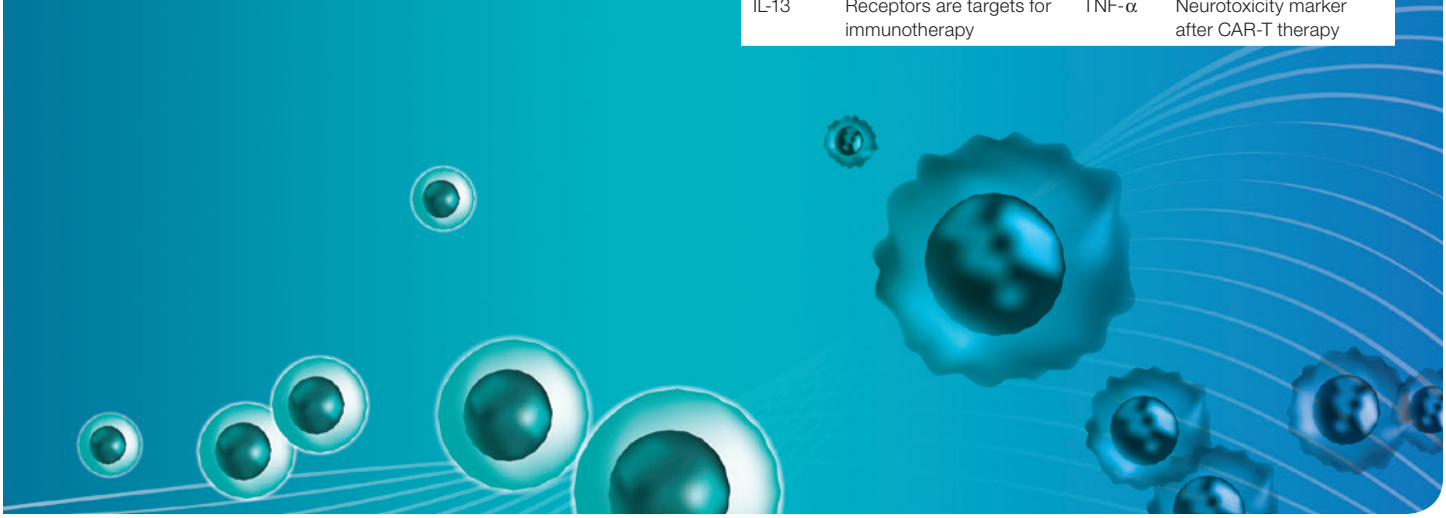
This multiplex panel is composed of cytokine biomarkers selected specifically for the investigation of immune responses associated with checkpoint inhibitors, chimeric antigen receptor T cells (CAR-T), oncolytic viruses, and cytokine release syndrome.

- **Validated on human serum, plasma, and tissue lysate**
- **Only 12.5 µl of sample required**
- **Data obtained in ~3 hr**
- **For use on Bio-Plex Multiplex Immunoassay Systems**

Refer to the following publications, which describe these cytokine biomarkers, for more information.

Analytes in Panel

Analyte	Significance in Immunotherapy	Analyte	Significance in Immunotherapy
GM-CSF	Therapeutic cytokine	IL-15	Oncolytic virus therapy in conjunction with CAR-T therapies
IFN-γ	Cytokine release syndrome (CRS) marker	IL-17A	Biomarker for immunomodulating therapies
IL-2	Therapeutic cytokine	IL-18	Exhibits antitumor properties
IL-4	Cancer biomarker; receptors are also potential therapeutic target	IP-10	Biomarker of response to combination epigenetic immuno-oncology therapies; CRS marker
IL-5	CRS marker	MCP-1	Necrosis biomarker; CRS marker
IL-6	CRS marker	MIG	CRS marker
IL-7	Survival marker of CAR-T cells	MIP-1α	General inflammation marker
IL-8	CRS marker	MIP-1β	CRS marker
IL-10	CRS marker	RANTES	Oncolytic virus therapy in conjunction with CAR-T therapies
IL-13	Receptors are targets for immunotherapy	TNF-α	Neurotoxicity marker after CAR-T therapy



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Publications

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GM-CSF

GM-CSF is critical to the regulation of antitumor immune responses, mainly by the activation of both innate and adaptive immunity. GM-CSF is also used as a therapeutic cytokine to supplement other oncological treatments.

Hong IS (2016).
Stimulatory versus suppressive effects of GM-CSF on tumor progression in multiple cancer types.
Exp Mol Med 48, e242.

Ozkaynak MF et al. (2018).
A comprehensive safety trial of chimeric antibody 14.18 with GM-CSF, IL-2, and isotretinoin in high-risk neuroblastoma patients following myeloablative therapy: Children's oncology group study ANBL0931.
Front Immunol 9, 1,355.

IFN-γ

IFN-γ may function as a biomarker for cytokine release syndrome in patients undergoing CAR-T therapy.

Graham C et al. (2017).
Preliminary results of UCART19, an allogeneic anti-CD19 CAR T-cell product, in a first-in-human trial (CALM) in adult patients with CD19^{+} relapsed/refractory B-cell acute lymphoblastic leukemia.
Blood 130 (suppl 1), 887.

Magalhaes I et al. (2018).
CD19 chimeric antigen receptor T cells from patients with chronic lymphocytic leukemia display an elevated IFN-γ production profile.
J Immunother 41, 73–83.

IL-2

Therapeutic IL-2 not only induces immune cell stimulation but may also induce hypotension and capillary leak syndrome. Bristol-Myers Squibb partnered with Nektar Therapeutics to investigate PEGylated IL-2 in conjunction with checkpoint inhibitors (anti–PD-1 antibody).

Garber K (2018).
Cytokine resurrection: Engineered IL-2 ramps up immuno-oncology responses.
Nat Biotechnol 36, 378–379.

Ozkaynak MF et al. (2018).
A comprehensive safety trial of chimeric antibody 14.18 with GM-CSF, IL-2, and isotretinoin in high-risk neuroblastoma patients following myeloablative therapy: Children's oncology group study ANBL0931.
Front Immunol 9, 1,355.

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IL-4

Increased IL-4 production has been found in breast, prostate, lung, renal, and other cancer cells. IL-4 receptors can be used for targeted therapies as well.

Nappo G et al. (2017).
The immunosuppressive cytokine interleukin-4 increases the clonogenic potential of prostate stem-like cells by activation of STAT6 signalling.
Oncogenesis 6, e342.

Suzuki A et al. (2015).
Targeting of IL-4 and IL-13 receptors for cancer therapy.
Cytokine 75, 79–88.

IL-5

IL-5 may be a biomarker for neurotoxicity associated with CAR-T therapy. In addition, changes in serum inflammatory cytokines, such as IL-5, may serve as biomarkers of response to treatment and could underpin future combined treatment modalities, including immunomodulating agents such as combination chemotherapy and poly ADP ribose polymerase (PARP) inhibitor treatments.

Anderson E et al. (2018).
Combined chemoradiotherapy and PARP inhibition in pancreatic cancer to induce a synchronous inflammatory cytokine response.
J Clin Oncol 36 (suppl), 29.

Park JH et al. (2017).
Baseline and early post-treatment clinical and laboratory factors associated with severe neurotoxicity following 19-28z CAR T cells in adult patients with relapsed B-ALL.
J Clin Oncol 35 (suppl), 7024.

IL-6

IL-6 may be part of a collection of biomarkers for cytokine release syndrome after anti-CD19 CAR-T therapy.

Gödel P et al. (2018).
Understanding cytokine release syndrome.
Intensive Care Med 44, 371–373.

Graham C et al. (2017).
Preliminary results of UCART19, an allogeneic anti-CD19 CAR T-cell product, in a first-in-human trial (CALM) in adult patients with CD19^{+} relapsed/refractory B-cell acute lymphoblastic leukemia.
Blood 130 (suppl 1), 887.

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IL-7

Changes in serum inflammatory cytokines, such as IL-7, may serve as biomarkers of response to treatment and could underpin future combined treatment modalities, including immunomodulating agents such as combination chemotherapy and PARP inhibitor treatments. In addition, IL-7 levels can help CAR-T cells survive in tumor conditions.

Adachi K et al. (2018).
IL-7 and CCL19 expression in CAR-T cells improves immune cell infiltration and CAR-T cell survival in the tumor.
Nat Biotechnol 36, 346–351.

Anderson E et al. (2018).
Combined chemoradiotherapy and PARP inhibition in pancreatic cancer to induce a synchronous inflammatory cytokine response.
J Clin Oncol 36 (suppl), 29.

IL-8

IL-8 may be part of the collection of biomarkers that can be used to predict the success of CD19-directed CAR-T therapies. It can also be used to predict cytokine release syndrome after therapy.

Gödel P et al. (2018).
Understanding cytokine release syndrome.
Intensive Care Med 44, 371–373.

Siddiqi T et al. (2017).
Patient characteristics and pre-infusion biomarkers of inflammation correlate with clinical outcomes after treatment with the defined composition, CD19-targeted CAR T cell product, JCAR017.
Blood 130 (suppl 1), 193.

IL-10

IL-10 may be part of a collection of biomarkers for cytokine release syndrome after anti-CD19 CAR-T cell therapy.

Gödel P et al. (2018).
Understanding cytokine release syndrome.
Intensive Care Med 44, 371–373.

Graham C et al. (2017).
Preliminary results of UCART19, an allogeneic anti-CD19 CAR T-cell product, in a first-in-human trial (CALM) in adult patients with $CD19^{+}$ relapsed/refractory B-cell acute lymphoblastic leukemia.
Blood 130 (suppl 1), 887.

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IL-13

IL-4 and IL-13 receptors on cancer cells provide targets for therapeutic agents for cancer therapy.

Martínez-Reyes CP et al. (2018).
Serum levels of interleukin-13 increase in subjects with insulin resistance but do not correlate with markers of low-grade systemic inflammation.
J Diabetes Res 2018, 7209872.

Suzuki A et al. (2015).
Targeting of IL-4 and IL-13 receptors for cancer therapy.
Cytokine 75, 79–88.

IL-15

IL-15 is an immunostimulatory factor targeting CD8 T cells and natural killer cells that can promote antitumor responses and, thus, is included in the arsenal for immuno-oncology therapies. In addition, changes in serum inflammatory cytokines, such as IL-15, may serve as biomarkers of response to treatment and could underpin future combined treatment modalities, including immunomodulating agents such as combination chemotherapy and PARP inhibitor treatments. IL-15 is also used in oncolytic virus therapy in conjunction with CAR-T therapies.

Anderson E et al. (2018).
Combined chemoradiotherapy and PARP inhibition in pancreatic cancer to induce a synchronous inflammatory cytokine response.
J Clin Oncol 36 (suppl), 29.

Robinson TO and Schluns KS (2017).
The potential and promise of IL-15 in immune-oncogenic therapies.
Immunol Lett 190, 159–168.

IL-17A

Changes in serum inflammatory cytokines, such as IL-17A, may serve as biomarkers of response to treatment and could underpin future combined treatment modalities, including immunomodulating agents such as combination chemotherapy and PARP inhibitor treatments.

Anderson E et al. (2018).
Combined chemoradiotherapy and PARP inhibition in pancreatic cancer to induce a synchronous inflammatory cytokine response.
J Clin Oncol 36 (suppl), 29.

IL-18

IL-18 is an immunostimulatory cytokine that augments antibody-dependent cellular cytotoxicity mediated by human natural killer cells against antibody-coated lymphoma cells in vitro and has antitumor activity in animal models.

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Robertson MJ et al. (2018).
A dose-escalation study of recombinant human interleukin-18 in combination with ofatumumab after autologous peripheral blood stem cell transplantation for lymphoma.
J Immunother 41, 151–157.

Shimabukuro-Vornhagen A et al. (2018).
Cytokine release syndrome.
J Immunother Cancer 15, 56.

IP-10

IP-10 (CXCL10) may be a predictive biomarker of response to combination epigenetic immuno-oncology therapies. IP-10 may also be implicated in cytokine release syndrome.

Katoh M (2018).
Combination immuno-oncology therapy with immune checkpoint blockers targeting PD-L1, PD-1 or CTLA4 and epigenetic drugs targeting MYC and immune evasion for precision medicine.
J Thorac Dis 10, 1,294–1,299.

Lin EM et al. (2018).
Advances in immuno-oncology biomarkers for gastroesophageal cancer: Programmed death ligand 1, microsatellite instability, and beyond.
World J Gastroenterol 24, 2,686–2,697.

MCP-1

MCP-1 can be used to predict cytokine release syndrome after therapy. In addition, CP-1 levels can be an indicator of necrosis in glioblastoma. Necrosis is linked to poor prognosis in patient populations.

Gödel P et al. (2018).
Understanding cytokine release syndrome.
Intensive Care Med 44, 371–373.

Jung Y et al. (2017).
Abstract 5924: Necrotic cells promote microglia infiltration in glioblastoma through regulating MCP-1 and MIP-3α expression.
Cancer Res 77 (suppl 13), 5924.

MIG

MIG is elevated in cytokine release syndrome.

Shimabukuro-Vornhagen A et al. (2018).
Cytokine release syndrome.
J Immunother Cancer 15, 56.

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MIP-1α

MIP-1α is a general inflammation marker.

Mevorach D et al. (2016).
Apoptotic cells for the prevention of cytokine release syndrome (CRS) in CAR T-cell therapy.
Blood 128 1,626.

MIP-1β

MIP-1β is elevated in cytokine release syndrome.

Mevorach D et al. (2016).
Apoptotic cells for the prevention of cytokine release syndrome (CRS) in CAR T-cell therapy.
Blood 128 1,626.

Shimabukuro-Vornhagen A et al. (2018).
Cytokine release syndrome.
J Immunother Cancer 15, 56.

RANTES

CAR-T cell therapy has also been combined with oncolytic virus expressing the chemokine RANTES and the cytokine IL-15, and showed enhanced function of CAR-T cells by improving CAR-T cell trafficking and recruiting innate immune cells.

Zhang H et al. (2016).
New strategies for the treatment of solid tumors with CAR-T cells.
Int J Biol Sci 12, 718–729.

Zhang S et al. (2018).
CCL5-deficiency enhances intratumoral infiltration of $CD8^+$ T cells in colorectal cancer.
Cell Death Dis 9, 766.

TNF-α

TNF-α is a biomarker for neurotoxicity after CAR-T therapy.

Magalhaes I et al. (2018).
CD19 chimeric antigen receptor T cells from patients with chronic lymphocytic leukemia display an elevated IFN-γ production profile.
J Immunother 41, 73–83.

Mevorach D et al. (2016).
Apoptotic cells for the prevention of cytokine release syndrome (CRS) in CAR T-cell therapy.
Blood 128, 1,626.

Visit bio-rad.com/ImmunotherapyKit for a wide range of videos, technical reports, published findings, and other resources describing Bio-Plex Pro Assays.

Ordering Information

Catalog #	Description
12007975	**Bio-Plex Pro Human Immunotherapy 20-Plex Panel**, 1 x 96-well, includes coupled magnetic beads, detection antibodies, standards, assay buffer, wash buffer, detection antibody diluent, streptavidin-phycoerythrin, flat bottom plate, sealing tape, standard diluent, sample diluent, for the detection of GM-CSF, IFN-γ, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-13, IL-15, IL-17A, IL-18, IP-10, MCP-1, MIG, MIP-1α, MIP-1β, RANTES, TNF-α

Bio-Plex Pro Human Singleplex Sets

171B5018M	GM-CSF Set
171B5019M	IFN-γ Set
171B5003M	IL-2 Set
171B5004M	IL-4 Set
171B5005M	IL-5 Set
171B5006M	IL-6 Set
171B5007M	IL-7 Set
171B5008M	IL-8 Set
171B5010M	IL-10 Set
171B5012M	IL-13 Set
171B5013M	IL-15 Set
171B5014M	IL-17A Set
171B5020M	IP-10 Set
171B5021M	MCP-1 (MCAF) Set
71B6015M	MIG Set
171B5022M	MIP-1α Set
171B5023M	MIP-1β Set
171B5025M	RANTES Set
171B5026M	TNF-α Set

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