

SALIVARY CYTOKINES

QUICK START GUIDE



BIOLOGICAL CONSIDERATIONS

Cytokines are small signaling proteins that are essential in coordinating many different cell types that make up your immune system. In a complex signaling network, they initiate immune responses, attract various cell types to sites of inflammation, activate specific cells, and also slow down the immune responses. They are produced at sites of inflammation and infection by a number of different cell types, including macrophages, monocytes, fibroblasts, and dendritic cells. Based on their structure and function they can be categorized into several different families including interleukins, interferons, chemokines, and tumor necrosis factors. Research now shows evidence that the impact of stress also causes the release of pro-inflammatory cytokines. Over time, chronic stress can disrupt the balance of cytokine levels in circulation, which may alter the body's ability to fight infections or control disease symptoms and progression. Due to the wide array of cytokine functionality, a multitude of fields benefit from studying cytokines. Cytokine research is found in oral cancer, periodontics, oral lichen planus disease, acute and chronic stress, asthma, and chronic obstructive pulmonary disease research.

Biological Representation	Immune Response
Assay Methodology	Multiplex Immunoassay

SAMPLE TIMING AND DESIGN

Due to the nature and context of cytokine signaling, sample timing and study design are dependent on the aims of your study. Passive drool is recommended over swabs, and cold chain management is critical. Researchers can customize a panel of cytokines to specifically address their research questions. Since oral inflammation can result in local cytokine production and influence cytokine levels in oral fluid, it is recommended to have information about the oral health of your participants. Since cytokines are macromolecules, it is recommended that salivary flow rate is accounted for. Salimetrics has a program that determines fit for purpose and validates additional cytokines upon request, so please inquire if you are interested.

FREQUENTLY STUDIED WITH

C-Reactive Protein (CRP), total IgA, Cortisol, SARS-CoV-2 IgG, Cotinine, total IgG, total IgM, total protein

TECHNICAL SUMMARY

150 µL* of passive drool is recommended and allows you to test all cytokines. Salivabio swabs are compatible for IL-1B and IL-6.

*Add 300 µL to the total collection volume for all analytes of interest.

Cytokine	Function/Key roles
TNF- α	Innate inflammatory response, development of acquired immunity from infection, remodeling of tissues, and causing apoptosis of tumor cells.
IL-1β	Pro-inflammatory cytokine, involvement in the body's inflammatory response to acute or chronic infections and conditions that are associated with a persistent low-grade inflammatory state, such as obesity.
IL-8	Neutrophil chemotactic factor. Immune mediator of neutrophil-dependent acute inflammation. Targets the changes in response to infection, inflammation, trauma, environmental stress, and steroid hormones.
IL-6	Pro and anti- inflammatory. Stimulates the immune response to infection or trauma by inducing the production of acute-phase proteins such as CRP and by fever induction. Also studied in periodontal disease, sleep dysfunction, psychosocial factors, and stress.
IL-5	Dysregulation is associated with eosinophilia, atopic dermatitis, and pulmonary fibrosis. Expressed in mast cells of asthmatic airways.

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IL-7	Important for every stage of T cell development and survival of naïve T cells, generation and maintenance of CD4 and CD8 T cell memory, and for the formation of lymphoid structure and defense mechanisms mediated by lymphoid cells. Pathologies associated with IL-7 are those mediated by the dysregulation of lymphoid function leading to autoimmune diseases such as diabetes, multiple sclerosis, chronic inflammatory diseases, rheumatoid arthritis, and inflammatory bowel disease.
IL-2	Immune tolerance and immunity against pathogens, primarily by its direct effects on T lymphocytes. Can function to initiate or dampen immune response.
IL-10	Anti-inflammatory that inhibits the synthesis of numerous cytokines that suppress TH1 proinflammatory responses involved in promoting phagocytosis. Enhances B lymphocyte survival, proliferation, and antibody production.
IL-12p70	Activates T cells and natural killer cells that stimulate the production of IFN- γ . It is also involved in several disorders including periodontitis and chronic toxoplasmosis.
IL-13	Stimulates B-cell proliferation, macrophage activation, immunoglobulin production, protein secretion, and phosphorylation of Stat6 protein. It is a central regulator of IgE synthesis, mucus hypersecretion and a mediator of allergic inflammation. Involved in a number of disorders including asthma, COPD, allergic rhinitis, atopic dermatitis, inflammatory bowel disease, and colorectal cancer.
IFN-γ	Central regulator of innate and adaptive immune responses mounted against viral infection, mediates cell mediated immunity such as anti-tumor immune responses, and is a hallmark of T helper type 1 (Th1) immune responses. Dysregulation is associated with disorders including autoimmune diseases and Huntington's disease. IFN-gamma levels are increased during hepatitis C infection and tuberculosis. It is also a general indicator of active viral infection. IFN-gamma is elevated during stress induced and may be used for stress related immune suppression.
IL-17A	T-helper cells that produce IL-17A (Th17) are a distinct proinflammatory lineage from Th1 or Th2. IL-17A in general is categorized as an inflammatory cytokine that can induce the expression of other cytokines such as IL-6. Dysregulation of IL-17A has been associated with autoimmune and chronic inflammatory diseases including multiple sclerosis, psoriasis, rheumatoid arthritis, inflammatory bowel disease, and is a target for FDA approved therapeutics.
IL-23	IL-23 has an important role in maintenance and expansion of Th17 cells and induces Th17 cytokine secretion. It is mainly made by activated dendritic cells, macrophages or monocytes in response to antigen stimulation. It has many roles in the inflammatory response and is a therapeutic drug target to treat inflammatory diseases.
sTNF-R1	Soluble TNF-R1 is a surface receptor for TNF that can be shed by enzymatic cleavage and retains the ability to bind TNF. When TNF signaling occurs this can be a mechanism to dampen the response and prevent damage that may ensue from unregulated inflammation. It is also shed from tumor cells to avoid immune surveillance. Soluble TNF receptors have been associated with cancer of various origins.

Pathology Driven by Dysregulated Cytokine Activity**

Acute and chronic stress: : IL-1 β , IL-6, IL-18

Asthma and chronic obstructive pulmonary disease research: Current: IL-5, IL-13, Future: IL-8, IL-6, IL-1 β , IL-17/23

Disease for gingivitis periodontal disease, and caries research: TNF, IL-1 β , IL-6, IFN- γ , IL-17/23, IL-10/TGF- β

Oral Cancer Research: IL-8, IL-1 β , IL-6, TNF- α

Cytokines associated with disease severity of oral lichen planus: IL-6, IL-8, IL-17, IFN- γ , TNF- α

Summarized in Salimetrics SBB**

Please note: Salimetrics salivary IL-6 and IL-1 β ELISA kits are available to purchase.

KEY RESOURCES

1. Granger, DA, Taylor, MK. (2020). Salivary Bioscience: Foundations of Interdisciplinary Saliva Research and Applications. Springer <https://link.springer.com/book/10.1007/978-3-030-35784-9>
2. Turner, M. D., et al., (2014). Cytokines and chemokines: At the crossroads of cell signalling and inflammatory disease. Biochimica et biophysica acta, 1843(11), 2563–2582.
3. Chauhan, P et al., (2021) A primer on cytokines.Science Direct, Vol 145, 1555458 <https://www.sciencedirect.com/science/article/abs/pii/S104346621000387>
4. **Granger, D and Granger, S. (2019). Clarifying Cytokines in Saliva. Salimetrics. <https://salimetrics.com/clarifying-cytokines-in-saliva/>

