



IL-6 (INTERLEUKIN 6)

The Singulex IL-6 assay is sensitive enough to quantify IL-6 concentrations in plasma from healthy, normal human subjects, a fundamental requirement in monitoring IL-6 changes during disease and potential therapeutic intervention.

BIOLOGY AND DISEASES

Interleukin-6 (IL-6) is a pro-inflammatory cytokine secreted by T cells and macrophages to stimulate immune response to trauma, especially burns or other tissue damage leading to inflammation. IL-6 is also secreted by macrophages in response to specific microbial molecules, referred to as pathogen associated molecular patterns (PAMPs), which trigger the innate immune response and initiate inflammatory cytokine production. IL-6 is one of the most important mediators of fever and of the acute phase response. IL-6 is also called a “myokine,” a cytokine produced from muscle that increases in response to muscle contraction. Additionally, osteoblasts secrete IL-6 to stimulate osteoclast formation.

THERAPIES

IL-6 has therapeutic potential as a drug target that results in an anti-inflammatory and inhibition of the acute phase response. In terms of host response to a foreign pathogen, IL-6 has been shown, in mice, to be required for resistance against the bacterium *Streptococcus pneumoniae*. Inhibitors of IL-6 (including estrogen) are used to treat postmenopausal osteoporosis. There is also therapeutic potential for cancer, as IL-6 is essential for hybridoma growth and is found in many supplemental cloning media such as briclone.

UNMET NEED

It is difficult to determine the circulating levels of IL-6 in the plasma of healthy subjects with many currently available assays, thus it is difficult to differentiate disease from healthy states. Furthermore, when used as a therapeutic target, it is desirable to measure therapeutic efficacy by measuring IL-6 levels as they decrease below normal state levels. This cannot be achieved with assays currently available, and there are few IL-6 diagnostic assays on the market at the present time. One IL-6 assay is currently available outside the U.S. for diagnostic use, and for research use only (RUO) in the U.S. and Japan.

SINGULEX ANSWER

Singulex's IL-6 assay enables the quantification of very low levels of plasma IL-6 and allows for accurate measurement of small changes in its level due to disease processes or therapeutic intervention. This high level of sensitivity can provide insights into therapeutic efficacy. The IL-6 assay has an LLoQ of 0.1 pg/mL and a reading range of 0.01-250 pg/mL, enabling accurate quantification of IL-6 in human plasma obtained from healthy subjects.

This assay will allow investigators to:

1. Measure the efficacy and dosing of therapeutics designed to interfere with the inflammatory response.
2. Design more robust clinical and preclinical studies in which IL-6 concentration is used as a therapeutic endpoint.
3. Understand how IL-6 levels change in patients as they transition from healthy to diseased states.

ERENNA TECHNOLOGY ACCESS PROGRAM.

Through the Erenna Technology Access Program (ETAP), Singulex offers an interactive, results-driven solution to biomarker challenges faced by the pharmaceutical industry during product development. Singulex assists the development programs of our ETAP collaborators by developing customer-driven assays and access to a menu of fully-validated assays. Participants in ETAP gain access to the Singulex Erenna Immunoassay System, our proven expertise developing high-value immunoassays and our world-class customer support. Together with Singulex, our ETAP collaborators are expanding the utility of protein biomarkers and using them as tools to measure disease progression, drug efficacy and toxicity.

TABLE 1: Analytical sensitivity of the Singulex IL-6 assay.

Lower Limit of Detection (LoD)	0.01 pg/mL
Lower Limit of Quantification (LLoQ)	0.1 pg/mL
Reading Range	0.01-250 pg/mL

Erenna® System



TABLE 2: IL-6 assay low-end standard curve data.

[IL-6] pg/mL	Detected Events	Std Dev	CV
0.78	2565	155	6%
0.39	1368	65	5%
0.20	735	26	4%
0.10	416	57	14%
0.05	272	4	2%
0.02	188	16	8%
0.00	116	5	4%

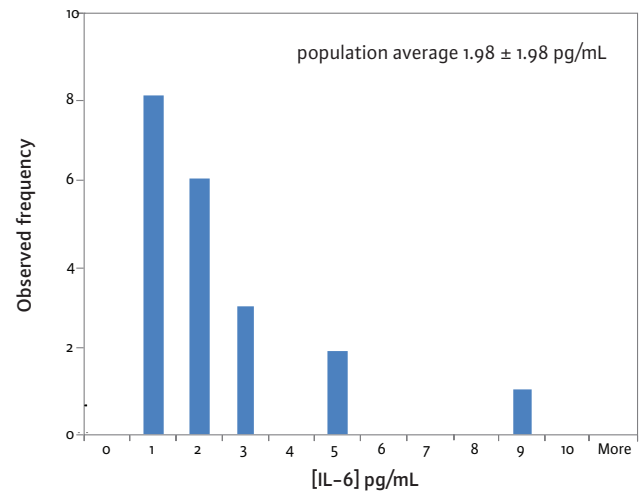


FIGURE 1: Plasma IL-6 concentration in healthy human subjects.

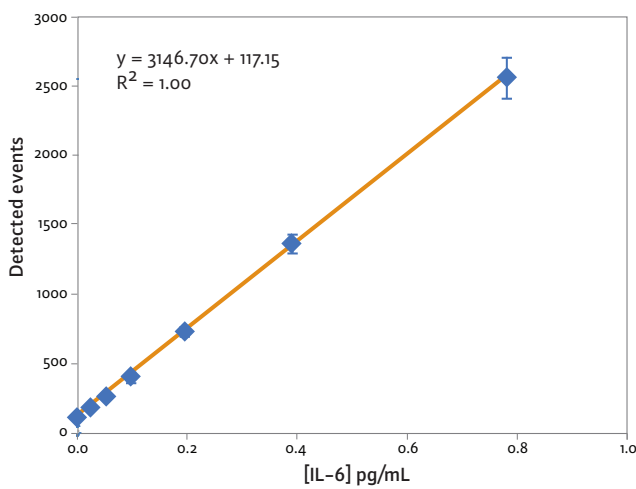


FIGURE 2: IL-6 low-end standard curve signal.

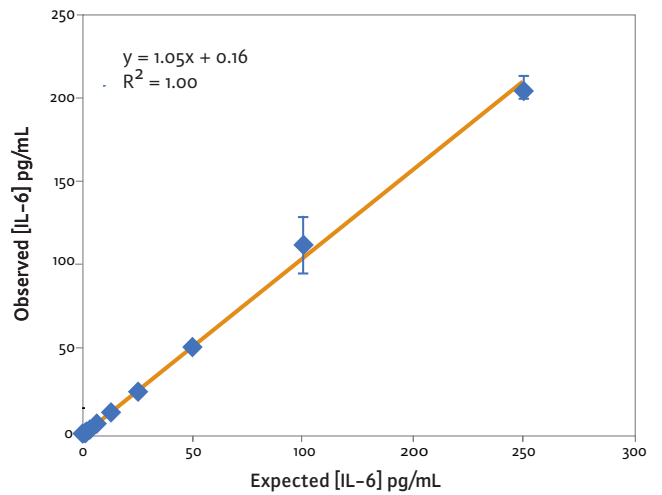


FIGURE 3: IL-6 assay curve fit.

These standard curves are for representational purposes only. A standard curve must be run with each assay.

Copyright © 2009, Singulex Inc. Singulex and Erenna are trademarks of Singulex, Inc.