



IL-17A (INTERLEUKIN 17, A)

The Singulex IL-17A assay is sensitive enough to quantify IL-17A concentrations in plasma from healthy, normal human subjects and monitor changes in plasma IL-17A during disease and potential therapeutic intervention.

BIOLOGY AND DISEASES

Interleukin-17A (IL-17A) is the founding member of a group of cytokines called the IL-17 family. There are several members of the IL-17 family, from IL-17A to IL-17F (IL-17E is also called IL-25). They all have very similar structures, however they bear no resemblance to other cytokines. Most notably, IL-17A is involved in mediating pro-inflammatory responses by inducing the production of many other cytokines, chemokines, and prostaglandins from many cell types. The increased expression of chemokines attracts other cells, including neutrophils. IL-17A has many physiological functions, such as airway remodeling. As a result of these roles, the IL-17 family has been linked to many immune/autoimmune related diseases, including rheumatoid arthritis (RA), asthma, allergic responses, lupus, allograft rejection and anti-tumor immunity.

THERAPIES

Recently, intense interest has focused on IL-17A as a therapeutic target. This cytokine is involved in many inflammatory diseases, including rheumatoid arthritis, multiple sclerosis, asthma and systemic lupus erythematosus. In rheumatoid arthritis patients, levels of IL-17A are present in much higher levels in synovial fluid compared with osteoarthritis patients, suggesting this protein may become a significant target for new rheumatoid arthritis drugs. Recent studies have shown IL-17A to be involved in bone destruction through a number of mechanisms.

UNMET NEED

IL-17A will continue to be a diagnostic biomarker for inflammatory diseases like rheumatoid arthritis. Normal levels of IL-17A in plasma cannot be measured with currently available ELISA technology. Hence, no baseline level of IL-17A has been established with which to differentiate diseased from healthy states, an essential parameter for establishing proper dosing to bring IL-17A down to normal levels. In order for IL-17A to be an effective marker, there is great need for an assay with enough sensitivity to detect the velocity of subtle changes in IL-17A concentration, and to quantify the baseline concentration of IL-17A in normal, healthy plasma.

SINGULEX ANSWER

The Singulex IL-17A assay increases the clinical utility of IL-17A by providing the sensitivity to detect very low levels of IL-17A and the velocity to measure small changes in concentration that can provide insights into drug efficacy or disease progression. The IL-17A assay has a LLoQ of 0.05 pg/mL and a reading range of 0.01–200 pg/mL, enabling accurate quantification of IL-17A in platelet depleted plasma. The Singulex IL-17A assay has also been validated for use in serum.

This assay will allow investigators to:

1. Measure the efficacy and dosing of therapeutics designed to interfere with the inflammatory response.
2. Aid in the development of anti-IL-17A drugs to evaluate early phase efficacy.
3. Design robust clinical and preclinical studies when IL-17A concentration is used as a therapeutic endpoint.
4. Understand how IL-17A 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-17A assay.

Lower Limit of Detection (LoD)	0.01 pg/mL
Lower Limit of Quantification (LLoQ)	0.05 pg/mL
Reading Range	0.01-200 pg/mL



TABLE 2: IL-17A assay low-end standard curve data.

[IL-17A] pg/mL	Detected Events	Std Dev	CV
3.10	1959	97	5%
1.56	1179	104	9%
0.78	715	34	5%
0.39	434	13	3%
0.20	316	35	11%
0.10	210	17	8%
0.05	196	15	8%
0.02	162	18	11%
0.00	144	28	19%

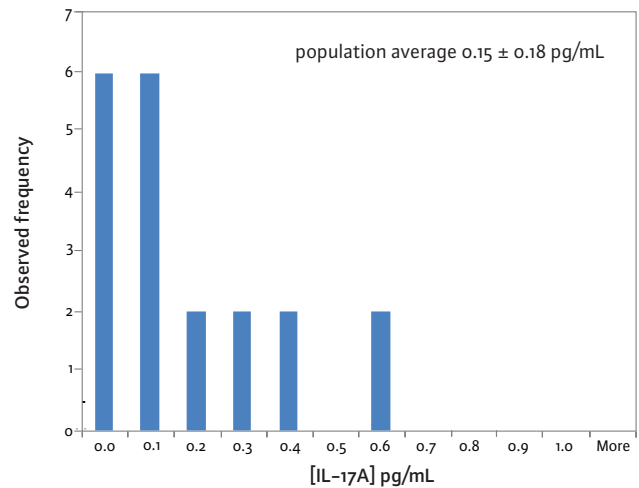


FIGURE 1: Plasma IL-17A concentration in healthy human subjects.

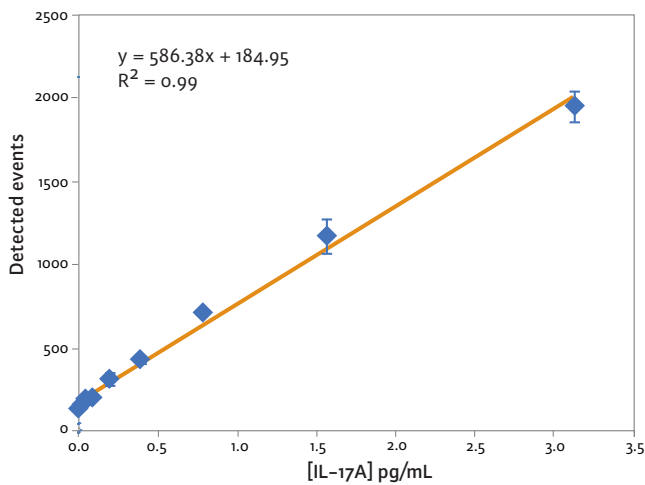


FIGURE 2: IL-17A low-end standard curve signal.

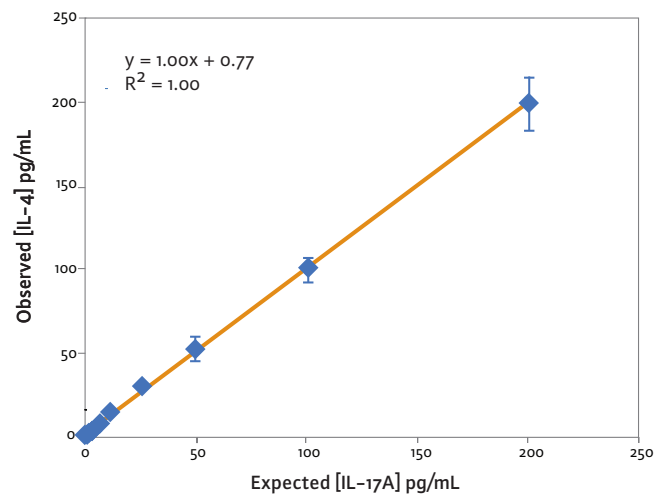


FIGURE 3: IL-17A assay curve fit.

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

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