

IFN- γ (INTERFERON GAMMA)

The Singulex IFN- γ assay allows sensitive quantification of plasma IFN- γ between healthy controls and diseased patients, enabling clinical studies and diagnostic research in the area of immuno-regulatory diseases.

BIOLOGY AND DISEASES

Interferon-gamma (IFN- γ) is a cytokine with antiviral and tumor-suppressing properties that is actively involved in the innate immune system. As the only member of the Type 2 IFN family, IFN- γ is expressed by Th1 cells, Tc cells, dendritic cells and natural killer cells. Once bound to its heterodimeric receptor IFN- γ R, the activated glycoprotein recruits and directs macrophages to the site of infection and escalates the inflammatory response. IFN- γ has also been documented to up-regulate the expression of IL-1 and down-regulate the production of IL-8, both of which are pro-inflammatory cytokines.

THERAPIES

Due to its key role in the autoimmune system, IFN- γ has been a focus in treatments targeted for malignant osteoporosis, HIV infection and conditions arising from chronic granulomatous disease. The potency, specificity and rapid action of IFN- γ make it an attractive target for the pharmaceutical development of immuno-regulatory diseases. A bioengineered form (IFN- γ 1b) is marketed under the trade name Actimmune. Results have shown that IFN- γ effectively reduces both the frequency and severity of infection related to chronic granulomatous disease. Moreover, studies are underway to address the safety and efficacy of IFN- γ in treating chronic hepatitis C and pulmonary diseases, and as a diagnostic tool for children with TB.

UNMET NEED

The complexity of IFN- γ 's involvement in the innate immune response calls for more sensitive assay technology to establish its diagnostic utility as a predictive biomarker for disease. The ELISA-based whole-blood IFN- γ assay was developed as an alternate test procedure for pulmonary tuberculosis in place of the traditional tuberculin skin test. However, some studies have suggested that the assay was unable to significantly differentiate the concentrations of plasma IFN- γ in healthy controls versus in TB patients. Therefore, a sensitive assay with superior accuracy and precision is needed to measure baseline concentrations of IFN- γ in healthy subjects, as well as to track subtle changes in IFN- γ between healthy and diseased states.

SINGULEX ANSWER

The Singulex IFN- γ assay, optimized for use on the Erenna System, improves the clinical utility of IFN- γ by allowing researchers to detect very low concentrations of IFN- γ and measure small changes in concentration that can provide insights into drug efficacy or disease progression. The Singulex IFN- γ assay has an LLoQ of 0.20 pg/mL and a reading range of 0.14–2000 pg/mL, enabling accurate quantification of low concentrations of IFN- γ in healthy subjects and elevated levels in diseased states using the same assay.

This assay will allow investigators to:

1. Measure the potential cardiac safety and dosing of therapeutics in both preclinical and clinical settings.
2. Perform time-course studies using individual small animals or precious samples, when sample volume is an issue.
3. Understand how IFN- γ concentrations change in patients as they transition from a healthy to diseased state.

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 IFN- γ assay.

Lower Limit of Detection (LoD)	0.14 pg/mL
Lower Limit of Quantification (LLoQ)	0.20 pg/mL
Reading Range	0.14–2000 pg/mL



TABLE 2: IFN- γ assay low-end standard curve data.

[IFN- γ] pg/mL	Detected Events	Std Dev	CV
12.5	2841	137	5%
6.25	1528	109	7%
3.13	878	21	2%
1.56	500	20	4%
0.78	321	24	7%
0.39	212	18	9%
0.20	166	11	7%
0.10	148	14	9%
0.00	110	16	14%

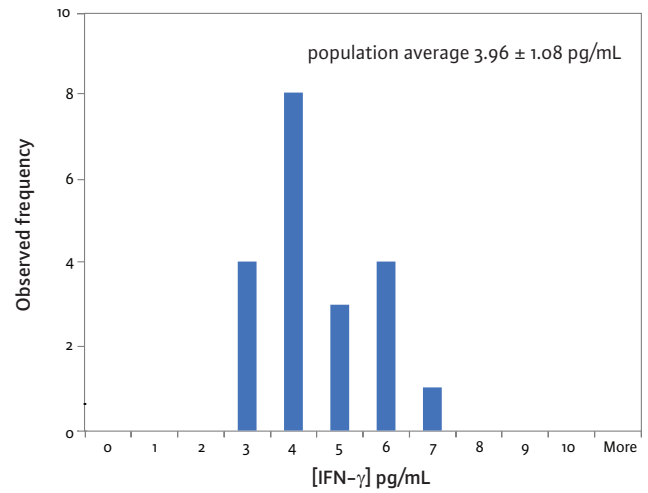


FIGURE 1: Plasma IFN- γ concentration in healthy human subjects.

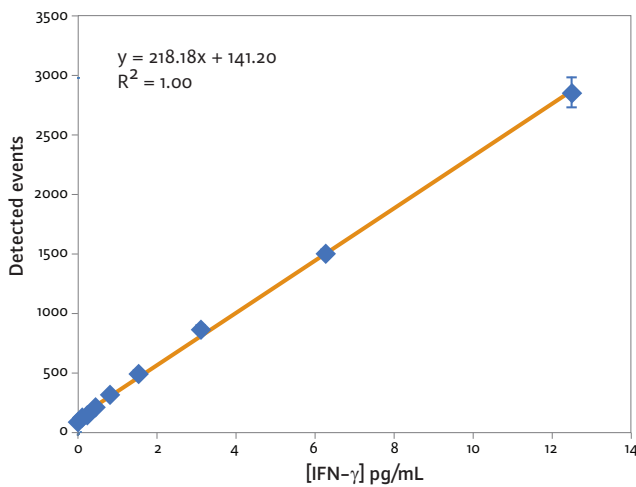


FIGURE 2: IFN- γ low-end standard curve signal.

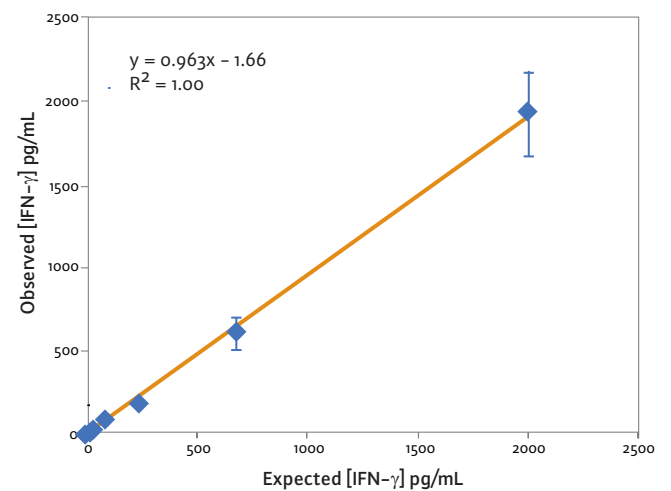


FIGURE 3: IFN- γ assay curve fit.

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

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