

cTNI (CARDIAC TROPONIN-I)

Normal levels of endogenous cTnI and small changes in plasma cTnI can be quantified in humans, rats, dogs and monkeys, providing previously intractable answers around cardiomyocyte pathophysiology. This allows for earlier assessment of ischemia and cardiotoxicity, providing valuable insight into potential drug safety.

BIOLOGY AND DISEASES

Cardiac Troponin-I (cTnI) is specific to cardiomyocytes and is released into blood following heart damage. Extensive studies have shown that cTnI, which is slowly released from damaged cardiomyocytes, often requires 4–8 hours post-trauma to be detectable. Measurement of cTnI concentrations in plasma are the standard of care for diagnosing non-STEMI acute myocardial infarction (AMI). In addition, this biomarker has been widely accepted in preclinical and clinical drug development settings as an indicator of myocardial damage and hence, heart damage.

THERAPIES

cTnI is accepted as a biomarker to assess potential cardiotoxicity of experimental therapies. It is extensively studied in preclinical settings and included in clinical drug development programs when preclinical data suggests a potential for cardiac-related adverse events.

UNMET NEED

Even though cTnI is used as the standard of care for diagnosing AMI, as well as in preclinical and clinical development, until recently its concentration in the plasma of apparently healthy humans and preclinical animal models had not been reported. Thus, it was impossible to benchmark a “normal” level within a given animal or human and measure small increases (velocity) of cTnI that might be associated with subtle cardiac damage. Furthermore, many assays do not equally quantify cTnI across different species and require large plasma sample volumes, limiting their use in preclinical settings, especially in rodent model systems.

SINGULEX ANSWER

Singulex’s cTnI assay, optimized for use on the Erenna System, provides cTnI quantification to 0.8 pg/mL (10%CV). The assay was designed to equilaterally quantify cTnI across humans, rats, dogs and monkeys. The Singulex cTnI assay has also been validated for use in serum.

Current ETAP investigators have used this assay to:

1. Define the concentration of plasma cTnI in healthy humans, rats, dogs and monkeys .
2. Identify AMIs earlier in patients and in retrospective studies.
3. Measure heart damage earlier under physical stress or known cardiotoxins.
4. Study cTnI concentrations in a single rat using only 10 µL plasma.

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. Design more robust clinical and preclinical studies when velocity of cTnI concentration change from a baseline normal level is used as an endpoint.
4. Understand how cTnI levels change from normal levels in a variety of cardiac-related diseases.
5. Understand the utility of cTnI as a biomarker to serve as a surrogate endpoint for clinical events.

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 cTnI assay.

Species	LoD pg/mL	Healthy Levels
Human	0.08	1–12 pg/mL
Rat	0.2	9–20 pg/mL
Dog	0.1	1–4 pg/mL
Monkey	0.4	4–5 pg/mL

Erenna® System

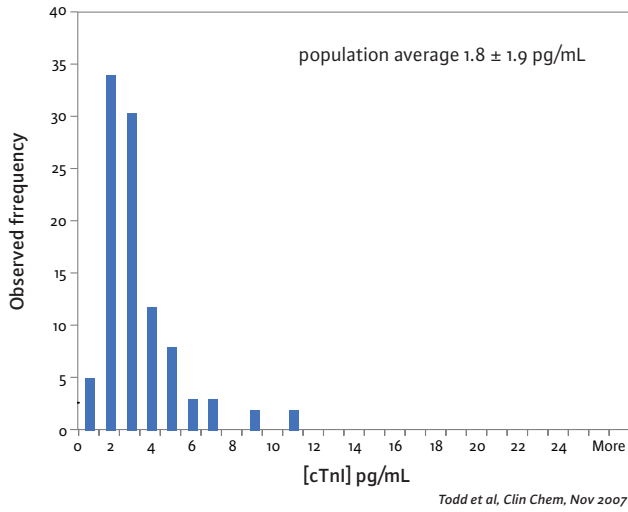


FIGURE 1: Distribution of cTnI levels in healthy human subjects.

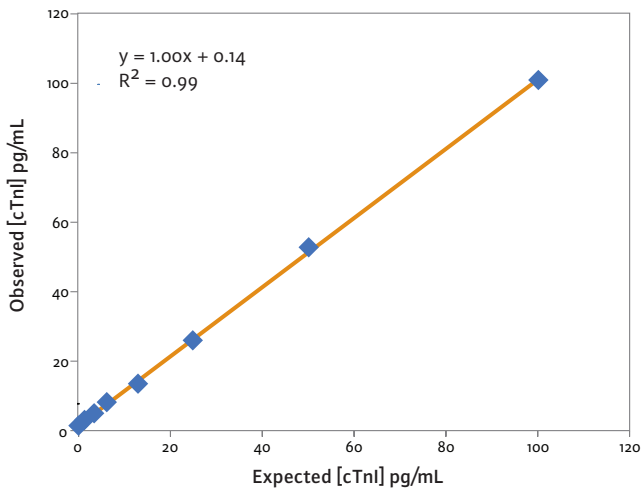


FIGURE 2: cTnI assay curve fit.

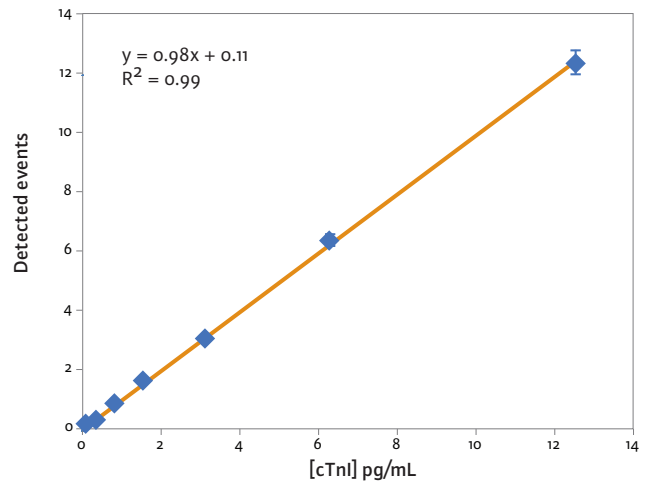


FIGURE 3: cTnI assay low-end standard curve signal.

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

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