

Spx HD™ Enhanced Testing

1. What SpxHD™ enhanced tests are offered in the Singulex Clinical Laboratory?

The Singulex Clinical Laboratory currently offers three proprietary tests based upon our innovative technology, including cardiac troponin-I (Sgx HD cTnI) and the inflammatory markers Interleukin-6 (Sgx HD IL-6) and Interleukin-17A (Sgx HD IL-17A).

2. What is cardiac troponin-I (cTnI)?

Cardiac troponin-I (cTnI) is a protein produced specifically by heart muscle cells, and injury to heart muscle tissue results in the release of cTnI into the blood.

3. How is cTnI different from cTnT?

Cardiac troponin-I (cTnI) and cardiac troponin-T (cTnT) are two different proteins that are both made in heart muscle cells. Because they are two different proteins with different characteristics, a test for cTnI does not measure cTnT, and vice versa.

4. How do troponins function in a healthy heart?

Together, cardiac TnI, TnT and another protein called troponin-C (TnC) form the Troponin Complex, which regulates the contraction of heart muscle fibers. These contractions are essential for proper heart function, and allow the heart to pump blood throughout the body.

5. Can cTnI be measured in blood from healthy people?

Until recently, it was thought that cTnI could only be measured in the blood of patients undergoing serious heart muscle injury, such as a heart attack [1]. It is now known that cTnI is present at low concentrations in the blood of all people [2], and is believed to represent healthy, physiological turnover of heart muscle cells [3]. Recent studies also show that low level troponin elevations above the physiological healthy levels may indicate a patient's risk of future cardiovascular events [4-5].

6. What are the cutoffs for the high sensitivity Spx HD™ cTnI test?

95% of healthy people have troponin-I values that are less than 4.6 pg/mL and 99% of healthy people have troponin-I values less than 7.1 pg/mL when measured with the ultrasensitive Sgx HD cTnI test.

Test results above the 99th percentile reference range value may indicate an increased risk for

future adverse cardiovascular events. In addition, test results above the 95th but below the 99th percentile reference range value may be approaching a category of increased risk.

7. What are the benefits of a high sensitivity cTnI test to physicians and their patients?

Cardiac troponin-I testing has traditionally been used in an emergency room setting to rule-in or rule-out diagnosis of an ischemic event, such as a heart attack in a patient with severe chest pain. Recently, it has been suggested that high sensitivity cTnI tests can enable clinicians and practitioners with new information that may improve outcomes for both inpatients (hospitalized, short term risk) and outpatients (post hospitalization, long term risk). This information can be used by physicians to better identify patients, who often present without clinical symptoms, who may be at risk of cardiac related adverse outcomes in the future [4].

8. What might low level elevations in cTnI mean about my heart health?

Elevated cTnI measurements are prognostic indicators for heart disease [5], but elevated cTnI can also be measured in patients who are not experiencing acute (heart attack) or chronic (heart failure) coronary symptoms [6]. Small elevations in otherwise healthy people have been shown to predict increased risk for future cardiovascular disease [7] and may provide insight for predicting future cardiovascular disease [8]. Small elevations of cTnI may also be measured in some patients after stress testing [9], after strenuous exercise [10], and after prolonged walking of up to 4 days [3].

9. What do the **SoxHD IL-6 and **SpxHD" IL-17A** tests measure?**

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The **Sgx HD IL-6** and **Sgx HD IL-17A** tests each measure pro-inflammatory cytokines called interleukins. These proteins are secreted into the blood by the immune system during inflammation.

10. What might elevated levels of IL-6 and IL-17A mean?

The presence of elevated cytokine levels in the blood may be an indication of vascular inflammation when they accompany other indications of atherosclerosis and heart disease. Together with other inflammatory markers like MPO, and tests for heart pathology like Sgx HD cTnI, these tests may provide insight into the likelihood of future cardiovascular events [11-13].

11. What is the role of inflammation in heart disease?

The role of inflammation in CVD has become well established over the past decade as part of the atherosclerosis process [14-16]. These referenced studies have linked inflammatory processes as a causative force behind atherosclerosis, a disease of the vascular system. Atherosclerosis in turn results in narrowed or blocked blood vessels, leading to increased blood pressure. This exertion can cause heart muscle deterioration, plaque formation and subsequent heart attack.

