

# NK Vue™ Test Overview

NK Vue™ is the first commercially available test to measure natural killer (NK) cell activity, and is used for *in vitro* diagnostic monitoring of the immune status of individuals.

## MEASUREMENT OF NK CELL ACTIVITY

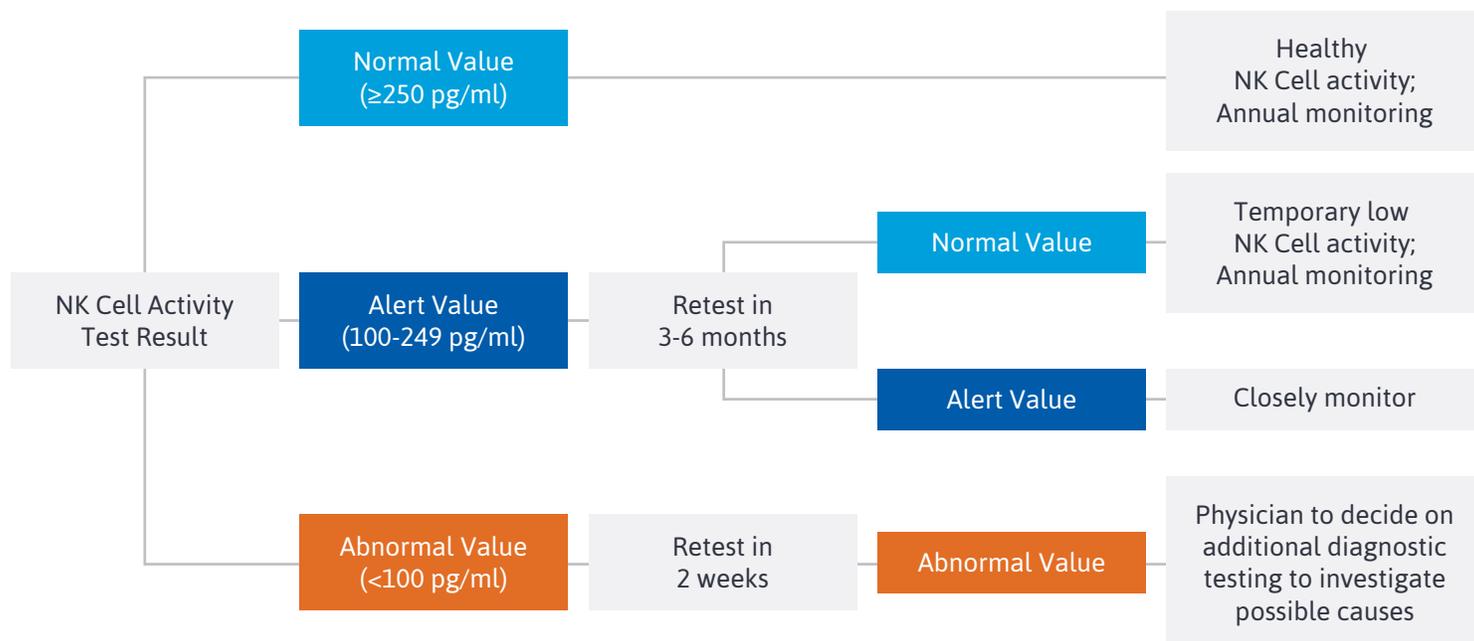
Measurement of NK cell activity has been shown to be a useful tool for assessing immunosurveillance, which may reveal an underlying condition or disease where NK cell activity may be affected.

NK Vue™ is a simple test, requiring only 1 mL of blood, that measures the ability of NK cells to remove tumor cells or infected cells present in whole blood. If the test result indicates low NK cell activity, the physician may follow-up with additional screening tests, such as a PSA test, mammogram, stool test or colonoscopy.

## RECOMMENDED TESTING ALGORITHM

Based on the current experience with NK Vue™ in Korea and Canada, we can provide the following preliminary recommendations.

This recommendation is provided as a tool to help in the interpretation of results; it is not a guideline. This recommendation may be changed at any time without notice when new clinical data becomes available.



## NK VUE™ AND DISEASE



Individuals with low cytotoxic activity of NK cells have been shown in an epidemiological study to be at significantly higher risk of cancer. It has been well-established that decreased NK cell activity is found in patients with a variety of solid tumors and large tumor burdens, and that this may be associated with development of distant metastases. Families with high incidences of cancer have shown reduced NK cell activities compared to control families.

Low NK cell activity has been found in patients with autoimmune disorders such as multiple sclerosis, rheumatoid arthritis and lupus and in patients suffering from chronic fatigue syndrome. In the elderly, low NK cell activity has been associated with increased risk of infections and associated morbidities, whereas well preserved NK cell activity has been linked to increased longevity. Studies in colorectal and prostate cancers have shown reduced NK cell activity in patients with those cancers.

### The NK Vue™ Difference

The activity of NK cells can be measured using the classical cytotoxicity assays (Chromium-51) or newer non-radioactive fluorescent dye cytotoxicity assays. These tests measure only the cytotoxic potential of NK cells and do not measure their ability to engage other cell types involved in the adaptive immune response.

NK cell activity *in vitro* cannot be measured without stimulating NK cells since NK cells do not secrete effector cytokines *ex vivo* in the absence of appropriate activating stimuli. Using a stimulatory cytokine, we can analyze NK cell activity in whole blood, which will include measurement of both the cytotoxic potential of the whole NK cell population (both CD56bright and CD56dim subsets) as well as the ability of these cells to amplify the immune response to tumors.

Both of these NK cells subsets release IFN- $\gamma$  following cytokine stimulation. The amount of IFN- $\gamma$  released is indicative of both the cytotoxic ability of the CD56dim subset and the immunomodulation by this cytokine, released from both subsets (CD56dim and CD56bright), to stimulate immune cells, and aid in the T-cell mediated anti-tumor response.

### NK Cell Activity and Colorectal Cancer

The correlation between low NK cell activity (as measured by NK Vue) and the presence of colorectal cancer has been demonstrated in a published clinical trial. In a study of 41 patients with newly diagnosed colorectal cancer, researchers at Yonsei University College of Medicine in Korea discovered that the NK cell activity of patients in their study group was significantly lower than it was in the 41 healthy patients in the control group.<sup>1</sup>

In Canada, a large clinical trial evaluated 872 high-risk subjects undergoing colonoscopy. The study showed that NK cell activity, as measured by a simple blood test, was able to predict a higher risk of colorectal cancer. Patients with low NK cell activity had a 10-fold higher risk of colorectal cancer compared with subjects with high NK cell activity.<sup>2</sup>

### NK Cell Activity and Prostate Cancer

The correlation between low NK cell activity (as measured by NK Vue) and the presence of prostate cancer has also been demonstrated in a published clinical trial. In a study of 54 newly diagnosed, biopsy-confirmed prostate cancer patients, researchers at Yonsei University College of Medicine in Korea found that NK cell activity in these patients was significantly lower than it was in the 54 healthy individuals in the control group.<sup>3</sup>

An association between NK cell activity and prostate cancer was demonstrated in a 43 patient (men undergoing prostate biopsy) study. Results showed that patients with NKA levels below 200 pg/ml had an 86% absolute risk of having prostate cancer at biopsy.<sup>4</sup>

A clinical study was performed on 94 patients (men undergoing prostate needle biopsy for an elevated PSA and/or abnormal DRE). The study analyzed NK cell activity in the blood and found that men scheduled for prostate biopsy were five-times more likely to have a prostate cancer diagnosis when NKA levels were below 200 pg/ml, as measured by NK Vue.<sup>5</sup>

NK Vue was approved by Health Canada in 2014 and the Korean Ministry of Food and Drug Safety in Oct 2012 and recognized as Novel Health Technology after assessment by NECA (National Evidence-based healthcare Collaborating Agency) in June 2014.

<sup>1</sup> Lee, S.-B. et al. A high-throughput assay of NK cell activity in whole blood and its clinical application. *Biochem. Biophys. Res. Commun.* 2014 Mar 14;445(3):584-590.

<sup>2</sup> Jobin, G. et al. Association between natural killer cell activity and colorectal cancer in high-risk subjects undergoing colonoscopy. *Gastroenterology*. 2017 Oct;153(4):980-987.

<sup>3</sup> Koo, K. C. et al. Reduction of the CD16(-)CD56bright NK cell subset precedes NK cell dysfunction in prostate cancer. *PLoS ONE*. 2013 Nov 4;8(11):e78049.

<sup>4</sup> Barkin J, et al. Association between natural killer cell activity and prostate cancer: a pilot study. *Can J Urol*. 2017 Apr;24(2):8708-8713.

<sup>5</sup> Vidal AC, et al. Natural Killer cell activity and prostate cancer risk in veteran men undergoing prostate biopsy. *Cancer Epidemiol.* 62:101578 [Epub ahead of print 1 Aug 2019] PMID: 31377571



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