For Healthcare Professionals

MASTO CHECK

The Next Generation of Early Breast Cancer Screening

AVAILABLE THROUGH:

Singapore Diagnostics

0917-777-LABS(5227)

www.singaporediagnostics.com

ONLY AVAILABLE IN SINGAPORE DIAGNOSTICS METRO MANILA BRANCHES

The Next Generation Early Breast Cancer Screening with A Single Drop of Blood

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“We aim to bring a healthy life for every woman by creating a new paradigm for diagnostics.”

1 Early cancer biomarker discovery platform

Provides early detection solutions for a wide range of diseases, from chronic diseases to major cancers such as breast cancer

2 Enabler of personalized medicine through companion diagnostics

Develops an optimized proteomics biomarker platform for companion diagnostics that enables personalized medicine

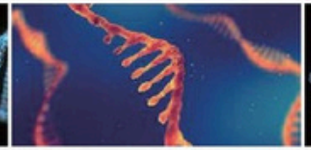
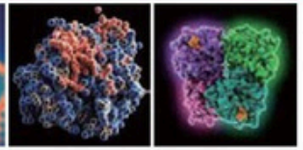
3 IT convergence technology

Rapid development of effective Proteomics big data and innovative artificial intelligence (AI) software using machine learning technology based on extensive expertise in developing diagnostic solution

Era of Multi-Omics Led to Increased Attention to Proteomics

Proteomics is the study of proteins at a macro level, which can unlock the potential to diagnose most cancers and diseases. Integration of proteomics with other omics technology is expected to further maximize diagnostic accuracy.

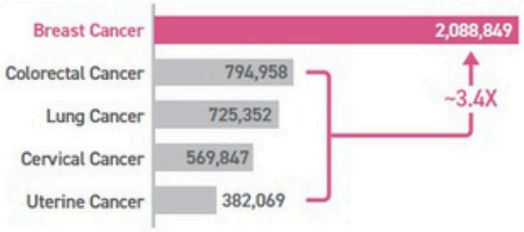
Multi-Omics

	Genomics	Transcriptomics	Proteomics
			
Analysis Target	~ 25,000 genes and the Genome (DNA)	+ ~ 100,000 and more transcripts (RNA)	+ ~1,000,000 (Protein)
Description	• Genomic analysis of cellular activities and metabolic pathways - DNA, ctDNA, cfDNA and etc. • Mutational analysis	• Analysis of RNA, which is the intermediate step from DNA to protein - miRNA, mRNA - Expression analysis	• Analysis of proteins, the final product of central dogma • Discover protein markers that show disease-specific expression patterns

Breast Cancer Incidence

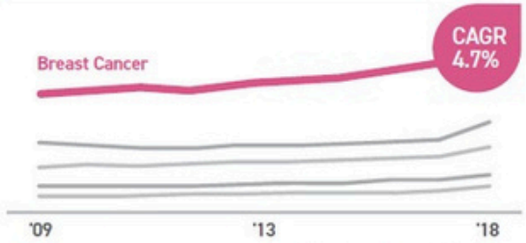
Breast cancer is by far the most common cancer in women globally, and its prevalence continues to increase.

Ranking of Cancer Incidence in Women



(2018, unit: headcount)

Steady Growth in Incidence Rate



Source : World Cancer Research Fund

MASTOCHECK

Specially designed to overcome the limitations of conventional breast cancer screening methods

Multiple-marker early screening test with just a tiny amount of blood (~1ml)

High accuracy (77%) for stage 1 breast cancer

Precise diagnosis based on quantitative information of LC-MS/MS

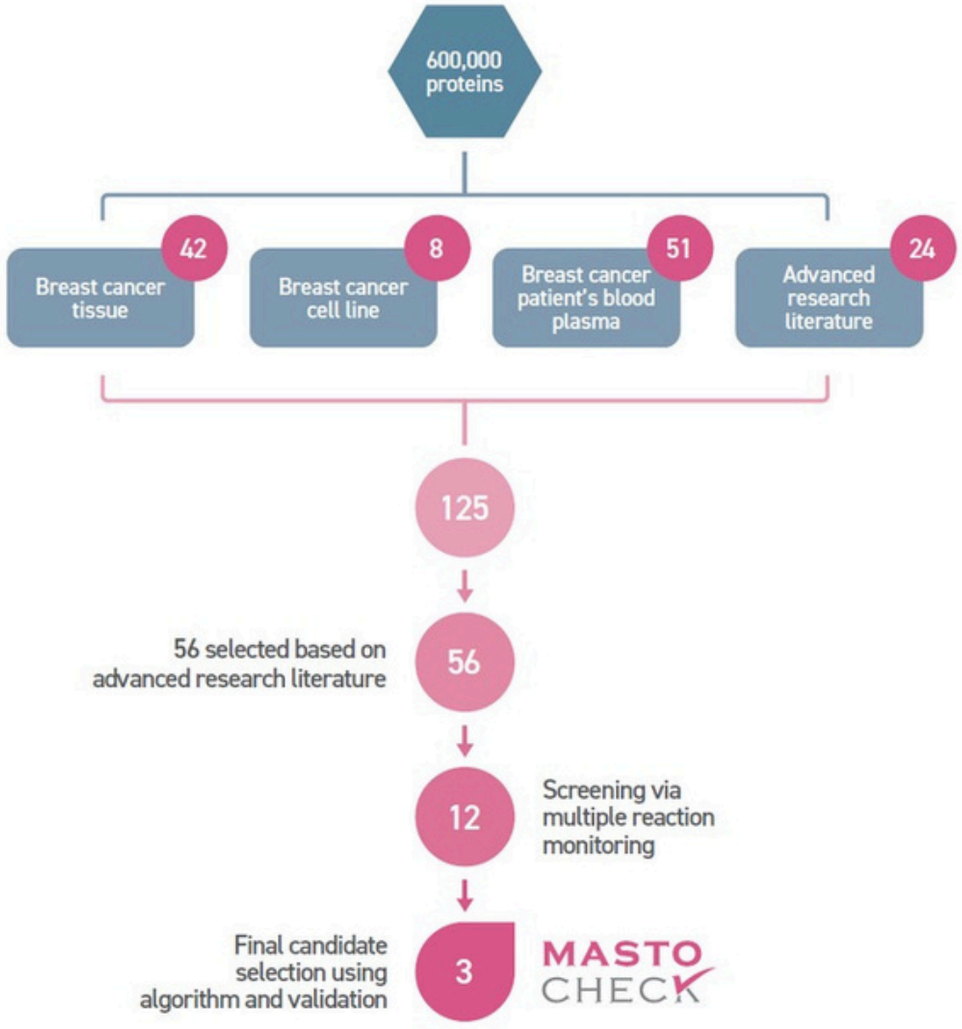
- Non-invasive
- Painless
- Radiation-free
- Developed by Breast Cancer Professionals

Accessible to young woman (20-40 years old), pregnant woman, patient with breast implant or dense breast

Proven to show 10%-30% higher sensitivity compared to Mammography alone

MASTOCHECK Development Process

A team led by professor Dong Young Noh of Breast Surgery of Seoul National University spearheaded the development of MASTOCHECK since 2008; ~600,000 proteins were analyzed to select three markers showing optimal accuracy.



Biomarkers

Known Functions and Implications as a Breast Cancer Marker

Related Papers

CA1

(Carbonic anhydrase1)

- Carbonic anhydrase (CA) protein is an enzyme involved in cellular respiration. In the process of tumorigenesis, the CA enzyme is overexpressed, resulting in increased cellular respiration which is a key mechanism for driving proliferation of cancer cells. During which, the increased activity of CA is also presumed to support angiogenesis.
- Research has shown that overexpression of CA9 (one of 15 CA isoforms) is strongly associated with cancer. In one study, the CA9 enzyme is found in both cell membrane and cell nucleus of cancer cell tissues.
- CA1 is another enzyme in the CA family that exists both inside and outside of cells. In particular, the plasma levels of CA1 has been proven to increase when breast cancer occurs.

- Hypoxia-induced carbonic anhy drase IX as a target for cancer therapy: From biology to clinical use (Semin Cancer Biol. 2015 Apr;31:52-64.)
- Carbonic anhydrase IX is an in dependent predictor of survival in advanced renal clear cell car cinoma (Clin Cancer Res. 2003 Feb;9(2): 802-11)
- Expression of hypoxia-inducible carbonic anhydrase-9 relates to angiogenic pathways and independently to poor outcome in non-small cell lung cancer(Cancer Res. 2001 Nov 1:61(21):7992-8)

CHL1

(neural Cell Adhesion Molecule like L1 protein)

- Close Homologue of L1 (CHL1) is part of the L1 gene family of neural cell adhesion molecules (L1-CAM), which has been shown to be highly associated with metastasis.
- Based on the comparison of CHL1 gene expression levels, breast cancer cells exhibited highest sensitivity among several types of primary cancer tissues.
- The sensitive response of CHL1 was also observed in the plasma of breast cancer patients, and we have obtained a patent to apply the use of CHL1 as a diagnostic marker for breast cancer.

- Differential Expression of CHL1 Gene during Development of Major Human Cancers (PLoS One. 2011 Mar 7:6[3]:e15612)
- CHL1 is involved in human breast tumorigenesis and progression (Biochem Biophys Res Commun. 2013 Aug 23:438(2):433-8.)
- Loss of cell adhesion molecule CHL1 improves homeostatic adaptation and survival in hypoxic stress (Nature Cell Death Dis. 2013 Aug 15:4:e768.)
- CHL1 hypermethylation as a potential biomarker of poor prognosis in breast cancer. Oncotarget. 2017 Feb 28819:15789-15801)

APOC1

(Apolipo -protein C1)

- Apolipoprotein C1 (APOC1) is a type of liposomal protein responsible for signal transmission of lipoproteins, especially as an inhibitor of Cholesteryl-ester transfer protein (CETP). CETP converts LDL (Low-density Lipoprotein) and LDL cholesterol factors into HDL High-Density-Lipoprotein) cholesterol.
- In breast cancer patients, the blood concentration of APOC1 is reported to be lower among the lipoprotein of breast cancer patients. In contrast, the concentration of APOC1 is shown to increase in ovarian cancer and pancreatic cancer patients, which enhance its specificity for breast cancer screening. We have thus patented APOC1 as a breast cancer diagnostic marker.
- APOC1 is also proven to be useful as a marker for recurrence prognosis in recurrent breast cancer patients [(A Goncalves (2006)], and can be effective for monitoring post cancer treatment.

- Identification of Apolipoprotein C-I Peptides as a Potential Biomarker and its Biological Roles in Breast Cancer (Med Sci Monit. 2016 Apr 7:22:1152-60)
- Apolipoprotein C-1 maintains cell survival by preventing from apoptosis in pancreatic cancer cells (Increased concentrations in pancreatic cancer) (Nature Oncogene. 2008 May 1;27(20):2810-22)
- Proteomics Analysis for Finding Serum Markers of Ovarian Cancer (Increased Concentration in Ovarian Cancer) (Biomed Res | Int. 2014:2014:179040.)
- Detection and identification of potential biomarkers of non small cell lung cancer.(Technol Cancer Res Treat. 2009 Dec;8[6]:455-66.] (Decreased Concentration in Non-Small Cell Carcinoma)

MASTOCHECK Performance

Analysis of diagnostic performance showed higher accuracy
when mammography + MASTOCHECK is conducted together, vs just mammography alone.

Comparison of Diagnosis Performance (JBD 2019)

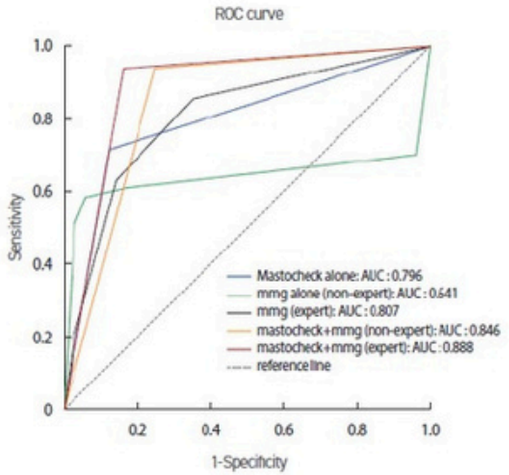
Higher accuracy for MASTOCHECK + mammography

Diagnosis performance comparison of women with dense breasts (level 3, 4)
MMG with MASTOCHECK vs. MMG only (breast specialist vs non-breast specialist)

- The sensitivity, specificity, and accuracy were 59.2%, 84.8% and 69.0%, respectively, when dense breasts, which are grade 3 or higher, were classified and analyzed. In the same cases who underwent mammography review, the sensitivity, specificity, and accuracy of MASTOCHECK were 71.6%, 85.3% and 77.0%, respectively, as confirmed by the final experiment.
- The sensitivity, specificity and accuracy of subgroup analysis on dense breasts are 93.2%, 72.8%, and 85.4%, as shown in Table 4, with a 30% improvement in sensitivity over mammography alone. The accuracy has also been improved by 15%.
- Mammography + MASTOCHECK (AUC 0.846) was better than mammography alone (AUC 0.641), and it was statistically significant ($p<0.001$) (Figure 1).

Result of validation

	Mammography alone	Mammography +MASTOCHECK
Total		**%**
Sensitivity	63.0	93.9
Accuracy	71.3	87.1
Dense Breast (Grade 4)		**%**
Sensitivity	47.2	84.9
Accuracy	63.5	79.2



Comparison with Conventional Single Breast Cancer Marker

CA 15-3 Conventional Single Marker	MASTOCHECK Multiple Markers
Single Marker Composition 10%* Diagnosis Accuracy at Stage 1-2 Breast Cancer	Accuracy 77%** for Stage 1-2 Breast Cancer Screening
CA 15-3 inferred False Negative Over 90%	MASTOCHECK False Negative 28%

MASTOCHECK, BREAST CANCER SCREENING TEST WITH A SINGLE DROP BLOOD

* Neoplasma. 1994;41(4):213-6., Isr J Med Sci. 1988 Sep-Oct;24(9-10):623-7
** Patent registered (10-1431062) Efficacy of Mastocheck for Screening of Early Breast Cancer: Comparison with Screening Mammography, 2019

FAQ

When results from imaging examination and MASTOCHECK are different?

There's no one-size-fits all rule for breast cancer screening. If imaging and MASTOCHECK show conflicting results, it is recommended to observe breast cancer more closely.

i.e. if the result of the imaging test is negative and the result of MASTOCHECK is positive, 3-6 months follow ups for the first 1-3 years could be considered. As more data are accumulated on MASTOCHECK in large scale, updated information with reliable advice would be followed.

Why MASTOCHECK should be taken?

For breast cancer screening test, very limited options are available such as mammograms and MRI according to worldwide evidence-based guideline. Given the concerns about radiation exposure due to pregnancy and difficulties for imaging test because of dense breast or breast implant, MASTOCHECK is the excellent alternative for breast cancer screening test. Young women under 40 years old but with Above-Average Breast Cancer Risk due to family history, other genetic predisposition (for example, women with a BRCA mutation) or of other cancer history are also good candidates for MASTOCHECK.

MASTOCHECK is radiation-free, simple and convenient, and accurate for dense breast. With only a small volume (1ml) of blood, MASTOCHECK is an excellent substitute and a supplement tool for all women looking for alternative breast cancer screening methods.

1 "Breast Cancer Screening Guidelines for Women", Center for Disease Control