GENE SOLUTIONS

SPOT-MAS
MULTI–CANCER EARLY DETECTION

Introduction to

Multi–Cancer Early Detection

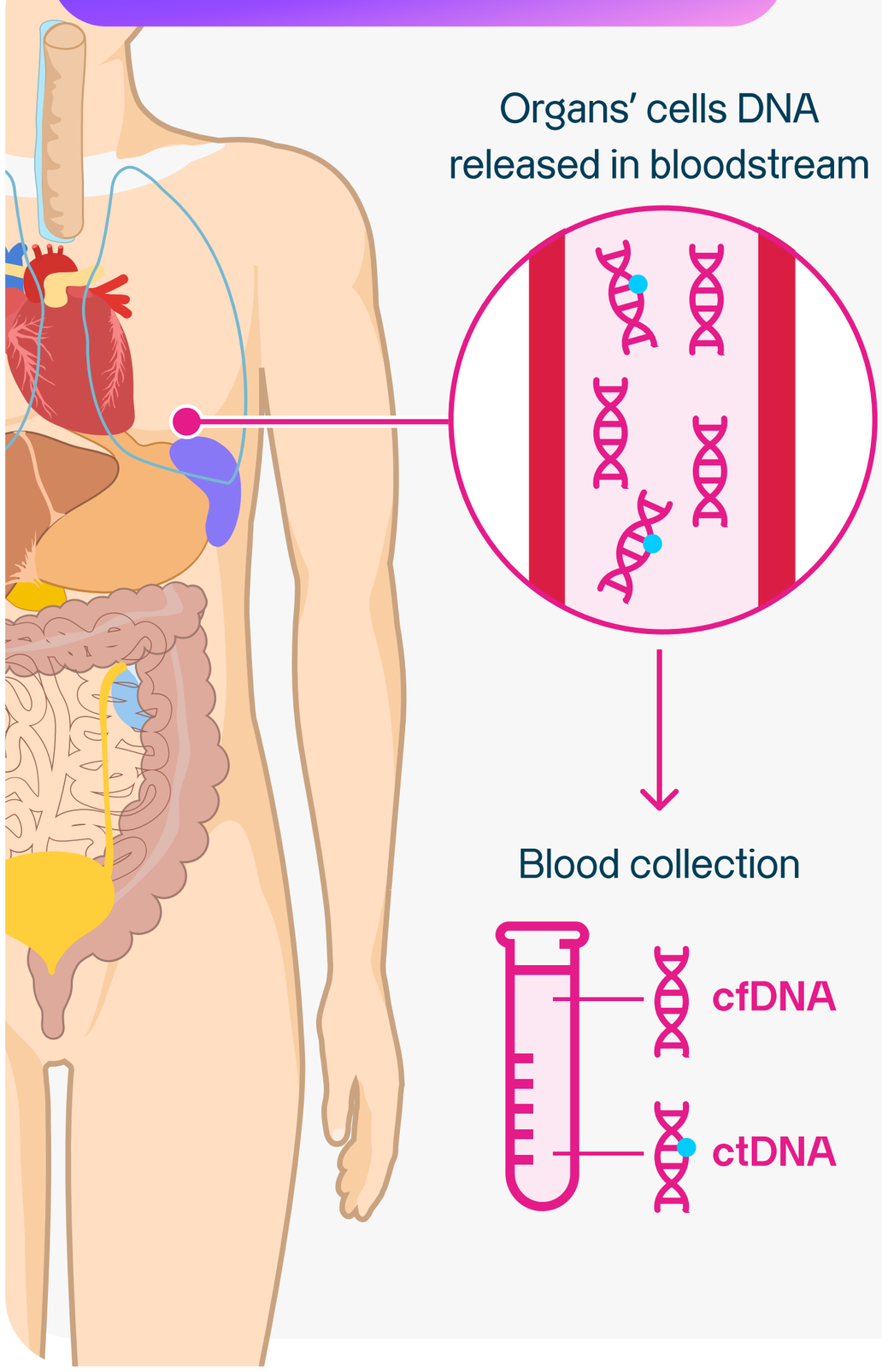
Spot early signs of 10 common and aggressive cancers, by analyzing DNA shed by cancer cells (ctDNA).

Spot cancer signals early

- What is ctDNA Multi–Cancer Early Detection?
- Why should we care?
- What should we do to improve early detection?
- What screening options are available for me and my family?
- Who should consider starting ctDNA screening?
- Why SPOT–MAS and what do the results mean?

01 | What is ctDNA Multi–Cancer Early Detection?

WHAT IS ctDNA TECHNOLOGY?



Cells from all organs carry DNA. Throughout their life cycle, cells release fragments of their DNA into the bloodstream. Examining these DNA fragments can provide valuable clinical insights.

cfDNA (cell–free DNA): DNA fragments released passively from cells into bloodstream.

Since 2011, cfDNA sequencing technology has been used to detect genetic abnormalities of the fetus through the collection of blood from pregnant women. This test is known as Non–invasive Prenatal Testing (NIPT).

ctDNA (circulating tumor DNA): cell–free DNA released from tumor cells. Tumor cells release ctDNA actively with multiple features significantly different with cfDNA.

Following a similar concept, ctDNA technology is applied to detect and examine tumor DNA in the blood. This enables early detection of cancer for healthy individuals, as well as profiling and tracking tumor progress in cancer patients.

BENEFITS OF ctDNA IN MULTI–CANCER EARLY DETECTION

Convenience: one single blood draw during a healthcare visit.

Early Detection: the potential to identify cancer signals at an early stage.

High Accuracy: high specificity limits false positive and unnecessary work-up.

Efficiency: capability to test for cancers that do not have recommended screenings to improve patient outcomes.

The practice of early detection for multiple cancers is an active search for a signal that many cancers share, thereby improving the probability of identifying cancer at an early stage.

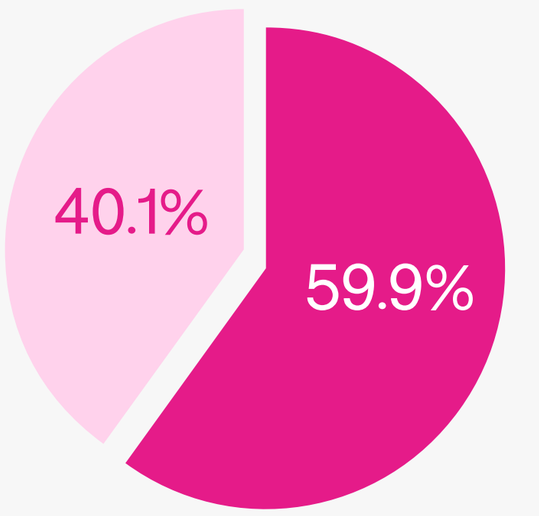
ctDNA has been proved as an insightful signal in multi–cancer screening. [1][2]

(1) Le Son Tran, et al. (2023) eLife 12:RP89083. (2) Daniel C. Chung, et al. (2024) The New England Journal of Medicine.

02 | Why should we care?

STATUS OF 10 COMMON AND AGGRESSIVE CANCERS

Mortality



(1) WHO – GLOBOCAN 2022. South–Eastern Asia

10 cancer types

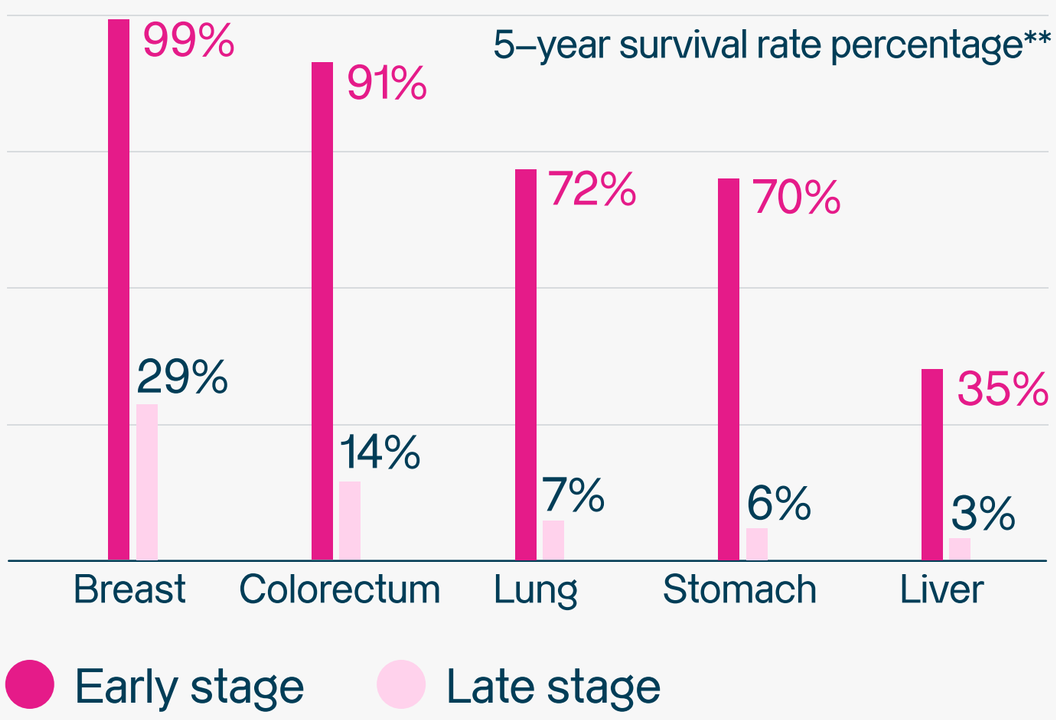
Breast
Lung
Colorectum
Stomach*
Liver*
Ovary*
Pancreas*
Esophagus*
Uterus*
Biliary tract*

*** 7/10**
Cancer types that currently have no standard-of-care screening program available.

The WHO GLOBOCAN South–East Asia Report (2022) tracks the incidences of more than 3,000 new cases a day, spanning a total of 32 reported cancer types[1]. Remarkably, 10 types of cancer, accounted for 56.2% of total new incidences and 59.9% of total mortality.

Only three among them (Breast, Lung, Colorectum) have established screening programs. The need for early–stage screening for more cancer types is crucial, given the rising incidence of cancers. Early detection can significantly improve survival rates and save lives.

THE NEED FOR EARLY DETECTION



Early detection is key in the fight against cancer. It not only increases the chances of successful treatment but also significantly improves the quality of life for patients.

(2) Statistics adapted from the American Cancer Society's (ACS) publication, Cancer Facts & Figures 2022 and Cancer Facts & Figures 2021; the ACS website; and the International Agency for Cancer Research website.
(3) Sankaranarayanan, R., Ramadas, K., Qiao, Y., 2014. Managing the changing burden of cancer in Asia. BMC Med 12, 3.
(4) ACTION (Asean CosTs in Oncology) STUDY, Singapore 2020.

Common cancer types like breast or colorectum have >90% survival rate if detected early[2]. However, more than 70% of cancers in low–income and middle–income Asian countries are diagnosed in late stage [3].

Main reasons for late detection:

- People with no obvious signs of cancer do not go for early cancer screening.
- Only a few cancer types have recommended screening.
- Cancer symptoms mostly occur at late stage.

Late–stage diagnosis leads to[4]:

- 5x higher mortality rate within 12 months.
- 50% higher chance of financial catastrophe.

03 | What should we do to improve early detection?

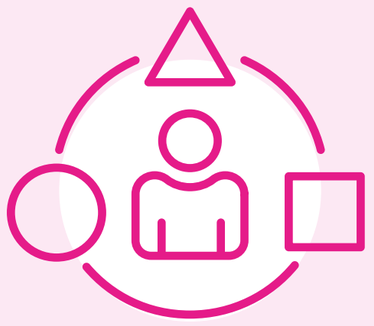
UNDERSTAND WHAT CAUSES CANCER

Hereditary & Familial

25–30%(1) attributed to all cancers

Occurred mutations

70%(1) attributed to all cancers



Hereditary & Familial	Occurred mutations
Inherited from familial gene	Caused by age, environment & lifestyle habits
Mutations in a person genome from birth	Mutations acquired over time
All cells in the body have these mutations	New mutations are present at the tumor only
May be passed to future generations	Will not be passed to future generations
Screen for hereditary cancer risks: common genes associated with specific types of cancer.	Screen for tumor presence at early stages by annual screening checkup or using ctDNA multi–cancer early detection test.

(1) Garber J.E., Offit K. Hereditary Cancer Predisposition Syndromes. J. Clin. Oncol. 2005;23:276–292

AWARENESS OF SCREENING METHODS

Proactive screening

- Detect possible presence of cancer
  - Single approach: Imaging for single organ, HPV test for cervical cancer, Selected biomarker for single organ.
  - Multi approach: Full body CT scan, PET–CT, ctDNA early cancer detection test.
- Germline mutations for hereditary cancer risks
  - Multiple hereditary cancer testing.

04 | What screening options are available for me and my family?

SCREENING AVAILABILITY

Once in a lifetime

Hereditary cancer risks test by informed choice. (Related genes that recommended by American Cancer Society or National Comprehensive Cancer Network)

+ Routine cancer screening

Screening programs are available for some cancer types. Talk to your primary care doctor for advice.

+ Complementary Screening

Annual screening with SPOT-MAS covers multiple cancers that do not have formal screening programs. Discuss with your primary care doctor to learn more about the test.

SCREENING PROGRAMS AND ctDNA SCREENING

Recommended programs:[1][2]

Breast cancer
Annual mammography for women above 40 years old.

Colorectal cancer
Start regular Stool–based test or Colonoscopy at age 50.

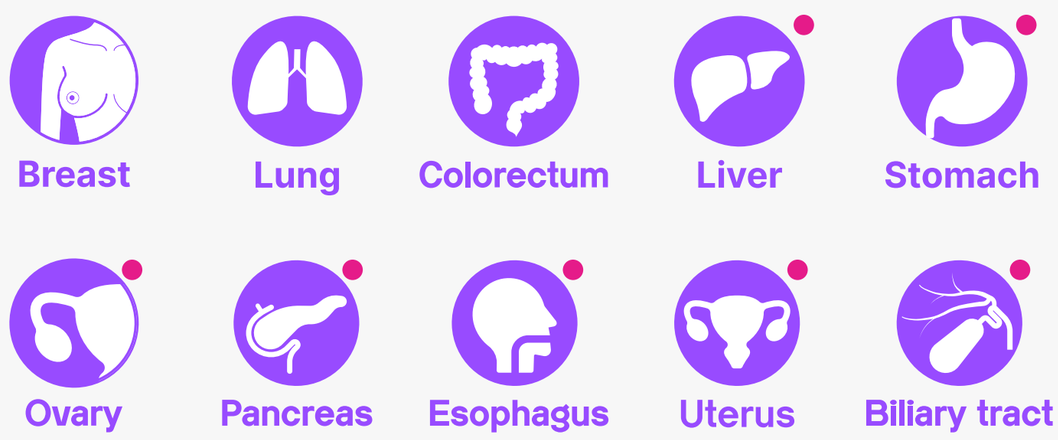
Lung cancer
Annual low–dose CT scan people age 50–80 who smoke or used to smoke.

Cervical cancer
Cervical cytology, HPV test every 05 years and PAP test every 03 years for people from the age of 25-65.

(1) National Cancer Centre Singapore (2) American Cancer Society

SPOT–MAS multi-cancer early detection test:

Spot for early cancerous signal of:



- **7/10** currently have no standard-of-care screening program available.

Screening methods complementary to standard–of–care programs are available as informed choices. Talk to your healthcare provider about the pros and cons of testing to make decision.

05 | Who should consider starting ctDNA screening?

01 Heavy smoking
People who have a 20 pack–year history of smoking.[1]

02 Heavy drinking
People who drink 15 cans of beer a week (for men) or 08 cans of beer a week (for women).[2]

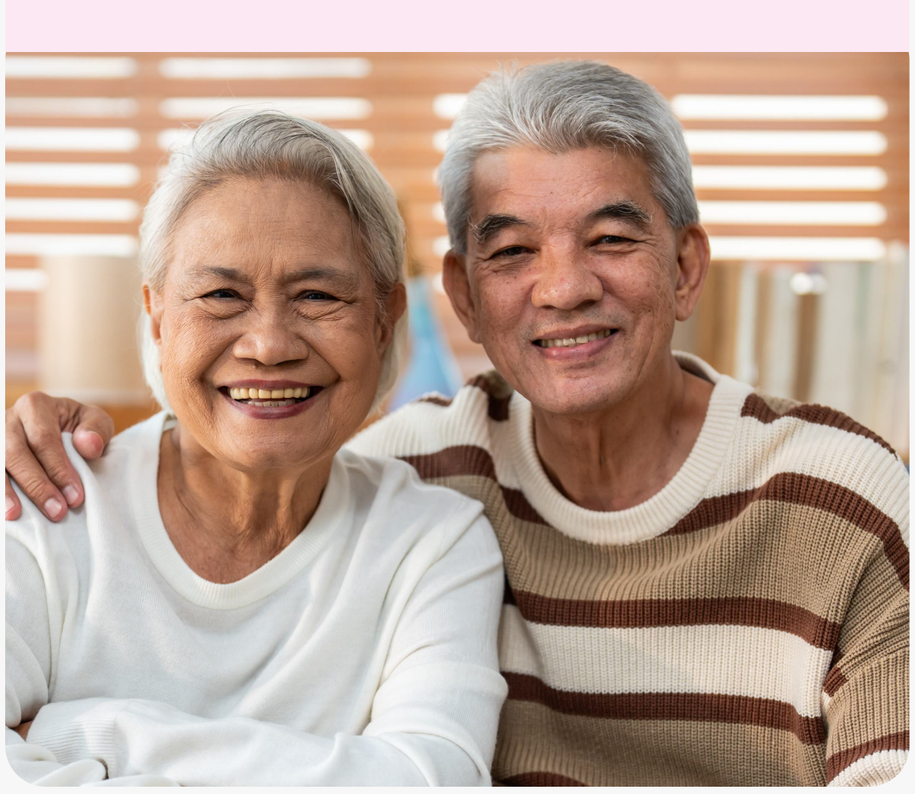
03 Hereditary risks
Those who have tested positive for inherited cancer genes such as BRCA1, BRCA2, TP53.[3]

04 Liver diseases
People who have Hepatitis B or C.[4]

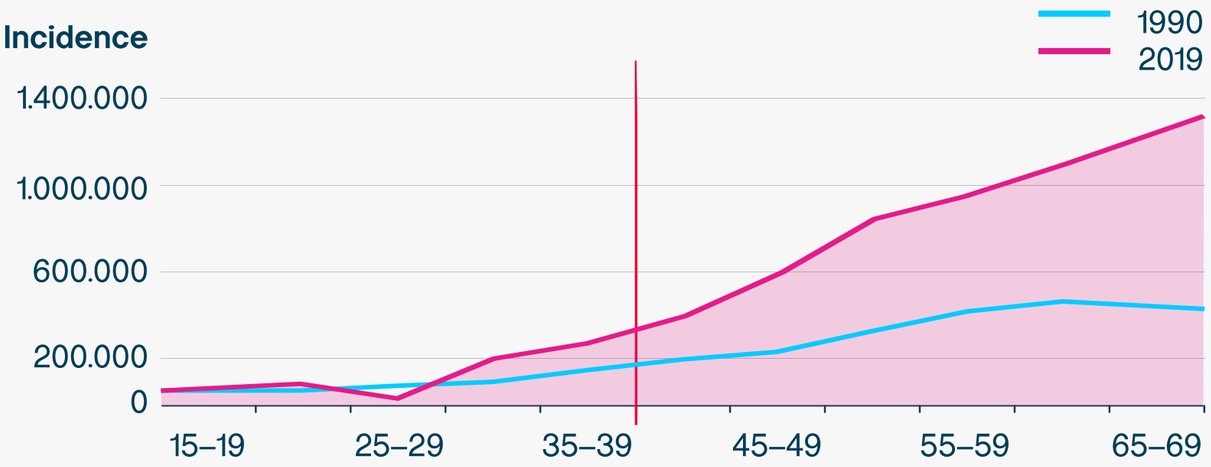
05 Familial history
People whose family members had been diagnosed with cancer.[5]

Adults aged less than 40 years but have high risks

Adults aged 40 years & older



The incidence of cancer has increased since 1990. Older persons are at higher risk for cancer.[1]



Cancer incidence by age in Asia between 1990 and 2019 [1]

Globally, breast cancer screening is recommended for women above 40 years old[2]. Some countries recommend to screen for colon[3], stomach[4], lung[5], and liver[6] starting from as early as 40 years old.

(1) Chen et al., 2021. American Journal of Otolaryngology 42, 102915. (2) Connor et al., 2017. Addiction 112, 222–228. (3) Garber et al., 2005. JCO 23, 276–292. (4) Petruzziello et al., 2018. TOVJ 12, 26–32. (5) Brewer et al., 2017. Breast Cancer Res Treat 165, 193–200.

(1) Sharma et al., 2024. The Lancet Regional Health – Southeast Asia 21, 100333. (2) Renet al., 2022. The Breast 64, 85–99. (3) Azad NS et al., 2020. Prev Med. 2020;133:106003. (4) Mabe et al., 2022. Digestive Endoscopy 34, 412–419. (5) Nawa et al., 2019. Japanese Journal of Clinical Oncology 49, 130–136. (6) Lee et al., 2014. Cancer Res Treat 46, 223–233.

06 | Why SPOT–MAS?

Largest clinical validation in Asia: SPOT–MAS performance is validated in a research involves **9.024 participants**, showing proven accuracy in cancer signal detection (78.1% Sensitivity, **99,8% Specificity**) and tumor location prediction (84% Accuracy).[1]

Testing Laboratory: The blood specimen is processed and tested at Gene Solutions Genomics Pte Ltd, a MOH-licensed clinical laboratory in Singapore. Results will be delivered to your doctor.

International Awards: Gene Solutions' award winning studies to screen for multi–cancer has been featured in:

- American Society of Clinical Oncology (ASCO) Breakthrough 2023
- European Society for Medical Oncology (ESMO) Asia 2023
- >14 peer–reviewed international biomedical journal articles, including eLife, Nature publications, etc

(1) Nguyen, et al. "Analytical and clinical validation of a ctDNA based assay for multi–cancer early detection" (2023). doi:10.1101/2023.12.22.23300420

WHAT DO SPOT–MAS RESULTS MEAN?

Negative:
No ctDNA signal detected

ctDNA was not detected when the SPOT–MAS test was conducted. This test provides a snapshot of the blood at the time of collection and does not predict for future cancer risks.

Next step

Continue with the SPOT–MAS test annually or other screens as recommended by your doctor. Do not ignore cancer signs or symptoms if they occur, as this could lead to a delayed diagnosis.

Positive:
ctDNA signal detected

ctDNA signal associated with tumor cells was detected in the blood. The result may include 1–2 predictions of the origins of tumor in the body where the cancer may be found.

Next step

As the SPOT–MAS test is a screening test, a confirmatory imaging test is required to confirm if cancer is truly present. Your doctor will advise you on the required following tests.

Patient Support Programs

For patients with a positive test result, partial reimbursement for follow up diagnostic tests are available. Discuss with your doctor to learn more.

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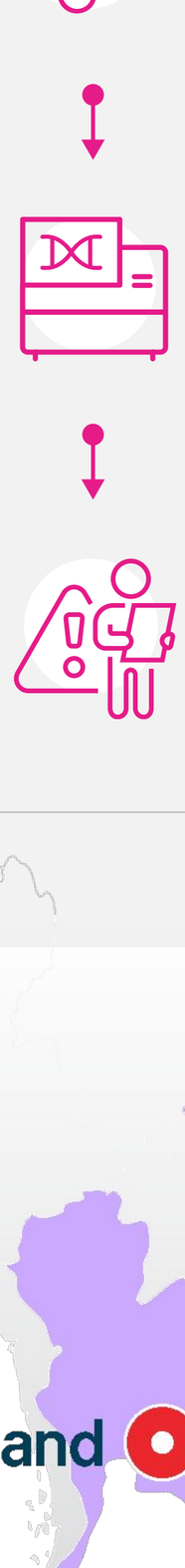
Test Process:

01 Request the test through your primary care doctor.
1 tube (10mL) of blood will be collected.

02 Your extracted DNA from the plasma will be processed using Next–generation sequencing to analyze methylation profile and multi–feature of DNA.

03 Receive your test results after 20 working days from the time sample is received at Gene Solutions Genomics Singapore laboratory.



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Simply reach out to your healthcare provider or Gene Solutions to learn more.

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