FOUNDATION MEDICINE®

Roche

Intelligent Diagnosis
Precision Medicine

Comprehensive Genomic Profiling

Find Out More About

Comprehensive Genomic Profiling

A Step in the Right Direction for the Best Treatment

Introduction

Upon being diagnosed with cancer, patients are keen to start treatment as soon as possible.

However, it is important to first gain accurate knowledge of the biological characteristics of a tumor before deciding on a treatment plan.

Tumor cells have their own genome profiles as different mutations or alterations accumulate on their DNA. Corresponding targeted cancer therapy options have been developed to tackle different kinds of gene mutations, and these have been clinically proven to be more efficacious than conventional treatments.

A variety of gene alterations may be present in cancer cells. With recent advances in technology for detecting and analyzing the DNA of cancer cells, genomic alterations present on as many as several hundred cancer-related genes can now be detected. A genome profile can thus serve as an important tool to assist healthcare professionals in their decision-making processes, allowing treatments to be tailored to specific patients and treatment outcomes to be more accurately predicted.

With the right medicine, your treatment can be more effective.

This, together with the support and company of family and friends, can help you walk confidently on your treatment journey.

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The first step in cancer treatment

There are a large number of cancer-related genomic alterations, and many targeted drugs have been developed for these. In fact, there can be different genomic alterations even in the same type of cancer. It is therefore very important for a doctor first to understand the biological characteristics of a patient's tumor.

"Precision medicine" is a new trend in cancer treatment that identifies the unique biological characteristics of a tumor and then suggests a personalized treatment strategy for the individual patient.

For example, patients with the same type of breast cancer may have different genomic alterations. Consequently, their treatment may need to be different too. In other words, cancer treatment is no longer homogeneous, but can now be both "precise" and "personalized".

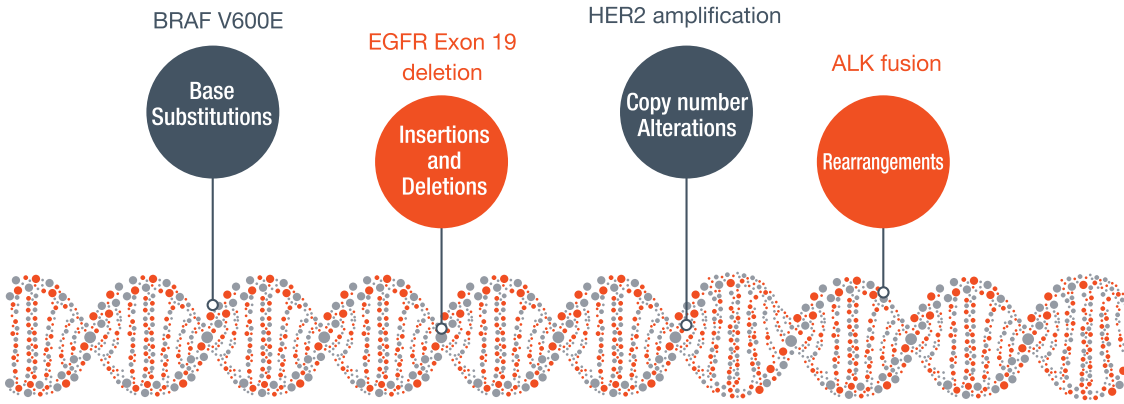
A comprehensive genomic profiling test - the first step in cancer treatment - is a cancer testing method that can identify the gene mutations in cells that may be causing your cancer to grow. The test helps your doctor develop personalized treatment options based on your unique genomic profile and cancer type, options focused on maximizing the curative effects of your treatment while minimizing any side effects as far as possible.

What is the relationship between genomic alterations and cancer?

Our body is made up of countless cells. Normally, cells grow and divide in an orderly manner; old cells are replaced and damaged cells repaired. This mechanism is controlled by specific DNA.[1]

Cancer occurs when these DNA get damaged or when they mutate in such a way that the body is unable to identify the problem and repair it. Abnormal cells can grow out of control and form tumors that invade healthy tissue and organs.[2] These tumors may become metastatic and spread throughout the body.[3]

There are 4 classes of genomic alterations that can drive tumor growth



BRAF (V-raf Murine Sarcoma Viral Oncogene Homolog B); EGFR (Epidermal Growth Factor Receptor); HER2 (Human Epidermal Growth Factor Receptor 2); ALK (Anaplastic Lymphoma Kinase)

What kinds of cancer genomic tests are available?

Single Marker Tests

- These tests look for mutations in single genes, or changes within single proteins, known to be associated with specific type of cancer
- Repeated tests may be needed, and each test may take from a few to up to ten days

Hotspot Gene Panel Tests

- Hotspot Gene Panel Tests only look for specific mutations in groups of genes known to be associated with cancer
- These tests may miss less common mutations, or mutations not normally associated with specific types of cancer

A paradigm shift on cancer treatment

In comparison with above 2 tests, a comprehensive genomic test is the latest technologies for cancer genomic test. A comprehensive genomic profiling can offer additional benefits, including:

(i) Patients **do not have to take multiple invasive tests** involving multiple tumor tissue samples, delaying their treatment
(ii) Doctors can more easily develop the **most appropriate treatment plan** for patients and evaluate the treatment effects; and
(iii) Patients can get a better grasp of their condition, facilitating consultations with the doctor about the best treatment plan and **improving their participation and confidence** in the treatment

- Considerations to take into account before selecting the appropriate cancer genomic test include:

  - **Time required**
  - **Reliability**
  - **Type of cancer covered**
  - **Treatment advice**
  - **Cost**

For further details or enquiries, please consult your doctor.

How can comprehensive genomic profiling help you?

Foundation Medicine

A Decisive Step

After using advanced technology to 'read' your genes and simultaneously identify the known to be implicated in cancer (including even some **rare and unknown genetic mutations**), Foundation Medicine provides a detailed report containing information about your tumor's genomic makeup.

This enables your doctor to see the potential genomic alterations and therefore explore the potential targeted therapies or treatment approaches that might benefit your individual case, including therapies that may not otherwise have been considered.

How to choose a genomic testing service?

The technology should be approved by international regulatory bodies

(For example: the US Food and Drug Administration)
Technology associated with genomic profiling that has been approved by international regulatory bodies can provide highly reliable analysis results. For example, approval by the **US Food and Drug Administration** (FDA) is a strong guarantee of the efficacy and safety of genomic testing technology.

Results should have been published in medical journals

The technology should have undergone a series of clinical trials and clinical studies, and the results of these should have been accepted by and published in renowned international medical journals. Such reports provide a **solid basis for healthcare professionals to make informed decisions about testing**.

What can companion diagnostics achieve?

Companion diagnostics can achieve improved **safety or effectiveness** by:
1. Identifying patients who are most likely to benefit from a particular therapeutic product;
2. Identifying patients likely to be at increased risk of serious side effects as a result of treatment with a particular therapeutic product; and
3. Monitoring responses to treatment adjustments, e.g. changes to treatment schedules, doses, treatment interruptions, etc.

Foundation Medicine – Our diagnostic portfolio

Advanced comprehensive techniques are used to analyze tumor tissue, thus avoiding the need for multiple different invasive tests and minimizing wastage of tumor samples. Foundation Medicine is breaking through the 'blind spots' in current cancer treatment, quickly identifying the alterations in genes known to be implicated in cancer.

FOUNDATIONONE® CDx

- The **world's first FDA-approved** genomic testing method for cancer[5]
- Applies next-generation sequencing to identify genomic alterations across **324** cancer-related genes known to be drivers of solid tumors, plus select introns of 34 genes[4]
- **High sensitivity* of up to 99%**[4,6]
- Microsatellite instability (MSI) and tumor mutational burden (TMB) results **inform eligibility for immunotherapies**, and identify clinical trial options

Suitable for:
- Patients with solid tumors
- Before using targeted therapy for the first time; or,
- Recurrent and metastatic cases, patients looking for treatment options

Sample type: Tissue biopsy

* Sensitivity is subject to the quality of the tumor tissue sample and biomarker.

FOUNDATIONONE® LIQUID CDx

- **FDA-validated**, liquid biopsy comprehensive genomic profiling service[11]
- Reveals clinically relevant genetic variations leading to cancer growth by detecting circulating tumor DNA (ctDNA) in the patient's blood[8]
- Analyzes **over 300** cancer-related genes[8] and tumor fraction values
- High microsatellite instability (MSI-H), blood tumor mutational burden (bTMB), or pan-tumour biomarkers results **inform eligibility for immunotherapies**[10] and identify clinical trial options

Suitable for:
- For whom tissue biopsy is inaccessible or impractical;
- For whom tissue biopsy is insufficient
- For whom with disease progression or a relapse in targeted therapies

Sample type: Blood sample

FOUNDATIONONE® HEME

- Specifically analyzes and identifies DNA sequence information of **406** genes and RNA (cDNA) sequence information on **265** common rearranged genes in hematologic malignancies and sarcomas[9]
- Reports TMB & MSI

Suitable for: Patients with blood cancers (leukemia, lymphoma and myeloma) or patients with sarcoma. Quickly and efficiently guides therapy selection

Sample type: Tumor tissue sample/blood sample/bone marrow aspiration

FoundationOne simplifies the practice of precision medicine by analysing guideline-recommended genes in **a single comprehensive test**

FOUNDATIONONE® CDx

Companion diagnostic indications[4]

Biomarker(s) detected	Therapy
Non-small cell lung cancer (NSCLC)	
EGFR exon 19 deletions and EGFR exon 21 L858R alternations	afatinib, erlotinib, gefitinib or osimertinib
EGFR exon 20 T790M alternations	osimertinib
ALK rearrangement	alectinib, crizotinib or ceritinib
BRAF V600E	dabrafenib with trametinib
MET SNVs and indels* that lead to MET exon 14 skipping	capmatinib
Melanoma	
BRAF V600E	dabrafenib or vemurafenib
BRAF V600E or V600K	trametinib or cobimetinib combination vemurafenib
Breast Cancer	
ERBB2 (HER2) amplification	trastuzumab, ado-trastuzumab-emtansine or pertuzumab
PIK3CA C420R, E542K, E545A, E545D [1635G>T only], E545G, E545K, Q546E, Q546R, H1047L, H1047R, and H1047Y alterations	alpelisib
Colorectal cancer	
KRAS wild-type (absence of mutations in codons 12 and 13)	cetuximab
KRAS wild-type (absence of mutations in exons 2, 3, and 4) and NRAS wild type (absence of mutations in exons 2, 3, and 4)	panitumumab
Ovarian Cancer	
BRCA1/2 alterations	olaparib or rucaparib
Cholangiocarcinoma	
FGFR2 fusions and select rearrangements	pemigatinib
Prostate cancer	
Homologous Recombination Repair (HRR) gene (BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D and RAD54L) alterations	olaparib
Solid tumors	
TMB ≥ 10 mutations per megabase	pembrolizumab
NTRK1/2/3 fusions	larotrectinib

The test is also used for detection of genomic loss of heterozygosity (LOH) from formalin-fixed, paraffin-embedded (FFPE) ovarian tumor tissue. Positive homologous recombination deficiency (HRD) status (F1CDx HRD defined as tBRCA-positive and/or LOH high) in ovarian cancer patients is associated with improved progression-free survival (PFS) from rucaparib maintenance therapy in accordance with the rucaparib product label.

FFPE=formalin-fixed, paraffin-embedded
* SNVs= single nucleotide variants, Indels=Insertion–deletion mutations

FOUNDATIONONE®LIQUID CDx

Companion diagnostic indications[8]

Biomarker(s) detected	Therapy
Non-small cell lung cancer (NSCLC)	
EGFR exon 19 deletions and EGFR Exon 21 L858R substitution	gefitinib, osimertinib or erlotinib
ALK rearrangement	alectinib
Prostate cancer	
BRCA1, BRCA2 alterations	rucaparib#
BRCA1, BRCA2 ATM alterations	olaparib
Ovarian cancer	
BRCA1, BRCA2 alterations	rucaparib#
BRCA1, BRCA alterations	rucaparib#
Breast Cancer	
PIK3CA mutations C420R, E542K, E545A, E545D [1635G>T only], E545G, E545K, Q546E, Q546R; and H1047L, H1047R, and H1047Y	alpelisib

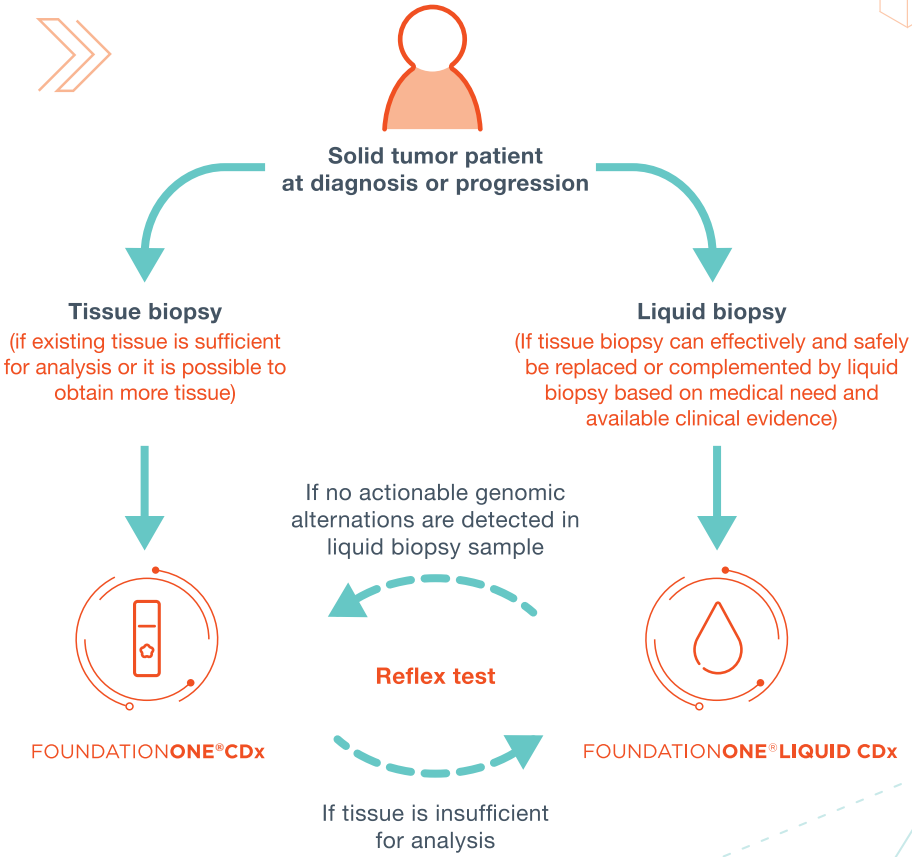
A negative result from a plasma specimen does not mean that the patient's tumor is negative for genomic findings.

Patients with the tumor types above who are negative for the mutations listed in the above table should be reflexed to routine biopsy and their tumor mutation status confirmed using an FDA-approved tumor tissue test, if feasible.

rucaparib is not registered in Hong Kong.

How to choose a suitable testing service?

To carry out personalized cancer treatment, your doctor will choose the test that's right for you based on your type of cancer and the type of sample that will be tested.



How testing works?

To carry out personalized cancer treatment, your doctor will choose the test that's right for you based on your type of cancer, and the type of sample that will be tested.

01 The doctor arranges to send a **biopsy sample** of your tumor to the Boston Laboratory for testing

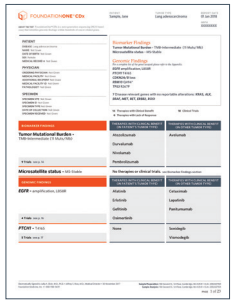
02 Foundation Medicine analyzes your sample to find **any cancer-causing genomic mutations**

03 Comprehensive analysis is carried out based on your personal data, medical records and genomic alteration data, which is **paired with other clinical medical research and drug database data**

04 It typically takes **14 days*** from the time your tissue sample is received in Boston, USA for Foundation Medicine to complete the test. Your doctor will then receive a **comprehensive and easy-to-understand report**.

* The number of days required depends on the quality of the tumor tissue samples

What the results mean?



The Foundation Medicine report includes the following information:

- The number of genomic alterations identified, and the number of matched therapy options
- The number of clinical trials the patient may be eligible for
- The genomic alterations identified in the patient
- US FDA-approved therapies available for the patient's tumor type
- US FDA-approved therapies available for another tumor type that shares a genomic alteration with the tumor that this patient has
- Details of clinical trials that are enrolling patients with this genomic profile

- **FoundationOne®CDx and FoundationOne®Heme are also designed to provide clinically actionable information. Every test result includes tumor mutational burden or microsatellite instability status#**
- **FoundationOne® Liquid CDx provides bTMB & MSI-H results and historic patient findings from earlier FoundationOne tests**

What is the relationship between tumor mutational burden & microsatellites and my cancer?

Tumor mutational burden and microsatellites are **emerging biomarkers of tumors**, that can provide **guidance** to oncologists who are deciding to treat their patients with **immunotherapies**. The results can also be used to assess the patient's likely response to immunotherapy. Tumors with **high TMB** may represent a **greater eligibility for immunotherapy**.[10]

Tumour mutational burden (TMB) is defined as the total number of somatic mutations per coding area of a tumor genome.

Microsatellites are short, repeated sequences of DNA. Microsatellite instability-high (MSI-H) cells have an accumulation of errors in genetic sequences that are normally repeated. When a cell is unable to repair mistakes made during the division process, errors in DNA start accumulating and may cause cancer.

Tumor fraction includes an estimate of the percentage of ctDNA present in the cfDNA sample, which is reflective of the total tumour burden.

Comprehensive genomic profiling consultation service

Any questions?

Our cancer genetics consultant will help with your concerns and ease your worries, assisting you to further understand the benefits and limitations of comprehensive genomic profiling. This enables patients to choose the right treatment with confidence.

Make an appointment

Please send an email to hk.fmi@roche.com with your personal information and contact no. in advance, and our service team will follow up the appointment.

Note: The counseling service will not recommend any treatment options to patients

Case sharing

Case 1

Patient profile >>

50+ year-old female

Diagnosed with non-small cell lung cancer with metastasis in hip joint, lymph node and liver in 2015

Treatment status >>

- Progression in chemotherapy and radiotherapy
- Received immunotherapy due to her worsening condition. The results were satisfactory. When the tumor had almost completely disappeared, she was diagnosed with pneumonia and was forced to stop treatment

FoundationOne®CDx analysis and subsequent treatment >>

- Identified rare gene mutations in NTRK fusion
- Joined the clinical trial of a target therapy for NTRK fusion at CUHK

Able to control the tumors in patient brain, lung and lymph nodes

Case 2

Patient profile >>

58-year-old female

5-year history of ER/PR–positive and HER2–amplified invasive ductal breast carcinoma

Treatment status >>

- Considered ineligible for HER2-targeted therapy, progression on multiple systemic combination regimens (taxanes, bevacizumab, dasatinib, ixabepilone and gemcitabine)

FoundationOne®CDx analysis and subsequent treatment >>

- Identified 2 activating mutations in ERBB2 (V777L and S310F) and mutations in PIK3CA and TP53
- Initiation of combination therapy with a tyrosine kinase
  - inhibitor targeting HER2 & EGFR
  - HER2 inhibitor
  - chemotherapy

Dramatic changes on pharmacodynamic imaging accompanied by significant symptomatic improvements in the patient

Frequently asked questions

What are the chances that Foundation Medicine CGP will find a relevant genomic alteration for my tumor?

Foundation Medicine Comprehensive Genomic Profiling (CGP) includes different types of alterations in genes known to be involved in cancer, to make sure nothing is missed. Depending on the type of mutation and our currently available knowledge, the report may highlight approved therapies, therapy approved for another tumor type, or relevant clinical trials. However, not genomic alterations that have been identified to date have corresponding potential treatments. Furthermore, your doctor may recommend an alterations treatment based on other factors which the report does not look at. For example, the side effects of some treatments may mean they are not suitable for you.

Will I need to have another biopsy taken for the genomic profiling test?

Foundation Medicine CGP can be run on a tissue sample at an earlier time. If there is not enough tissue left from an earlier biopsy to run the analysis, a new biopsy may need to be taken. Your doctor may also recommend a new biopsy to obtain a more recent sample.

Will Comprehensive Genomic Profiling identify the best treatment for me?

Only you and your doctor can identify the best treatment for you. However, because Foundation Medicine CGP look for your types of alterations in genes known to be involved in cancer, you can be confident that if an alteration is present in your tissue sample, there is a strong chance that Foundation Medicine CGP will detect it.The profile may identify potential avenues of treatment that you can explore with your doctor. It is important to understand that some therapies or trials identified by the profile may not be currently available in your country.

Can Foundation Medicine CGP predict if chemotherapy will work for me?

No. Foundation Medicine CGP is not designed to predict how your cancer will respond to chemotherapy. However, Foundation Medicine CGP can help your doctor to potentially match the genomic alterations present in your cancer with a treatment that can specifically target this cancer type. This could be either an approved treatment or one being investigated in clinical trials.

Response to a particular therapy involves a multifactor assessment and requires information such as previously administered treatment options, performance status, and ability to tolerate treatment. Therefore, this decision is best made by your doctor.

Can Foundation Medicine CGP predict if a mutation was genetically inherited (germline)? Can Germline Mutations be detected for family members?

While Foundation Medicine CGP can detect many genetic alterations, it cannot specify whether your specific genomic alteration was inherited (germline) or acquired over time. For example, your profile may indicate that you have a rare genetic mutation, but it can't determine if you have inherited this mutation or acquired it over time.

Foundation Medicine CGP is designed to interrogate your known genomic mutations associated with human cancers, regardless of whether they have been inherited or not. If you and your family would like to determine whether your specific cancer type is inherited, you will need to request a separate germline test. Your report will indicate whether your genomic alteration has been associated with germline cancer-predisposition syndromes, which may help you decide whether to proceed with further testing.

- This brochure is for reference only.
  If you have any queries, please consult your healthcare professional.

Consult your doctor or visit the following website for details of genomic profiling
www.cancertest-fmi.com.hk

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