FRANCE MÉDECINE GÉNOMIQUE 2025

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Document d'information en vue d'un examen des caractéristiques génétiques d'une tumeur

Genetic testing for cancer patients - information document

In consultation with a team of medical specialists, your doctor has prescribed a test to determine the genetic characteristics of your tumour.

The purpose of this information document is to explain the nature of this genetic test and its possible consequences for you and, in certain scenarios, your family. It will provide you with answers to the following questions:

This document supplements the explanations given by your doctor or genetic counsellor who remains your first point of contact should you have any questions that will help you to make your decision. If you decide to have this test, the doctor will ask you to sign a consent form.

1 Why determine the genetic characteristics of a tumour?

The mechanisms responsible for the development and progression of cancers are very diverse and vary from one patient to the next. Each tumour has its own specific characteristics, which may concern the tumour cells themselves or their interaction with the surrounding cells and organs.

There is no one type of cancer for each organ in the body but a multitude of subtypes, each characterised by specific abnormalities. Better knowledge of these abnormalities, particularly those of tumour cell DNA (the genes of a tumour) and how they impact the mechanisms of cancer development, has made it possible to implement new treatments that lead to the specific destruction of the tumour cells.

Based on these recent advances in genomics research, the aim of precision medicine is to offer the patient treatment that is tailored to the genetic characteristics of the tumour (targeted therapy), if such treatment exists. The aim is not to replace the treatments that the patient is already receiving but to supplement them when they are not effective enough.

2 What does this test involve?

It involves taking a fragment of your tumour to sequence (decode) the DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) contained in its cells.

As part of your diagnosis and care, you have already given samples of your blood, cells, fluids and tissues. These samples are stored for several years and can be used to establish the genetic profile of your tumour.

However, a new biopsy may be needed.

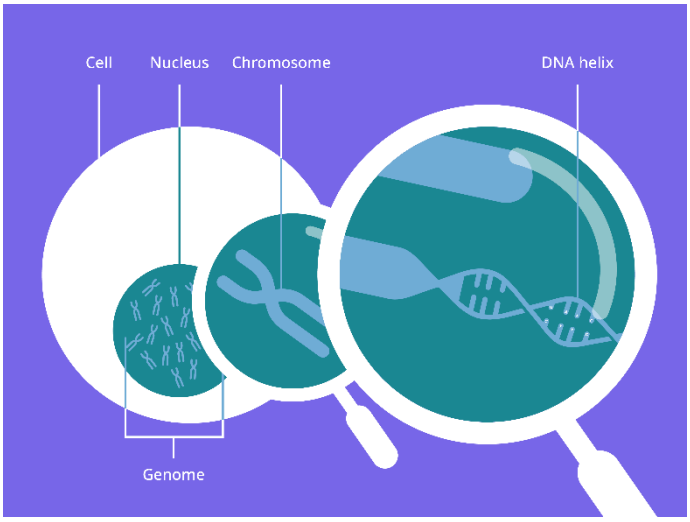
If so, the doctor will discuss it with you and request your consent.

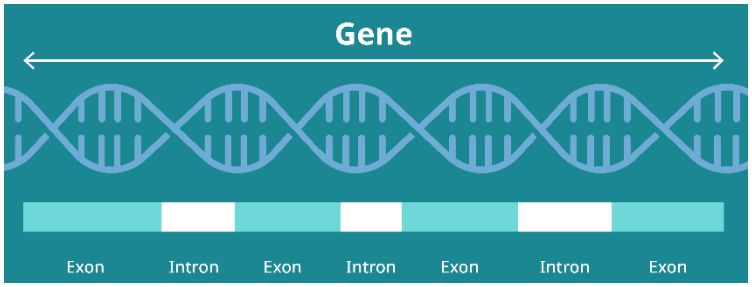
3 What do *DNA*, *gene*, *genome* and *exome* mean?

Your body is made up of billions of cells. Your genome is the complete set of your genetic material. Your genome is found in the nucleus of most of your body's cells and is unique to you. No-one else in the world has the exact same genome as you (unless you have an identical twin).

Your genome is all the DNA that makes up your chromosomes. DNA is written using four letters: A (adenine), T (thymine), G (guanine), and C (cytosine). The DNA sequence - or genetic sequence - forms a 'blueprint' containing all the information your body needs to develop and function.

Containing over 3 billion letters, your genome would fill the pages of 400 dictionaries.





A gene is a fragment of the genome. It is a specific piece of genetic information that leads to the production in the cell of a component necessary for it to function: a protein.

Around 20 000 genes have been found to code for proteins. Each protein plays a different role. For example, haemoglobin is the protein used to transport oxygen in the blood. Other proteins play a role in defining eye colour.

The genes contain exons, which serve as the 'construction plan' of the protein for which the gene codes. The complete set of the exons in the genome is called the exome. Although it represents less than 1% of the genome, it is the exome that contains most of the variants known to cause certain diseases, such as rare diseases. The rest of the genome is referred to as non-coding. For a given gene, the RNA is produced in our cells from the exons of the DNA. This RNA constitutes a sort of blueprint for the production of the protein that is coded from the sequence of this gene.

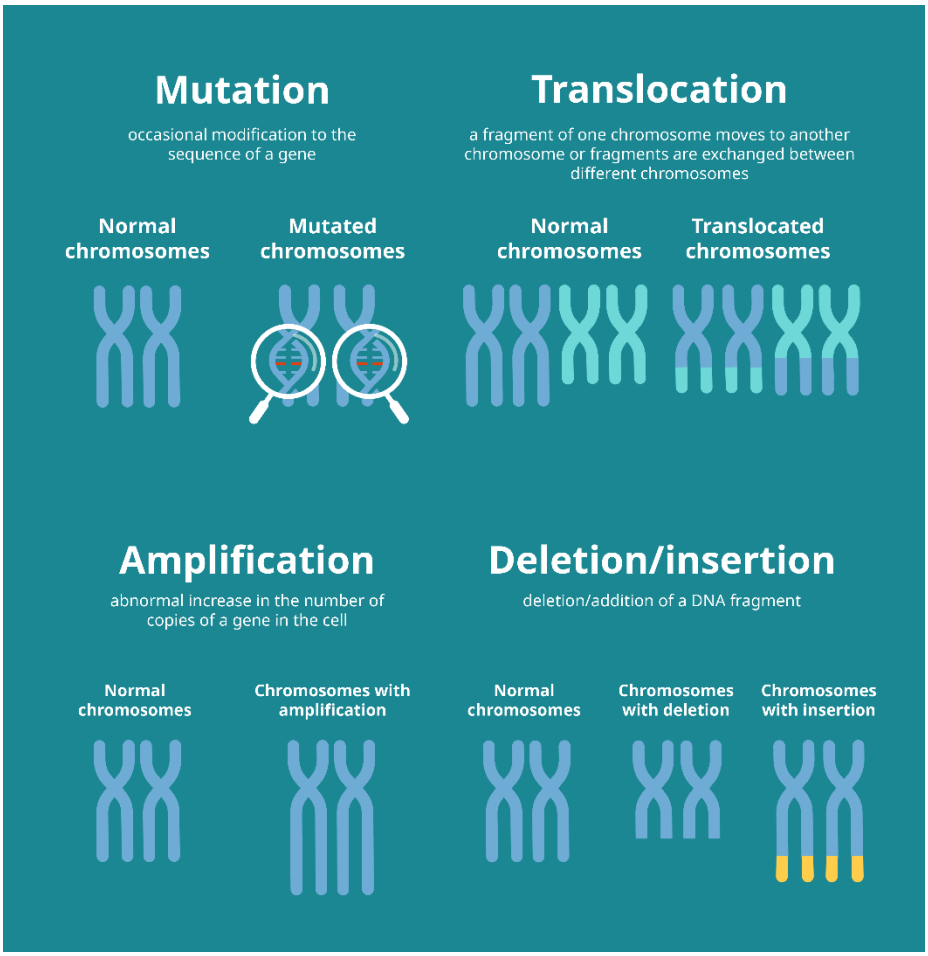
On average, the genomes of two people are 99% identical. The remaining 1% is where they differ and these differences are called variants. These variants, in addition to how a person interacts with his or her living environment, are responsible for the unique nature of each human being. These variants can be common or rare, ranging from the change of one single DNA letter to the addition or deletion of a chromosome.

More detailed information on this subject can be found on the French Biomedicine Agency website www.genetique-medicale.fr.

4 What are the genetic characteristics of a tumour?

A tumour develops following the uncontrolled division and proliferation of certain cells. These dysfunctions are caused by a build-up of errors within their DNA. These errors, abnormalities or molecular alterations can cause disruptions within the cells and their environment leading to the development, growth and possibly the propagation of the tumour.

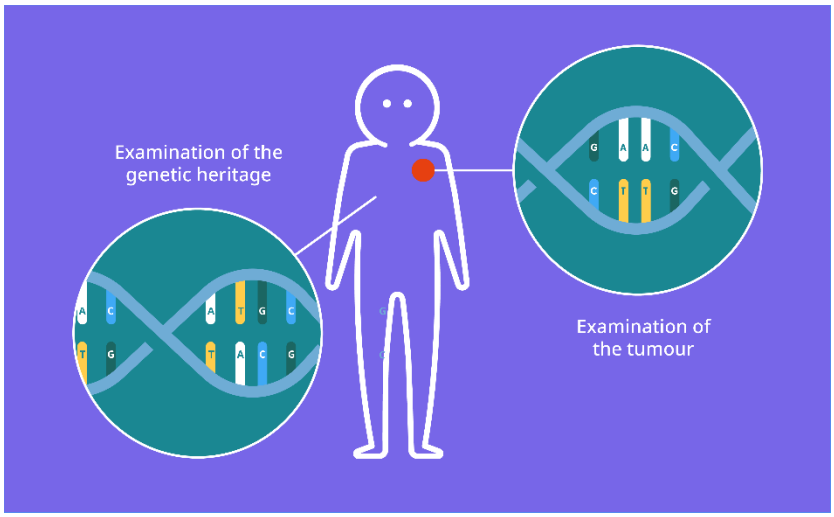
These abnormalities may take the following forms:



In most cases, these abnormalities appear in the tumour cells during the development of the disease and are not found in the other 'normal' cells of the body. They are therefore not hereditary. However, some do form part of the patient's genetic heritage and can be passed down to the next generation.

More detailed information on this subject can be found on the French National Cancer Institute website www.e-cancer.fr.

5 What do *genome sequencing* and *exome sequencing* mean?



The genetic test offered to you consists of reading the DNA and RNA of your tumour as well as the DNA of your genetic heritage: this is known as sequencing. It may look at all the exons (whole exome) or all the DNA (whole genome).

The result of the sequencing is presented as a succession of the four letters that constitute the DNA molecule: A T G and C (see section 2).

Although it is now possible to read a whole exome or a whole genome, interpreting the readings remains difficult and restricted to current knowledge. The vast quantities of data produced by these new technologies are analysed using powerful computerised tools combined with the expertise of bioinformaticians, genetic technologists and clinical geneticists. Given the large number of molecular abnormalities present in tumours, it is not easy to identify those which have a real impact on the development of the disease. What is more, treatments are not yet available for all the molecular abnormalities that may be identified within a tumour.

6 What are the possible results of the genetic test?

In addition to sequencing your tumour, it is also necessary to sequence your genetic heritage (using a blood sample) in order to better understand the genetic characteristics of your tumour and determine the most appropriate treatment for your cancer. The sequencing of your genetic heritage (referred to as germline genetic characteristics) may reveal factors that increase your risk of developing cancer in relation to the average risk in the general population. These abnormalities existed before the development of the tumour. They may have been inherited and can be passed on to offspring. Other members of your family may therefore be concerned (see point 8).

More detailed information on this subject can be found on the French National Cancer Institute website www.e-cancer.fr.

The genetic test may therefore detect molecular abnormalities in your tumour and possibly in your genetic heritage. You can choose to be informed of all the results of the genetic test or just some.

The care offered by your doctor will depend on the abnormalities identified:

Abnormalities in the tumour

Depending on the molecular abnormalities identified during the sequencing of your tumour, two types of treatment can be envisaged:

- *either* the molecular abnormalities enable your doctor to prescribe a targeted medicine (or therapy) or suggest that you participate in a clinical trial evaluating a new medicine;
- *or* the molecular abnormalities do not enable your doctor to prescribe a targeted medicine, in which case he or she will suggest that you continue the therapeutic strategy that is most appropriate at this time.

Abnormalities in the genetic heritage

If hereditary genetic variants responsible for the development of your cancer are identified, and if you have given your consent to be informed of the results:

- your doctor will refer you for a genetic oncology consultation. Personalised care will be arranged for you and for the affected members of your family.
- in some cases, the molecular abnormalities identified enable your doctor to prescribe a targeted medicine (or therapy) or suggest that you participate in a clinical trial evaluating a new medicine.

7 Must I inform my family? If so, how?

If you are found to be the carrier of a genetic abnormality, then other members of your family may also be carriers.

The genetic heritage passed down from the parents is to some extent shared by different members of the same family (brother, sister, cousin, uncle, aunt, etc.).

If there is the risk of serious consequences for which preventive measures or treatment exist, the law requires that family members be informed of the genetic abnormality.

They then have the option to consult a clinical geneticist who will advise them on the appropriateness of a genetic test. If required, their medical care will be adjusted based on the results of the test.

It is the role of the prescribing doctor or genetic counsellor to define who, within the family, is or is not at risk of carrying a familial genetic abnormality. The genetic abnormality and degree of kinship are taken into account when evaluating this risk.

Who informs the family? Which family members?

If you have been diagnosed with a hereditary genetic abnormality that may be the cause of a serious condition (whether or not related to the reason for your consultation), for which preventive measures exist, including care and genetic counselling, you can inform your affected family members directly. If you do not wish to do this, you can ask the doctor to inform them for you.

You can request this when signing the consent form.

If you choose to inform them yourself, your doctor or genetic counsellor can assist you, for example with the help of a document explaining the disease and how it is inherited. Psychologist support is also available, if required. Finally, the contact details of patient associations may be useful for you so that you can discuss things with them and get the benefit of their experience. Your doctor can advise you.

If you ask your doctor to inform your family members, he or she will send a letter advising them to make an appointment for a genetic consultation. Neither you nor the diagnosis of your disease will be mentioned.

Although this solution helps some families, it is not the most appropriate. Family communication is preferable.

If you refuse to inform your family members yourself or if you refuse to have the doctor inform them for you, your civil liability may be incurred.

The family members concerned, having been unable to make arrangements for appropriate care, may seek compensation for the harm suffered.

It is also envisaged that:

- You can ask not to be informed of your own test results and to have the doctor inform the other members of your family (this can be requested when signing the consent form).
- You can ask for this information to be sent anonymously.
- If you have donated your gametes (eggs or sperm), the doctor, with your authorisation, will inform the fertility clinic (which has allocated your gametes to one or more infertile couples), so that it can take the necessary measures for any children born as a result of this donation.

8 How might the biological samples and data from this test be used?

Biological samples

Thanks to advances in sequencing techniques, the amount of biological material (number of cells) required to perform the test is becoming increasingly small. It may be that some of the sample collected (for example, blood) is still available for use.

You can accept or oppose this storage on the consent form.

If you accept, the law envisages that this sample may be used:

- *Either* as part of the same healthcare approach (use of a different technique, confirmation of the results): in which case you will not be asked to sign a new consent form.
- *Or* for research purposes. This research may directly concern the disease for which you have sought medical advice, or another genetic disease, or another research subject. The researcher is then obliged to inform you of his or her research and check that you do not oppose the use of your samples in it.

Data

Likewise, the data resulting from the genetic test (the sequence of your exome or your genome) are sensitive data subject to specific legislation:

- If the analysis of your sequence does not provide any information on your disease, the data will be stored for reanalysis as and when new information becomes known about the genes potentially implicated in the disease.

You will not be asked to sign a new consent form.

- As with the biological samples, the data resulting from the sequencing may help to further knowledge through research, particularly on genetics.

If you accept the principle of this, your data may be communicated to other research teams, private or public, national or international, within the framework of research that is authorised in advance, with the appropriate safeguards to ensure confidentiality that are set out in a data-sharing contract/agreement between Inserm and the data recipient(s).

You can, freely and at any time, without affecting your medical care, oppose the subsequent use of your data in research by contacting your doctor.

The 2025 French Genomic Medicine Initiative website (https://pfmg2025.aviesan.fr/en/projets-de-recherche/) contains all the necessary information that is specific to these projects. You have the right to obtain a copy of the documents relating to the transfer of your data and you will be informed of the purpose of any new processing of that data at the relevant time on the website (https://pfmg2025.aviesan.fr/en/projets-de-recherche/).

Reminder of your rights

- Freedom to choose
- **Right to be informed:** if you have difficulty understanding the information that has been given to you verbally or in writing and if you have any questions, please do not hesitate to ask them. The medical teams are there to answer them.
- **Right to access your personal data:** you have the right to access and rectify your data.
- **Right to oppose the transmission of your data:** you have the right to oppose the transmission of your data (including your genetic data and ethnic origins) which are covered by the obligation of professional secrecy and may be used and processed as part of research programmes. These rights can be exercised by contacting your doctor/geneticist who is the only one to know your identity.
- **Right to erase data:** you have the right, except in a limited number of cases, to request the deletion of your personal data. However, please note that any useful data collected before you exercise your right to oppose or withdraw your consent may continue to be processed in a confidential manner so as to meet a legal obligation and not compromise the fulfilment of the research objectives.
- **Right to restrict processing:** you have the right to request that the use of some of your data be temporarily frozen. The objective is to avoid the dissemination of information that needs to be verified by temporarily suspending its processing throughout the time needed to perform those verifications.
- **Right to data pseudonymisation and confidentiality:** your identity is protected. Your name will never be disclosed. The rule of medical secrecy applies to all of your data.
- **Right to your health information:** with your agreement, you will be informed of any information relating to your health.
- **Right to change your mind at any time:** without having to give a reason, regarding the use of your biological samples for research purposes by contacting your doctor/geneticist.

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