myDNAmap
cancer

myDNAmap
the power of your genetics

myDNAmap is a medical genome company that was established with the aim of helping the general public to access all of the information included in their DNA, so they can better care for their health and that of their family.

myDNAmap offers a unique and comprehensive service in the field of preventative medicine. We sequence the whole genome containing all of the genes associated with a person's health and wellbeing. We provide pre- and post-sequencing advice, which will answer any questions and explain the results. We have developed **myDNAapp,** a mobile app where you can consult your results, contact health and science professionals and enter information regarding your health, which helps to personalise your genetic report. Furthermore, **myDNAmap** offers annual updates, which include the most recent discoveries in the field of genetics.

We know that every one of us is unique and individual just like our DNA.

Knowing your genetic profile will help you to take care of your health and that of your family. Today, tomorrow and always.

Always check **mydnamap.com** for the latest updates of our services.

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What are the benefits of the myDNAmap Cancer panel?

- early detection of variants associated with different types of hereditary cancers.

- opportunity to choose a personalised treatment based on the genetics of the individual.

- in positive cancer cases, family members can receive oncological genetic counselling and undergo screening tests.

- healthy individuals can learn about their predisposition to certain types of hereditary cancer to take consequent preventative measures.

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Preventative, Predictive, Personalised and Participatory Medicine.

Cancer is a disease present in all medical specialisms and is the second cause of death worldwide. In men, the most prevalent cancers are prostate, lung, bronchial, colon, rectal and bladder cancers. In females, the prevalence of cancer is higher in the breasts, lungs, colon, rectum, uterus, ovaries and thyroid glands. In children, prevalence is with cancers that affect the blood and those associated with the brain and lymph nodes.

Cancer aetiology is complex and can be caused by various hereditary and acquired genetics. Acquired genetic variants can develop "spontaneously" as a response to carcinogenic environmental factors (tobacco smoke, radiation, viruses and bacteria etc.), or as a result of errors in DNA replication. These genetic changes occur after conception and are called somatic.

Hereditary cancers represent approximately 5% of all cancers. They are transmitted from generation to generation and are caused by genetic variants in the germline (ovule and sperm). These variants occur in susceptibility genes, are present in all cells of the body and, in the majority of cases, present in an autosomal dominant manner.
Normally, hereditary cancer manifests at an earlier age than normal.

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Having a pathogenic germinal mutation is only a predictor of cancer and does not necessarily mean that the individual will develop it. Nevertheless, families and individuals with a hereditary likelihood of cancer can benefit from early detection programmes. That is why it is important to identity them early.

During the tumour process there is an uncontrollable cellular cycle. That is why many genes associated with cancer play a significant role in DNA cell-proliferation and repair processes.

At **myDNAmap** we study more than 150 genes associated with hereditary cancers.

Some hereditary tumours included in the panel:

Hereditary breast and ovarian cancers
It is estimated that 1 in 8 women may develop breast cancer throughout their life. The majority of breast cancer (male and female) and ovarian cancer cases are sporadic. However, it is calculated that 5-10% are due to a hereditary genetic predisposition, where dominant autosomal pathogenic variants in *BRCA1* and *BRCA2* are responsible for the majority of cases. In men, variants in *BRCA1* and *BRCA2*, although less frequently, are responsible for cases of prostate cancer, pancreatic cancer and melanoma, among others.

Approximately 50% of women with breast cancer have no history of the disease and therefore are unaware that they are carriers of the pathogenic variants in *BRCA1* and *BRCA2*. For this reason, international experts have already started to recommend the preventative analysis of these genes in women over 30 years old. There are other genes associated with breast, ovarian and endometrial cancer included in this panel, which are associated with cell cycle control and DNA repair.

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Gastrointestinal cancer

Gastrointestinal cancer is a complex disease, resulting from a combination of environmental and lifestyle habits with specific genetic variants. The majority of gastrointestinal cancers are sporadic cancers and approximately 5 to 10% of them have a hereditary component as a consequence of germinal mutation.

Lynch syndrome or hereditary non-polyposis colorectal cancer most frequently predisposes adenomas and colorectal cancers and is associated with dominant variants in *MLH1, MSH2, MSH6, PMS2* and *EPCAM*. The probability that a person who is a carrier of a pathogenic variant in any of those genes will develop Lynch syndrome is very high, leading to 80-90% of cases. There are also genes associated with gastrointestinal cancer. All of these are associated with cellular control and DNA proliferation and are included in this panel.

Li-Fraumeni syndrome

Li-Fraumeni syndrome is a rare autosomal dominant disease caused by variants in the *TP53* gene, a key regulator in the cell cycle. 85% of patients with pathogenic variants in this gene develop the illness. This syndrome is characterised by the occurrence of multiple tumours at an early age. Due to its broad tumour spectrum, there are no early detection programmes available. For this reason, only sequencing this gene enables us to take preventative measures.

Prostate cancer

Prostate cancer is one of the most common types of cancer in men (1 in 7). In many cases, it is a silent disease that may not show any symptoms in its initial stages. If it is detected when it is still limited to the prostate gland, a successful treatment is more likely, as it has still not affected other tissues. The genes most commonly associated with these cases and other types of cancer in men are *BRCA1, BRCA2* and *HOXB13*.

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Familial adenomatous polyposis

Familial adenomatous polyposis is a type of early onset colorectal cancer and is associated with the emergence of multiple adenomatous polyps in the rectum and colon. It is estimated that 1 in every 8,300 newborns suffer from this condition. It represents less than 1% of colorectal cancer cases.

The majority of familial adenomatous polyposis is caused by known susceptibility genes and presents dominant and recessive patterns of Mendelian inheritance. The classic form of familial adenomatous polyposis is dominantly inherited and is associated to pathogenic genetic variants in the *APC* gene and accounts for approximately 0.5% of all colorectal cancers. A frequency rate of 20% is calculated for de novo mutations, which would mean the absence of family history in these cases. Variants in the *MUTYH* gene are associated with an autosomal recessive form and are responsible for 0.5% of all colorectal cancers.

Hereditary lung cancer

Lung cancer is the most common cancer worldwide. The majority of cases are caused by somatic variants associated with environmental factors like smoking. Only 8% are associated with germinal mutations, which in turn are difficult to identify, given that this type of cancer is significantly influenced by the environment. Despite its rarity, various genes have been associated with a predisposition to lung cancer, among others *BRCA2, CDKN2A, TP53* and *EGFR*.

Melanoma

Melanoma is a type of skin cancer which affects cells called melanocytes; these produce brown pigment or melanin which colours our skin. Skin cancer can have an unfavourable prognosis if it is not detected and treated at an early age. Only 10% of cases present a familial aggregation. Various genes have been associated with this type of cancer, the most common being *CDKN2A*. People who present a pathogenic variant of this gene have a greater disposition to developing various melanomas, where other organs are also affected like the pancreas.

Tumours of the central nervous system
Tumours affect the nervous cells of the brain and spinal cord.

Neuroblastoma: This is a childhood cancer that is most commonly diagnosed during a child's first year of life and represents between 10 and 15% of all cancer deaths in children. It occurs when neuroblasts or embryonic cells start to multiply uncontrollably forming a tumour. Normally, these cancers are sporadic due to somatic mutations. Familial cases are quite rare; only 1-2% are due to germinal mutations. Some of the genes associated with neuroblastoma are *PHOX2B, ALK, KIF1B* and *RAS*. Mutations in the latter are associated with a predisposition to neuroblastoma, accompanied by other clinical syndromes like Costello syndrome, Noonan syndrome and neurofibromatosis type 1.

Glioblastoma: This is the most aggressive and common form of brain cancer, which stems from nervous cells, called astrocytes, which support neurons. Hereditary cases are rare and are frequently associated with other tumours like neurofibromatosis type 1 (associated with *NF1*), Li-Fraumeni syndrome (associated with *TP53*), melanoma (associated with *CDKN2A*) and Lynch syndrome (associated with *MSH2* and *MSH6*).

Meduloblastomas: Is a type of very common cancer that affects children. The medulloblastoma starts in the brain, in the area responsible for muscular coordination, movement and balance. Subsequently, it tends to disseminate to other parts of the brain and spinal cord via the cerebrospinal fluid. Hereditary cases are rare and are frequently associated with other tumours like Li-Fraumeni syndrome (associated with *TP53*), Gorlin syndrome (associated with *PTCH1*) and Turcot syndrome (associated with *APC*).

Neurofibromatosis type 1: It is a genetic neurocutaneous disorder that is clinically very heterogeneous. It is characterised by white coffee colour patches, Lisch nodules in the iris, axillar or inguinal freckles and multiple neurofibromas. It is estimated to be prevalent in 1 in 3000 newborns. Neurofibromatosis is generally diagnosed during infancy and follows an autosomal dominant inheritance pattern in the *NF1* gene. Tumours are usually benign but in some cases they can become malignant.

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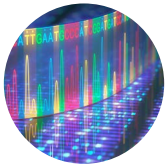
The following hereditary cancers are included in the **myDNAmap Cancer Panel:**

- **Gynaecological:** breast, ovary, uterus
- **Urological:** bladder, kidney, prostate
- **Gastrointestinal:** colon, pancreas, stomach, polyposis, oesophagus, nasopharyngeal, liver
- **Endocrine:** thyroids, paragangliomas
- **Haematological:** acute myeloid leukemia, chronic myelomonocytic leukemia, juvenile myelogenous leukemia, non-Hodgkin lymphoma, myelodysplastic syndrome, multiple myeloma
- **Skin:** melanoma
- **Nervous system:** neuroblastoma, glioblastoma, medulloblastoma
- **Pulmonary**
- **Otros:** osteosarcoma, neurofibromatosis type I
- **Síndromes relacionados a tumores:** Li-Fraumeni syndrome, Lynch syndrome, Ataxia telangiectasia, Type 1 Cowden syndrome, Cowden syndrome 5, Cowden syndrome 6, Perlman syndrome, Costello syndrome, Nijmegen breakage syndrome, Werner syndrome, tuberous sclerosis, Bloom syndrome.

Related panels



myDNAmap neurology

myDNAmap pharmacogenetic

myDNAmap offers a study based on pharmacogenetics, the objective of which is to design an effective pharmacological treatment based on the genetics of the individual (personalized medicine). The pharmacogenetics panel analyses more than 60 drugs associated with cancer treatments.

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Technology used

Whole genome sequencing (WGS) using Illumina HiSeq X10 or NovaSeq 6000 systems. Illumina PE150, QQ30 ≥80%, aligned with the human reference genome GRCh37/hg19. The classification and analysis of variants is carried out based on the recommendations of the American College of Medical Genetics and Genomics (ACMG). The variants reported are mentioned based on the recommendations of the Human Genome Variation Society (HGVS).

The technology used at **myDNAmap** cannot detect somatic mutations or deletions, insertions and complex rearrangements. We cannot detect: large deletions, large duplications/insertions, translocations, inversions, structural reorderings, aneuploidies, copy number variations (CNVs), long repeated sequences, triplet repeat expansion, somatic variants, mosaicism, heteroplasmy, epigenetic defects or methylation status.

Our report: is the scientific-technical communication of the results. It is written in a precise yet simple manner, intended for both our users and health professionals. It is provided within the framework of a consultation with one of our genetic counsellors. This can take place via videoconference. During the consultation the specialised professional will explain the details, answer any user queries and clear up any doubts that may occur.

Note: the detection of genetic variants only provides a predisposition or potential, but never provides a certainty of developing diseases. Under no circumstances is the genetic information provided valid for diagnostic use. It does not imply the potential to determine the age you will be when it starts nor the type or severity of the disease(s); nor does it allow us to rule out the existence of clinical or genetic heterogeneity.

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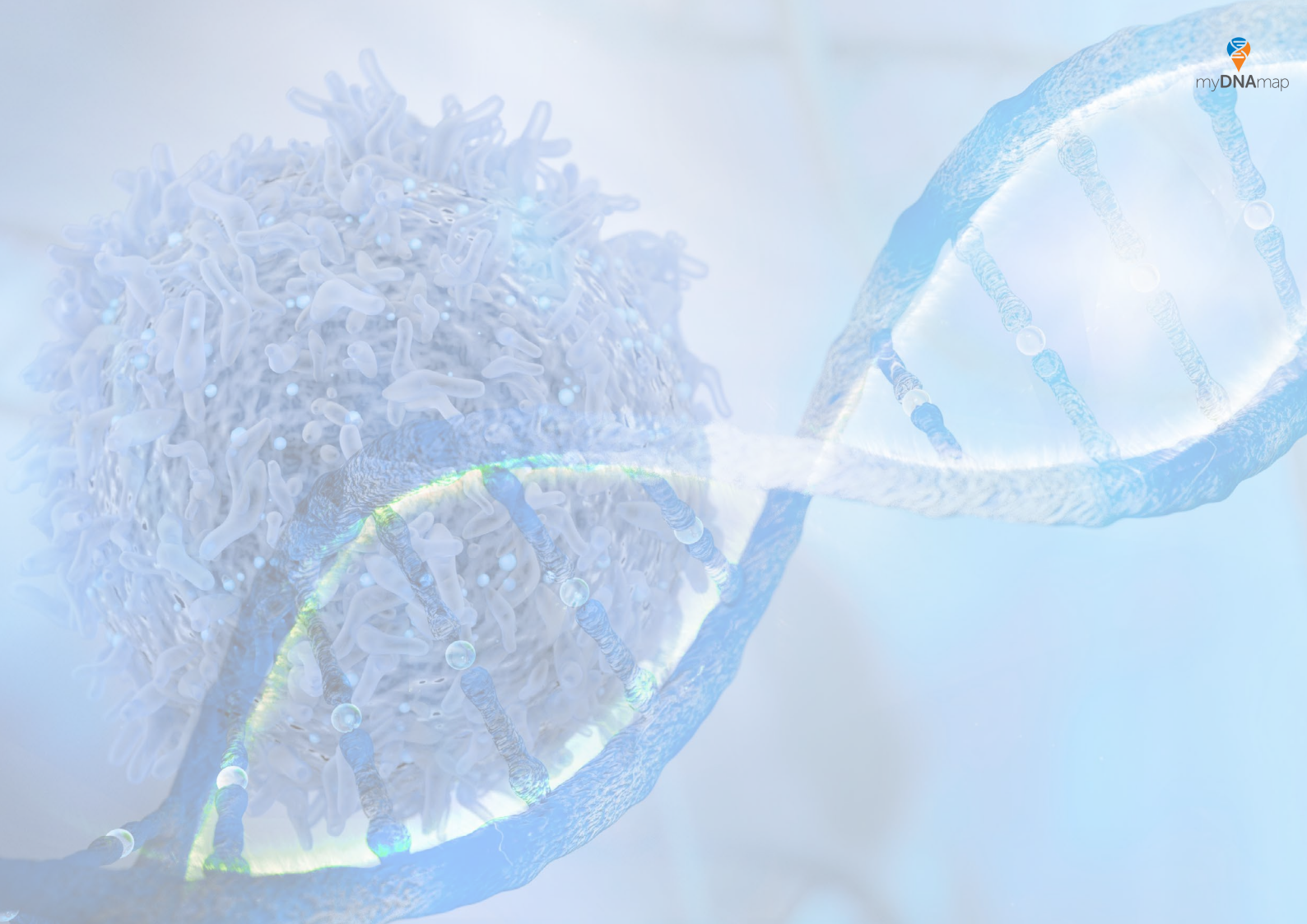
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