GENDIA

CANCER RISK test

DESCRIPTION: The CANCER RISK test determines your risk for hereditary cancer through the analysis of 30 genes involved in the genetic predisposition to cancer.
The CANCER RISK test therefore does not detect or diagnose existing cancer, but is a screening test to assess your genetic risk of developing cancer, particularly cancer of the breast, ovaries, uterus, intestines, stomach, pancreas, skin and prostate. When the CANCER RISK test detects a gene variant which results in an increased risk of cancer, a cancer screening and prevention plan can be developed.

WHY WOULD I HAVE A CANCER RISK TEST? More than 1 in 3 people develop cancer during their life, and more than 1 in 5 people die of cancer. Most cancers are non-hereditary but cancer of the breast, ovary, uterus, intestines, stomach, pancreas, skin (melanoma), and prostate is sometimes inherited. Some people have a high risk of these cancers due to the presence of a gene variant in their genetic material (DNA), which can be detected by the CANCER RISK test. In that case a cancer screening and prevention plan can be made, in order to prevent cancer or allow cancer detection at an early stage. An authorized healthcare provider will review your information, and upon his or her determination that the test is appropriate for you, he or she will order the test.
In addition, the CANCER RISK test can determine whether your children or other family members may also have an increased risk of cancer.

SAMPLE: The test is performed on saliva in an Oragene recipient, which can be provided by GENDIA. The saliva kit can be returned in compliance with the included instructions at room temperature to GENDIA (Emiel Vloorsstraat 9, 2020 Antwerp, Belgium).

TURNAROUND TIME: The CANCER RISK test takes 2 months to complete from arrival of the sample at GENDIA to the result report.

METHODS: The CANCER RISK test analyzes 30 genes including *BRCA1, BRCA2, APC, ATM, BAP1, BARD1, BMPR1A, BRIP1, CDH1, CDKN2A CDK4, CHEK2, EpCAM, GREM1, MLH1, MSH2, MSH6, MITF, MUTYH, NBN, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, SMAD4, STK11* and *TP53*.
The analysis consists of next generation sequencing (NGS) that detects both sequence variants and larger deletions-duplications in these 30 genes. The assay fully sequences the coding sequences and intron/exon boundaries for the genes of interest. Intronic sequences (other than in highly duplicated regions) are also included to allow for copy number variant and other analyses.
The lab will de-identify the genetic information that it obtains from its analysis of your DNA and submit this de-identified genetic information to public databases in order to advance our understanding of how human gene variants impacts risk to develop cancer. The CANCER RISKtest was developed and is performed by a test lab in California, USA, which operates a clinical testing laboratory that is accredited by the College of American Pathologists (CAP) and meets the certification requirements for high complexity laboratory testing as established under the Clinical Laboratory Improvement Amendments (CLIA). By signing this Informed Consent, you acknowledge and agree that your sample and personal information will be transferred to the test laboratory in California, USA, for testing, use, processing, and storage.

RESULTS: The results will be sent to you personally by email. If you want to have third parties to receive a copy, you can indicate this on the submission form below. Genetic counseling with explanation of the test results and recommended follow-up steps if necessary can be provided by genetic counselors from GENDIA.

There are 3 possible test results:

1. **In case a pathogenic gene variant is found:** You may have an increased risk of developing one or more of the cancer, but it does not necessarily mean that you have cancer or that you will definitely develop cancer in your lifetime. But it is important that you share your results with your healthcare provider to create a personalized screening and prevention plan, in order to prevent cancer or allow cancer detection at an early stage.

2. **In case no gene variant is found:** You then do not have an increased risk to develop cancer due to a gene variant in one of the 30 genes analyzed in the CANCER RISK test. It is important to note that results indicating that no pathogenic gene variant was found in the 30 genes analyzed do not guarantee that you will never develop cancer.

3. **In case a gene variant with unknown significance (VUS) is found:** VUS will not be reported, but re-evaluated by the test lab every 6 months. If these variants are reclassified as associated with an increased risk to develop cancer, we will contact you to let you know about the new classification.

LIMITATIONS: The CANCER RISK test is designed to detect gene variants in 30 genes implicated in cancer. However, no currently available test can detect every mutation associated with increased risk for disease, and no test can analyze all genetic causes for diseases, as not all causes are known. As with all medical tests, there is a chance of a false positive or a false negative result. A false positive result means a genetic mutation was detected, which is not in fact present. A false negative result means the test failed to identify a genetic mutation that is in fact present. If a patient has a rare biological condition (e.g., mosaicism), had an allogenic bone marrow transplant (bone marrow from a donor), a blood transfusion within 7 days prior to providing a sample, or an active hematologic malignancy (blood-related cancer such as leukemia, lymphoma, or multiple myeloma), the CANCER RISK test cannot be performed as these conditions may limit the accuracy of the results. Other sources of error, while rare, include sample mix-up, poor sample quality or contamination, inherent DNA sequence properties, and technical errors in the laboratory. The performing test laboratory specifically disclaims any liability for the inaccuracy of test results resulting from such conditions or the failure to provide accurate or complete patient information. Analysis of results is based on currently available information in the medical literature and scientific databases. Because literature and scientific knowledge are constantly being updated, new information may replace or add to the information that was used to analyze your results.

Only gene variants that are clearly associated with an increased risk to develop cancer are reported. As part of the test, the laboratory may also identify the presence of Variants of Uncertain Significance (VUS), which are genetic changes that require further research to determine if they are associated with an increased risk for disease. The laboratory will provide further detail about these VUS's only if you actively elect to receive such information, or if additional research enables us to reclassify a particular VUS. You should discuss the results of the Test and the presence of VUS's (if any), and any need for further testing of these and other conditions, with your healthcare provider or a genetic counselor.

The CANCER RISK test is not a diagnostic test. The test report is not intended to replace seeing a healthcare provider. By signing this Informed Consent, you understand and agree that your results must be considered in the context of broader medical management by a healthcare provider, and that you should not make medical decisions without consulting a healthcare provider.

PRIVACY and CONFIDENTIALITY: Your sample and the DNA extracted from it will only be used for the CANCER RISK test and as set forth herein. Your DNA will be stored at the performing test laboratory in the United States, unless you ask GENDIA to destroy it. The results from the CANCER RISK test will be stored at GENDIA and the performing test laboratory in the United States, GENDIA will comply with the laws and regulations of Belgium and the EU regarding data privacy and the collection, use, processing and storage of patient information, and the performing test laboratory in the United States will comply with the laws and regulations of the United States regarding data privacy and the collection, use, processing and storage of patient information. The results of the CANCER RISK test will only be reported to you personally, and never to third parties, including family members, insurance companies and physicians, unless required by law or regulation, or if you ask GENDIA to do so.

USE OF DATA: By signing this Informed Consent, you agree that your sample, personal information and results may be anonymized, stored and used by the performing laboratory for internal quality control, validation studies, and research and development. You also consent to (a) the use of your anonymized sample, personal information, and results in the performing laboratory's research with third party collaborators; and (b) the storage of your sample and DNA at the performing laboratory to allow you to have additional testing in the future. You have the option of requesting that your sample be destroyed or your personal information be deleted at any time from our active databases, subject to the applicable laws and regulations. Please note that deletion of this information prior to completion of the CANCER RISK test will result in a cancellation of the CANCER RISK test, and no results will be provided to you or your healthcare provider. Although we can delete your personal information from our active databases, some or all of your personal information will remain archived in back-ups for compliance with legal, regulatory, and other requirements. Information that has already been de-identified, anonymized, and/or aggregated may not be retrievable or traced back for destruction, deletion, or amendment. If you choose to have your sample destroyed or your personal information deleted from the performing laboratory's active databases, please contact your ordering healthcare provider.

GENETIC COUNSELING: A consultation with genetic counseling and discussion of the CANCER RISKtest results and the follow up steps is indicated certainly when a pathogenic gene variant is identified that is associated with an increased cancer risk.
Such consultation is available at GENDIA. You can make an appointment by emailing at info@gendia.net

SUBMISSION FORM: Submission forms can be obtained by emailing info@gendia.net

PRICE: 299 Euro.

PAYMENT: Payment is due one month after the issue date of the invoice.

TABLE 1 : Genes analysed in the CANCER RISK test

GENE	Breast	Ovaria	Uterus	Intestine	Stomach	Pancreas	Skin	Prostate
BRCA1	●	●				●		●
BRCA2	●	●				●	●	●
MLH1		●	●	●	●	●		
MLH2		●	●	●	●	●		
MSH6		●	●	●	●			
PMS2		●	●	●				
EPCAM		●	●	●	●	●		
APC				●	●	●		
MUTYH				●				
MITF							●	
BAP1							●	
CDKN2A						●	●	
CDK4							●	
TP53	●	●	●	●	●	●	●	●
PTEN	●		●	●			●	
STK11	●	●	●	●	●	●		
CDH1	●				●			
BMPR1A				●	●	●		
SMAD4				●	●	●		
GREM1				●				
POLD1				●				
POLE				●				
PALB2	●	●				●		
CHEK2	●			●				●
ATM	●					●		
NBN	●							●
BARD1	●	●						
BRIP1	●	●						
RAD51C		●						
RAD51D		●						

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TABLE 2: Life-time risk for several frequent tumors in men and women.
An increased risk for the tumors in blue is detected with the CANCER RISK test.

CANCER	FEMALES	MALES
Breast	1 / 8	1 / 769
Ovarian	1 / 76	-----
Uterus	1 / 36	-----
Intestines	1 / 23	1 / 21
Stomach	1 / 152	1 / 93
Pancreas	1 / 67	1 / 65
Skin	1 / 61	1 / 38
Prostate	-----	1 / 7
Lung	1 / 17	1 / 14

TABLE 3 : Percentage of the different cancers that is inherited.
An increased risk for the tumors in blue is detected with the CANCER RISK test

CANCER	% INHERITED
Breast	1 / 10
Ovarian	1 / 8
Uterus	1 / 10
Intestines	1 / 20
Stomach	1 / 50
Pancreas	1 / 10
Skin	1 / 20
Prostate	1 / 20
Lung	< 1 / 100

SUBMISSION FORM CANCER RISK test (Please complete)

P 6 - 10 Please complete and put the submission form in the saliva kit
P 1 – 5 You can keep this for personal information

INFORMED CONSENT

1. I confirm that I have read all of the information in this authorization and informed consent document, and I understand what it says and agree to it.

2. I confirm that I have filled out the patient submission form below to the best of my knowledge.

3. I agree to the Terms of Service and privacy policy of GENDIA.

Signature: …

Date: …

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Please put barcode sticker here
(Attach 1 barcode form clear tray)

IMPORTANT

- Stick only 1 barcode on this form
- Leave 1 barcode on the clear tray
- Put the capped tube again in the clear tray and shipping box.

Please complete in capitals		
Patiënt Information		
*** In order to guarantee maximal patient privacy GENDIA only works with patient codes and not with patient names. Please use a CODE (with at least 6 numbers and/or letters) instead of your NAME and keep this code in a safe place, as GENDIA will only use this code in all documents.**		
Patient Code*	…	
Date of Birth	…	
Sex	☐ Male	☐ Female
Address	… …	
Phone Number	…	
Email	…	

Referring Physician	
Last Name + First Name	…
Address	… …
Phone Number	…
Email	…

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PERSONAL HEALTH HISTORY

1. Have you had a genetic test for hereditary cancer risk?

☐ No

☐ Yes, the test was performed

- On the following genes: …
- By the following lab: …

Please list any pathogenic or likely pathogenic mutations that were identified:

…

2. If you have ever had cancer, please provide details.

☐ No

☐Yes,

☐ Breast cancer, diagnosed in *(year)* …

☐ Breast cancer affected both breasts, diagnosed *(year)* … and in (*year)* …

☐ Ovarian or fallopian tube cancer, diagnosed in (*year)* …

☐ Primary peritoneal, diagnosed in (*year)* …

☐ Uterine cancer, diagnosed in *(year)* …

☐ Intestinal cancer, diagnosed in *(year)* …

☐ Stomach cancer, diagnosed in *(year)* …

☐ Pancreas cancer, diagnosed in *(year)* …

☐ Skin cancer, diagnosed in *(year)* …

☐ Prostate cancer, diagnosed in *(year)* …

☐ Hematological malignancy (for example, Leukemia, Lymphoma, or Multiple myeloma)

☐ I am in active treatment

☐ I have been in remission for … years.

3. Did you ever received radiation therapy ?

☐ No ☐ Yes

If yes, please provide details: …

4. Did you ever received chemotherapy ?

☐ No ☐ Yes

If yes, please specify: …

PERSONAL HEALTH HISTORY

5. Have you ever had a surgical removal ?

☐ No
☐ Yes, removal of breasts in *(year)* …
☐ Yes, removal of ovaries in (*year)* …
☐ Yes, removal of uteries in *(year)* …
☐ Yes, removal of colon-rectum in (*year)* …
☐ Yes, removal of intestinal polyps in *(year)* …
☐ Yes, removal of melanoma (skin cancer) in (*year)* …
☐ Yes, removal of prostate in *(year)* …

6. Have you had a biopsy ?

☐ No
☐ Yes, of following organ(s): …
and result(s): …

7. Were you ever diagnosed with intestinal, colon or rectal polyps ?

☐ No
☐ Yes : In which part of the intestines ? …
How many polyps have been found in total ? …
When was your last colonoscopy / rectoscopy ? …

8. Have you had a bone marrow transplant ?

☐ No
☐ Yes - Was the transplanted bone marrow your own ?
☐ No ☐ Yes

9. Have you had a blood transfusion in the week before providing your saliva sample to GENDIA?

☐ No ☐ Yes

FAMILY HEALTH HISTORY

1. **Please provide cancer history for your biological family members, including:**

   - Parents
     ….
   - Grandparents
     …
   - Child(ren)
     …
   - Sib(s)
     …
   - Aunt(s)
     …
   - Uncle(s)
     …

   Only the following cancers are of relevance to the test : cancer of the breast, ovaries, uterus, intestines, stomach, pancreas, skin and prostate.

2. **Have any of these relatives had a genetic test for hereditary cancer risk?**
   - ☐ No
   - ☐ Yes

     If yes, please provide reports of previous testing if available.
     For any gene variants found: list the relative, gene, and gene variant.
     …

FAMILY HEALTH HISTORY

3. Family pedigree

If anybody of the family (you, parents, grandparents, children, uncles, aunts, nieces nephews) had cancer of the breast, ovaries, uterus, intestines, stomach, pancreas, skin and prostate, please make a family pedigree and indicate everybody that had such cancer.

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