GeneMate®

Hereditary cancer risk

Report date: 2020-xx-xx
Sample received: 2020-xx-xx
Sample date (saliva): 2020-xx-xx

Customer

Kalle Persson
Male
YYMMDD-XXXX
Email: first.last@gmail.com

iCellate Support

iCellate Medical AB
Industrivägen 1
171 48 Solna
Email: support@icellate.se

Sample

Type: Saliva
Barcode: xxxxxxxxxx
iCellate ref.nr: ICEL000XX

No pathogenic variants were found in your sample

A note from our clinical team:

Based on the test result, in combination with the provided information regarding your family cancer history, you do not have an inherited increased risk of cancer.

About your result

No pathogenic or likely pathogenic genetic variants (also called mutations) were identified in any of the analyzed genes. Note that the analysis does not rule out the possibility that someone in your family carry a pathogenic variant, given that the test is limited to the analysis of your genes and not those of your family members.

Upon ordering, you submitted your family cancer history. Based on the information provided, there is **no suspicion** of hereditary cancer in your family. This assessment is based on national guidelines for who should be screened for hereditary cancer. In the case that the information you have provided is incorrect, or that you receive additional information, a new assessment could be warranted.

It is important to participate in national screening programs (please find more information below), even in the absence of hereditary cancer risk.

If you have **questions regarding your result**, please schedule an appointment for genetic counseling by clicking here.

Analyzed genes

The following genes were analyzed. Please see sections Test method and Limitations for further information.

APC	*ATM*	*BAP1*	*BARD1*	*BMPR1A*
BRCA1	*BRCA2*	*BRIP1*	*CDH1*	*CDKN2A*
CHEK2	*DICER1*	*EPCAM*	*FLCN*	*FH*
MAX	*MEN1*	*MLH1*	*MSH2*	*MSH6*
MUTYH	*NF1*	*NF2*	*PALB2*	*PMS2*
PTEN	*RAD51C*	*RAD51D*	*RB1*	*RET*
SDHA	*SDHAF2*	*SDHB*	*SDHC*	*SDHD*
SMAD4	*SMARCB1*	*STK11*	*TMEM127*	*TP53*
TSC1	*TSC2*	*VHL*	*WT1*	

Your result has been approved by:

Geneticist Jönsson
Clinical Laboratory Geneticist

Geneticist Jansson
Genetic Counsellor

Geneticist Jonsson, Med Dr
Clinical Geneticist

What is the average risk of developing cancer?

For Swedish men, the cumulative risk of developing cancer by 80 years of age is 39.2%. The risk increases with age and varies by cancer type. The below table summarizes average cancer risk for men.

SWEDAC ACKREDITERING
Ackred. nr. 10473
Provning
ISO 15189

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Cancer type	<40 years	<50 years	<60 years	<70 years	<80 years
All cancer types	1.33%	2.92%	7.90%	21.34%	39.20%
Prostate	0.00%	0.21%	2.08%	8.49%	16.33%
Skin cancer (other)	0.01%	0.05%	0.20%	0.90%	3.25%
Malignant melanoma	0.19%	0.45%	0.93%	1.74%	3.01%
Urinary tract (except kidney)	0.02%	0.07%	0.30%	1.19%	3.15%
Colon	0.04%	0.15%	0.44%	1.31%	3.23%
Lung, trachea, and bronchi	0.01%	0.05%	0.29%	1.21%	2.95%
Rectum and anus	0.02%	0.11%	0.33%	1.03%	2.16%
Kidney	0.04%	0.13%	0.33%	0.72%	1.33%
Brain and nervous system	0.23%	0.36%	0.60%	0.98%	1.39%
Pancreas	0.01%	0.04%	0.16%	0.53%	1.13%

Table 1. Cumulative risk of developing cancer by 80 years of age for men.

For Swedish women, the cumulative risk of developing cancer by 80 years of age is 32%. The risk increases with age and varies by cancer type. The below table summarizes average cancer risk for women.

Cancer type	<40 years	<50 years	<60 years	<70 years	<80 years
All cancer types	2.14%	5.36%	10.53%	19.93%	32.02%
Breast	0.44%	1.89%	3.95%	7.22%	10.11%
Malignant melanoma	0.30%	0.77%	1.20%	1.83%	2.70%
Lung, trachea, and bronchi	0.02%	0.08%	0.39%	1.40%	3.22%
Colon	0.03%	0.15%	0.44%	1.29%	2.96%
Skin cancer (other)	0.02%	0.06%	0.20%	0.70%	2.11%
Uterus	0.01%	0.09%	0.39%	1.03%	2.03%
Brain and nervous system	0.34%	0.55%	0.77%	1.08%	1.44%
Rectum and anus	0.03%	0.11%	0.11%	0.75%	1.38%
Ovaries and fallopian tubes	0.07%	0.14%	0.35%	0.67%	1.11%
Urinary tract (except kidney)	0.01%	0.03%	0.17%	0.51%	1.15%
Kidney	0.03%	0.07%	0.19%	0.39%	0.66%
Pancreas	0.01%	0.04%	0.16%	0.44%	1.05%

Table 2. Cumulative risk of developing cancer by 80 years of age for women.

How can I manage my cancer risk?

Lifestyle

Approximately 30% of all cancers can be prevented through a healthy lifestyle. Adopting the following recommendations decreases an individual's risk for cancer. For more information, please see cancercentrum.se.

- Do not use any form of tobacco.
- Maintain a healthy body weight.
- Be physically active in everyday life. Limit the time spent sitting.
- Maintain a healthy diet:

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  - Eat plenty of whole grains, pulses, vegetables, and fruits.
  - Limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks.
  - Avoid processed meat; limit red meat and foods high in salt.
- If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention.
- Avoid too much sun, especially children. Use sun protection. Do not use tanning beds.
- For women: Breastfeeding reduces the mother's cancer risk. If you can, breastfeed your baby.
- Hormone replacement therapy (HRT) increases the risk of certain cancers. Limit use of HRT.
- Take part in vaccination programs and cancer screening programs.

Screening

The National Board of Health and Welfare has issued the following recommendations for national screening programs, with the aim of creating conditions for equal care.

For women:

- Cervical cancer screening with a gynecological pap smear test should be offered
  - Every third year for women between 23–29 years
  - Every third year for women between 30–49 years, which should include HPV analysis and a complementary analysis with cytology at approximately 41 years
  - Every seventh year for women between 50–64 years, which should include HPV analysis
- Breast cancer screening with mammography should be offered every 18 – 24 months between 40 and 74 years of age.

For everyone:

- Colorectal cancer screening by fecal occult blood test should be offered every second year to men and women between 60 and 74 years of age.

Recommendations regarding prevention and screening may differ for individuals with a high risk of cancer. Different recommendations may apply to individuals currently undergoing cancer treatment. Please consult your doctor for an individualized plan.

Frequently asked questions

Please find more information and answers to frequently asked questions in our FAQ. Additional information about hereditary cancer could be found at:

Cancerfonden
1177
Socialstyrelsen (The National Board of Health and Welfare)
The American website cancer.net
Cancer.se

Support

If you are in need of support you can contact Cancerrådgivningen, where you will be able to talk to a nurse specialized in cancer care with experience supporting individuals in their questions and concerns about cancer. Your call will be anonymous and employees at Cancerrådgivningen are bound by confidentiality. You can reach Cancerrådgivningen by calling 08 - 123 138 00 or by emailing cancerradgivningen@sll.se.

Test method

GeneMate® is a Next Generation Sequencing (NGS) service, optimized for analyzing DNA associated with a predisposition for certain hereditary cancers. Genomic DNA is extracted from saliva provided by the customer and the specific regions of interest are amplified with an amplicon-based technique and then sequenced on an Illumina NextSeq550Dx platform. The sequencing reads are then mapped to the reference genome, after which different and precise bioinformatic tools are used to identify single nucleotide variants (SNV), copy number variants (CNV) and small insertions/deletions (INDELS). Identified variants are reported using the recommended HGCS-nomenclature.

The classification of genomic variants is performed in accordance with established guidelines issued by the American College of Medical Genetics and Genomics (ACMG) and are described with the recommended nomenclature for classification as one of the

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following: pathogenic, likely pathogenic, unknown significance, likely benign, or benign. The classifications are evaluated by our clinical team consisting of a clinical laboratory geneticist, a genetic counsellor and a clinical geneticist (medical doctor). Results will be reported as positive if a pathogenic or likely pathogenic variant is detected in conjunction with data collection. Results will be reported as negative if no variant, a benign variant or a likely benign variant is detected in conjunction with data collection. Variants of unknown significance are generally reported as negative unless otherwise recommended by the clinical team. Variants of unknown significance (VUS) are reclassified regularly as the medical literature and scientific knowledge is updated. In cases where the customer noted that they wish to be informed about future updates when ordering the test, iCellate will update customers if a variant of unknown significance is reclassified. Reported variants will be confirmed with an orthogonal test via a referral laboratory. The clinical team will also do an interpretation based on the family history of cancer if provided.

This test has been developed and its performance characteristics determined by iCellate Medical AB, an ISO 15189:2012-ackredited laboratory (Accred. no. 10473) and IVO-registered healthcare provider (Health and Social Care Inspectorate).

Limitations

iCellate Medical AB only detects and reports findings within the genes found in the panel (please see the list of genes covered by the test). There may exist clinically significant variants in the tested genes that the current technology is not designed to detect. Additional variants that are associated with hereditary cancer but not part of GeneMate® product panel and/or variants that associated with disease other than hereditary cancer will not be reported by iCellate. A follow-up consultation with a genetic counsellor is recommended to ensure complete understanding of your test result.

The GeneMate® test does not report chromosomal aneuploidies (i.e. an abnormal number of chromosomes), complex gene conversions, fusions, inversions, balanced translocations, certain repeat expansions, non-coding intronic variants deeper than 10 base pairs from exon-intron boundary and copy number variations spanning less than 6 exons/target region as defined by the panel. The sensitivity/specificity to detect specific variants may vary. This variation includes deletions and insertions in the range of 40-150 bp, deletions and insertions of certain repetitive elements, deletion-duplications or copy number variations, variants in regions with low/high GC content and within or in the vicinity of homopolymers, variants in simple sequence repeats, and in pseudogene and duplicated segments. Since we know that standard target enrichment protocols cannot reliably analyze some genomic regions, variations from those areas will not be reported. In selected genes analysis is restricted only to positions known to impact cancer risk.

Results of the current test may be inaccurate in patients receiving blood transfusion, bone marrow transplant(s), and in patients with certain hematological malignancies.

Disclaimer

While comprehensive efforts are taken by iCellate to avoid any analytical errors, iCellate is not responsible for errors in sample collection, transportation, and/or any other errors made prior to receipt of the sample at our laboratory. Laboratory and diagnostic errors may occur due to sample processing, DNA contamination, or operational procedures (including but not limited to equipment or reagent errors, or supplier errors) at any stage of the GeneMate® test. While rare, any of the above errors may limit and or affect the sensitivity, specificity, and/or accuracy of the GeneMate® test results.

All classifications are based on review, interpretation, and/or analysis of evidence available at the time of reporting, including medical literature and scientific databases, and will change as new evidence becomes available. Standard risk models may be employed to report risk assessments if pathogenic or likely pathogenic variants were not identified by guidelines following risk identification for the GeneMate® test.

The accuracy of the risk estimation for each individual based on the family history depends on the accuracy of the information provided by the tested individual. If the family history provided is incorrect or incomplete this will influence the risk estimation. Even in the case of a negative result there may be an increased risk for cancer that motivates a more detailed investigation of the family history and in some cases inclusion in screening programs.

References

1. Faktablad Cancerdiagnostik. NORDCAN. https://www-dep.iarc.fr/nordcan/SW/frame.asp. Published March 26, 2019. Accessed September 9, 2020.