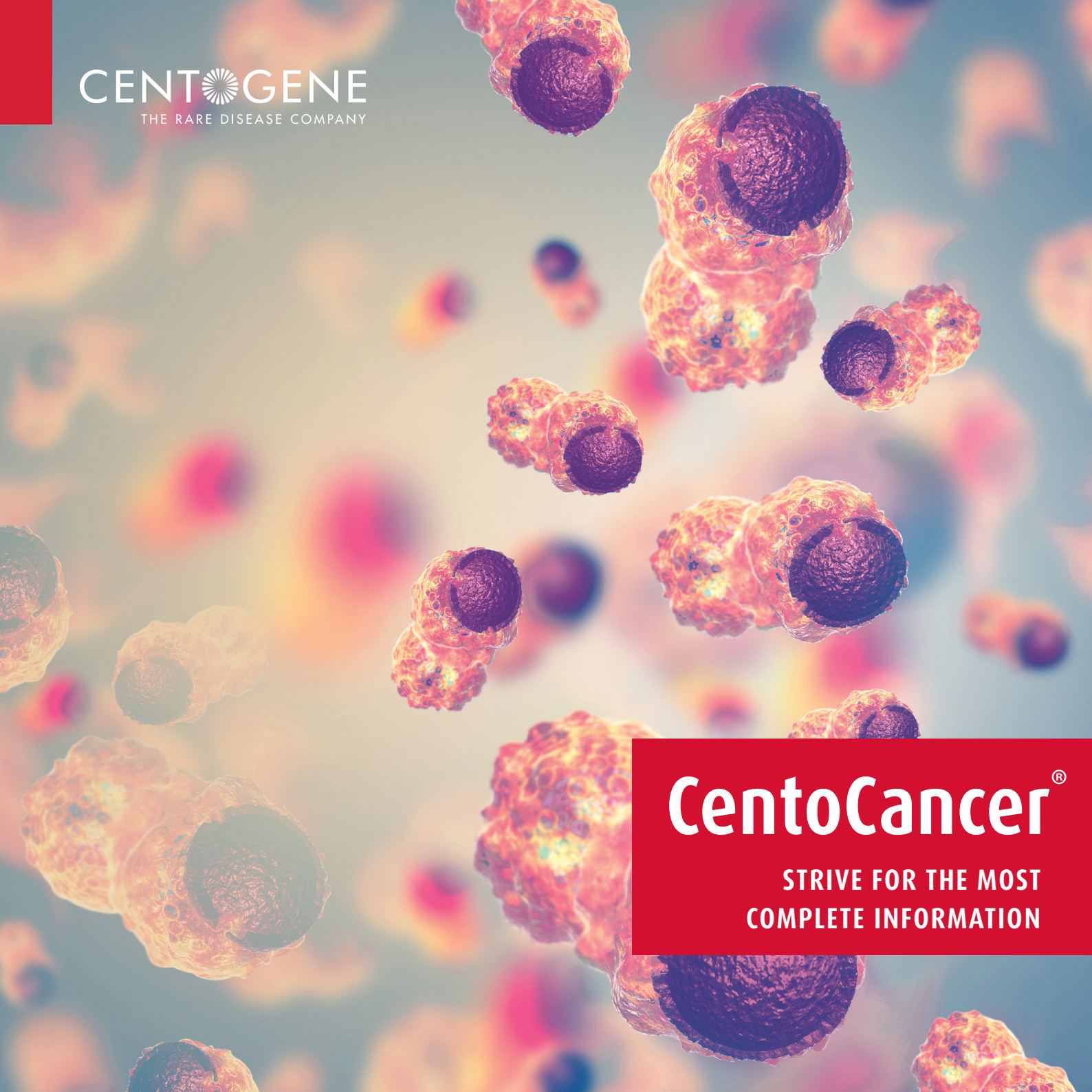
CENTOGENE
THE RARE DISEASE COMPANY



CentoCancer®

STRIVE FOR THE MOST COMPLETE INFORMATION

CentoCancer® – our most comprehensive **oncogenetics panel** for **hereditary mutations**

Hereditary pathogenic variants confer an increased risk of developing cancers during an individual's lifetime. Early identification of pathogenic variants in genes which have a predisposition to cancer is a fundamental first step in the diagnosis, management and treatment of individuals and families with hereditary cancer syndromes.

PANEL COMPOSITION

CentoCancer®, our most comprehensive cancer panel with 56 genes, offers complete answers to help you choose the best possible therapeutic approach for your patients. Each gene in CentoCancer® has been carefully selected based on its risk potential in the development of one or more of the following cancers:

- Breast
- Ovarian
- Colorectal
- Gastric
- Thyroid
- Endometrial
- Pancreatic
- Melanoma
- Renal
- Prostate

WHO SHOULD CONSIDER CentoCancer® FOR GENETIC TESTING?

CentoCancer® is appropriate for:

- Individuals with a positive personal history of early-onset cancer, rare cancer, bilateral cancer, or multiple primary cancers
- Unaffected individuals with a positive family history of multiple generations of cancers, rare cancers, or early-onset cancers
- Individuals in whom the suspected genetic diagnoses for a suspected familial cancer risk are not covered by a single targeted panel, or if a targeted panel testing was previously negative

CentoCancer® – Panel composition and methodology

CentoCancer® includes the following 56 most relevant cancer associated genes:

APC	CDH1	HNF1B	MSH2	POLD1	RAD51D	STK11
ATM	CDK4	HOXB13	MSH6	POLE	RET	TP53
BARD1	CDKN2A	MC1R	MUTYH	POT1	SDHA	TSC1
BLM	CHEK2	MEN1	NBN	PRSS1	SDHAF2	TSC2
BMPR1A	EPCAM	MET	NTHL1	PTCH1	SDHB	VHL
BRCA1	FH	MITF	PALB2	PTEN	SDHC	WT1
BRCA2	FLCN	MLH1	PMS1	RAD50	SDHD	XRCC2
BRIP1	HNF1A	MRE11A	PMS2	RAD51C	SMAD4	XRCC3

KEY PANEL FACTS

- Bidirectional next-generation sequencing (NGS) of all 56 genes in the panel, including coding regions (all exons) and +/-10bp exon/intron boundaries
- Coverage: >99% of target bases covered at >20x; mean coverage ≥180x
- 100% coverage of core genes: BRCA1, BRCA2, TP53
- Copy number variant (CNV) analysis from NGS data included for all genes
- Low quality single nucleotide variants (SNVs) and all relevant deletion/insertion variants are confirmed by Sanger sequencing or MLPA/qPCR prior to reporting
- All indel variants are also confirmed by Sanger sequencing prior to reporting
- CNVs are confirmed by MLPA/qPCR prior to reporting
- All relevant deep intronic variants described in the current version of HGMD® and CentoMD® are included
- Turnaround Time: 15 business days
- Required Material: ≥1µg DNA or ≥1ml EDTA blood or ≥1 CentoCard®

Some common cancer predisposition syndromes covered by CentoCancer®

Syndromes	Associated cancers
HEREDITARY BREAST/OVARIAN CANCER BRCA1, BRCA2	Breast, ovarian, prostate, pancreatic, melanoma
LI-FRAUMENI SYNDROME TP53	Breast, sarcomas, adrenocortical carcinoma, leukemia, brain tumors
COWDEN SYNDROME PTEN	Breast, thyroid, benign lesions of skin, hamartoma, renal cell carcinoma, uterine
HNPCC (LYNCH SYNDROME) MLH1, MSH2, MSH6, PMS1, PMS2	Colorectal (often right sided and multifocal), endometrial, ovarian, small bowel, stomach, pancreas, ureter, renal pelvis
FAMILIAL ADENOMATOUS POLYPOSIS APC	Polyposis, colorectal, thyroid, gastric, periampullary carcinoma, hepatoblastoma
VON HIPPEL-LINDAU VHL	Renal cell carcinoma, retinal angioma, cerebellar hemangioblastoma, pheochromocytoma, pancreatic cysts, islet cell tumor
MULTIPLE ENDOCRINE NEOPLASIA MEN1, RET	Parathyroid tumors, pancreatic tumors, pituitary tumors, medullary thyroid cancer, pheochromocytoma, neuromas

HEREDITARY CANCER AND/OR SUSCEPTIBILITY

Selection of genetic test/panel according to family history and clinical data

BRCA1, BRCA2 panel	BRCA1, BRCA2
Breast ovarian cancer panel	ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, MEN1, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, PALB2, PMS1, PMS2, PTEN, RAD50, RAD51C, RAD51D, STK11, TP53, XRCC2
CentoBreast® panel	ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, NBN, PALB2, PTEN, RAD51C, STK11, TP53
Colon cancer with polyps panel	APC, BMPR1A, MUTYH, PTEN, SMAD4, STK11
Colon cancer non-polyposis panel	EPCAM, MSH2, MLH1, MSH6, PMS2
CentoColon extended panel	APC, BMPR1A, CDH1, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, NTHL1, PMS2, POLD1, POLE, PTEN, SMAD4, STK11, TP53
Gastric cancer panel, targeted	BMPR1A, CDH1, EPCAM, MLH1, MSH2, MSH6, PMS1, PMS2, SMAD4
Ovarian cancer panel, targeted	BARD1, BRCA1, BRCA2, BRIP1, EPCAM, MLH1, MRE11A, MSH2, MSH6, NBN, PMS1, PMS2, RAD50, RAD51C, RAD51D, STK11, TP53
Prostate cancer panel	BRCA1, BRCA2, CHEK2, HOXB13, MLH1, MSH2, MSH6, NBN, PTEN, TP53
Pancreatic cancer panel, targeted	APC, ATM, BMPR1A, CDKN2A, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS1, PMS2, PRSS1, SMAD4, STK11
Renal cancer panel, targeted	EPCAM, FH, FLCN, HNF1A, HNF1B, MET, MITF, MLH1, MSH2, MSH6, PMS1, PMS2, PTEN, SDHB, SDHD, TSC1, TSC2, VHL, WT1
Skin cancer panel, targeted	CDKN2A, EPCAM, MC1R, MITF, MLH1, MSH2, MSH6, PMS1, PMS2, POT1, PTCH1, XRCC3
Thyroid cancer panel, targeted	APC, PTEN, RET
Uterine cancer panel, targeted	EPCAM, MLH1, MSH2, MSH6, PMS1, PMS2, PTEN
PGL / PCC / GIST panel, targeted	GDNF, KIF1B, MAX, MEN1, NF1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127, TP53, VHL
Multiple endocrine neoplasias / paraganglioma/pheochromocytoma panel	CDKN1B, MAX, MEN1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127, VHL

Identification of specific cancer-causing pathogenic variant

Genetic counseling, genetic testing of all family members with consent

No pathogenic variants identified

Complex family history, variability of cancers and absence of known genetic cause in the family

CentoCancer® panel	APC, ATM, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, FH, FLCN, HNF1A, HNF1B, HOXB13, MC1R, MEN1, MET, MITF, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, NTHL1, PALB2, PMS1, PMS2, POLD1, POLE, POT1, PRSS1, PTCH1, PTEN, RAD50, RAD51C, RAD51D, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, STK11, TP53, TSC1, TSC2, VHL, WT1, XRCC2, XRCC3

Identification of specific cancer-causing pathogenic variant

No pathogenic variant identified

WES analysis on a research basis

Research reporting

Genetic counseling, genetic testing of all family members with consent

Please visit our website
for more information:

www.centogene.com

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