NutriPATH
INTEGRATIVE PATHOLOGY SERVICES

INFORMATION SHEET

Comprehensive Hereditary Cancer Screening

Clinical Summary

The Comprehensive Hereditary Cancer Screening Panel analyzes **49 genes**: APC, ATM, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDKN2A, CDK4, CHEK2, EPCAM, GREM1, FH, FLCN, MAX, MEN1, MITF, MLH1, MSH2, MSH6, MUTYH, NF1, NBN, NF2, PALB2, POLD1, POLE, PMS2, PTEN, RAD50, RAD51C, RAD51D, RB1, RET, SDHAF2, SDHA, SDHB, SDHC, SDHD, SMAD4, STK11, TMEM127, TSC1, TSC2, TP53, VHL, WT1

These genes are associated with hereditary disposition to various cancers, across multiple organ systems. This panel includes analysis of genes associated with predisposition to the most common hereditary cancer syndromes such as such as breast and ovarian cancer, colorectal cancer and Lynch syndrome.

Cancer is a common disease with a lifetime risk of affecting about 1 in 3 individuals in the USA (1). Majority of these cancers are sporadic. However, some cancers are hereditary and can cause increased risk of cancer in certain families. Overall, approximately 5-10% of all cancer cases are thought to involve hereditary predisposition (2). Indications of possible hereditary cancer predisposition include: Several members of the same family affected with the same type of cancer or similar types, early unset of cancer in an individual or personal history of several primary cancers (3). Identifying those at risk may help with early intervention through additional screening, increased surveillance and other interventions.

Most of the genes on the panel, with few exceptions, are associated inherited cancer syndromes with an autosomal dominant inheritance pattern. However, some also include rare diseases with an autosomal recessive inheritance pattern.

Technical Summary

We evaluated the accuracy of the NGS panel assay using benchmark samples with true positive/negative sites based on GeT-RM and NIST GIAB data. The technical sensitivity and specificity are ~99%. The average depth of coverage of the current test is > 100X with ~ 98% of targeted regions covered >=10X.

This assay also detects large deletions and duplications (CNVs) using the Atlas-CNV method (4).

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Genes and Associated Disorders

GENE	INHERITANCE	ASSOCIATED DISEASE
APC	AD	Colorectal cancer somatic, Gastric cancer somatic Adenomatous polyposis coli, Brain tumor-polyposis syndrome 2, Gardner syndrome, Desmoid disease hereditary, Hepatoblastoma somatic
ATM	AD/AR	Breast cancer susceptibility, Prostate cancer susceptibility, Pancreatic cancer susceptibility, Ataxia-telangiectasia
BAP1	AD	Tumor predisposition syndrome
BARD1	AD	Breast cancer, susceptibility
BMPR1A	AD	Colorectal cancer, Pancreatic cancer susceptibility, Juvenile polyposis syndrome infantile form, Polyposis syndrome hereditary mixed 2, Polyposis juvenile intestinal
BRCA1	AD/AR	Breast-ovarian cancer familial 1, Pancreatic cancer susceptibility, Prostate cancer susceptibility, Fanconi anemia complementation group S
BRCA2	AD/AR	Breast-ovarian cancer, Breast cancer male susceptibility, Breast cancer Fanconi anemia complementation group D1, Glioblastoma 3, Medulloblastoma, Pancreatic cancer 2, Prostate cancer, Wilms tumor
BRIP1	AD	Breast cancer, early-onset, susceptibility to
CDH1	AD	Breast cancer lobular, Endometrial carcinoma somatic, Gastric cancer hereditary diffuse, Ovarian cancer somatic, Prostate cancer susceptibility
CDKN2A	AD	Melanoma and neural system tumor syndrome, Melanoma-pancreatic cancer syndrome, Melanoma, cutaneous malignant 2
CDK4	AD	Melanoma, cutaneous malignant 3
CHEK2	AD	Breast cancer susceptibility, Li-Fraumeni syndrome, Colorectal and gastric cancer susceptibility, Osteosarcoma somatic, Prostate cancer familial susceptibility
EPCAM	AD	Colorectal cancer, hereditary nonpolyposis, type 8
GREM1	AD	Colorectal cancer risk association
FH	AD	Leiomyomatosis and renal cell cancer
FLCN	AD	Birt-Hogg-Dube syndrome
MAX	AD	Pheochromocytoma susceptibility
MEN1	AD	Multiple endocrine neoplasia 1
MITF	AD	Melanoma susceptibility
MLH1	AD/AR	Colorectal cancer hereditary nonpolyposis type 2, Mismatch repair cancer, Muir-Torre syndrome, Lynch syndrome
MSH2	AD/AR	Colorectal cancer hereditary nonpolyposis type 1, Mismatch repair cancer syndrome, Muir-Torre syndrome, Lynch syndrome
MSH6	AD/AR	Colorectal cancer hereditary nonpolyposis type 5, Endometrial cancer familial, Mismatch repair cancer syndrome, Lynch syndrome
MUTYH	AR	Adenomas multiple colorectal, Colorectal adenomatous polyposis autosomal recessive with pilomatricomas, Gastric cancer somatic, Breast cancer susceptibility, Uterine cancer susceptibility
NF1	AD	Leukemia juvenile myelomonocytic, Neurofibromatosis familial spinal, Neurofibromatosis type 1, Neurofibromatosis-Noonan syndrome, Watson syndrome, Breast cancer susceptibility, Gastric cancer susceptibility, Pancreatic cancer susceptibility
NBN	AD	Leukemia, acute lymphoblastic, Breast cancer susceptibility
NF2	AD	Neurofibromatosis, type 2
PALB2	AD	Breast cancer susceptibility, Fanconi anemia complementation group N, Pancreatic cancer susceptibility to 3, Lynch syndrome
POLD1	AD	Colorectal cancer, susceptibility to, 10
POLE	AD	Colorectal cancer, susceptibility to, 12

Genes and Associated Disorders (Cont'd)

PMS2	AR	Colorectal cancer hereditary nonpolyposis type 4, Mismatch repair cancer syndrome, Pancreatic cancer susceptibility
PTEN	AD	Cowden syndrome Glioma susceptibility 2, Lhermitte-Duclos syndrome, Meningioma, Prostate cancer somatic, Breast cancer susceptibility
RAD50	AD/AR	Breast cancer susceptibility, Ovarian cancer susceptibility, Nijmegen breakage syndrome-like disorder
RAD51C	AD/AR	Breast-ovarian cancer familial susceptibility, Fanconi anemia complementation group O
RAD51D	AD	Breast-ovarian cancer familial susceptibility to 4
RB1	AD	Retinoblastoma
RET	AD	Multiple endocrine neoplasia IIA; Multiple endocrine neoplasia IIB; Medullary thyroid carcinoma; Hirschsprung disease, susceptibility to
SDHAF2	AD	Paragangliomas 2
SDHA	AD	Paragangliomas 5, Gastric cancer susceptibility
SDHB	AD	Gastrointestinal stromal tumor, Paraganglioma and gastric stromal sarcoma, Paragangliomas 4, Pheochromocytoma
SDHC	AD	Gastrointestinal stromal tumor, Paraganglioma and gastric stromal sarcoma, Paragangliomas 3
SDHD	AD/AR	Paraganglioma and gastric stromal sarcoma, Paragangliomas 1, Pheochromocytoma
SMAD4	AD	Juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome, Pancreatic cancer somatic, Polyposis juvenile intestinal
STK11	AD	Pancreatic cancer somatic, Peutz-Jeghers syndrome, Testicular tumor somatic, Colorectal cancer susceptibility, Gastric cancer susceptibility, Breast cancer susceptibility
TMEM127	AD	Pheochromocytoma
TSC1	AD	Tuberous sclerosis-1
TSC2	AD	Tuberous sclerosis-2, Pancreatic cancer
TP53	AD	Adrenocortical carcinoma pediatric, Basal cell carcinoma 7, Bone marrow failure syndrome, Breast cancer somatic, Choroid plexus papilloma, Colorectal cancer, Glioma susceptibility 1, Hepatocellular carcinoma somatic, Li-Fraumeni syndrome, Nasopharyngeal carcinoma somatic, Osteosarcoma, Pancreatic cancer somatic
VHL	AD/AR	Pheochromocytoma, Renal cell carcinoma somatic, von Hippel-Lindau syndrome
WT1	AD	Wilms tumor, type 1

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