Laboratory of Personalized Genomic Medicine
Department of Pathology and Cell Biology

COLUMBIA
COLUMBIA UNIVERSITY
IRVING MEDICAL CENTER

630 West 168th Street
P&S 11th Floor, Room 453
New York, NY 10032
Tel: 212-305-9706
Fax: 212-342-0420

Internal Use Only CUMC MRN: _____ Acc #:_____

Columbia Comprehensive Cancer Panel

Informed Consent for Genetic Testing

Please read the following form carefully and discuss with your ordering physician or genetic counselor before signing consent.

This consent is intended for sequencing of malignant ("cancerous") and non-malignant tumors and diseases of the blood cells along with DNA from normal cells. If this consent form is signed by an authorized representative of a patient, the word "you" also refers to the patient. You have the option to seek genetic counseling with a genetic counselor, geneticist, or other qualified health care practitioner before signing the consent.

Description of the Columbia Comprehensive Cancer Panel Sequencing Test

The test analyzes DNA, which carries the instructions for the body's development and function. DNA is contained in all the cells that make up the body's tissues. The DNA of tumors includes variants (mutations) that allow abnormal growth. It is recommended that both normal and tumor DNA, and tumor RNA be tested. The test can be performed without normal DNA. When normal DNA is also tested the test will compare the genetic information (DNA) in the tumor cells with normal cells to understand which mutations may be found in the body and which may have developed only in the tumor. The test will only analyze the genes on the accompanying panel. The primary purpose of this test to identify variants that may help in the treatment of your tumor, but the test can also identify mutations found in your body, that may indicate a heritable predisposition to cancer. In addition to hereditary predisposition to cancer, the panel also includes genes that cause treatable conditions. It is up to you whether you would like to know about mutations in your body in these genes. When available, we will also analyze RNA from the tumor to understand more of the effects of the DNA changes on the tumor. Testing RNA will not identify mutations in your body.

Reasons for Testing

Taking part in this test is voluntary. The decision to undergo the Columbia Comprehensive Cancer Panel test is made by you and your doctor. In general, the test is used when your doctor would like to have information about genetic changes that might explain the characteristics of your tumor or blood disorder or to assess the likelihood that the disease will respond to specific medications.

Testing

The test requires using a piece of tumor tissue, that may come from a biopsy, with or without a sample from unaffected parts of the body such as blood or saliva to serve as a sample of your normal cells. DNA and RNA will be isolated from tumor cells tissue and DNA will be isolated from normal cells. The DNA and RNA will then be sequenced for the genes on this panel.

Test Interpretation

Once the DNA/RNA is read, the information obtained is analyzed for differences between your own normal cells and that obtained from your tumor cells. Some changes may cause the disease, determine its behavior, or affect the treatment chosen for your condition. To find the changes most likely to have caused or influenced your disease, we will do the following:

The changes in your DNA will be compared with a list of changes that are known to cause diseases with symptoms similar to yours. Changes found in the disease sample will be compared with your normal cells to confirm that the changes are specific to your tumor. Sometimes changes occur that are not important to disease. These changes, also called "variants," may be present in your normal sample. We will exclude these from our report. Sometimes we will find changes in your normal DNA unrelated to your tumor or blood disorder that may be of significance to your health. You will have a chance below to tell us whether you want to receive this information.

Results Reporting

There are several kinds of results that may be reported. Results will go directly to your doctor or your other healthcare provider who ordered the test.

1. **Positive - A disease causing (pathogenic) variant is identified. The person tested may:**
    a. Carry a genetic change in the body or tumor that is a target for therapy.
    b. Identify a genetic change that may explain disease but is not a genetic target for therapy.

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c. Carry a genetic change in their body that increases the risk for certain cancers. This may include types of cancer that were not previously diagnosed in the individual or family.

d. Show that other blood-related family members may have increased risks for certain cancers. Other family may have inherited the same genetic change in non-tumor cells.

2. **Negative – No disease-causing variants identified. The person tested may:**
   a. Have no changes made to diagnosis or care based on the results of this test.
   b. Carry a genetic variant that explains or predisposes them to cancer or a medical problem, but which was not identified on this test. A negative result does not rule out a genetic basis for cancer or other health problems.
   c. Have further testing recommended by their provider.

3. **Uncertain – A variant of uncertain significance (VUS) was identified.**
   a. With current technology and research, it is unclear if a VUS caused or will cause a disorder or predisposition to a health condition.
   b. A VUS does not establish a diagnosis.
   c. In the future, a VUS may be reclassified as either pathogenic or benign. Check periodically with your provider for any changes in the understanding of a VUS.
   d. Testing other family members either affected or unaffected by cancer may provide more information about a VUS. Your medical provider may recommend family testing if a VUS is identified.

Secondary Findings

You may choose to be informed or not to be informed of secondary findings in genes that increases the risk for certain cancers or in genes that cause treatable conditions. Since this test provides information about changes in a large number of genes, changes might be detected that are not related to the disease for which the test was performed. Some of these findings might have significant immediate effects on your health care management. On an attached sheet is a list of genetic conditions that may be found by this testing.

These secondary findings in risk genes may also have implications for your family. Based on your results we may suggest that you speak to a genetic counselor or discuss genetic testing on your family members. Any such additional testing would be discussed with the appropriate family member and addressed in a different consent.

Potential Risks, Benefits, and Limitations

1. Results of the test may be limited by DNA quality, inherent DNA properties, amount of tumor in the sample, or other types of limitations.
2. There is a small risk of errors due to but not limited to technical errors in the laboratory.
3. You may learn medical information about yourself or your family that you did not expect. Unexpected information could lead to emotional or psychological distress.
4. Your relatives may be upset to learn that they may be at risk for a disease.
5. If you have had a bone marrow transplant, it may be difficult to tell whether variants in “normal” tissue are from your body, or from the donor’s cells. This will also make it more difficult to determine whether variants seen in your tumor are in the tumor only, or also in your body.

Cost of Testing

You will be responsible for any deductible and co- payments required by your insurance company for your medical care. If your insurance company denies payment for the tests and services, you may be personally responsible for these costs. Sometimes these payments count towards your annual out of pocket maximum. Please check with your health plan of insurance company to find out what they will cover.

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Privacy Protections

Results of testing will be reported through the medical provider who ordered the testing.

The test results will be a part of my medical record and will be available to physicians and genetic counselors involved in my care. Columbia University, New York-Presbyterian and Weill Cornell Medicine and their related entities participate in an Organized Health Care Arrangement (OHCA). This allows us to share health information to carry out treatment, payment and our joint health care operations, including integrated information system management, health information exchange, financial and billing services, insurance services, insurance, quality improvement, and risk management activities. Organizations that will follow this Notice include Columbia University, New York-Presbyterian sites, Weill Cornell Medicine, and their related entities.

Specific consent is required for releasing results to other entities, such as healthcare providers outside the OHCA or researchers.
If you do not want the secondary findings included with Columbia Comprehensive Cancer Panel results sent to these personal medical records, you must inform us about this below. Unless you tell us not to transmit them, the complete Columbia Comprehensive Cancer Panel report, including secondary findings in risk genes will become part of your EMR. Even if they do not become part of the EMR, the results may be made available to individuals/ organizations with legal access to your medical record, on a strict "need-to- know" basis. Those with legal access include, but are not limited to, the doctors and nursing staff directly involved in your care, your current and future insurance carriers (after your consent is obtained), and others specifically authorized by you or your authorized representative to gain access to your medical records.

The Genetic Information Non-Discrimination Act (GINA) is a federal law prohibiting use of genetic information or testing in decisions regarding health insurance and employment. There are some exceptions, and the law does not apply to other types of insurance, such as life insurance. For more information about GINA, see http://www.genome.gov/10002328.

Options for Reporting:

Please select one of the following for reporting of hereditary cancer genes:

[ ] Identify genetic variants in tumor cells and compare to genetic variants in non-tumor/non-cancerous ("normal") cells. Variants may indicate a heritable predisposition to certain cancers or indicate targets for therapy. An inherited predisposition may increase an individual's risk to have cancer. Please identify those variants that are present in my body ("germline variants) in cancer predisposition genes.
[ ] Identify genetic variants in tumor cells and compare to genetic variants in non-tumor/non-cancerous ("normal") cells. For hereditary cancer predisposition genes please report significant variants without identifying whether they are in the tumor only or in my body.

Please select one of the following for reporting of mutations in genes associated with treatable non-cancer conditions.

[ ] I want to know whether I have mutations in my body ("normal cells") in the genes on this panel associated with treatable non-cancer conditions.
[ ] I do not want to know whether I have mutations in my body ("normal cells") in the genes on this panel associated with treatable non-cancer conditions.

Sample storage:

New York state law specifies all normal samples for genetic testing will be discarded after 60 days or at the end of the test process, whichever is later. Please select

[ ] I allow the laboratory to de-identify my normal sample for use in education, test validation or research.
[ ] Destroy my normal sample after 60 days or at the end of the test process, whichever is later.

Statement of Consent

I have read the consent form and talked about the Columbia Comprehensive Cancer Panel testing, including the purpose, procedures, risks, benefits and alternatives with my doctor. Any questions I had were answered to my satisfaction.

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SIGNATURES:

Columbia Comprehensive Cancer Panel Testing Participant

Print Name: _____ Signature:_____ Date: _____

Patient, or patient representative.

Print Name: _____ Signature: _____Date: _____

Patient name (if signed by patient representative): _____

Practitioner Obtaining Consent

Print Name: _____ Signature: _____Date: _____

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Columbia Comprehensive Cancer Panel **List of Cancer Predisposition Genes recommended for reporting of secondary conditions by ACMG**	
Gene	**Disorder**
APC	Familial adenomatous polyposis
BMPR1A	Juvenile polyposis syndrome
BRCA1	Hereditary breast and ovarian cancer
BRCA2	Hereditary breast and ovarian cancer
MAX	Hereditary paraganglioma-pheochromocytoma syndrome
MEN1	Multiple endocrine neoplasia type 1
MLH1	Lynch syndrome
MSH2	Lynch syndrome
MSH6	Lynch syndrome
MUTYH	*MUTYH*-associated polyposis
NF2	Neurofibromatosis type 2
PALB2	Hereditary breast cancer
PMS2	Lynch syndrome
PTEN	*PTEN* hamartoma tumor syndrome
RB1	Retinoblastoma
RET	Familial medullary thyroid cancer
RET	Multiple endocrine neoplasia type 2A
RET	Multiple endocrine neoplasia type 2B
SDHAF2	Hereditary paraganglioma-pheochromocytoma syndrome
SDHB	Hereditary paraganglioma-pheochromocytoma syndrome
SDHC	Hereditary paraganglioma-pheochromocytoma syndrome
SDHD	Hereditary paraganglioma-pheochromocytoma syndrome
SMAD4	Juvenile polyposis syndrome
STK11	Peutz-Jeghers syndrome
TMEM127	Hereditary paraganglioma-pheochromocytoma syndrome
TP53	Li-Fraumeni syndrome
TSC1	Tuberous sclerosis complex
TSC2	Tuberous sclerosis complex
VHL	Von Hippel-Lindau syndrome
WT1	*WT1*-related Wilms tumor

Ref. ACMG SF v3

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Columbia Comprehensive Cancer Panel **Additional Cancer Predisposition Genes (Not on ACMG list of genes for reporting of secondary variants) for reporting of germline mutations.**	
Gene	**Disorder with germline variants***
ATM	Cancer susceptibility (heterozygous mutation)
ALK	Susceptibility to neuroblastoma
AXIN2	Colorectal cancer susceptibility (rare) with autosomal dominant ectodermal dysplasia
BAP1	BAP1 tumor predisposition syndrome (uveal melanoma, mesothelioma)
BARD1	Cancer susceptibility
BLM	Hereditary cancer predisposition (heterozygous mutations)
BRIP1	Cancer susceptibility (heterozygous mutations)
CDC73	Hyperparathyroidism; parathyroid adenoma; parathyroid carcinoma.
CDH1	Diffuse gastric and lobular breast cancer syndrome
CDK4	Cutaneous malignant melanoma
CDKN1B	Multiple Endocrine Neoplasia type IV (MEN4)
CDKN2A	Melanoma, Melanoma pancreatic cancer syndrome
CEBPA	Acute Myeloid Leukemia
CHEK2	Cancer susceptibility
CTNNA1	Hereditary diffuse gastric cancer
DICER1	DICER1 syndrome
EGFR	Susceptibility to non small cell lung cancer (germline T790M)
EPCAM	Lynch Syndrome (3' deletion)
FH	Leiomyomatosis and renal cell cancer (heterozygous mutations)
FLCN	Birt-Hogg-Dube syndrome
GATA2	AML and MDS susceptibility
HOXB13	Prostate cancer susceptibility
HRAS	Rhabdomyosarcoma and bladder cancer in Costello syndrome
KIT	Familial gastrointestinal stromal syndrome; cutaneous mastocytosis (activating heterozygous mutations)
MET	Familial Papillary Renal Cell Carcinoma
MITF	Cutaneous melanoma susceptibility
MSH3	Autosomal recessive familial adenomatous polyposis
NBN	Susceptibility to multiple cancers (heterozygous mutations)
NF1	Neurofibromatosis1
NTHL1	Autosomal recessive familial adenomatous polyposis
PDGFRA	Familial GIST
PHOX2B	Neuroblastoma susceptibility with or without Hirschsprung's disease
POLD1	Colorectal cancer susceptibility
POLE	Colorectal cancer susceptibility
POT1	Melanoma and Glioma susceptibility

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PRKAR1A	Carney complex, type 1, intracardiac myxoma, Primary pigmented nodular adrenocortical disease
PTCH1	Basal cell nevus (Gorlin) syndrome
RAD50	Cancer susceptibility (heterozygous mutations)
RAD51C	Cancer susceptibility including familial breast-ovarian cancer (heterozygous mutations)
RAD51D	Cancer susceptibility including familial breast-ovarian cancer (heterozygous mutations)
RECQL4	Osteosarcoma susceptibility
RUNX1	AML, platelet disorder associated with myeloid malignancy
SDHA	Paragangliomas (rare)
SMARCA4	Rhabdoid tumor
SMARCB1	Rhabdoid tumor
SMARCE1	Familial meningioma susceptibility
SUFU	Basal cell nevus syndrome, desmoplastic medulloblastoma, susceptibility to meningioma
TERT	Susceptibility to AML and cutaneous malignant melanoma

With some genes, homozygous or compound heterozygous germline mutations are associated with a severe clinical syndrome, while heterozygous germline mutations are associated cancer susceptibility. Only the cancer susceptibility is listed.

Columbia Comprehensive Cancer Panel **List of Genes on Panel that predispose to non-cancer heritcable conditions and recommended for reporting of secondary findings by ACMG.**	
Gene	**Disorder**
HNF1A	Maturity-Onset of Diabetes of the Young
SMAD3	Loeys-Dietz syndrome
TGFBR1	Loeys-Dietz syndrome
TGFBR2	Loeys-Dietz syndrome

Ref. ACMG SF v3