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 the sequencing of malignant ("cancerous") and non-malignant tumors and diseases of the blood cells. If this consent form is used for a pediatric patient, the word "you" also refers to your child. 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. 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, and also a sample from unaffected parts of the body such as blood or saliva to serve as a sample of your normal cells. A sample from tumor cells and/or from unaffected normal cells are required for this test. If you have a disease of the blood, we will obtain blood and/or bone marrow as the disease samples, and a swabbing of cheek cells from your mouth to serve as the normal cells instead. DNA and RNA will be isolated from your disease tissue, blood and/or cheek cells, and then read by a machine called a sequencer.

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 or abnormal blood 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 from your blood or cheek cells to confirm that the changes are specific to your tumor or abnormal blood cells. 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.

Privacy Protections

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

The test results in the clinical report will be a part of my medical record and will be available to physicians and genetic counselors involved in my care. Reported test results are stored in the laboratory’s computer records, and are normally automatically sent to the electronic medical records (EMRs) of New York Presbyterian Hospital, Columbia University Medical Center and Weill Cornell Medicine. Columbia University, NewYork-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

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services, insurance services, insurance, quality improvement, and risk management activities. Organizations that will follow this Notice include Columbia University, NewYork-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 Clinical Sequencing

Please read each sentence below and think about your choices for the Columbia Comprehensive Cancer Panel test performed. We want to know 1) whether you want to learn about secondary findings, 2) whether a complete report including secondary findings in risk genes should be transmitted to the EMR, 3) whether we can store your sample for future use, and 4) whether you wish to be contacted in the future. No matter what you decide to do, it will not negatively affect your current care.

You may say "I do" or "I do NOT" agree to each of the following choices. Please **circle your choice and write your initials** next to it.

1) **Secondary Findings:**

   I do _____ (Initial)

   I do NOT _____ (Initial)

   want to learn about secondary findings in risk genes, specifically those related to cancer predisposition and other treatable conditions linsted on the attached table.

2) **Electronic Medical Records (EMRs):**

   Please answer only if you selected to learn about secondary findings in question 1. If you chose not to learn about secondary findings, these findings will not be transmitted to your EMR.

   I do _____ (Initial)

   I do NOT _____ (Initial)

   want my complete Columbia Comprehensive Cancer Panel reported results transmitted to my EMRs within the New York-Presbyterian (NYP) hospital, Columbia University Medical Center and Weill Cornell Medicine. If I do NOT want my complete Columbia Comprehensive Cancer Panel reported results transmitted to my EMR, I understand that this means that my results related to secondary findings in risk genes will not be reported in the EMR and all other results related to my condition will be transmitted to my EMR. I understand that the complete Columbia Comprehensive Cancer Panel results will continue to be part of the laboratory's electronic information system. If complete test results are not entered into the hospital or university medical center EMRs, future doctors may not have access to those results, which may include secondary findings in risk genes. I understand that I must assume responsibility for informing my future doctors about such findings of the Columbia Comprehensive Cancer Panel test that relate to my healthcare.

3) **Sample Storage:**

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We recognize that your clinical condition may change and/or newer sequencing technologies may become available over time. We would like to store your tissue, DNA, and RNA samples and the data they generate in case new information becomes available that we think might benefit you or your family.

I do _____ (Initial)

I do NOT _____ (Initial)

give permission for Columbia University Medical Center to store my samples for future clinical testing.

4) **Future Contact for Clinical Purposes:**

In the event that new information becomes available that might benefit me:

I do _____ (Initial)

I do NOT _____ (Initial)

give permission for Columbia University Medical Center to contact me.

Research

Information learned from additional research testing may help future patients with cancer or other diseases. The results of testing done solely for the purposes of research will be returned to you only if the findings have a direct impact on your current condition and if performed or confirmed in an approved clinical laboratory. In all other cases research results will not be returned to you and not become a part of your medical record. It is important to keep track of the types of genetic changes we find at the time the test was ordered and are able to connect to particular diseases. This helps us improve our diagnostic capabilities. Hence, whichever choice you make below regarding storage and future use of your samples and Columbia Comprehensive Cancer Panel data, information about the type of disease and symptoms associated with the reported genetic findings at the time of initial testing will be preserved. This might not directly benefit you, but it might benefit future patients with similar conditions.

5) ***Samples:*** Your blood or buccal sample will be discarded after 60 days or after the result is finalized, whichever is later. We will attempt to store your leftover tumor DNA and RNA samples indefinitely and may use these specimens to evaluate and improve our laboratory testing (quality control, quality improvement and test validation/verification). In addition, we would like to be able to use these leftover specimens for research. Any such research will need to be approved by an institutional review board (IRB). Samples used solely for the purpose of research about the disease may be de-identified by removing your name, medical record number and other identifying information

I do _____ (Initial)

I do NOT _____ (Initial)

give permission for Columbia University Medical Center to use my leftover samples for research.

6) ***Sequencing data:*** Your sequencing data will be stored by the laboratory linked to your clinical information for at least as long as is required by regulations (which may change with time). If you agree, we would like to store the results of your Columbia Comprehensive Cancer Panel and related testing in a database. It is possible to store these data with or without identifying information. If the data are stored in a manner that includes your name and other identifying information the opportunity will still exist to link back to you and your clinical situation in the future. If, during a re-analysis, we discover something that would directly impact your care for your current condition, every effort will be made to communicate this information to you. We will do our best to make sure that the personal information contained in this database is kept private. For example, if information from this testing is published or presented at scientific meetings, your name and other personal information will not be used. However, we cannot guarantee total privacy. Your personal information may be given out if required by law.

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agree to my Columbia Comprehensive Cancer Panel and related data being stored indefinitely in a database for potential research.

7) **(Please answer only if you have chosen "I do" above for question 7):**

I do _____ (Initial)

I do NOT _____ (Initial)

agree to having my stored Columbia Comprehensive Cancer Panel and related data in a database that includes identifiers.

8) **Future Contact for Research Purposes**:

I do _____ (Initial)

I do NOT _____ (Initial)

give permission for Columbia University Medical Center to contact me for the purposes of participating in future research.

Cost of Testing

Although research funds will pay for certain research-related items and services, you will be responsible for any deductible and co-payments required by your insurance company for clinical tests and services you receive as part of 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.

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. I am aware that by signing below, I am agreeing to take part in this testing and associated research. I can stop being a part of the research database at any time. I am not waiving (giving up) any of my legal rights by signing this consent form. I will be given a copy of this consent form to keep for my records.

SIGNATURES:

Columbia Comprehensive Cancer Panel Testing Participant

Print Name: _____ Signature:_____Date: _____

Parent/Guardian of Columbia Comprehensive Cancer Panel Testing Participant (if participant <18 years old)

Print Name: _____ Signature: _____Date: _____

Person 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 to
POLE	Colorectal cancer, susceptibility to
POT1	Melanoma and Glioma, susceptibility to

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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