The PTEN Study: Eligibility Criteria and Clinical Features Checklist

Please note that patient results will not be released until all required study documents and confirmatory records have been received.

If this information is not available to you for inclusion with the patient's sample and other required paperwork, please ensure that the institution(s) where these records may be found is listed on the medical release form so our research team can retrieve this information.

Also please note: **whether macrocephaly is present or not, an OFC measurement is now a requirement for study participation.** Our study will allow the following measurements to "count" as macrocephaly for adults:

- Men: Minimum of 58.0 cm
- Women: Minimum of 57.3 cm

Eligibility Criteria

Patients with the following will **automatically** qualify for study participation:

- Known *PTEN* mutation or variant of uncertain significance
- Lhermitte-Duclos disease
- Pigmented macules of the glans penis
- Clinical diagnosis of Proteus or Proteus-like syndrome
- Adult patients with a score of 10 or greater per the Cleveland Clinic *PTEN* Risk Calculator (website: http://www.lerner.ccf.org/gmi/ccscore/)
- Pediatric patients with macrocephaly plus at least one of the following:
    - Autism/mental retardation/developmental delay
    - Lipoma, biopsy-proven trichilemmoma, oral papillomatosis, or hemangioma
    - Arteriovenous malformation
    - One or more gastrointestinal polyp(s)

In addition, patients with the following combination of findings from our clinical features checklist will qualify for study participation:

- Two major criteria
- One major plus two minor criteria
- Three minor criteria

Exclusion Criteria

Please do not submit the following:

- Patients with genetic tests (i.e. *BRCA* testing) pending
- Patients with other diagnostic testing that explains their major features (example: patient has endometrial cancer, fibrocystic breast disease, and lipoma but also has deleterious *MSH2* mutation)
- Patients for whom pathology records are unattainable or at an unknown institution.

If you have a question about whether or not your patient qualifies for this study, please send a clinical summary and a copy of the pedigree to the study team for review by fax: (216) 636-0009 or email: pten@ccf.org.

The Cleveland Clinic, IRB 8458
Molecular Mechanisms Involved in Cancer Predisposition

Subject Consent to Contact Form

I have reviewed the information provided about the research study and I am interested in learning more. A representative from The Genomic Medicine Institute has permission to contact me regarding study participation.

Phone number: (_____)_____ Preferred days/times: _____

Alternate number: (_____)_____ Preferred days/times: _____

Today's date: _____

Your signature: _____

Print your name: _____

If you are consenting on behalf of a child (under 18 years old), please print the child's name: _____

Participant's date of birth: _____

Contact information for health care provider facilitating study participation:

Name: _____ Title: _____

Institution: _____

E-mail: _____ Phone number: (_____) _____

Please mail this form to:

The Cleveland Clinic Genomic Medicine Institute
9500 Euclid Avenue, NE5
Cleveland, OH 44195

OR

FAX to:

FAX #: (216) 636-0009
Attn: Beth Crouser, MBA

Cleveland Clinic

AUTHORIZATION TO DISCLOSE HEALTH INFORMATION TO CLEVELAND CLINIC

1. Patient Information:		
Name *(First, Middle, Last)*		Cleveland Clinic Medical Record # if known:
Current Address		City State Zip
Last 4 Digits of Social Security # N/A	Email	Phone Number ( ) Date of Birth / /

2. Release Information From:	3. Release Information To: CLEVELAND CLINIC
Facility/Provider:	Name of Recipient: Beth Crouser, MBA Facility and/or Mail Code: Genomic Medicine Institute / NE50
Address City/State Zip	Address: 9500 Euclid Avenue — City/State Zip: Cleveland, OH 44195
Phone Number ( )	Phone Number: (216) 445-5850 — Fax Number: (216) 636-0009
	Select one: ☒ Paper ☒ Secure electronic delivery (If secure delivery, provide email): crouseb2@ccf.org

Purpose for Disclosure: ☐ **Continuity of Care** ☒ **Other (please indicate)** Referral to research study
(Purpose for disclosure must be completed prior to processing.)

Dates of service to release (FROM): _____ **(TO):** Present

☐ Office Visits	☐ History & Physical	☒ Research paperwork including medical records
☐ Emergency Department Reports	☐ Other _____	☐ _____
☐ Discharge Summary	☐ _____	☐ _____
☐ Operative Reports	☐ _____	☐ _____

I, the undersigned, authorize the above named sending Facility/Provider as described in Section 2 to release health information as indicated/described above. I understand and acknowledge that the requested health information may contain information regarding physical and mental illness, HIV test results ordiagnosis, treatment of AIDS/AIDS-related conditions, and/or alcohol/drug abuse. **This authorization does not include permission to release outpatient Psychotherapy Notes as defined below.* Release of Psychotherapy Notes requires a separate authorization.**

This authorization and consent will expire one year from the date of authorization written below, unless revoked by me (or my legal representative) through written notice presented to above named Facility/Provider as described in Section 2. Any revocation will not apply to information that has already been released in response to this authorization. I understand that treatment, payment, enrollment, or eligibility for benefits will not be based on whether or not I sign this authorization.

I understand that the sender of my health information may charge for the service of disclosing medical information and I am responsible for inquiring about these potential charges.

If Authorization is not complete, signed and dated, it may be returned and result in my information not being released until completed.

_____ / _____ ____/____/____

Signature of Patient/Patient's Personal Representative *Printed Name* *Date Signed*

_____

Relationship, if not Patient

**Psychotherapy Notes are defined as notes that document private, joint, group, or family counseling sessions that are separated from the rest of a patient's medical records.*

Submit completed request to the Cleveland Clinic Facility/Mailcode identified in Section 3 above.

NOTICE: If you send health information to Cleveland Clinic via email, please know that your message may be sent in an unencrypted email. An unencrypted email means there is a risk that the information in the email and any attachments could potentially be read by a third party when it is sent through the internet.

Banking Checklist: To be completed for all studies

Subject Name: _____ DOB: _____

Date of blood draw: _____ *If CCF patient*: CCF# _____

MANDATORY

Has another family member enrolled into any of our studies? *(please circle one)* Yes No

-If so, what is the family member's first and last name: _____

-What is this patient's relationship to the above family member: _____

MANDATORY Subject Sex: ☐ Male ☐ Female

Subject Race (check all that apply):
☐ American Indian and Alaska Native
☐ Asian
☐ Black or African American
☐ Native Hawaiian and Other Pacific Islander
☐ White
☐ Other

Subject Ethnicity: ☐ Hispanic or Latino ☐ Not Hispanic or Latino

Country/countries of origin: _____

Enrolling Healthcare Provider: _____

Please note: patient results will be sent to this individual via confidential e-mail.

Title: _____ Institution: _____

Phone: _____ E-mail: _____

- **Check off each required document to signify that it is included**
- **Check the box by the study/studies for which you are submitting a patient**

Required from non-IRB approved outside sites (most sites):	**Required from IRB-approved outside sites:**
☐ Subject consent to contact form ☐ Authorization for release of medical information ☐ Pedigree ☐ Copy of available records per study **DO NOT** send patient's sample with these documents.	☐ Copy of signed informed consent form ☐ Contact information page ☐ Authorization for release of medical information ☐ Pedigree ☐ Copy of available records per study ☐ Informed consent process documentation form/ other forms required by enrolling site's IRB ☐ Patient sample in provided collection kit

☐	**The PTEN Study** ☐ Meets study criteria per checklist ☐ Participant does not fully meet study criteria, but pre-approval for participation has been obtained from genetic counselor study coordinator ☐ Family member of previous study participant **Additional required documents:** ☐ Completed PTEN Clinical Features Checklist
☐	**The SDH Study – Additional required documents:** ☐ Completed SDH Clinical Features Checklist
☐	**The Velosano Study** ☐ Clinic Note
☐	**General Cancer Banking:** If not a CCF patient, submission for this study was pre-approved by the following research team member: _____ ☐ Diagnosis: _____
☐	**The U54 Autism Study** ☐ Clinic Note ☐ Completed Questionnaires

The PTEN Study: Clinical Features Checklist, page 1 of 2

Patient Name: _____ DOB: _____ Gender: _____

Patient Height: _____ Patient Weight: _____ Patient OFC (in cm): _____

AQ = automatic qualification; M = major criteria; m = minor criteria; **see revised eligibility criteria on above page to ensure your patient qualifies.**

√ if present	CNS Features	AQ/M/m	Documentation requested
	Lhermitte-Duclos disease	AQ	MRI and/or biopsy
	Macrocephaly	M	Clinic note
	Autism	m	Clinic note
	Mental retardation	m	Clinic note
	Developmental delay	m	Clinic note
√ if present	**Endocrine Features**	**AQ/M/m**	**Documentation requested**
	Thyroid cancer (not medullary)	M	Pathology report
	Goiter	m	Imaging
	Thyroid nodule(s)	m	Imaging
√ if present	**Breast Features**	**AQ/M/m**	**Documentation requested**
	Invasive carcinoma	M	Pathology report
	Ductal carcinoma in situ	m	Pathology report
	Lobular carcinoma in situ	m	Pathology report
	Breast papilloma	m	Pathology report
	Breast fibroadenoma	m	Pathology report
	Fibrocystic breast disease	m	Pathology report, imaging, and/or clinic note
√ if present	**Dermatologic Features**	**AQ/M/m**	**Documentation requested**
	Pigmented macules of the glans penis	AQ	Clinic note
	Biopsy-proven trichilemmoma(s)	M	Pathology report
	Oral-mucosal papillomatosis	M	Clinic note
	Lipoma(s)	m	Pathology report
√ if present	**Cardiovascular Features**	**AQ/M/m**	**Documentation requested**
	Arteriovenous malformation	m	Pathology report and/or imaging
√ if present	**Gastrointestinal Features**	**AQ/M/m**	**Documentation requested**
	Hamartomatous (juvenile, Peutz-Jegher) polyp(s)	M	Pathology report
	Ganglioneuroma(s)	M	Pathology report
	Hyperplastic polyp(s)	m	Pathology report
	Glycogenic acanthosis	m	Endoscopy report
√ if present	**Genitourinary Features**	**AQ/M/m**	**Documentation requested**
	Endometrial (uterine) cancer	M	Pathology report
	Uterine fibroid(s)	m	Pathology report and/or imaging
	Renal cell (kidney) cancer	m	Pathology report
	Congenital genitourinary defect	m	Imaging or clinic note
	Other genitourinary tumor (specify): _____	m	Pathology and/or imaging
√ if present	**Other Features**	**AQ/M/m**	**Documentation requested**
	Clinical diagnosis of Proteus or Proteus-like syndrome	AQ	Clinic note

The PTEN Study: Clinical Features Checklist, page 2 of 2

Patient Name: _____ DOB: _____ Gender: _____

Other Findings: Please circle present (P), absent (A), or unknown (U) for each.

MRI-proven megencephaly	P	A	U	Dermatofibroma	P	A	U
Malignant CNS tumor	P	A	U	Fibroma of other organ	P	A	U
Benign CNS tumor	P	A	U	GI polyp other than listed previously	P	A	U
Demyelinating leukodystrophy	P	A	U	Colon cancer	P	A	U
Hemangioma of skin	P	A	U	Other GI malignancy	P	A	U
Hemangioma of other organ	P	A	U	Melanoma	P	A	U
Acral keratoses	P	A	U	Other malignant skin cancer	P	A	U
"Skin tags", pathology unknown	P	A	U	Hearing loss	P	A	U
Hashimoto's (chronic lymphocytic) thyroiditis	P	A	U	Other invasive cancer(s) Specify: _____	P	A	U

Other History: Please circle yes (Y) or no (N) to indicate whether or not the patient has undergone the following:

Brain CT	Y	N	Breast mammogram	Y	N
Brain MRI	Y	N	Breast ultrasound	Y	N
Brain biopsy	Y	N	Breast MRI	Y	N
Thyroid ultrasound	Y	N	Breast biopsy	Y	N
Other thyroid scan: _____	Y	N	Breast lumpectomy	Y	N
Thyroid FNA	Y	N	Unilateral mastectomy	Y	N
Partial thyroidectomy	Y	N	Bilateral mastectomy	Y	N
Total thyroidectomy	Y	N	Hysterectomy	Y	N
Abdominal ultrasound	Y	N	Unilateral oophorectomy	Y	N
Abdominal CT	Y	N	Bilateral oophorectomy	Y	N
Abdominal MRI	Y	N	CT Angiography (specify organ): _____	Y	N
Pelvic ultrasound	Y	N			
Pelvic CT	Y	N	MR Angiography (specify organ): _____	Y	N
Pelvic MRI	Y	N			
Colonoscopy	Y	N	Biopsy of other organ(s): _____	Y	N
EGD/Upper endoscopy	Y	N			
Partial colectomy	Y	N	Other scans or procedures not listed here: _____ _____	Y	N
Total colectomy	Y	N			
Biopsy of any skin lesion	Y	N			

Other Testing: Please check to indicate whether or not the patient has had any of the following genetic tests and give results. Please include a copy of the lab report for any tests that have been done.

✓	Test name	Result
	BRCA1/2 sequencing and 5-site rearrangement panel	☐ Positive ☐ Negative ☐ VUS
	BRCA1/2 Multisite-3 panel	☐ Positive ☐ Negative
	BART	☐ Positive ☐ Negative ☐ VUS
	Chromosome analysis (Karyotype or array)	☐ Abnormal ☐ Normal ☐ VUS
	Clinical *PTEN* sequencing	☐ Positive ☐ Negative ☐ VUS
	Clinical *PTEN* MLPA	☐ Positive ☐ Negative ☐ VUS
	Clinical *PTEN* promoter analysis	☐ Positive ☐ Negative ☐ VUS
	Fragile X testing	☐ Positive ☐ Negative ☐ VUS
	MSI testing	☐ High ☐ Stable ☐ Low
	IHC analysis	☐ Positive ☐ Negative ☐ Equivocal
	Other gene testing (specify): _____	☐ Positive ☐ Negative ☐ VUS
	Other gene testing (specify): _____	☐ Positive ☐ Negative ☐ VUS