Indications for Referrals for Genetic Counseling

Hereditary Cancer Risk Program

Baylor Scott & White HEALTH

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Referral Process for Genetic Counseling

Paperwork requested from the physician:

1. Genetics Referral form signed by the physician
2. Pathology reports, if applicable
3. Recent clinic notes
4. Previous genetic testing results

Paperwork requested from the patient:

1. Electronic family health questionnaire
2. Previous genetic testing results

*Once an appointment has been scheduled, physician will be notified via fax confirmation.

After the genetic counseling appointment:

1. Patient will be notified via telephone of his or her test results.
2. Patient will receive summary letter, test results, and family tree via US Mail.
3. Referring physician will receive summary letter and test results via fax.

The genetics department is only able to fax results to referring physicians, per Baylor Scott & White Health, Health Information Management department policy.

For more information about the Hereditary Cancer Risk Program, contact us at:

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15 Rare Tumors that Warrant a Genetics Evaluation

1. Adrenocortical carcinoma
2. Thymic gland carcinoid tumor
3. Diffuse gastric cancer
4. Ovarian, Fallopian tube, Primary peritoneal cancer
5. Medullary thyroid cancer
6. Renal cell carcinoma (chromophobe or oncocytic)
7. Paraganglioma, Pheochromocytoma
8. Sex cord tumors with annular tubules
9. Leiomyosarcoma
10. Sebaceous carcinoma
11. Choroid Plexus Carcinoma (CPC)
12. Desmoid tumor
13. Hemangioblastoma
14. Retinoblastoma
15. Sertoli cell tumor

Brain/CNS

- Brain tumor and any second primary cancer
- Brain tumor with two additional cases of any *Lynch syndrome-related cancers in the same person or in relative
- Brain tumor and one additional *Li-Fraumeni related cancer in ≥ 2 close relatives with one dx ≤45y
- Choroid plexus carcinoma at any age
- Hemangioblastoma (CNS or retinal) at any age
- Astrocytoma and melanoma in the same person or in ≥ 2 first degree relatives
- Medulloblastoma and ≥10 cumulative colon polyps
- ≥ 2 neurofibromas
- ≥ 1 plexiform neurofibroma
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative that meets one of the above criteria

*See pages 20, 21

Breast

- Breast cancer dx ≤ 45y
- Breast cancer dx ≤ 50y with a family history of breast or prostate cancer (Gleason score ≥ 7) or unknown or limited family history
- Triple negative (ER-, PR-, HER2-) breast cancer dx ≤ 60y
- Two breast cancer primaries in the same individual, with one ≤ 50y
- Male breast cancer at any age
- Ashkenazi Jewish descent with breast cancer at any age
- Breast cancer at any age with:
  - ≥ 1 close relative with breast cancer dx ≤ 50y
  - ≥ 1 close relative with ovarian cancer at any age
  - ≥ 1 close relative with metatastic prostate cancer at any age
  - ≥ 1 close relative with pancreatic cancer at any age
  - ≥ 2 close relatives with breast cancer and/or prostate cancer (Gleason score ≥ 7) at any age
  - *BRCA1/2* mutation detected by tumor profiling in the absence of germline mutation analysis
  - Two additional *Cowden syndrome criteria
  - One additional *Li-Fraumeni related cancer
- Lobular breast cancer with a personal or family history of diffuse gastric cancer
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative that meets one of the above criteria

*See page 21

Colorectal

- Colorectal cancer dx ≤ 50y
- Colorectal cancer with abnormal tumor screening:
  - MSI-High
  - Immunohistochemistry staining showing the absence of one or more mismatch repair proteins*
- Colorectal cancer at any age with one of the following:
  - Synchronous or metachronous *Lynch syndrome related cancers
  - ≥ 1 first degree relative with any *Lynch syndrome related cancer dx ≤ 50y
  - ≥ 1 close relative with pancreatic cancer at any age
  - ≥ 2 close relatives with any *Lynch syndrome related cancers regardless of age
  - Two additional *Cowden syndrome criteria
- ≥ 2.5% Risk score on mutation prediction models such as MMRPro or PREMM[1,2,6]
- Personal or family history of polyposis:
  - ≥ 20 adenomas
  - Multiple GI hamartomatous polyps
  - Multiple juvenile polyps
  - ≥ 5 serrated polyps
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative that meets one of the above criteria

*See pages 20, 21

Endocrine, Other

- Parathyroid cancer with one of the following:
  - Dx < 30y
  - Multiple glands involved
  - Second neuroendocrine primary
  - Family history of hyperparathyroidism, pituitary adenoma, pancreatic islet cell tumor, or carcinoid of foregut
- Personal history and/or first degree relative with two of the following: pituitary adenoma, parathyroid adenoma, PNET, thymic or bronchial carcinoid, and/or adrenal tumor
- Pheochromocytoma and/or paraganglioma at any age
- Thymic gland carcinoid tumor at any age
- Adrenocortical carcinoma at any age
- Primary pigmented nodular adrenocortical dysplasia at any age
- An individual with a known familial cancer genetic mutation
- Unaffected individual with a close relative that meets the above criteria

Endometrial

- Endometrial cancer dx ≤ 50y
- Endometrial cancer with abnormal tumor screening:
  - MSI-High
  - Immunohistochemistry staining showing the absence of one or more mismatch repair proteins*
- Endometrial cancer at any age with one of the following:
  - Synchronous or metachronous *Lynch syndrome related cancers
  - ≥ 1 first degree relative with any *Lynch syndrome related cancers dx ≤50y
  - ≥ 1 close relative with pancreatic cancer at any age
  - ≥ 2 close relatives with any *Lynch syndrome related cancers, regardless of age
  - Two additional *Cowden syndrome criteria
  - Leiomyosarcoma histology
- ≥ 2.5% Risk score on mutation prediction models such as MMRPro or PREMM[1,2,6]
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative that meets one of the above criteria

*See pages 20, 21

Hematologic Malignancies

- Adults with MDS/AML/ALL/CLL with one or more of the following:
  - Dx ≤ 45y
  - Family history with at least 2 relatives with MDS/AML/ALL/CLL
  - Thrombocytopenia
  - Macrocytosis
  - Personal history of head/neck or anogenital squamous cell carcinoma
  - Somatic mutations in *RUNX1, GATA2, CEBPA, DDX41* at ~50% variant allele frequency or ≥ 90% variant allele frequency
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative who meets one of the above criteria

Ovarian/Fallopian Tube/Peritoneal

- Ovarian, fallopian tube, or primary peritoneal cancer at any age, regardless of family history
- Ovarian sex cord tumor with annular tubules at any age
- Sertoli cell tumor at any age
- An individual with a known familial cancer genetic mutation
- Unaffected individual with a close relative that meets one of the above criteria

Pancreatic

- Pancreatic cancer, at any age, regardless of family history
- Neuroendocrine subtype (PNET) with one of the following:
  - Personal history of parathyroid adenoma, thymic or bronchial carcinoid tumor, pituitary tumor, or adrenal tumor
  - Multiple PNETs
  - Personal history of or a first degree relative with gastrinoma
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative that meets the above criteria

*See page 20

Prostate

- Family history of two prostate cancers diagnosed ≤55y
- Metastatic prostate cancer dx at any age regardless of family history (radiographic evidence or biopsy proven disease)
- Prostate cancer diagnosed at any age (Gleason Score ≥ 7) with one of the following:
  - ≥ 1 close relative with ovarian cancer at any age
  - ≥ 1 close relative with pancreatic cancer at any age
  - ≥ 1 close relative with metatastic prostate cancer at any age
  - ≥ 1 close relative with breast cancer ≤ 50y
  - ≥ 2 close relatives with breast, pancreatic or prostate (Gleason score ≥ 7) cancer at any age
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract

Renal

- Renal cell carcinoma at any age with one of the following:
  - Bilateral or multifocal presentation
  - Dx < 50y
  - Papillary histology (type 1 or type 2)
  - Collecting duct histology
  - Tubulopapillary histology
  - BHD-related histology (chromophobe, oncocytoma, or oncocytic hybrid)
  - ≥ 1 close relative with pancreatic cancer at any age
  - Two additional *Cowden syndrome critera
- Personal history of angiomyolipomas of the kidney and one additional *Tuberous Sclerosis criteria
- Clear cell RCC diagnosed before 50
- Clear cell RCC and at least one relative with clear cell renal carcinoma
- Urothelial carcinoma or transitional cell carcinoma and a personal or family history of any *Lynch syndrome related cancers
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative that meets the above criteria

*See pages 20, 21, 22

Skin

- Melanoma with ≥ 1 close relative with pancreatic cancer at any age
- Melanoma with ≥ 1 close relative with metatastic prostate cancer at any age
- ≥ 3 primary melanomas in the same person
- ≥ 5 basal cell carcinomas in the same person
- Melanoma and pancreatic cancer in the same person
- Melanoma and astrocytoma in the same person or in close relatives
- Uveal melanoma with a family history of uveal melanoma or cutaneous melanoma
- Sebaceous adenoma/carcinoma and one additional case of any *Lynch syndrome related cancer in the same person or in relatives
- Cutaneous leiomyomas
- Fibrofolliculomas, perifollicular fibromas, trichodiscomas/ angiofibromas, and acrochordons (≥5)
- ≥ 6 café-au-lait macules
- Freckling in the axillary and inguinal regions
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative that meets the above criteria

*See page 20

Stomach

- ≥ 2 cases of gastric cancer, one dx <50y in close relatives
- ≥ 3 cases of gastric cancer in close relatives
- Diffuse gastric cancer dx <40y
- Personal or family history of diffuse gastric cancer and lobular breast cancer
- Gastric cancer at any age with one of the following:
  - Synchronous or metachronous *Lynch syndrome related cancers
  - ≥ 1 close relative with pancreatic cancer at any age
  - ≥ 2 close relatives with any *Lynch syndrome related cancers
- Personal or family history of ≥ 3 Gastrointestinal Stromal Tumor (GIST)
- Personal or family history of GIST with personal or family history of a paraganglioma or pheochromocytoma at any age
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative that meets the above criteria

*See page 20

Thyroid

- Medullary thyroid cancer
- Papillary thyroid cancer (cribriform-morular variant)
- Non-medullary thyroid cancer and two additional *Cowden syndrome criteria
- An individual with a known familial cancer genetic mutation
- Personal or family history of ≥ 3 cases of breast cancer, pancreatic cancer, prostate cancer (Gleason score ≥ 7), melanoma, sarcoma, adrenocortical carcinoma, brain tumors, leukemia, diffuse gastric cancer, colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatologic manifestations, macrocephaly, and/or hamartomatous polyps of the gastrointestinal tract
- Unaffected individual with a close relative that meets the above criteria

*See page 21

Other Rare Benign and Malignant Tumors that Warrant a Genetics Referral

Site	Rare Finding
Brain/CNS	• Rhabdoid tumor at any age • Lhermitte-Duclos (dysplastic gangliocytoma of the cerebellum) dx >18y • Subependymal giant cell astrocytoma and one additional *Tuberous Sclerosis criteria in the same person
Bone	• Bone cysts and one additional *Tuberous Sclerosis criteria in the same person
Cervix	• Adenoma malignum of the cervix at any age
Connective Tissue	• Desmoid tumor at any age • Sarcoma (non- Ewing sarcoma) dx <18y • Sarcoma (non- Ewing sarcoma) and a personal or family history of any additional *Li-Fraumeni related cancers
Duodenum	• Gastrinoma at any age
Ear	• Endolymphatic sac tumor at any age
Eye	• Retinoblastoma at any age • Retinal achromic patch and one additional *Tuberous Sclerosis criteria in the same person • Retinal hamartoma and one additional *Tuberous Sclerosis criteria in the same person • Ocular neuroma, at any age • Optic glioma at any age • Uveal melanoma with family history of uveal or cutaneous melanoma • ≥ 2 Lisch nodules (iris hamartomas)
Foregut	• Carcinoid tumor of the foregut (e.g., thymic, bronchial) and a personal history of parathyroid adenoma, PNET, anterior pituitary tumor, and/or adrenal tumor
Gonads	• Sertoli cell tumor at any age • Macular pigmentation of glans penis and 2 additional *Cowden syndrome criteria
Heart	• Cardiac rhabdomyoma (especially prenatal/newborn) and one additional *Tuberous Sclerosis criteria in the same person
Kidney	• Rhabdoid tumor at any age • Renal cysts and one additional *Tuberous Sclerosis criteria in the same person
Liver	• Hepatoblastoma dx <5y
Lungs	• Lung cysts leading to multiple pneumothoraces • Non-small cell lung cancer at any age with a T790M somatic variant in the *EGFR* gene prior to treatment
Mouth	• Pitting in dental enamel (>3) and one additional *Tuberous Sclerosis criteria in the same person • Oral neuroma at any age
Skin	• Trichilemmoma (≥ 3), acral keratoses (≥ 3), mucocutaneous neuromas, macular pigmentation of glans penis, or oral papillomas and 2 additional *Cowden syndrome criteria • Hypomelanotic macules, shagreen patch, ungual fibromas, facial angiofibromas, gingival fibroma, or “confetti” skin lesions and one additional *Tuberous Sclerosis criteria in the same person

*See pages 21, 22

Hereditary Breast and Ovarian Cancer Syndrome-Related Cancers:

- Breast Cancer (male and female)
- Ovarian Cancer
- Prostate Cancer (Gleason score ≥7)
- Pancreatic Cancer
- Melanoma

Lynch Syndrome-Related Cancers:

- Colorectal Cancer
- Endometrial Cancer
- Gastric Cancer
- Ovarian Cancer
- Pancreatic Cancer
- Prostate Cancer
- Cancer of the Ureter and Renal Pelvis
- Cancer of the Biliary Tract
- Brain Cancer (usually glioblastomas)
- Cancer of the Small Intestines
- Sebaceous Adenomas
- Keratoacanthomas

***For colon or endometrial cancers with abnormal immuno-histochemistry studies, additional testing may be warranted:**

Colon cancer:

If MLH1/ PMS2 Absent:

✓ BRAF studies needed

✓ MLH1 Methylation studies needed

Endometrial cancer:

If MLH1/ PMS2 Absent:

✓ MLH1 Methylation studies needed

Li-Fraumeni Syndrome-Related Cancers:

- Early Onset Breast Cancer
- Soft Tissue Sarcoma
- Osteosarcoma
- Brain Tumors
- Adrenocortical Carcinoma
- Leukemia

Cowden Syndrome-Related Findings:

- Breast Cancer
- Endometrial Cancer
- Thyroid Cancer, Non-Medullary
- Colon Cancer
- Renal Cell Carcinoma
- GI Hamartomas
- Macrocephaly
- Macular pigmentation of glans penis
- Autism Spectrum Disorder
- Esophageal glycogenic acanthoses
- Lipomas
- Intellectual Disability
- Thyroid structural lesions (adenomas, nodules, goiter)
- Testicular lipomatosis
- Vascular anomalies

Tuberous Sclerosis Complex-Related Findings:

- Angiofibromas (≥3) or fibrous cephalic plaque
- Cardiac rhabdomyoma
- Cortical dysplasias, including tubers and cerebral white matter migration lines
- Hypomelanotic macules
- Lymphangioleiomyomatosis
- Multiple retinal nodular hamartomas
- Renal angiomyolipoma
- Shagreen patch
- Subependymal giant cell astrocytoma
- Subependymal nodules
- Ungual fibromas
- “Confetti“ skin lesions (numerous 1-3-mm hypopigmented macules scattered over regions of the body, such as the arms and legs)
- Dental enamel pits (>3)
- Intraoral fibromas (≥2)
- Multiple renal cysts
- Nonrenal hamartomas
- Retinal achromic patch

Notes

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