IntelligeneDx
Cancer Genomics

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Possible Indications for Genetic Testing and Potential Testing Options*

(to be completed by healthcare provider)

Patient Name: _____ Date: _____

Unless otherwise noted, criteria refer to the patient or any of their close relatives. Close relatives include the patient's parents, siblings, children, aunts, uncles, nieces, nephews, grandparents, and grandchildren. Third degree relatives such as 1st cousin, great aunt/uncles, great grandparents and grandniece/nephews should be included in the family history, but are not enough on their own to necessitate testing.

If you have questions about whether or not testing is indicated for your patient, please contact IntelligeneDx's in-house genetic counselor at 913.258.2306 or inovikova@intelligenedx.com

Patient's Personal & Family History	Potential Test
☐ Renal Cell Carcinoma (RCC) with clear cell histology, if any of the following criteria are met: ☐ Diagnosed at age <50; ☐ Bilateral or multifocal tumors; ☐ ≥1 close relative with clear cell RCC ☐ RCC with papillary type 1 or 2 histology ☐ RCC with collecting duct or tubulopapillary histology ☐ RCC with Birt–Hogg–Dubé syndrome-related histology (chromophobe, oncocytoma, oncocytic hybrid) ☐ Urothelial carcinoma (or transitional cell carcinoma) and 2 additional cases of any Lynch Syndrome-associated cancer in the same person or in relatives ☐ RCC and 2 additional Cowden syndrome criteria in the same person ☐ Angiomyolipomas of the kidney and one additional TSC criterion in the same person	Bladder and Renal Cancer Panel
☐ Personal or close relative with breast cancer diagnosed age ≤50 ☐ Personal or family history of ovarian cancer at any age ☐ Personal or family history of male breast cancer at any age ☐ Triple-negative breast cancer diagnosed at age ≤60 ☐ ≥2 primary breast cancers in the same person ☐ Ashkenazi Jewish decent ☐ ≥3 cases of breast, ovarian, pancreatic, and/or aggressive prostate cancer in close relatives, including the patient ☐ Lobular breast cancer and diffuse gastric cancer in the same person ☐ Lobular breast cancer in one person and diffuse gastric cancer in a different person in the family, with at least one of those cancers diagnosed at or before age 50	Breast and Ovarian Cancer Panel
☐ Colorectal cancer diagnosed at age <50 ☐ ≥10 adenomatous colon polyps in the same person ☐ Colorectal cancer diagnosed at age ≥50 if there is a first degree relative with colorectal or endometrial cancer at any age ☐ Synchronous or metachronous colorectal or endometrial cancers in the same person ☐ Colorectal cancer and two additional cases of any Lynch Syndrome, Cowden Syndrome or Li-Fraumeni Syndrome cancers in the same person or in close relatives ☐ Colorectal cancer showing mismatch repair deficiency on tumor screening	Colorectal Cancer Panel

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☐ Personal history of or a first degree relative with medullary thyroid cancer ☐ Parathyroid adenoma diagnosed at age <30 ☐ Parathyroid adenoma with multiple glands involved ☐ Two of any of the following in the same person: parathyroid adenoma, thymic or bronchial carcinoid, pancreatic neuroendocrine tumor (e.g., gastrinoma, insulinoma, glucagonoma, VIPoma), pituitary tumor, or adrenal tumor ☐ Parathyroid adenoma and a family history of hyperparathyroidism, pituitary adenoma, pancreatic islet cell tumor, or foregut carcinoid tumor ☐ Growth hormone–producing adenoma with acromegaly and one additional Carney complex criterion in the same person ☐ Multiple primary neuroendocrine tumors in the same person ☐ Gastrinoma in the patient or a first degree relative	Endocrine Neoplasia Panel
☐ ≥2 cases of gastric cancer in close relatives; one diagnosed at age <50 ☐ ≥3 cases of gastric cancer in close relatives ☐ Diffuse gastric cancer diagnosed at age <40 ☐ Diffuse gastric cancer and lobular breast cancer in the same person ☐ Diffuse gastric cancer in one relative and lobular breast cancer in another; one diagnosed at age <50 ☐ Gastric cancer and 2 additional cases of any Lynch-syndrome associated cancer in the same person or in close relatives	Gastric Cancer Panel
☐ Personal history of or first degree relative with breast cancer diagnosed before age 30 ☐ Personal history of or a first degree relative with an adrenocortical tumor ☐ Personal history of or a first degree relative with a choroid plexus tumor ☐ Sarcoma diagnosed at age <18 ☐ ≥2 close relatives with a tumor in the Li-Fraumeni Syndrome (LFS) spectrum, one diagnosed at ≤45 ☐ Personal history of ≥2 LFS associated tumors, one diagnosed at age ≤45	Li-Fraumeni Syndrome Cancer Panel
☐ ≥3 cases of melanoma and/or pancreatic cancer in close relatives ☐ ≥3 primary melanomas in the same person ☐ Melanoma and pancreatic cancer in the same person ☐ Melanoma and astrocytoma in the same person or in 2 first degree relatives	Melanoma Cancer Panel
☐ Pancreatic cancer dx at any age, if any of the following criteria are met: ☐ ≥2 cases of pancreatic cancer in close relatives; ☐ ≥2 cases of breast, ovarian, and/or aggressive prostate cancer in close relatives; ☐ Ashkenazi Jewish ancestry ☐ Pancreatic cancer and ≥1 Peutz–Jeghers polyp in the same person ☐ Pancreatic cancer and two additional cases of any Lynch Syndrome associated cancer in the same person or in close relatives ☐ ≥3 cases of pancreatic cancer and/or melanoma in close relatives ☐ Pancreatic cancer and melanoma in the same person	Pancreatic Cancer Panel
☐ ≥2 cases of prostate cancer diagnosed at age ≤55 in close relatives ☐ ≥3 first degree relatives with prostate cancer ☐ Aggressive (Gleason score >7) prostate cancer and ≥2 cases of breast, ovarian, and/or pancreatic cancer in close relatives	Prostate Cancer Panel
☐ If criteria above were met for multiple hereditary panels please select the 94 gene panel on the requisition.	94 Gene Panel
☐ Known familial mutation – someone in the patient's family had genetic testing and a mutation was found. The patient will be tested only for the familial mutation. A copy of the relative's test result is required for this test.	Variant Testing

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☐ This test allows physicians to make a possible diagnosis of cases whose common analysis of genes and other different approaches were inconclusive. Please contact our genetic counselor prior to ordering this test.	Exome Testing

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☐ Patient appropriate for further risk assessment and/or genetic testing ☐ Bladder/Renal ☐ Breast/Ovarian ☐ Colorectal ☐ Endocrine Neoplasia ☐ Gastric ☐ Li-Fraumeni Syndrome ☐ Melanoma ☐ Pancreatic ☐ Prostate ☐ 94 Gene ☐ Variant ☐ Exome	☐ Discussed cancer risk with patient ☐ Patient offered genetic testing ☐ Accepted ☐ Declined

Tumors associated with Li–Fraumeni syndrome

• Adrenocortical tumor
• Brain tumor
• Breast cancer (often early onset)
• Bronchoalveolar cancer
• Colorectal cancer
• Leukemia
• Osteosarcoma
• Soft-tissue sarcoma

Tumors associated with Lynch syndrome

• Biliary tract cancer
• Colorectal adenocarcinoma
• Endometrial adenocarcinoma
• Gastric cancer
• Glioblastoma
• Ovarian cancer
• Pancreatic cancer
• Sebaceous adenocarcinoma
• Small bowel cancer
• Urothelial carcinoma (ureter and renal collecting ducts)

Cowden syndrome major criteria

• Breast cancer
• Endometrial cancer (epithelial)
• Thyroid cancer (follicular)
• Gastrointestinal hamartomas (including ganglioneuromas but excluding hyperplastic polyps; ≥3)
• Lhermitte–Duclos disease (adult)
• Macrocephaly (≥ 97th percentile: 58 cm for adult women, 60 cm for adult men)
• Macular pigmentation of the glans penis
• Multiple mucocutaneous lesions (any of the following): - Multiple trichilemmomas (≥3, at least 1 proven by biopsy) - – Acral keratoses (≥3 palmoplantar keratotic pits and/or acral hyperkeratotic papules) - Mucocutaneous neuromas (≥3) - Oral papillomas (particularly on tongue and gingival), multiple (≥3) OR biopsy proven OR dermatologist diagnosed

Cowden syndrome minor criteria

• Autism spectrum disorder
• Colon cancer
• Esophageal glycogenic acanthosis (≥3)
• Lipomas (≥3)
• Intellectual disability (i.e., intelligence quotient ≤75)
• Renal cell carcinoma
• Testicular lipomatosis
• Thyroid cancer (papillary or follicular variant of papillary)
• Thyroid structural lesions (e.g., adenoma, multinodular goiter)
• Vascular anomalies (including multiple intracranial developmental venous anomalies)

Carney complex criteria

• Spotty skin pigmentation on lips, conjunctiva and inner or outer canthi, and/or vaginal or penile mucosa
• Myxoma (cutaneous and mucosal)
• Cardiac myxoma
• Breast myxomatosis or fat-suppressed magnetic resonance imaging findings suggestive of this diagnosis
• Acromegaly due to growth hormone–producing adenoma
• Large cell calcifying Sertoli cell tumor or characteristic calcification on testicular ultrasonography
• Primary pigmented nodular adrenocortical dysplasia
• Thyroid carcinoma (nonmedullary) or multiple hypoechoic nodules on thyroid ultrasonography in a young patient
• Psammomatous melanotic schwannoma
• Blue nevus, epithelioid blue nevus (multiple)
• Breast ductal adenoma (multiple)
• Osteochondromyxoma

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Nevoid basal cell carcinoma syndrome major criteria
• Lamellar calcification of the falx in an individual younger than age 20
• Jaw keratocyst
• Palmar or plantar pits
• Multiple basal cell carcinomas (>5 in a lifetime) or a basal cell carcinoma diagnosed before age 30 (excluding basal cell carcinomas that develop after radiotherapy)
• First-degree relative with nevoid basal cell carcinoma syndrome

Nevoid basal cell carcinoma syndrome minor criteria
• Childhood medulloblastoma (primitive neuroectodermal tumor)
• Lymphomesenteric or pleural cysts
• Macrocephaly (occipital frontal circumference >97th percentile)
• Cleft lip or cleft palate
• Vertebral or rib anomalies observed on x-ray
• Preaxial or postaxial polydactyly
• Ovarian or cardiac fibromas
• Ocular anomalies (cataract, developmental defects, and pigmentary changes of the retinal epithelium)

Tuberous sclerosis complex (TSC) major criteria
• Facial angiofibromas or forehead plaque
• Non-traumatic ungual or periungual fibroma
• Hypomelanotic macules (≥3)
• Shagreen patch (connective tissue nevus)
• Cortical tuber in the brain
• Subependymal glial nodule
• Subependymal giant cell astrocytoma
• Multiple retinal nodular hamartomas
• Cardiac rhabdomyomas, single or multiple
• Lymphangiomyomatosis
• Renal angiomyolipoma

Tuberous sclerosis complex (TSC) minor criteria
• Multiple, randomly distributed pits in dental enamel
• Hamartomatous rectal polyps
• Bone cysts
• “Confetti” skin lesions
• Multiple renal cysts
• Non-renal hamartoma
• Cerebral white matter radial migration lines
• Retinal achromic patch
• Gingival fibromas

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