UVEAL MELANOMA-RELATED GENE PANEL: GNAQ, GNA11 AND BAP1

Background: Uveal melanoma (UM) is a rare ocular cancer that affects the uveal tract, comprising the iris, ciliary body, and choroid. UM is the most common primary malignancy of the eye with an incidence of ~1,200 new cases diagnosed per year in the United States. Clinical features associated with increased risk for developing metastatic disease, most commonly to the liver, include large tumor diameter, ciliary body involvement, and epithelioid cell type. Chromosomal aberrations, particularly monosomy for chromosome 3 and amplification of chromosome 8q, or Class 2 classification by gene expression profile, predict a >50% risk for developing metastasis within 5 years of the initial diagnosis.

Initiating events in a normal uveal melanocyte toward becoming a nevus include activating mutations in GNAQ or GNA11. Melanomas undergo additional genetic changes. Mutations of BAP1, located at 3p21, and loss of the other copy of chromosome 3 have been identified in metastatic UMs.

BAP1 germline analysis is warranted in patients with ocular melanoma and a strong personal or family history of cancers.


Utility: Prognostic evaluation, clinical management, and prediction of metastasis-free survival.

Sensitivity: Testing targets specific gene mutations and does not detect mutations that are outside of the targeted area. The testing will detect alterations >99% of the time and the overall prognosis is poor in most patients who are found to have a GNAQ or GNA11 mutation in conjunction with bi-allelic loss of BAP1. In the event that there is admixture of the tumor sample with normal cells, the sensitivity can be compromised.

Turn around: 4-6 weeks

Fees: $1,200

CPT codes: 81403, 81404, 81406


INSTRUCTIONS FOR SAMPLE SUBMISSION

Documentation:
Each sample must be accompanied by:
1. A request form for DNA analysis completed by the physician, nurse or genetic counselor requesting screening. Please note: ICD-9 code is required for billing purposes. If ICD-9 code is unknown, please provide patient’s clinical symptom(s) or family history that prompted testing.
2. A completed registration form with check, money order, credit card authorization or information for billing the referring institution.
3. An informed consent signed by the patient (if under 18 years of age, the parent or guardian should sign) and the professional obtaining the consent. Please have the patient initial at the top of each page and send all pages of the consent.
4. A verification of blood tubes form signed by the patient, parent or guardian. The form should be signed at the time of the blood draw.
5. The patient’s pedigree to include three generations, if possible.

IN THE EVENT THAT ALL PROPERLY COMPLETED FORMS DO NOT ACCOMPANY THE SPECIMEN, YOU WILL BE NOTIFIED, AND TESTING WILL BE HELD UNTIL PAPERWORK IS COMPLETE

Sample Requirements:
• Fine needle aspirate of ocular tumor collected in HBSS (Hanks Solution) before plaque therapy, stored at 4°C and shipped on ice.
• Obtain 2 EDTA tubes (lavender top) of blood - approximately 4 mL per tube
• For a newborn sample, obtain 2 EDTA tube (lavender top) of blood - approximately 1-2 mL per tube
• Label each tube with the patient’s name, date sample was obtained, and patient’s date of birth
• We accept banked or recently extracted DNA; please include the concentration. Please call the laboratory to inquire about the amount needed for testing.

Shipping Sample:
Ship at room temperature via Federal Express or other overnight courier that guarantees AM delivery to arrive Monday-Friday. There is no one in the laboratory evenings and weekends to receive samples. If sample is drawn on a Friday, please refrigerate it until shipment on the following business day.

Shipping Address:
Genetic Diagnostic Laboratory
University of Pennsylvania
415 Anatomy-Chemistry Building
3620 Hamilton Walk
Philadelphia, PA 19104
REQUEST FOR UVEAL MELANOMA-RELATED GENE PANEL TESTING: GNAQ, GNA11, AND BAP1

Please provide the following information. We cannot perform your test without ALL of this information. PLEASE PRINT ALL ANSWERS

PATIENT INFORMATION

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CLINICAL INFORMATION

Do you have dermal nevi? □ No □ Yes; if yes, approximately how many? __________

Do you have a personal history of cancer? □ No □ Yes; if yes, describe: ____________________________________________

Do you have a family history of cancer? □ No □ Yes; If yes, please list who was affected and the cancer diagnosis: ____________________________________________

Do you have a history of smoking? □ No □ Yes; if yes, how long did you smoke? ____________________________

If the patient has a diagnosis of ocular melanoma:

Is the melanoma tumor in the iris or choroid? □ Iris □ Choroid □ Ciliary body involvement

Which eye is affected: □ Left □ Right

What color is the iris? □ Black □ Brown □ Blue □ Green □ Hazel

What is the risk stratification for prognosis of metastatic disease?

Chr. 3: □ Disomy □ Monosomy; Chr. 8: □ Disomy □ Amplification 8q

---OR---

□ Class 1a □ Class 1b □ Class 2

SAMPLE TYPE(S)

□ Venous blood □ FNAB □ Frozen tissue □ FFPE sections/block

TEST REQUESTED

□ Uveal melanoma-related gene panel testing: analysis of GNAQ, GNA11, and BAP1

* Please include a copy of genetic result for affected family member for any familial test requests.
# PATIENT REGISTRATION FORM

Please provide the following information. We cannot perform your test without ALL of this information. PLEASE PRINT ALL ANSWERS.

## PATIENT INFORMATION

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## PHYSICIAN INFORMATION

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## PAYMENT OPTIONS (must choose one) [a receipt will be mailed to the patient for self-pay options]

- [ ] I have enclosed a check payable to the “Genetic Diagnostic Laboratory” for $ ________________

- [ ] Please charge my credit card for the amount of $ ________________
  - [ ] VISA
  - [ ] Master Card
  - [ ] Discover
  - [ ] American Express

  Card Number: _______________________________ Exp date: ________________

  Name of cardholder as it appears on card: __________________________________________

- [ ] I have Pennsylvania Medicaid. A copy of my Medicaid card is attached.

- [ ] INSTITUTIONAL BILLING: The Institution where my testing originated has agreed to pay all charges for the testing.
  INCLUDE Billing Address, Person Authorizing Payment, Telephone, and Fax below:

  BILLING ADDRESS

  BILLING ADDRESS

  NAME OF INDIVIDUAL AUTHORIZING PAYMENT | PHONE | FAX
  ---------------------------------------|-------|-----
VERIFICATION OF CORRECTLY IDENTIFIED BLOOD TUBES

I am a participant in genetic DNA testing.

I have been shown the tubes containing my blood for this genetic testing and my name has been correctly placed on each one of these tubes.

I have signed a copy of the consent form regarding this genetic testing to be sent along with my blood samples. I have been given a copy of the consent form to keep.

Participant Name: _____________________________________________

Participant/Parent Signature: _______________________________________

Date: _______________
INFORMED CONSENT FOR GENETIC TESTING
UVEAL MELANOMA-RELATED GENE PANEL: GNAQ, GNA11 AND BAP1

I _______________________________ request molecular genetic testing for Uveal Melanoma-related genes: GNAQ, GNA11 and BAP1 to supplement knowledge about the biology of the ocular tumor. Genetic testing requires a sample of tissue from the ocular tumor and/or blood. DNA will be isolated from the sample(s) for molecular genetic testing.

Informed consent includes an understanding that:

1. The risk of disclosure of genetic information might include psychosocial concerns and concerns about genetic discrimination. Please discuss these concerns with your health care provider.

2. There are different types of results that may be reported including:
   a. It is disclosed that the tumor carries a clinically significant molecular alteration known to be associated with aggressive disease.
   b. The analysis did not detect a molecular alteration. The methods currently in use might be unable to detect all mutations in every gene, and the tumor might still have a DNA mutation that was not detected by the current technology.

3. Genetic information might be learned that implicate the presence of a germline genetic condition that could affect you and/or family members.

4. These tests are relatively new and are subject to change periodically to improve or expand the utility of the test. The tests are not considered research but are considered to be the best and newest laboratory service available. This DNA testing is often complex and utilizes specialized materials. While the testing is highly accurate for detection of the majority of disease causing mutations, a small fraction of mutations may be missed by the current technology. Due to the nature of the testing, there is a small possibility that the test will not work properly or that an error will occur. Occasionally, testing may reveal a variant of unknown significance that is unable to be definitively interpreted as positive or negative for disease-association based on our current knowledge of the variant.

Your signature below acknowledges your voluntary participation in this testing, but in no way releases the laboratory and staff from their professional and ethical responsibility to you.

5. The results are confidential; they will only be released to other medical professionals or other parties with your verbal or written consent.

6. After the specific tests requested have been completed and reported, the Laboratory may dispose of, retain, or preserve these specimens for research or for validation in the development of future genetic tests. In all circumstance described previously, your identity will be protected and research results will not be provided to you or to any other party. If use of this genetic material results in a scientific publication, it will not contain any identifying information. Indicate your consent or denial to the above sentence by initialing below. Your refusal to consent to research will not affect the reporting of your genetic results.

_____ I consent to the use of my DNA sample for future test validation and/or research purposes.

_____ I do not consent to the use of my DNA sample for future test validation or research purposes.

Initials _______
7. In the event that your sample is used for research purposes, the Laboratory may wish to contact you for additional information regarding your sample. This includes, but is not limited to, information on personal health and family history as it relates to the genetic testing. The Laboratory may also wish to contact you if additional genetic information about your sample is gained through the research testing. Indicate your consent or denial to the above sentence by initialing below. Your refusal to consent to research will not affect the reporting of your genetic results.

_____ I consent to be contacted by the Laboratory in the future for research purposes.

_____ I do not consent to be contacted by the Laboratory in the future for research purposes.

8. The Genetic Diagnostic Laboratory is not a DNA banking facility and your DNA or tumor sample may not be available for future clinical studies.

Physician/Counselor Statement: I have explained the potential clinical utility for the requested molecular test to this individual. I have addressed the limitations outlined above, and I have answered this individual’s questions.

Signature__________________________________________

Print Name________________________________________

Date ______________________

Patient Statement: I agree to the genetic analysis, and I have had the opportunity to ask questions about the testing.

Patient’s Name (PRINTED): ________________________________________

Relationship: _____ Self or _____ Child

Patient’s Date of Birth: _______________________

Signature of Patient or Parent: __________________________________________

Date Signed _________________________