Uncovering Periodic Paralysis

A sponsored no-cost Primary Periodic Paralysis (PPP) genetic testing program

PPP is a rare and potentially progressive genetic condition.[1-3] Xeris Pharmaceuticals® has partnered with Invitae to offer a periodic paralysis genetic test for those who have episodic muscle weakness or temporary paralysis provoked by common triggers for PPP.

A genetic test can help shorten the diagnostic journey and expedite clinical management of the disease.

ORDER A TEST TODAY

www.uncoveringperiodicparalysis.com

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PPP is a rare inherited condition[3]

- PPP includes several autosomal dominant inherited neuromuscular disorders which cause **recurrent, progressive, and debilitating episodes of extreme muscle weakness and temporary paralysis**[3-4]
  - Although there are other related variants, the most common forms of PPP are hypokalemic periodic paralysis and hyperkalemic periodic paralysis[5-8]

PPP IS OFTEN DIFFICULT TO DIAGNOSE[1-2]

- Patients in one study reported seeing an average of 4 doctors before receiving a correct diagnosis of PPP[1]*
- Average time from onset of symptoms to correct diagnosis **26 years**†[2]

PPP IS COMMONLY MISDIAGNOSED[1,2,9]

- Patients have reported being misdiagnosed with other conditions, including depression, malingering, conversion disorder, or myotonia congenita[1]

A negative test does not rule out a PPP diagnosis[3]

Patients with a negative test result may still have PPP. Genetic testing can confirm a diagnosis in about 70% of patients, but the remaining 30% don't have one of the commonly identified genetic mutations. These patients can be diagnosed by considering[3]:

- Clinical presentation of symptoms
- History of attacks (as well as serum potassium levels during attacks)
- Response to specific PPP triggers
- Family history
- Ruling out other conditions that mimic PPP
- Other testing such as ECG/EKG, EMG, and CMAP

xeris Care Connection™

Providing patients and their providers with expertise in managing critical aspects of the PPP treatment journey

*Based on a survey of 137 patients ages 19-84 years with a diagnosis of hyperkalemic periodic paralysis who were invited through the internet or one of several healthcare institutions worldwide.
† Based on a survey of 66 self-selected patients over the age of 40 years with a clinical diagnosis of Primary Periodic Paralysis who sought support via the Internet.

Genetic testing is a simple, convenient process

1. **Place your order:**
Online Order: Place an order through the ordering portal at **www.uncoveringperiodicparalysis.com**
-or-
Fax Order: Fill out the enclosed form, which is also available at **www.uncoveringperiodicparalysis.com,** and fax it to 415-276-4164

2. **Collect a specimen:** Order a specimen collection kit at **www.invitae.com/request-a-kit**. Make sure to label the sample with the patient's full name, date of birth, and sample collection date. Your Xeris Area Business Specialist can also provide you with a kit.

3. **Get the results:** Once Invitae receives the sample, you will receive the results in 10-21 calendar days, on average. If you create an online account, you will be able to track the status of your order and receive a notification email when the test results are ready.

Eligibility for Testing

- Patients must be 18+ years of age
- Have a history of episodic muscle weakness, paralysis attacks, or episodic pain after attacks (more than 1 occurrence)
- Have episodes provoked by at least 1 of the common triggers for PPP. Visit www.uncoveringperiodicparalysis.com to view the common triggers of PPP.

No-Cost Testing For Family Members*

- Xeris Pharmaceuticals® and Invitae offer no-cost family variant testing to any blood relative of a patient newly diagnosed through the Uncovering Periodic Paralysis genetic testing program
- Eligibility for family members:
  - A pathogenic or likely pathogenic variant was found on the original patient's Uncovering Periodic Paralysis gene panel test
  - The order for the genetic test must be placed within 90 days of the original patient's test report
- Direct family members do **not** have to meet any of the eligibility requirements (age, triggers, episodes, etc.) to receive family variant testing.

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The advantages of the PPP genetic testing panel

- **Screens for hyperkalemic, hypokalemic, and atypical periodic paralyses, as well as Andersen-Tawil syndrome,** including the 6 most commonly associated genes: ATP1A2, SCN4A, CACNA1S, KCNJ2, MCM2AP, and RYR1.

- On the requisition form, you have the opportunity to check a box that will automatically reflex to analysis using the Invitae Comprehensive Neuromuscular Disorders Panel should the initial result be negative. However, if you don't check that box, you still have 90 days to order re-requisition analysis.

- Turnaround time for the panel is rapid. Once Invitae receives the sample, you will receive the results in 10-21 calendar days, on average.

- Invitae's board-certified genetic counselors are available Monday through Friday, 5 AM to 5 PM Pacific time, to help review patient cases, differentiate between test options, and aid in interpreting results. If you have questions, you can reach the Invitae Customer Service team at 800-436-3037

A genetic test can help shorten the PPP diagnostic journey and expedite clinical management of the disease

ORDER A TEST TODAY

www.uncoveringperiodicparalysis.com

References: 1. Charles G, Zheng C, Lehmann-Horn F, Jurkat-Rott K, Levitt J. Characterization of hyperkalemic periodic paralysis; a survey of genetically diagnosed individuals. *J Neurol.* 2013;260:2606-2613. **2.** Cavel-Greant D, Lehmann-Horn F, Jurkat-Rott K. The impact of permanent muscle weakness on quality of life in periodic paralysis; a survey of 66 patients. *Acta Myol.* 2012;31:126-133. **3.** Statland JM, Fontaine B, Hanna MG, et al. Review of the diagnosis and treatment of periodic paralysis. *Muscle Nerve.* 2018;57:522-530. **4.** Cannon SC, Channelopathies of skeletal muscle excitability. *Compr Physiol,* 2015;5:761-790. **5.** Hypokalemic Periodic Paralysis. MedlinePlus. Updated March 1, 2020. Accessed July 26, 2023. https://medlineplus.gov/genetics/condition/hypokalemic-periodic-paralysis/. **6.** Hyperkalemic Periodic Paralysis. MedlinePlus. Updated February 1, 2019. Accessed July 26, 2023. https://medlineplus.gov/genetics/condition/hyperkalemic periodic-paralysis/. **7.** Paramyotonia Congenita. MedlinePlus. Updated August 1, 2015. Accessed July 18, 2023. https://medlineplus.gov/genetics condition/paramyotonia-congenita/. **8.** Andersen-Tawil Syndrome. MedlinePlus. Updated April 1, 2018. Accessed July 26, 2023. Available at: https://medlineplus.gov/genetics/condition/andersen-tawil-syndrome/. **9.** Arya SN. Periodic paralysis. *J Ind Acad Clin Med. 2002;3:374-382.*

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INVITAE

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ORDER ID
For Invitae internal use only

Requisition Form
Uncovering Periodic Paralysis Program TRF924-8

This requisition form can be used to submit an order for the **Uncovering Periodic Paralysis** program, a sponsored testing program for genetic disorders brought to you by **Xeris Pharmaceuticals** and **Invitae Corporation**.

INSTRUCTIONS: Review the ordering options and then complete all sections of this form. Your ordering option will be indicated in the test selection section.

ORDERING OPTIONS

1. UNCOVERING PERIODIC PARALYSIS PROGRAM

For individuals that meet the eligibility criteria below and wish to receive the program specific genetic testing panels.

REQUIRED: You must select below the appropriate eligibility criteria for this patient.

This program is available to patients in the US who meet the following eligibility criteria (both need to be checked to be eligible):

◯ Episodic muscle weakness/paralysis attacks **OR** episodic pain after attacks (more than one occurrence)

AND

◯ Episodes are provoked by at least one of the common triggers for hyperkalemic or hypokalemic primary periodic paralysis (see www.invitae.com/UncoveringPeriodicParalysis for more information)

2. GENE-SPECIFIC FAMILY FOLLOW-UP TESTING

For relatives of program participants who who received a Pathogenic/Likely Pathogenic result or approved VUS on the Invitae Periodic Paralysis Panel who want to receive gene specific family follow-up testing at no additional charge. Relatives do not need to meet the eligibility criteria listed above. Learn more at www.invitae.com/family.

PATIENT INFORMATION

First name	MI	Last name
Date of birth (MM/DD/YYYY)	Biological sex ◯ M ◯ F	MRN (medical record number)

Ancestry ◯ Asian ◯ Black/African American ◯ White/Caucasian ◯ Ashkenazi Jewish ◯ Hispanic ◯ Native American ◯ Pacific Islander ◯ French Canadian ◯ Sephardic Jewish ◯ Mediterranean ◯ Other: _____

Phone	Email address (report access after clinician releases)	
Address		City
State/Prov	ZIP/Postal code	Country

Ship a kit to this patient (optional) by faxing or emailing this completed form to Invitae

Kit type: ◯ Buccal swab kit ◯ Saliva kit

Ship to: ◯ Address above ◯ Alternate address: _____

SPECIMEN INFORMATION

Specimen type: Blood (3-mL purple EDTA) -OR- Buccal Swabs (OCD-100, 2 devices) -OR- Saliva (Oragene™) -OR- DNA source: _____

We are unable to accept blood/buccal/saliva from patients with:
- *Allogeneic bone marrow transplants*
- *Blood transfusion <2 weeks prior to specimen collection*

Specimen collection date (MM/DD/YYYY): ☐☐ ☐☐ ☐☐☐☐
If not provided, the day before specimen receipt will be used

Special cases: ◯ History of/current hematologic malignancy in patient

INVITAE PARTNER CODE UPP

CLINICIAN INFORMATION

Organization name		
Phone		Fax
Address		City
State/Prov	ZIP/Postal code	Country

Primary clinical contact name (if different from ordering provider)	NPI
Primary clinical contact email address (for report access)	

Ordering provider (select one ordering provider by marking the checkbox before the name)

	Name	NPI	Email address (for report access)
◯			
◯			
◯			
◯			
◯			
◯			

Additional clinical or laboratory contacts (optional, to share access to order online)

◯ **Share this order with the primary clinical contact's default clinical team, manage at invitae.com**

Name	Email address (for report access)
Name	Email address (for report access)

CLINICAL HISTORY

FAMILY HISTORY

Is there a family history of disease for which the patient is being tested? ◯ Yes ◯ No If yes, describe below and attach pedigree and/or clinical notes.

Relative's relationship to this patient	Maternal or paternal	Diagnosed condition	Age at diagnosis	Relative's relationship to this patient	Maternal or paternal	Diagnosed condition	Age at diagnosis

CLINICAL HISTORY

PERSONAL HISTORY

Is/was this patient affected or symptomatic?† ◯ Yes ◯ No
Provide details in the required clinical history questions (if applicable).

† Symptomatic means this patient has features or signs known or suspected to be related to the genetic testing being ordered and could include findings on physical examination, laboratory tests, or imaging.

REQUIRED CLINICAL HISTORY

Age of onset for signs/symptoms: _____

Family history of periodic paralysis: ◯ Yes ◯ No

Has the patient previously been diagnosed with periodic paralysis through another diagnostic test? ◯ Yes ◯ No

If "Yes," through which diagnostic test?
- ◯ Nerve connection/electromyogram (EMG)
- ◯ Electrocardiogram (EKG)
- ◯ Documented serum potassium (K+) changes during an attack
- ◯ Long exercise test (CMAP)
- ◯ Response to medication trial
- ◯ Other, please specify: _____

OPTIONAL - REQUESTED VARIANTS FOR THIS PATIENT'S REPORT, IF KNOWN

*To have the presence or absence of specific variants commented on in this patient's report, provide the details below. For gene-specific family follow-up see **Note** under Test Selection.*

Was the proband (individual with variant) tested at Invitae? ◯ Yes, Invitae Order ID: RQ# _____ ◯ No: Attach copy of lab results (*required*)

Variant(s) *(e.g. GENE c.2200A>T (p.Thr734Ser) NM_00012345) If left blank, all variants identified in the proband will be commented on.*		**This patient's relationship to proband:**
		◯ Parent ◯ Sibling ◯ Grandchild
		◯ Child ◯ Self ◯ Other: _____

TEST SELECTION – Select test(s) from either option 1 or 2 below:

1. UNCOVERING PERIODIC PARALYSIS PROGRAM – Indicate test(s) to be performed below:

Test code	Test name	# of genes	Gene list
◯ 03373	Invitae Periodic Paralysis Panel	6	ATP1A2, CACNA1S, KCNJ2, MCM3AP, SCN4A, RYR1

OPTIONAL AUTOMATIC REFLEX – Upon a negative result in the Invitae Periodic Paralysis Panel (results will be included in report 2)

◯ 03280	Invitae Comprehensive Neuromuscular Disorders Panel	131	ACTA1, ADSSL1, AGRN, ALG14, ALG2, AMPD1, ANO5, ATP2A1, B3GALNT2, B4GAT1, BAG3, BIN1, CACNA1S, CAPN3, CASQ1, CAV3, CCDC78, CFL2, CHAT, CHKB, CHRNA1, CHRNB1, CHRND, CHRNE, CLCN1, CNTN1, COL12A1, COL13A1, COL6A1, COL6A2, COL6A3, COLQ, CPT2, CRYAB, DAG1, DES, DMD, DNAJB6, DNM2, DOK7, DPAGT1, DPM1, DPM2, DPM3, DYSF, EMD, FHL1, FKBP14, FKRP, FKTN, FLNC, GAA, GFPT1, GMPPB, GNE, GOSR2, GYG1, GYS1, HACD1, HNRNPA2B1, HNRNPDL, ISCU, ISPD, ITGA7, KBTBD13, KCNJ2, KLHL40, KLHL41, LAMA2, LAMP2, LARGE1, LDB3, LMNA, LMOD3, MAP3K20, MATR3, MEGF10, MICU1, MTM1, MUSK, MYH2, MYH7, MYL2, MYO18B, MYOT, MYPN, NEB, ORAI1, PLEC, PNPLA2, POMGNT1, POMGNT2, POMK, POMT1, POMT2, PREPL, PYROXD1, RAPSN, RXYLT1, RYR1, SCN4A, SELENON, SGCA, SGCB, SGCD, SGCG, SLC18A3, SLC5A7, SMCHD1, SMN1, SMN2, SPEG, SQSTM1, STAC3, STIM1, SYT2, TAZ, TCAP, TIA1, TK2, TNNT1, TNPO3, TOR1AIP1, TPM2, TPM3, TRAPPC11, TRIM32, TTN, VAMP1, VCP, VMA21

2. GENE-SPECIFIC FAMILY FOLLOW-UP TESTING *For relatives of a program participant ('proband') who received a Pathogenic/Likely Pathogenic result or approved VUS.*

◯ Family follow-up testing for Proband's Invitae Order ID: RQ#_____	**This patient's relationship to proband:** ◯ Parent ◯ Sibling ◯ Grandchild ◯ Child ◯ Other: _____	**Gene(s) to be tested in this patient:**

***NOTE**: The presence or absence of all variants identified in the proband for the gene(s) ordered for gene-specific family follow-up will be commented on in this patient's report unless a limited selection is specified in the **Requested Variants** section above. Invitae will report any Pathogenic/Likely Pathogenic variants found in this patient for the gene(s) ordered.*

Invitae continually updates its panels based on the most recent evidence. If an order is placed using an outdated test requisition form, Invitae reserves the right to upgrade ordered tests to their current versions. Test IDs containing add-on codes will include the original panel as well as the add-on.

By signing this form, the medical professional acknowledges that the individual/family member authorized to make decisions for the individual (collectively, the "Patient") has been supplied information regarding and consented to undergo genetic testing, substantially as set forth in Invitae's Informed Consent for Genetic Testing (www.invitae.com/forms). The medical professional will retain evidence that the patient consented to genetic testing. The Patient has been informed that Invitae may notify them of clinical updates related to genetic test results (in consultation with the ordering medical professional as indicated) and has been informed that deidentified (also referred to as pseudonymized) patient data may be used and shared with third parties in connection with the Program, for research and commercial purposes. For orders originating outside the United States, the Patient has been informed that their personal information and specimen will be transferred to and processed in the United States. The medical professional warrants that (i) he/she will not seek reimbursement for this no-charge test from any third party, including but not limited to government healthcare programs; (ii) participation in the Program will not influence the his/her medical decisions; (iii) he/she is not obligated to purchase or prescribe any product or service offered by a sponsor of the Program; (iv) he/she is not obligated to participate in or to encourage patients to participate in any clinical trial or other research program conducted by a sponsor; and (v) he/she will participate in the Program in accordance with applicable laws. The medical professional consents to the sharing of organization and clinician contact information with third parties, including commercial organizations, who may contact the medical professional directly in connection with the Program. For California clinicians only: I have the right to opt-out of certain uses of my data, and additional rights as detailed in Invitae's privacy policy. A list of third party partners will be provided upon request. I attest that I am authorized under applicable law to order this test.

Medical professional signature (required)	**Date (MM/DD/YYYY)**

