Helix Pharmacogenomics (PGx) Tacrolimus CYP3A5 Test

Item	Description
Test Name	Helix Pharmacogenomics (PGx) Tacrolimus CYP3A5 Test
Test Type	Pharmacogenomics
Catalog Number	PTCR1
Procedure Code	H00223-1 (Helix)
Test Description	This test evaluates a patient's metabolizer status for *CYP3A5*, which can aid in optimal dosing of tacrolimus to maximize immune suppression efficacy to prevent organ rejection and reduce risk of side effects for transplant patients.
Genes Tested	*CYP3A5*
Genetics Information	This test utilizes next-generation sequencing to determine star alleles and metabolizer status for *CYP3A5*. These results are used to determine drug considerations for Tacrolimus.
Clinical Indication	Providing a genetic evaluation to determine whether oral use of tacrolimus can reduce risk of organ rejection for transplant patients.
Clinical Descriptions	Tacrolimus is an immunosuppressant prescribed to patients undergoing organ transplant to reduce risk of organ rejection. Tacrolimus reduces activity of the immune system, leading to reduced risk of organ rejection, specifically for adult patients who have received a kidney, liver, lung, or heart transplant. This drug may also be prescribed to children undergoing organ transplant under specific clinical circumstances. Blood concentrations and metabolism of tacrolimus are impacted by an individual's *CYP3A5* genotype. This information can help determine appropriate dosing in order to reduce risk of organ rejection leading to improved clinical outcomes for transplant patients.
Disease States	Adult patients undergoing organ transplant.
Interpretation	All detected variants are evaluated according to the Clinical Pharmacogenetics Implementation Consortium (CPIC). Variants are classified based on known, predicted, or possible impact on drug metabolism.
Reclassification of Variants	Helix does not systematically review variants evaluated and reported for this test looking for guideline updates or classification changes. Helix will review the classification of previously reported variants upon request of the ordering physician/provider. Ordering physicians/providers may contact Helix Customer Support to request a review of updates to CPIC guidelines and/or variant classification in terms of impact on drug metabolism. At the discretion of the laboratory director, the frequency of reclassification requests may be limited to once per year, no earlier than 12 months after initial evaluation has been performed.

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Variant Evaluation	Variant classification is performed using data provided by CPIC whenever available. When CPIC data is not available, a thorough literature search is performed to evaluate whether specific alleles have known and established impact on drug metabolism. Recommendations and interpretation for dosage and prescription are based on guidelines set forth by CPIC, the Food and Drug Administration (FDA), and the Pharmacogenomics Knowledgebase (PharmGKB). Variants are classified as having impact on drug metabolism with the following tiers: poor metabolizer, intermediate metabolizer, normal metabolizer, and ultrarapid metabolizer. These classifications are based on the combination of alleles found in the given individual and data set forth by CPIC and the other entities mentioned above. Variants of unknown significance on drug metabolism are not reported.
Turnaround Time	7 to 10 days
Available in NY State	No
Test Classification	This test was developed, and its performance characteristics determined, by Helix, Inc. in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.
Performing Laboratory Information	CLIA Laboratory Number: 05D2117342 Laboratory Hours of Operation: Monday-Saturday (7AM-10:30PM PST) Address: 10170 Sorrento Valley Road, Suite 100, San Diego, CA 92121 Helix Customer Service: (844) 211-2070 Email: support@helix.com
Regulatory Information	CLIA Complexity: High Test Classification: Non-Waived/ Laboratory Developed Test
CLIA Category	Chemistry / Routine Chemistry

Methods & Limitations for Helix Pharmacogenomics (PGx) Tacrolimus CYP3A5 Test

Data were generated from extracted DNA using the validated Helix Exome+ assay by the Helix clinical laboratory. The Exome+ assay is based on target enrichment followed by next generation sequencing using paired end reads on an Illumina DNA sequencing system. Star alleles were determined using a proprietary algorithm which performs variant calling and then determines star allele solutions based on a combination of defining SNPs and exon-level copy number. Star allele definitions came from PharmVar v5.2.22 for *CYP3A5*.

Metabolizer status was determined based on star allele solutions according to CPIC guidelines, with the following exceptions: (1) metabolizer status was set as Indeterminate if a novel nonsense or truncating novel mutation was observed within the gene, (2) metabolizer status was set as Indeterminate if the combination of defining SNPs and copy number suggested a novel star allele solution, and (3) if more than two copies of a gene were detected then metabolizer status was set as Indeterminate. Drug/gene considerations were limited to guidelines published by FDA, CPIC, or PharmGKB.

Phasing could not be performed for genotypes, and therefore in some cases the star allele solution could not be disambiguated between two or more equally likely possibilities. In these cases, if the metabolizer status was the same regardless of possible star allele solutions, the more common star allele solution was provided along with the metabolizer status. If the metabolizer status was different for the equally-likely star allele solutions, the star alleles were reported as Unknown and the metabolizer status was considered Indeterminate.

All samples were sequenced and interpreted in Helix's CLIA-certified (#05D2117342) and CAP-accredited (#9382893) laboratory in San Diego, California. These tests have not been cleared or approved by the U.S. Food and Drug Administration.

The reportable range includes the following star alleles:
CYP3A5: *1, *3, *6-*9.

Disclaimer:
The interpretations and drug considerations provided by Helix are intended solely for use by a medical professional and do not constitute medical advice by Helix. All treatment decisions and diagnoses remain the full responsibility of the treating provider. Results included in this report are based on the determined star alleles and guidelines published by the FDA and CPIC, and do not account for other factors that may impact drug response, such as environment, medical conditions, drug-drug interactions, or additional genetic variants. Helix is not responsible or liable for any errors, omissions, or ambiguities in the interpretation or use of the results of this report. Administration of any medication listed in this report requires careful therapeutic monitoring regardless of the drug considerations outlined in this report. All dates and times displayed are Pacific Time and may vary from the dates and times for Collection, Order and Report for the providers/patients.

Targeted Genes & Methodology for Helix Pharmacogenomics (PGx) Tacrolimus CYP3A5 Test

The following applies to the Helix Pharmacogenomics (PGx) Tacrolimus CYP3A5 Test. Next-generation sequencing is performed to test for the presence of star allele solutions in the genes analyzed, according to the reportable range listed.

This list is current from January 2025 to the present. For questions regarding genes, reference transcripts, or specific regions covered, Helix Customer Service at (844) 211-2070.

Catalog Number: PTCR1

Gene	Reportable Range
CYP3A5	*1, *3, *6 - *9