TEST ID: IBDGP
INFLAMMATORY BOWEL DISEASE PRIMARY IMMUNODEFICIENCY (PID) PANEL

USEFUL FOR

- Providing a comprehensive genetic evaluation for patients with a personal or family history suggestive of inflammatory bowel disease (IBD), enteropathy, hepatic primary immunodeficiency (PID), or intestinal manifestation associated with immunodeficiency
- Establishing a diagnosis and, in some cases, allowing for appropriate management and surveillance for disease features based on the gene involved
- Identifying variants within genes known to be associated with IBD, enteropathy, hepatic PID, or related disorders allowing for predictive testing of at-risk family members

GENETICS TEST INFORMATION

This test includes next-generation sequencing and supplemental Sanger sequencing to evaluate for the genes listed on the panel.

Targeted testing for familial variants (also called site-specific or known mutation testing) is available for all genes on this panel. See KVAR1 / Known Variant Analysis-1 Variant; KVAR2 / Known Variant Analysis-2 Variants; or KVAR3 / Known Variant Analysis-3+ Variants. Contact Mayo Medical Laboratories to confirm the appropriate test code for targeted testing if testing for a gene not included on this panel, or if testing for more than 5 variants is needed.

CLINICAL INFORMATION

Patients with a diverse spectrum of rare genetic disorders can present with inflammatory bowel disease (IBD). Patients with these disorders often develop symptoms during infancy or early childhood, along with endoscopic and histological features of Crohn's disease, ulcerative colitis (UC), or unclassified forms of IBD. Excessive and chronic bowel inflammation may occur as a reaction to normal gastrointestinal flora in genetically susceptible individuals. About half of the risk of developing Crohn's disease is genetically determined, while the remaining risk is modulated by environmental factors including diet and cigarette smoking. Inflammatory bowel disorders affect approximately 1 in 250 people in Western Europe, North America, and Australasia. The incidence is increasing in the developing world.

CONTENT AND VALUES SUBJECT TO CHANGE. SEE THE MAYO MEDICAL LABORATORIES TEST CATALOG FOR CURRENT INFORMATION.
Crohn's disease can affect any part of the bowel, from the mouth to the anus with inflammatory disease frequently progressing to cause strictures and fistulae in the bowel. The usual age of onset is between 15 and 30 years, but the disease can occur at any age.

UC is restricted to the colon, but has 2 important consequences: severe attacks with a high risk of urgent surgery, and an increased risk of bowel cancer.

Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome shares some common features with IBD. Diagnosis is based on clinical features and genetic testing.

Patients with features of humoral immunodeficiency may also develop enteropathy and features of IBD, for example with lipopolysaccharide (LPS)-responsive and beige-like anchor protein (LRBA) deficiency.

There are several monogenic disorders that can present with an IBD-like pathology. The prevalence of these monogenic diseases is relatively low compared to more intestinal diseases, including infections, celiac disease, and IBD. However, since the monogenic disorders are associated with high morbidity and mortality, it is imperative to diagnose them early.

IBD developing in the neonatal or infantile periods is classified as very early-onset IBD (VEOIBD) and accounts for less than 1% of pediatric patients. However, the clinical course is very severe and there is a high rate of resistance to immunosuppressive treatment.

**INTERPRETATION**

Evaluation and categorization of variants is performed using the most recent published American College of Medical Genetics and Genomics (ACMG) recommendations as a guideline. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and predictions made by these tools may change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.

**CLINICAL REFERENCE**