# Early Onset Inflammatory Bowel Disease Panel: Sequencing and CNV Analysis

## Test Code: MM160

<table>
<thead>
<tr>
<th>Turnaround time:</th>
<th>6 weeks</th>
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<td>CPT Codes:</td>
<td>81404 x1, 81406 x1, 81321 x1</td>
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## Condition Description

Inflammatory bowel disease (IBD), encompassing Crohn's disease, ulcerative colitis, and unclassified IBD (IBDU) is characterized by chronic intestinal inflammation and has multi-factorial etiology with complex interactions between genetic and environmental factors. Although the genetics of IBD is believed to be common and complex, over 150 genetic loci have been described to be associated with IBD. The genetic contribution of the majority of those common loci towards explained heritability or their effect sizes are low. Recent studies have revealed an increasing spectrum of human monogenic diseases with high effect sizes/penetrance that can present with IBD or IBD-like intestinal inflammation. A substantial proportion of patients with those genetic defects present with very early onset intestinal inflammations, particularly if the onset of IBD occurs in subjects less than 10 years of age. There is also considerable overlap between primary immunodeficiency and very early onset IBD. Over 20 monogenic defects/genetic loci have been selected in this genetic diagnostic panel to test for very early onset IBD or IBD-like diseases. In addition to IBD or IBD-like diseases, these monogenic disorders also overlap with immunodeficiency affecting granulocyte and phagocyte activity, hyper- and autoinflammatory disorders, defects with disturbed T and B lymphocyte selection and activation, and defects in immune regulation affecting regulatory T cell activity and interleukin (IL)-10 signaling.

EGL is offering a next generation sequencing diagnostic gene panel for very early onset IBD or IBD-like intestinal inflammation. The Inflammatory Bowel Disease Panel will enable the fast, accurate, and cost effective sequencing to:

- Identify mutation associated very early onset IBD (onset in less than 10 years) or IBD-like diseases
- Make a molecular diagnosis with the basis of pathogenesis
- Obtain rationale for patient-specific early intervention with emerging or experimental therapeutics and cell based approaches
- Screen family members for carrier detection and genetic counseling

## References:

- OMIM

## Genes

- AICDA, BTK, CD40LG, CYBA, CYBB, DCLRE1C, FOXP3, HPS1, HPS4, HPS6, ICOS, IL10RA, IL2RA, LRBA, MEFV, MVK, NCF2, NCF4, PTEN, RET, SH2D1A, SLC37A4, STXB2, TTC37, WAS, XIAP

## Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of inflammatory bowel diseases (IBD).
- Carrier testing in adults with a family history of inflammatory bowel diseases (IBD).

## Methodology

### Next Generation Sequencing:

In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Copy Number Analysis:

Comparative analysis of the NGS read depth (coverage) of the targeted regions of genes on this panel was performed to detect copy number variants (CNV). The accuracy of the detected variants is highly dependent on the size of the event, the sequence context and the coverage obtained for the targeted region. Due to these variables and limitations a minimum validated CNV size cannot be determined; however, single exon deletions and duplications are expected to be below the detection limit of this analysis.

## Detection

### Next Generation Sequencing:

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical sensitivity for sequence variant detection is ~99%.
Copy Number Analysis: The sensitivity and specificity of this method for CNV detection is highly dependent on the size of the event, sequence context and depth of coverage for the region involved. The assay is highly sensitive for CNVs of 500 base pairs or larger and those containing at least 3 exons. Smaller (< 500 base pairs) CNVs and those that involving only 1 or 2 exons may or may not be detected depending on the sequence context, size of exon(s) involved and depth of coverage.

**Specimen Requirements**

**Submit only 1 of the following specimen types**

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**
EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

**Type: DNA, Isolated**

**Specimen Requirements:**
Microtainer
8µg
Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Saliva**

**Specimen Requirements:**
Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Related Tests**

- IBD Targeted Hotspot Panel
- Early Onset Inflammatory Bowel Disease: Deletion/Duplication Panel