Practitioner Detailed Appendix

TOOLBOX GENOMICS

GI Panel

October 1, 2019

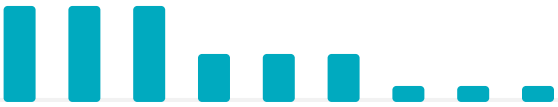
Demo Client

Kit #1234ABCD5678

Practitioner Report Key

1 Trait Impact Summary

A high level overview of which traits have the biggest impact based on our proprietary algorithm.



Impact Score	A potential impact of a variant type.
HIGH	Likely a large clinical impact
MEDIUM	Likely a slightly elevated clinical impact
LOW	Likely a low clinical impact

2 Variant Type

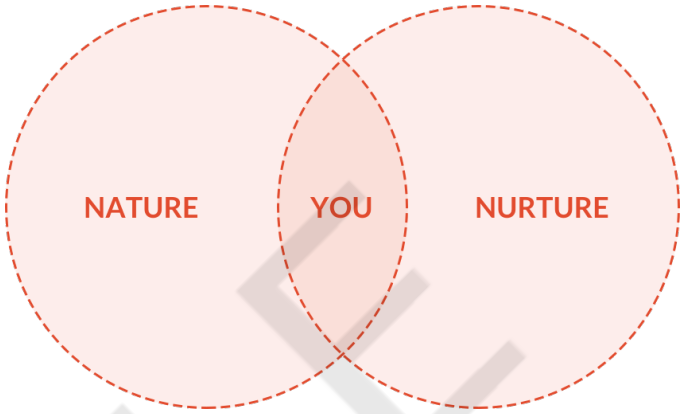
Genetic variants are the differences that make each person unique. In this report, variant refers to Single Nucleotide Polymorphisms (SNPs). + is the risk allele and - is the non-risk allele.

Variant Type	Definition
+/+	Both risk alleles present
+/-	One risk allele present
-/-	No risk allele present
+/U or -/U	Indeterminable allele
NR	Not Reportable, unable to determine variants present in the sample

3 Research Grade

The strength of the research after assessing for number of published studies, sample size of the population studied, degree of study replication, biological mechanism, and other factors.

Research Grade	Definition
***	High Research Validity
**	Medium Research Validity
*	Low Research Validity



UNDERSTANDING THE GENES

DNA is a long, ladder-shaped molecule. Each rung on the ladder is made up of a pair of interlocking units, called bases, that are designated by the four letters in the DNA alphabet - A, T, G and C. 'A' always pairs with 'T', and 'G' always pairs with 'C'.

Basic unit of heredity that is made of DNA and acts as instructions to make all body proteins. Humans have between 20,000 - 25,000 genes, half of which come from one's mother and the other half from one's father.

A SNP is a Single Nucleotide Polymorphism. DNA consists of 4 main building blocks (Adenine (A), Thymine (T), Guanine (G), and Cytosine (C)). In certain locations within DNA, one person may have an A, whereas another may have a G. This difference is often called a variant. This variant is a SNP. The rs number is a unique identifier used by researchers and databases to refer to specific SNPs. It stands for Reference SNP cluster ID.

Clinical Significance is the clinical or practical importance of a given SNP. Having a risk variant (+) for a particular SNP, increases one's predisposition to this clinical significance.

Disclaimer - This test is performed via DNA sequencing. As with all genetic testing with the highest possible standards, the data generated during the laboratory process will have a <99% sensitivity and specificity.

How These Traits Affect Your Client

This page provides a high-level snapshot of the clinical significance of each trait within this panel. The results are in two categories: traits that are ranked high, medium or low impact as well as traits for which there is an explicit result (i.e. categorical such as "yes" or "no"). At the end of this page are a summary of any non-reportable (NR) traits. The results for these traits are unable to be determined from the sample submitted. Recommendations are made for traits with high or medium impact only.

Impact Traits		Impact
1	Inflammation	HIGH
2	Celiac Disease	MEDIUM
3	Crohn's Disease	MEDIUM
4	Irritable Bowel Syndrome (IBS)	MEDIUM
5	Ulcerative Colitis	MEDIUM

Practitioner Detailed Appendix: GI Panel

Below is a summary of the genetic data that we test for in this Health Action Plan. Recommendations are given for traits with Medium and High Impact.

Traits are listed in order of trait impact. Please look at the Trait Impact Summary Report for more information.

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Inflammation	TNF-α	rs1800629	*Increased risk of elevated inflammatory response*	+/+	High	***	18676870, 27477483
Inflammation	IL6	rs1800795	*Increased risk of elevated circulating IL-6 cytokines*	+/+	High	***	15364891, 22493750
Inflammation	TNF-α	rs1799724	*Increased risk of elevated inflammatory response*	+/-	Medium	***	25835425, 30581618
Inflammation	PTPN22	rs2476601	*Increased risk of elevated inflammatory response*	+/-	Medium	***	20444268, 20453842
Inflammation	IL-10	rs1800872	*Increased risk of elevated inflammatory response*	+/-	Low	**	20444268, 24128120
Inflammation	TNF-α	rs1799964	*Increased risk of elevated inflammatory response*	-/-	Low	***	21102463, 28584644
Inflammation	IL23R	rs2201841	*Increased risk of elevated inflammatory response*	+/-	Low	**	20444268, 24128120
Inflammation	IL-10	rs3024505	*Increased risk of elevated inflammatory response*	-/-	Low	***	18836448, 20444268
Celiac Disease	KIAA1109	rs13119723	*Increased risk of Celiac Disease*	+/+	High	***	17558408, 21760890
Celiac Disease	BACH2	rs10806425	*Increased risk of Celiac Disease*	+/+	High	***	20190752
Celiac Disease	BACH2	rs7753008	*Increased risk of Celiac Disease*	+/+	High	*	22057235
Celiac Disease	CD247	rs864537	*Increased risk of Celiac Disease*	+/-	Medium	***	20190752, 27015091

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Celiac Disease	HLADQ2.5	rs2187668	*Increased risk of Celiac Disease*	-/-	Low	***	19500688, 21694611, 23936387, 24876751, 30013750
Celiac Disease	ICOS	rs4675374	*Increased risk of Celiac Disease*	-/-	Low	**	20190752, 27015091
Celiac Disease	ELMO1	rs6974491	*Increased risk of Celiac Disease*	-/-	Low	***	20190752
Celiac Disease	KIAA1109	rs4374642	*Increased risk of Celiac Disease*	-/-	Low	***	21383967, 21760890
Celiac Disease	ICOSLG	rs4819388	*Increased risk of Celiac Disease*	-/-	Low	**	20190752, 22592522
Celiac Disease	HLADQ8	rs7454108	*Increased risk of Celiac Disease*	-/-	Low	***	19500688, 21694611, 30013750
Celiac Disease	ELMO1	rs11984075	*Increased risk of Celiac Disease*	-/-	Low	**	21383967
Celiac Disease	ADAD1	rs7684187	*Increased risk of Celiac Disease*	+/-	Low	***	17558408, 19648293
Celiac Disease	ELMO1	rs79758729	*Increased risk of Celiac Disease*	-/-	Low	**	22057235
Celiac Disease	KIAA1109	rs13151961	*Increased risk of Celiac Disease*	-/-	Low	***	20190752, 24999842
Celiac Disease	BACH2	rs2474619	*Increased risk of Celiac Disease*	-/-	Low	**	24999842
Crohn's Disease	ZNF365	rs10995271	*Increased risk for Crohn's disease*	+/+	High	***	18587394, 21830272
Crohn's Disease	STAT3	rs744166	*Increased risk for Crohn's Disease and Ulcerative Colitis*	+/+	High	***	25286337, 27022745
Crohn's Disease	CDKAL1	rs6908425	*Increased risk for Crohn's disease*	+/+	High	***	17554300, 18587394
Crohn's Disease	IL23R	rs17375018	*Increased risk of Crohn's disease as well as increased likelihood of more severe symptoms*	+/+	High	***	22333126, 26678098

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Crohn's Disease	CDKAL1	rs7753394	*Increased risk for Crohn's disease*	+/+	High	***	17554300, 19956648
Crohn's Disease	IBD5	rs12521868	*Increased risk for Crohn's disease*	+/+	High	***	17213842, 27336838
Crohn's Disease	IL12B	rs10045431	*Increased risk for Crohn's disease*	+/+	High	***	18587394, 23300620
Crohn's Disease	CDKAL1	rs9469220	*Increased risk for Crohn's disease*	+/+	High	***	17554300, 27336838
Crohn's Disease	CDKAL1	rs1551398	*Increased risk for Crohn's disease*	+/+	High	***	21304977, 23300620
Crohn's Disease	BSN	rs9858542	*Increased risk for Crohn's disease*	+/+	High	***	17554300, 21618365
Crohn's Disease	TGFB1	rs1800471	*Increased risk for Crohn's disease and development of fibrosis in individuals with CD*	+/+	High	**	17047091, 27303667
Crohn's Disease	MST1	rs3197999	*Increased risk for Crohn's disease*	+/+	High	***	18438406, 18587394
Crohn's Disease	C11orf30	rs17582416	*Increased risk for Crohn's disease*	+/+	High	***	18587394, 27336838
Crohn's Disease	ICOSLG	rs762421	*Increased risk for Crohn's disease*	+/+	High	***	18587394, 19068216
Crohn's Disease	PTGER4	rs1992660	*Increased risk for Crohn's disease and other inflammatory bowel diseases*	+/+	High	**	17684544, 21548950
Crohn's Disease	PTGER4	rs2188962	*Increased risk for Crohn's disease*	+/+	High	***	21674708, 23300620
Crohn's Disease	ITLN1	rs2274910	*Increased risk for Crohn's disease*	+/+	High	***	18587394, 28243990
Crohn's Disease	ITLN1	rs11584383	*Increased risk for Crohn's disease*	+/-	Medium	***	18587394, 19068216
Crohn's Disease	ATG16L1	rs3828309	*Increased risk for Crohn's disease*	+/-	Medium	***	18587394, 23725363
Crohn's Disease	ATG16L1	rs2241880	*Increased risk for Crohn's disease*	+/-	Medium	***	17200669, 29960072

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Crohn's Disease	ORMDL3	rs2872507	*Increased risk for Crohn's, other inflammatory bowel disease, and accelerated colonic transit*	+/-	Medium	***	21752155, 27336838
Crohn's Disease	CDKAL1	rs6601764	*Increased risk for Crohn's disease*	+/-	Medium	**	17554300
Crohn's Disease	CDKAL1	rs7746082	*Increased risk for Crohn's disease*	+/-	Medium	***	21304977, 23300620
Crohn's Disease	IL23R	rs11805303	*Increased risk for Crohn's disease*	+/-	Medium	***	22333126, 26678098
Crohn's Disease	PTGER4	rs4613763	*Increased risk for Crohn's disease*	-/-	Low	***	18587394, 23300802
Crohn's Disease	CDKAL1	rs7807268	*Increased risk for Crohn's disease*	-/-	Low	**	17554300
Crohn's Disease	IL23R	rs11465804	*Increased risk for Crohn's disease*	-/-	Low	***	19175939, 26678098
Crohn's Disease	PTPN22	rs2476601	*Increased risk for Crohn's disease*	+/-	Low	***	18587394, 29456405
Crohn's Disease	LRRK2	rs11175593	*Increased risk for Crohn's disease*	-/-	Low	***	18587394, 29228965
Crohn's Disease	NOD2	rs2066844	*Increased risk for Crohn's disease*	-/-	Low	***	11385576, 30061834
Crohn's Disease	NOD2	rs2066845	*Increased risk for Crohn's disease*	-/-	Low	***	11385576, 30061834
Crohn's Disease	TNF-α	rs1799964	*Increased risk for Crohn's disease and Ulcerative Colitis*	-/-	Low	***	19673019, 21102463
Crohn's Disease	TLR9	rs5743836	*Increased risk for Crohn's, other inflammatory bowel disease, and accelerated colonic transit*	+/-	Low	**	21752155, 22346247
Crohn's Disease	AGT	rs5051	*Increased risk for Crohn's disease*	-/-	Low	**	17047091

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Crohn's Disease	IRGM	rs13361189	*Increased risk for Crohn's disease and Ulcerative Colitis*	-/-	Low	***	19491842, 29788077
Crohn's Disease	BSN	rs1000113	*Increased risk for Crohn's disease*	-/-	Low	***	17554300, 25944217
Crohn's Disease	BSN	rs10883365	*Increased risk for Crohn's disease*	-/-	Low	***	17554300, 18438406
Crohn's Disease	IRGM	rs4958847	*Inreased risk for ileal Crohn's disease*	-/-	Low	***	18580884, 29788077
Crohn's Disease	IL23R	rs1004819	*Increased risk for Crohn's disease*	+/-	Low	***	17786191, 18047539
Crohn's Disease	CDKAL1	rs8111071	*Increased risk for Crohn's disease*	-/-	Low	***	17554300, 20018022
Crohn's Disease	PTPN2	rs2542151	*Increased risk for Crohn's disease*	-/-	Low	***	17554300, 26833331
Crohn's Disease	NOD2	rs2076756	*Increased risk for Crohn's disease as well as increased risk of fistula development*	-/-	Low	***	21209938, 29434451
Crohn's Disease	NOD2	rs2066843	*Increased risk for Crohn's disease*	-/-	Low	***	21343918, 21887729
Crohn's Disease	PTPN3	rs12037606	*Increased risk for Crohn's disease*	-/-	Low	**	17554300
Crohn's Disease	CCR6	rs2301436	*Increased risk for Crohn's disease*	+/-	Low	***	18587394, 23300620
Crohn's Disease	BSN	rs10761659	*Increased risk for Crohn's disease*	-/-	Low	***	17554300, 26833331
Crohn's Disease	IRGM	rs11747270	*Increased risk of Crohn's disease as well as increased likelihood of more severe symptoms*	-/-	Low	***	18587394, 27336838
Crohn's Disease	JAK2	rs10758669	*Increased risk for Crohn's disease*	+/-	Low	***	18587394, 24385239
Crohn's Disease	CDKAL1	rs9286879	*Increased risk for Crohn's disease*	-/-	Low	***	18587394, 23300620
Crohn's Disease	NKX2-3	rs11190140	*Increased risk for Crohn's disease*	-/-	Low	***	18587394, 21830272

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Irritable Bowel Syndrome (IBS)	NPSR1	rs6972158	*Increased risk of severe symptoms related to IBS as well as accelerated GI transit times*	+/+	High	***	19732772, 25548468
Irritable Bowel Syndrome (IBS)	TLR9	rs352139	*Increased risk for post-infectious IBS (PI-IBS) and decreased response to anti-TNF treatment*	+/+	High	**	20044998, 26861312
Irritable Bowel Syndrome (IBS)	NPSR1	rs1379928	*Increased risk of severe symptoms related to IBS as well as accelerated GI transit times*	+/+	High	***	19732772, 25548468
Irritable Bowel Syndrome (IBS)	TNFSF15	rs4263839	*Increased risk for IBS and IBS-C*	+/+	High	***	21636646, 25824902
Irritable Bowel Syndrome (IBS)	FGFR4	rs351855	*Accelerated GI transit in IBS-D*	+/-	Medium	***	21396369, 25070056
Irritable Bowel Syndrome (IBS)	TNFSF15	rs7848647	*Increased risk of IBS*	-/-	Low	***	21487504, 22684480
Irritable Bowel Syndrome (IBS)	CRHR1	rs242924	*Increased risk of IBS*	-/-	Low	**	22957021, 27497153
Irritable Bowel Syndrome (IBS)	ADRA1D	rs1556832	*Increased symptom severity in patients with IBS*	+/-	Low	**	26288143
Irritable Bowel Syndrome (IBS)	TNF-α	rs1800629	*Increased risk of IBS as well as Crohn's disease*	-/-	Low	***	22684480, 28243990
Irritable Bowel Syndrome (IBS)	CDH1	rs16260	*Increased risk for post-infectious IBS (PI-IBS)*	+/-	Low	***	20044998, 21752155
Irritable Bowel Syndrome (IBS)	NXPH1	rs2349775	*Increased risk for IBD-D*	-/-	Low	**	24041540
Irritable Bowel Syndrome (IBS)	TLR9	rs5743836	*Increased risk for post-infectious IBS (PI-IBS)*	+/-	Low	***	20044998, 21752155
Irritable Bowel Syndrome (IBS)	FGFR4	rs1966265	*Accelerated GI transit in IBS-D*	-/-	Low	***	21396369, 24200957
Irritable Bowel Syndrome (IBS)	IL6	rs1800795	*Increased risk for post-infectious IBS (PI-IBS)*	-/-	Low	***	19034965, 28886490

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Irritable Bowel Syndrome (IBS)	CRHR1	rs7209436	*Increased risk of IBS*	-/-	Low	**	22957021, 27497153
Irritable Bowel Syndrome (IBS)	NPSR1	rs2609234	*Increased risk of severe symptoms related to IBS as well as accelerated GI transit times*	-/-	Low	***	19732772, 25548468
Irritable Bowel Syndrome (IBS)	TNFSF15	rs6478108	*Increased risk of IBS*	-/-	Low	***	17663424, 22684480
Irritable Bowel Syndrome (IBS)	TNFSF15	rs6478109	*Increased risk of IBS*	-/-	Low	***	22684480, 27336838
Ulcerative Colitis	STAT3	rs744166	*Increased risk of Ulcerative Colitis*	+/+	High	***	25133031, 25286337
Ulcerative Colitis	IL23R	rs1343151	*Increased risk of Ulcerative Colitis and Irritable Bowel Syndrome*	+/+	High	***	19175939, 27902482
Ulcerative Colitis	IL23R	rs76418789	*Increased risk of Ulcerative Colitis*	+/+	High	***	26398853, 27490946
Ulcerative Colitis	IRF5	rs4728142	*Increased risk of Ulcerative Colitis*	+/-	Medium	***	23971939, 26398853
Ulcerative Colitis	LAMB1	rs2158836	*Increased risk of Ulcerative Colitis*	+/-	Medium	***	19122664, 27336838
Ulcerative Colitis	IL-10	rs1800896	*Increased risk of Ulcerative Colitis in females*	+/-	Medium	**	18569989, 27528546
Ulcerative Colitis	TLR4	rs4986791	*Increased risk of Ulcerative Colitis*	+/-	Medium	*	15207785
Ulcerative Colitis	JAK2	rs1830610	*Increased risk of Ulcerative Colitis*	+/-	Medium	**	26398853
Ulcerative Colitis	INAVA	rs7554511	*Increased risk of Ulcerative Colitis*	+/-	Medium	***	19915572, 28436939
Ulcerative Colitis	IL23R	rs11805303	*Younger age of UC disease onset and increased disease lesions*	+/-	Medium	***	22333126, 25133031
Ulcerative Colitis	HLA	rs11554257	*Increased risk of Ulcerative Colitis*	-/-	Low	*	20848476

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Ulcerative Colitis	IL-10	rs1800872	*Increased risk of Ulcerative Colitis*	+/-	Low	**	28142034, 29720026
Ulcerative Colitis	IL-10	rs1800871	*Increased risk of Ulcerative Colitis*	+/-	Low	**	20509889, 24128120
Ulcerative Colitis	HNF4A	rs6017342	*Increased risk of Ulcerative Colitis*	+/-	Low	***	21297633, 27903283
Ulcerative Colitis	HLA-DRB1	rs2395185	*Increased risk of Ulcerative Colitis*	+/-	Low	***	19122664
Ulcerative Colitis	TLR4	rs4986790	*Increased risk of Ulcerative Colitis*	+/-	Low	**	15194649
Ulcerative Colitis	IL23R	rs2201841	*Increased risk of Ulcerative Colitis and Irritable Bowel Syndrome*	+/-	Low	***	19175939, 28210080
Ulcerative Colitis	IL23R	rs10489629	*Increased risk of Ulcerative Colitis*	-/-	Low	***	19175939
Ulcerative Colitis	IL-10	rs3024505	*Increased risk of Ulcerative Colitis*	-/-	Low	***	18836448, 25133031
Ulcerative Colitis	FCGR2A	rs1801274	*Increased risk of Ulcerative Colitis*	+/-	Low	**	26398853, 27156530
Ulcerative Colitis	CIITA	rs4781011	*Increased risk of Ulcerative Colitis*	+/-	Low	**	20228799, 25010687
Ulcerative Colitis	GPR12-USP12	rs17085007	*Increased risk of Ulcerative Colitis*	-/-	Low	***	26398853, 27156530
Ulcerative Colitis	HLA	rs3749946	*Increased risk of Ulcerative Colitis*	-/-	Low	***	20176734, 24837172