Practitioner Detailed Appendix

TOOLBOX GENOMICS

Immune Panel

October 1, 2019

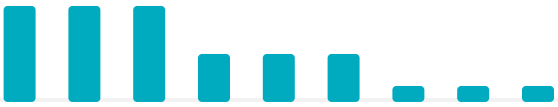
Demo Client

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

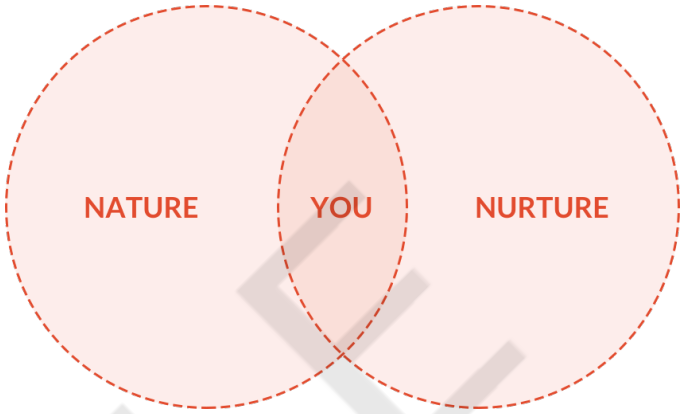
Genetic variants are the differences that make each person unique. In this report, variant refers to Single Nucleotide Polymorphisms (SNPs). + is the risk allele and - is the non-risk allele.

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	Rheumatoid Arthritis	MEDIUM
3	Hashimoto's Thyroiditis	LOW
4	Multiple Sclerosis	LOW
5	Psoriasis	LOW

Practitioner Detailed Appendix: Immune 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
Rheumatoid Arthritis	TNFAIP3	rs6920220	*Increased risk of RA*	+/+	High	***	28199970
Rheumatoid Arthritis	ANAPC4	rs3816587	*Increased risk of RA*	+/+	High	**	18794857, 20017963
Rheumatoid Arthritis	PTPN22	rs1217410	*Increased risk of RA*	+/+	High	*	16175503
Rheumatoid Arthritis	PTPN22	rs2476601	*Increased risk of RA*	+/-	Medium	***	20453842, 24449572

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Rheumatoid Arthritis	REL	rs13031237	*Increased risk of RA*	+/-	Medium	***	19503088, 23106574
Rheumatoid Arthritis	STAT4	rs7574865	*Increased risk of RA*	+/-	Medium	***	18576330, 19479340
Rheumatoid Arthritis	CCR6	rs3093024	*Increased risk of RA*	+/-	Medium	***	26131115
Rheumatoid Arthritis	NCF4	rs729749	*Increased risk of RA*	+/-	Medium	*	17897462
Rheumatoid Arthritis	AFF3	rs10865035	*Increased risk of RA*	+/-	Medium	***	20453842, 24449572
Rheumatoid Arthritis	TNFAIP3	rs5029937	*Increased risk of RA*	-/-	Low	***	28199970
Rheumatoid Arthritis	C6orf10	rs6910071	*Increased risk of RA*	-/-	Low	**	21383967, 24270849
Rheumatoid Arthritis	NOS3	rs2070744	*Increased risk of RA with possibility of increased clinical manifestations, e.g. pain*	-/-	Low	**	18830734, 27695991
Rheumatoid Arthritis	CDK6	rs42041	*Increased risk of RA, with possibility of increased rate of joint breakdown*	-/-	Low	**	19644859, 21586211
Rheumatoid Arthritis	TNFAIP3	rs2230926	*Increased risk of RA*	-/-	Low	***	28199970
Rheumatoid Arthritis	TLR3	rs3775291	*Increased risk of RA*	-/-	Low	**	19479340, 25304972
Rheumatoid Arthritis	CD40	rs4810485	*Increased risk of RA*	-/-	Low	***	18794853, 25908480
Rheumatoid Arthritis	HLA-DRB1	rs615672	*Increased risk of RA*	+/-	Low	*	17554300, 20017963
Hashimoto's Thyroiditis	ATXN2	rs653178	*Increased risk of being positive for TPO antiboties*	+/-	Medium	*	24586183
Hashimoto's Thyroiditis	MAGI3	rs1230666	*Increased risk for elevated TPO antibodies, TSH, hypothyroidism*	+/-	Medium	**	24586183

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Hashimoto's Thyroiditis	TNF-α	rs1800629	*Increased risk for Hashimotos*	-/-	Low	*	25127106
Hashimoto's Thyroiditis	PTPN22	rs12730735	*Increased risk for Hashimotos*	-/-	Low	*	22069277
Hashimoto's Thyroiditis	IL6	rs1800795	*Increased risk for Hashimotos*	-/-	Low	**	25127106
Hashimoto's Thyroiditis	BACH2	rs10944479	*Increased risk of being positive for TPO antiboties, increased TSH and hypothyroidism*	-/-	Low	*	24586183
Multiple Sclerosis	IL2RA	rs2104286	*Increased risk of MS*	+/+	High	***	22117963
Multiple Sclerosis	FLJ34870	rs1437898	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	C1orf125	rs12047808	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	MAF	rs404694	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	CRYBA4	rs5997184	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	CAST1	rs11719646	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	MGC13125	rs180358	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	JMJD2C	rs16925027	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	CBLB	rs9657904	*Increased risk of MS*	+/+	High	***	20453840, 21037273
Multiple Sclerosis	C16orf47	rs7191888	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	NALP11	rs299175	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	HIVEP2	rs263153	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	NPHP3	rs6794496	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	IL7R	rs6897932	*Increased risk of MS*	+/+	High	**	20194581, 25422737
Multiple Sclerosis	CHORDC1	rs1354913	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	CPAMD8	rs6512158	*Increased risk of MS*	+/+	High	*	19010793
Multiple Sclerosis	CPAMD8	rs11666377	*Increased risk of MS*	+/+	High	*	19010793

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Multiple Sclerosis	FOXO3	rs9486902	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	IRX1	rs4866550	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	CDH10	rs10078091	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	ZNF433	rs3745672	*Increased risk of MS*	+/-	Medium	*	20598377
Multiple Sclerosis	FUT9	rs6899560	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	WDR7	rs1557351	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	KIAA1706	rs1806468	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	FLJ16641	rs12638253	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	LRRC41	rs12142240	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	FOXO3	rs9480865	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	NAALADL2	rs7432623	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	C20orf133	rs368380	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	CHSY1	rs8043243	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	CHSY1	rs752092	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	FLJ16641	rs10936043	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	MKI67	rs7914524	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	FRS3	rs3804281	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	MLANA	rs2150702	*Increased risk of MS*	+/-	Medium	***	22190364
Multiple Sclerosis	IMMP2L	rs868824	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	CBLN2	rs337718	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	C1GALT1	rs10259085	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	CDCA1	rs10917727	*Increased risk of MS*	+/-	Medium	*	19010793
Multiple Sclerosis	KCNB2	rs2116078	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	TNFRSF1A	rs1800693	*Increased risk in TNF pathway stimulation which plays a role in development in MS*	-/-	Low	*	23624563, 24174586

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Multiple Sclerosis	IGF2R	rs12202350	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	NUBPL	rs2039485	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	CD6	rs17824933	*Increased risk of MS*	-/-	Low	***	27994359
Multiple Sclerosis	JARID2	rs6941421	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	CENPC1	rs10518025	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	C9orf150	rs12553535	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	HLA-DRA	rs3135388	*Increased risk of MS*	-/-	Low	***	22253788, 23186557
Multiple Sclerosis	NLGN1	rs13067869	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	MET	rs10243024	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	C6orf10	rs3129934	*Increased risk of MS*	-/-	Low	***	18941528, 22457343
Multiple Sclerosis	KCNIP1	rs11957313	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	IGF2R	rs6917747	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	GPR126	rs146250	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	LOC132321	rs1478091	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	COX10	rs7211577	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	HLA-DRA	rs3129871	*Increased risk of MS*	-/-	Low	*	23472185
Multiple Sclerosis	BICD1	rs261902	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	DKK2	rs10516537	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	C18orf24	rs2028455	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	LOC132321	rs2035213	*Increased risk of MS*	-/-	Low	*	19010793
Multiple Sclerosis	TNFRSF1A	rs4149584	*Increased risk of MS*	-/-	Low	*	21247752
Psoriasis	ETS1	rs3802826	*Increased risk for psoriasis*	+/+	High	*	23143594
Psoriasis	TNFSF15	rs6478109	*Increased risk for psoriasis*	+/+	High	**	24269700

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Psoriasis	IL23R	rs9988642	*Increased risk for psoriasis*	+/+	High	*	23143594
Psoriasis	STAT2	rs2066819	*Increased risk for psoriasis*	+/+	High	*	23143594
Psoriasis	RNF114	rs1056198	*Increased risk for psoriasis*	+/+	High	*	23143594
Psoriasis	TYK2	rs34536443	*Increased risk for psoriasis*	+/+	High	*	23143594
Psoriasis	IL13	rs1295685	*Increased risk for psoriasis*	+/+	High	*	23143594
Psoriasis	ZMIZ1	rs1250546	*Increased risk for psoriasis*	+/+	High	*	23143594
Psoriasis	KCNH7	rs17716942	*Increased risk for psoriasis; possible earlier age of onset*	+/-	Medium	*	23143594
Psoriasis	IL12B	rs3213094	*Increased risk for psoriasis*	+/-	Medium	**	20606885, 27073425
Psoriasis	FLJ16341	rs62149416	*Increased risk for psoriasis*	+/-	Medium	*	23143594
Psoriasis	EXOC2	rs9504361	*Increased risk for psoriasis*	+/-	Medium	*	23143594
Psoriasis	POLI	rs545979	*Increased risk for psoriasis*	+/-	Medium	*	23143594
Psoriasis	RPS6KA4	rs645078	*Increased risk for psoriasis*	+/-	Medium	*	23143594
Psoriasis	TNFAIP3	rs582757	*Increased risk for psoriasis*	+/-	Medium	***	23143594, 25521225
Psoriasis	CARD11	rs4722404	*Increased risk for psoriasis, most notably earlier onset*	+/-	Medium	**	27421022
Psoriasis	CARD14	rs11652075	*Increased risk for psoriasis*	+/-	Low	***	23905699, 27706581
Psoriasis	TSC1	rs1076160	*Increased risk for psoriasis*	+/-	Low	*	21623003
Psoriasis	TRAF3IP2	rs33980500	*Increased risk for psoriasis*	-/-	Low	*	23116200, 23143594

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Psoriasis	FOXP3	rs2232365	*Increased risk for psoriasis*	+/-	Low	*	22435141
Psoriasis	STX1B	rs12445568	*Increased risk for psoriasis*	-/-	Low	*	23143594
Psoriasis	DDX58	rs11795343	*Increased risk for psoriasis*	-/-	Low	*	23143594
Psoriasis	ELMO1	rs2700987	*Increased risk for psoriasis*	-/-	Low	*	23143594
Psoriasis	IL23R	rs2082412	*Increased risk for psoriasis*	+/-	Low	*	19169254
Psoriasis	PTRF	rs963986	*Increased risk for psoriasis*	-/-	Low	*	23143594
Psoriasis	TNIP1	rs2233278	*Increased risk for psoriasis*	-/-	Low	**	23143594, 29020033
Psoriasis	NOS2	rs28998802	*Increased risk for psoriasis*	-/-	Low	**	23143594, 26626624