Practitioner Detailed Appendix

TOOLBOX GENOMICS

Energy/Fatigue Panel

October 1, 2019

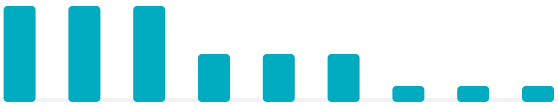
Demo Client

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

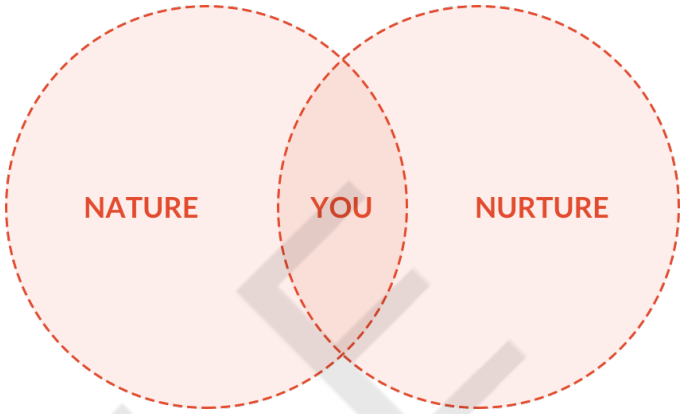
Genetic variants are the differences that make each person unique. In this report, variant refers to Single Nucleotide Polymorphisms (SNPs). + is the risk allele and - is the non-risk allele.

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.

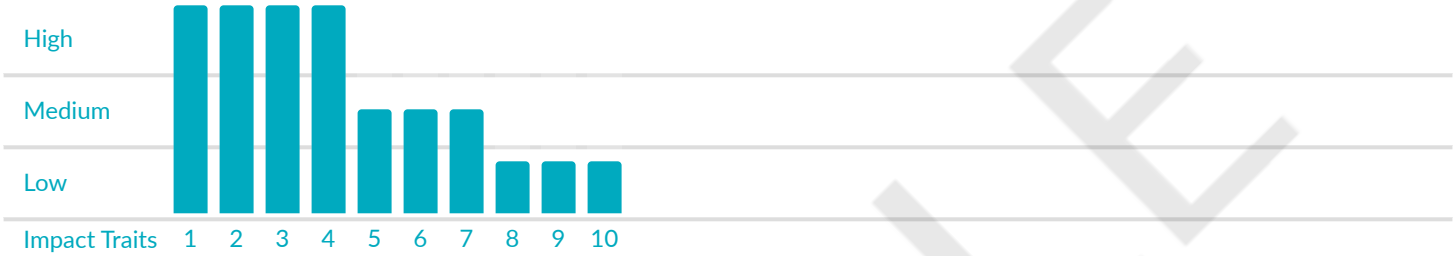
A SNP is a Single Nucleotide Polymorphism. DNA consists of 4 main building blocks (Adenine (A), Thymine (T), Guanine (G), and Cytosine (C)). In certain locations within DNA, one person may have an A, whereas another may have a G. This difference is often called a variant. This variant is a SNP. The rs 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	Cortisol	HIGH
2	Depression	HIGH
3	Inflammation	HIGH
4	Oxidative Stress	HIGH
5	Migraines	MEDIUM
6	Osteoarthritis	MEDIUM
7	Stress Response	MEDIUM
8	Chronic Fatigue Syndrome	LOW
9	Fibromyalgia	LOW
10	Musculoskeletal Pain	LOW

Practitioner Detailed Appendix: Energy/Fatigue 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)
Cortisol	FKBP5	rs1360780	*Reduced circulating levels of cortisol*	+/+	High	***	21316860
Cortisol	FKBP5	rs9470080	*Associated with impaired cortisol production*	+/+	High	***	24856550, 28850857
Cortisol	FKBP5	rs7748266	*Reduced circulating levels of cortisol*	+/-	Medium	***	21316860
Depression	HTR1A	rs6295	*Increased risk of major depressive disorder*	+/+	High	***	22752684, 30083112
Depression	HTR1A	rs878567	*Increased risk of major depressive disorder*	+/+	High	***	22752684, 27897266
Depression	FKBP5	rs3800373	*Increased risk of major depressive disorder following traumatic event*	+/+	High	***	21865530, 29466454
Depression	SLC6A4	rs25531	*Increased risk of major depressive disorder*	+/+	High	***	17938638, 30121542
Depression	FKBP5	rs1360780	*Increased risk of depressive disorders*	+/+	High	***	21865530, 29182159
Depression	FKBP5	rs9296158	*Increased risk of major depressive disorder following traumatic event*	+/+	High	***	21865530, 28889074
Depression	CRHR1	rs110402	*Increased risk of major depressive disorder*	+/+	High	***	22467522, 27544317
Depression	GNB3	rs5443	*Increased risk of major depressive disorder*	+/+	High	**	17938638, 30083112
Depression	CHRH2	rs3779250	*Increased risk of major depressive disorder*	+/+	High	**	22467522, 26543368
Depression	MTHFR	rs1801133	*Increased risk of major depressive disorder*	+/-	Medium	**	17938638, 30083112

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Depression	KSR2	rs7973260	*Increased risk for depression*	+/-	Medium	**	27089181, 27898078
Depression	LHPP	rs35936514	*Increased risk of major depressive disorder*	-/-	Low	***	26176920, 30083112
Depression	SLC6A15	rs1545843	*Increased risk of major depressive disorder*	+/-	Low	***	21521612, 30083112
Depression	SIRT1	rs12415800	*Increased risk of major depressive disorder*	-/-	Low	***	26176920, 30083112
Depression	PCLO	rs2522833	*Increased risk of depressive disorders*	+/-	Low	***	22386049, 30083112
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
Oxidative Stress	UGT	rs1105879	*Increased risk for elevated levels of oxidative stress*	+/+	High	***	19267064, 25355624

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Oxidative Stress	CDKN	rs10811661	*Increased risk for elevated levels of oxidative stress*	+/+	High	*	29777116
Oxidative Stress	GSTP1	rs1695	*Increased risk for elevated levels of oxidative stress*	-/-	Low	***	11535248, 28208751
Oxidative Stress	CYP1A1	rs1048943	*Increased risk for elevated levels of oxidative stress*	-/-	Low	***	17590289, 30068618
Oxidative Stress	LRRK2	rs34637584	*Increased risk for elevated levels of oxidative stress*	-/-	Low	***	28420983, 28927418
Oxidative Stress	SOD2	rs4880	*Increased risk for elevated levels of oxidative stress*	+/-	Low	***	27271305, 29331597
Migraines	TRPM8	rs10166942	*Increased risk of migraines*	+/+	High	***	22683712, 23294458
Migraines	PDRM16	rs2651899	*Increased risk of migraines*	+/+	High	***	21666692, 25388962
Migraines	ASTN2	rs6478241	*Increased risk of migraines*	+/-	Medium	***	22683712, 30256423
Migraines	PHACTR1	rs9349379	*Increased risk of migraines*	+/-	Medium	*	22683712
Migraines	ADH1B	rs1229984	*Increased risk of migraines*	+/-	Medium	*	19486361
Migraines	LRP1	rs11172113	*Increased risk of migraines*	+/-	Medium	***	21666692, 25667298
Migraines	SUGCT	rs4379368	*Increased risk of migraines*	-/-	Low	***	23793025, 28079315
Migraines	MEF2D	rs3790459	*Increased risk of migraines*	-/-	Low	*	22683712
Migraines	MEF2D	rs1925950	*Increased risk of migraines*	-/-	Low	*	22683712
Migraines	MEF2D	rs3790455	*Increased risk of migraines*	-/-	Low	**	22683712, 24674449
Migraines	MEF2D	rs1050316	*Increased risk of migraines*	-/-	Low	**	22683712

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Migraines	TRPM8	rs17862920	*Increased risk of migraines*	-/-	Low	*	22683712
Migraines	MEF2D	rs2274316	*Increased risk of migraines*	-/-	Low	**	22683712, 28058730
Migraines	FHL5	rs13208321	*Increased risk of migraines*	-/-	Low	***	23793025, 28079315
Migraines	MEF2D	rs12136856	*Increased risk of migraines*	-/-	Low	*	22683712
Osteoarthritis	MCF2L	rs11842874	*Increased risk of OA of the knee*	+/+	High	***	21871595, 22615457
Osteoarthritis	GLT8D1	rs6976	*Increased risk of OA*	+/+	High	**	22763110, 25939412
Osteoarthritis	FTO	rs8044769	*Increased risk of OA*	+/+	High	**	22763110, 27696742
Osteoarthritis	GNL3	rs11177	*Increased risk of OA*	+/+	High	**	22763110, 29942097
Osteoarthritis	TP63	rs12107036	*Increased risk of OA of the knee*	+/-	Medium	*	22763110
Osteoarthritis	COG5	rs3815148	*Increased risk for major joint OA and for enhanced disease progression*	+/-	Medium	**	20112360
Osteoarthritis	CHST11	rs835487	*Increased risk of OA at the hip and knee*	+/-	Medium	***	22763110, 27391021
Osteoarthritis	DUS4L	rs4730250	*Increased risk of OA of the knee*	-/-	Low	**	21068099
Osteoarthritis	BTNL2	rs10947262	*Increased risk of OA of the knee*	-/-	Low	**	20305777, 20691797
Osteoarthritis	HLA-DBQ1	rs7775228	*Increased risk of OA of the knee*	+/-	Low	**	20305777
Osteoarthritis	PTHLH	rs10492367	*Increased risk of OA*	-/-	Low	**	22763110
Osteoarthritis	RBFOX1	rs716508	*Increased risk for hand OA*	-/-	Low	***	19508968
Osteoarthritis	ASTN2	rs4836732	*Incresead risk of OA*	-/-	Low	**	22763110

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Osteoarthritis	ALDH1A2	rs3204689	*Increased risk for severe OA of the hand*	-/-	Low	**	24728293
Osteoarthritis	SENP6	rs9350591	*Increased risk of OA at all major joints*	-/-	Low	**	22763110
Osteoarthritis	CDC5L	rs10948172	*Increased risk of OA*	-/-	Low	*	22763110
Stress Response	COMT	rs4680	*Higher cortisol, depression and PTSD in response to stress*	+/-	Medium	***	23799032, 25068285
Stress Response	BDNF	rs6265	*Higher cortisol, depression, and anxiety in response to life stress*	-/-	Low	***	24433458, 25419135
Stress Response	HTR2C	rs6318	*Higher cortisol levels, increased risk of depression and eating dysregulation in response to life stress*	-/-	Low	***	21967853, 25457638
Chronic Fatigue Syndrome	NPAS2	rs356653	*Increased risk of chronic fatigue*	+/-	Medium	*	21912186
Chronic Fatigue Syndrome	GRIK2	rs2247215	*Increased risk of chronic fatigue*	-/-	Low	*	21912186
Fibromyalgia	ADRA1A	rs1383914	*Increased risk of fibromyalgia*	+/+	High	*	19565482
Fibromyalgia	ADRA1A	rs1048101	*Increased risk of fibromyalgia*	+/+	High	*	19565482
Fibromyalgia	FAM173b	rs13361160	*Increased risk for symptoms of chronic widespread pain*	+/+	High	***	22956598
Fibromyalgia	HTR2A	rs6313	*Increased fibromyalgia susceptibility*	+/-	Medium	*	18196244
Fibromyalgia	COMT	rs4818	*Increased risk of more severe pain symptoms in patients with fibromyalgia*	+/-	Low	**	21120493, 22528689
Fibromyalgia	ADRB3	rs4994	*Increased risk of fibromyalgia*	-/-	Low	*	19565482

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Fibromyalgia	COMT	rs6269	*Increased risk of pain and fatigue symptoms in patients with fibromyalgia*	+/-	Low	**	17961261, 22528689
Fibromyalgia	ADRA1A	rs574584	*Increased risk of fibromyalgia*	-/-	Low	*	19565482
Fibromyalgia	COMT	rs4680	*Increased risk of more severe pain symptoms in patients with fibromyalgia*	+/-	Low	*	21120493
Fibromyalgia	ADRA1A	rs573542	*Increased risk of fibromyalgia*	-/-	Low	*	19565482
Fibromyalgia	SCN9A	rs6754031	*Increased risk of more severe pain symptoms in patients with fibromyalgia*	-/-	Low	*	22348792
Musculoskeletal Pain	HTR2A	rs17289394	*Increased number of pain sites in musculoskeletal pain*	+/-	Medium	**	21305503
Musculoskeletal Pain	SERPINA6	rs8022616	*Increased number of pain sites in chronic widespread pain*	-/-	Low	**	19723618
Musculoskeletal Pain	MC2R	rs11661134	*Increased number of pain sites in chronic widespread pain*	-/-	Low	**	19723618
Musculoskeletal Pain	HTR2A	rs12584920	*Increased risk of chronic widespread pain*	-/-	Low	**	21305503
Musculoskeletal Pain	SERPINA6	rs941601	*Increased risk of experiencing musculoskeletal pain*	-/-	Low	**	19723618
Musculoskeletal Pain	CRHBP	rs1875999	*Increased number of pain sites in skeletal muscle*	-/-	Low	**	19723618