Practitioner Detailed Appendix

TOOLBOX GENOMICS

Detox Panel

October 1, 2019

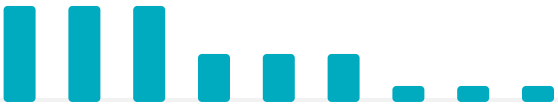
Demo Client

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

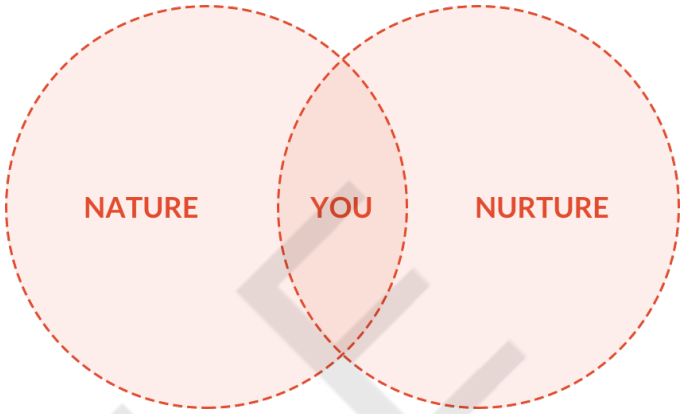
Genetic variants are the differences that make each person unique. In this report, variant refers to Single Nucleotide Polymorphisms (SNPs). + is the risk allele and - is the non-risk allele.

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.

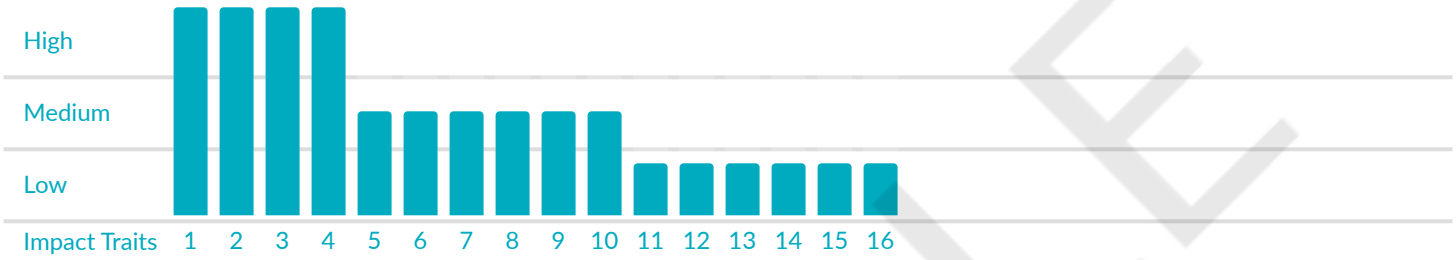
A SNP is a Single Nucleotide Polymorphism. DNA consists of 4 main building blocks (Adenine (A), Thymine (T), Guanine (G), and Cytosine (C)). In certain locations within DNA, one person may have an A, whereas another may have a G. This difference is often called a variant. This variant is a SNP. The rs 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 Oxidative Stress	HIGH
3 SOD	HIGH
4 SULT	HIGH
5 CYP1B1	MEDIUM
6 Estrogen Metabolism	MEDIUM
7 Glutathione	MEDIUM
8 MTHFR	MEDIUM
9 NAT	MEDIUM
10 SLC	MEDIUM
11 CYP1A1	LOW
12 CYP1A2	LOW
13 CYP2s	LOW
14 Nrf2	LOW
15 SUOX	LOW
16 UGT	LOW

Categorical Traits	Result	Learn More
1 COMT	Average Metabolizer	

Practitioner Detailed Appendix: Detox 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
Oxidative Stress	UGT	rs1105879	*Increased risk for elevated levels of oxidative stress*	+/+	High	***	19267064, 25355624
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

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
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
SOD	SOD2	rs4880	*Increased inflammation, impaired lipid metabolism*	+/-	Medium	***	19706356, 29681991
SULT	SULT1A1	rs1801030	*Decreased enzyme activity, altered drug and hormone metabolism*	+/+	High	***	25992585, 30068618
SULT	SULT1A1	rs1042157	*Decreased enzyme activity, altered drug and hormone metabolism*	+/-	Medium	***	20881232, 30120701
CYP1B1	CYP1B1	rs1056837	*Altered 17-beta-estradiol metabolism*	+/+	High	***	18763031, 18805939
CYP1B1	CYP1B1	rs1056836	*Increased enzyme activity, altered drug and hormone metabolism*	-/-	Low	***	18544568, 29344273
Estrogen Metabolism	GSTM1	rs366631	*Decreased enzyme activity, altered estrogen synthesis and metabolism*	+/+	High	*	15005800, 19383894
Estrogen Metabolism	CYP1A1	rs2606345	*Altered hormone and carcinogen metabolism, increased mammographic density, high toxin exposure*	+/-	Medium	***	18415690, 19630952
Estrogen Metabolism	CYP1A1	rs4646422	*Reduced enzyme activity in xenobiotic metabolism pathways*	-/-	Low	***	23139742, 24320736
Estrogen Metabolism	CYP2D6	rs1065852	*Inhibition of enzyme activity, altered drug and steroid metabolism*	-/-	Low	***	17115111, 19809024

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Estrogen Metabolism	GSTP1	rs1695	*Elevated inflammatory response, increased oxidative stress*	-/-	Low	***	18988661, 27043589
Estrogen Metabolism	CYP1A1	rs1048943	*Reduced enzyme activity in xenobiotic metabolism pathways*	-/-	Low	***	16949388, 18159984
Estrogen Metabolism	CYP1A2	rs2069514	*Decreased enzyme activity, altered estrogen synthesis and metabolism*	-/-	Low	***	20559687, 23128882
Estrogen Metabolism	CYP1A2	rs762551	*Increased enzyme activity, increased 2:16 estrogen ratio, also metabolizes caffeine*	+/-	Low	***	17507615, 18398030
Estrogen Metabolism	COMT	rs4680	*Moderate to poor antidepressent response due to lower enzyme activity, decreased enzyme activity in prefrontal cortex*	+/-	Low	***	18194538, 18989660
Estrogen Metabolism	CYP1A1	rs2470893	*Decreased xenobiotic and drug metabolism*	-/-	Low	***	19479063, 25228414
Estrogen Metabolism	CYP1A1	rs4646903	*Decreased enzyme activity, altered estrogen synthesis and metabolism*	-/-	Low	***	19608585, 29326607
Glutathione	GSTM1	rs366631	*Decreased enzyme activity, increased exposure to toxins, increased oxidative stress*	+/+	High	***	19383894, 20103664
Glutathione	GSTA1	rs3957357	*Decreased enzyme activity, reduced xenobiotic metabolism, and increased oxidative stress*	+/-	Medium	***	24471578, 27936036
Glutathione	GSTP1	rs1695	*Decreased enzyme activity resulting in altered catechol estrogen pathway and elevated estrogen quinones*	-/-	Low	***	18988661, 29785881

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Glutathione	GSS	rs17309872	*Reduced enzyme activity for xenobiotic drug metabolism pathway including clearance of pesticides*	-/-	Low	**	21636554, 21716162
Glutathione	GSTM5	rs3754446	*Decreased ezyme activity, altered steroid hormone metabolism*	-/-	Low	**	21487324, 27043589
MTHFR	MTHFR	rs1801133	*Associated with decreased enzyme activity, impaired folate metabolism and elevated homocysteine levels*	+/-	Medium	***	23824729, 29845757
NAT	NAT1	rs15561	*Intermediate/rapid-acetylators, increased potential for toxin accumulation*	+/-	Medium	***	16847422, 24151610
NAT	NAT2	rs1799930	*Intermediate/rapid-acetylators, increased potential for toxin accumulation*	+/-	Medium	***	16847422, 24151610
NAT	NAT1	rs6586714	*Intermediate/rapid-acetylators, increased potential for toxin accumulation*	+/-	Medium	**	22552404
NAT	NAT2	rs1801280	*Intermediate/rapid-acetylators, increased potential for toxin accumulation*	-/-	Low	***	16847422, 24151610
NAT	NAT2	rs1799929	*Decreased enzyme activity resulting in low acetylator status*	-/-	Low	***	19823052, 29505746
NAT	NAT2	rs1208	*Decreased enzyme activity resulting in low acetylator status*	-/-	Low	***	21989592, 22092036
NAT	NAT1	rs4987076	*Intermediate/rapid-acetylators, increased potential for toxin accumulation*	-/-	Low	***	16847422, 24151610
NAT	NAT2	rs1799931	*Intermediate/rapid-acetylators, increased potential for toxin accumulation*	-/-	Low	***	16847422, 24151610

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
NAT	NAT1	rs4986988	*Decreased enzyme activity, poor acetylator*	-/-	Low	**	26409796
NAT	NAT2	rs4271002	*Decreased enzyme activity, slow acetylator, increased inflammatory response*	-/-	Low	**	22389292, 23622008
NAT	NAT1	rs4986782	*Intermediate/rapid-acetylators, increased potential for toxin accumulation*	-/-	Low	***	16847422, 24151610
NAT	NAT2	rs1801279	*Decreased enzyme activity resulting in low acetylator status*	-/-	Low	***	16112301, 27223070
NAT	NAT2	rs1041983	*Decreased enzyme activity, poor acetylator*	+/-	Low	***	18936436, 26409796
SLC	SLC19A1	rs1888530	*Impaired folate metabolism*	+/-	Medium	**	20683905
SLC	SLC19A1	rs3788189	*Altered folate metabolism, increased promoter region activity*	+/-	Low	***	24732178
CYP1A1	CYP1A1	rs2470893	*Decreased enzyme activity, decrease for B[a]P epoxidation and phenylimidazopyridine metabolism*	-/-	Low	***	19479063, 23492908
CYP1A1	CYP1A1	rs4646903	*Increased enzyme activity, altered estrogen synthesis and metabolism, increased toxin exposure*	-/-	Low	***	19608585, 29326607
CYP1A1	CYP1A1	rs1048943	*Decreased enzyme activity in xenobiotic metabolism pathways*	-/-	Low	***	18159984, 18990750
CYP1A2	CYP1A2	rs762551	*Increased enzyme activity, fast caffeine metabolizer, increased 2:16 estrogen ratio*	+/-	Low	***	17507615, 18398030
CYP1A2	CYP1A2	rs2069514	*Decreased activity, impaired drug and steroid hormone metabolism*	-/-	Low	***	20559687, 23128882

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
CYP2s	CYP2A3	rs1801272	*Decreased enzyme activity, impaired xenobiotic metabolism*	-/-	Low	***	23049750, 29724170
CYP2s	CYP2D6	rs3892097	*Poor drug and steroid hormone metabolism*	-/-	Low	***	18070221, 30093869
CYP2s	CYP2A3	rs28399433	*Decreased enzyme activity, impaired drug metabolism*	-/-	Low	***	19339270, 22046326
Nrf2	NFE2L2	rs2364723	*Decreased enzyme activity and increased serum HMOX1 levels*	+/-	Medium	***	27374075, 27866025
Nrf2	NFE2L2	rs10497511	*Decreased enzyme activity, elevated glycosyltransferase activity*	-/-	Low	**	27374075
Nrf2	NFE2L2	rs13001694	*Decreased enzyme activity, elevated glycosyltransferase activity*	-/-	Low	**	24790085, 27374075
Nrf2	NFE2L2	rs1806649	*Decreased enzyme activity, elevated glycosyltransferase activity*	-/-	Low	***	24790085, 27374075
Nrf2	NFE2L2	rs6726395	*Decreased enzyme activity*	-/-	Low	**	16252231, 20196834
Nrf2	NFE2L2	rs1962142	*Decreased enzyme activity, elevated glycosyltransferase activity*	-/-	Low	**	27226772, 27374075
SUOX	SUOX	rs121908007	*Impaired sulfite oxidase activity as well as decreased serum molybdenum levels, and B12 deficiencies*	-/-	Low	**	9428520, 9600976
UGT	UGT	rs10929302	*Decreased enzyme activity, altered drug metabolism or drug response*	-/-	Low	***	18992148, 30093869
UGT	UGT	rs1105879	*Decreased enzyme activity, altered drug metabolism or drug response*	-/-	Low	***	18992148, 29425227

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
UGT	UGT	rs4148323	*Decreased enzyme activity, altered drug metabolism or drug response*	-/-	Low	***	19238116, 28900877
UGT	UGT	rs199539868	*Decreased enzyme activity, altered drug metabolism or drug response*	-/-	Low	**	24856997
UGT	UGT	rs114982090	*Decreased enzyme activity, altered drug metabolism or drug response*	-/-	Low	**	24856997
UGT	UGT	rs28934877	*Decreased enzyme activity, altered drug metabolism or drug response*	-/-	Low	***	19572200, 30093869
UGT	UGT	rs4124874	*Decreased enzyme activity, altered drug metabolism or drug response*	-/-	Low	***	18992148, 30093869
UGT	UGT	rs2070959	*Decreased enzyme activity, altered drug metabolism or drug response*	-/-	Low	***	18992148, 29425227
COMT	COMT	rs4680	*Average enzyme activity, average drug metabolism and stress management*	+/-	Medium	***	18989660, 19071221, 24816252, 29941295