Practitioner Detailed Appendix

TOOLBOX GENOMICS

Hormone Panel

October 1, 2019

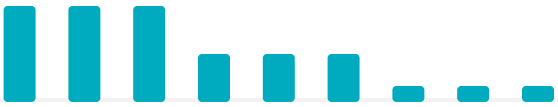
Demo Client

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

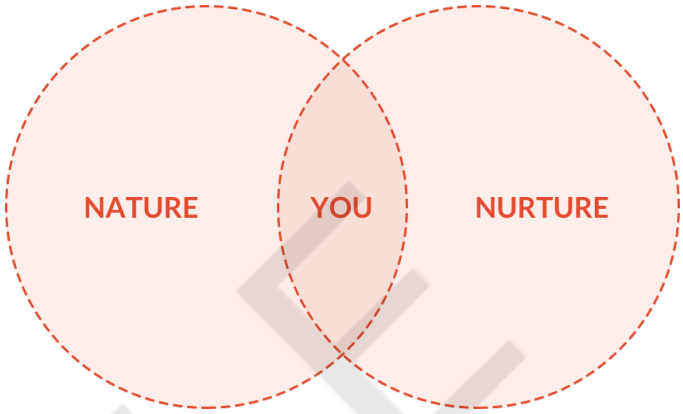
Genetic variants are the differences that make each person unique. In this report, variant refers to Single Nucleotide Polymorphisms (SNPs). + is the risk allele and - is the non-risk allele.

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	DHEA	HIGH
3	Estrogen	MEDIUM
4	Estrogen Metabolism	MEDIUM
5	Testosterone in Men	MEDIUM
6	Progesterone	LOW

Practitioner Detailed Appendix: Hormone 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
DHEA	SULT2A1	rs2637125	*Decreased serum DHEA levels, as well as altered steroid and drug metabolism*	+/+	High	***	21533175
DHEA	BCL2L11	rs6738028	*Decreased DHEA levels and potentially altered steroid metabolism*	+/+	High	***	21533175
DHEA	HHEX	rs2497306	*Decreased DHEA levels and potentially altered steroid metabolism*	+/+	High	***	21533175
DHEA	TRIM4	rs17277546	*Decreased serum DHEA levels as well as impaired xenobiotic metabolism*	+/-	Medium	***	21533175
DHEA	CYP2C9	rs2185570	*Decreased DHEA levels and potentially altered steroid metabolism*	+/-	Medium	***	21533175
DHEA	ZKSCAN5	rs11761528	*Decreased serum DHEA levels as well as impaired xenobiotic metabolism and potentially altered linoleic acid metabolism*	-/-	Low	***	21533175

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Estrogen	ESR1	rs9340799	*Lower circulating levels of estrogen and decreased mammographic density in females*	+/-	Medium	***	17889406, 27717337
Estrogen	ESR1	rs2077647	*Altered estrogen synthesis and metabolism in both males and females*	+/-	Medium	***	16477637, 27717337
Estrogen	LOC101928278	rs13387042	*Altered estrogen signaling, increased levels of 16-OH estradiols*	+/-	Medium	***	17529974
Estrogen	SHBG	rs6259	*Increased circulating levels of estradiol and SHBG hormones*	-/-	Low	***	22633539
Estrogen	ESR2	rs1256049	*Altered estrogen signaling, increased levels of 16-OH estradiols*	-/-	Low	***	23352710, 29414691
Estrogen	TNRC9/ CASC16	rs3803662	*Altered estrogen signaling, increased levels of 16-OH estradiols*	-/-	Low	***	17529974
Estrogen	ESR1	rs728524	*Altered estrogen synthesis and metabolism*	-/-	Low	***	16949394, 17889406
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
Testosterone in Men	FAM9B	rs5934505	*Low circulating serum testosterone levels in males*	+/+	High	***	21998597
Testosterone in Men	SHBG	rs727428	*Elevated serum SBHG levels and impaired androgen hormone metabolism in males*	+/+	High	**	21252242, 22936694
Testosterone in Men	PDE7B	rs7774640	*Low circulating serum testosterone levels in males*	+/-	Medium	**	21383644
Testosterone in Men	SHBG	rs12150660	*Low circulating serum testosterone levels in males*	-/-	Low	***	21998597
Testosterone in Men	SHBG	rs6258	*Low circulating serum testosterone levels in males*	-/-	Low	***	21998597

Trait	Gene	SNP/RSID	Clinical Significance	Variant Type	SNP Impact Score	Research Grade	References (PMID)
Testosterone in Men	FSHB	rs10835638	*Lower FSH levels in males as well as significantly reduced circulating levels of free testosterone*	-/-	Low	**	18567894
Progesterone	PGR	rs608995	*Altered progesterone receptor signaling, decreased circulating levels of progesterone*	-/-	Low	***	20547493
Progesterone	PGR	rs10895068	*Increased progesterone receptor transcription activity, altered progesterone to estrogen ratio*	-/-	Low	***	19462450
Progesterone	PGR	rs1042838	*Altered progesterone receptor signaling, decreased circulating levels of progesterone*	-/-	Low	***	15632380, 16614108, 18628428