



# dnapain

## Welcome

Example2 Example1

## to your DNA Pain report

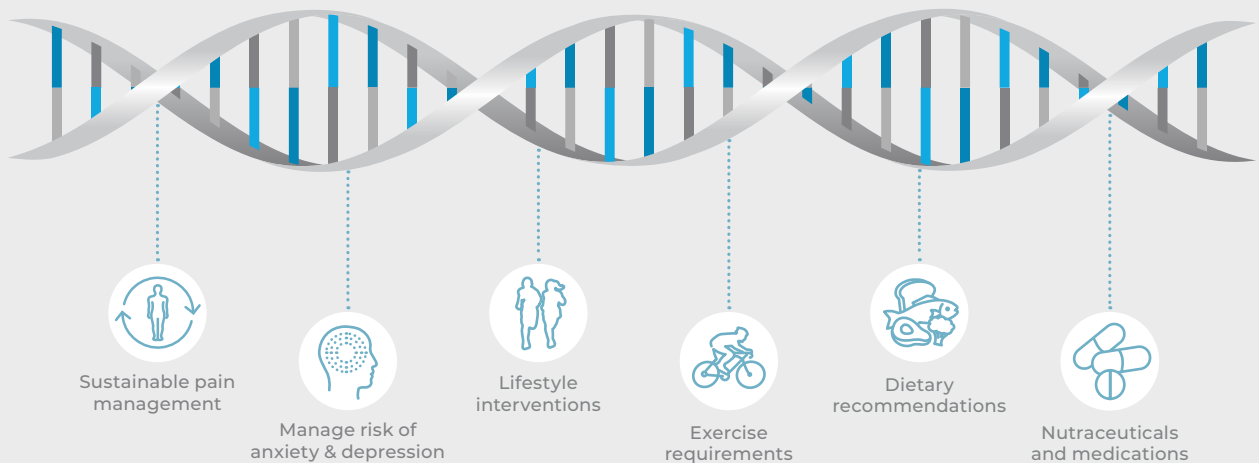
Date of birth: 01 Jan 2001

Date reported: 15 May 2024

Sample number: 12345678-New

Referring practitioner: Private

DNA Pain is a genetic test that offers insight into key biological pathways that influence chronic pain and comorbid conditions, offering personalised diet, nutraceutical, exercise and lifestyle recommendations for improved chronic pain management.



## Genetics and personalised medicine

Genes are segments of DNA that contain the instructions your body needs to make each of the many thousands of proteins required for life. Each gene is comprised of thousands of combinations of "letters" (called bases) which make up your genetic code. The code gives the instructions to make the proteins required for proper development and function.

Genetic variations (small differences in our DNA) can affect the expression of a gene, thereby affecting metabolic processes that are important for maintaining cellular health and how we respond to environmental interventions such as diet, lifestyle, supplements, and medication. Knowledge of these genetic variations offers unparalleled insight into your biological systems, allowing your healthcare practitioner to recommend precise interventions aimed at helping you reach your goals and achieve optimal health.



### NORMAL GENE

Genotype resulting in baseline risk for chronic pain



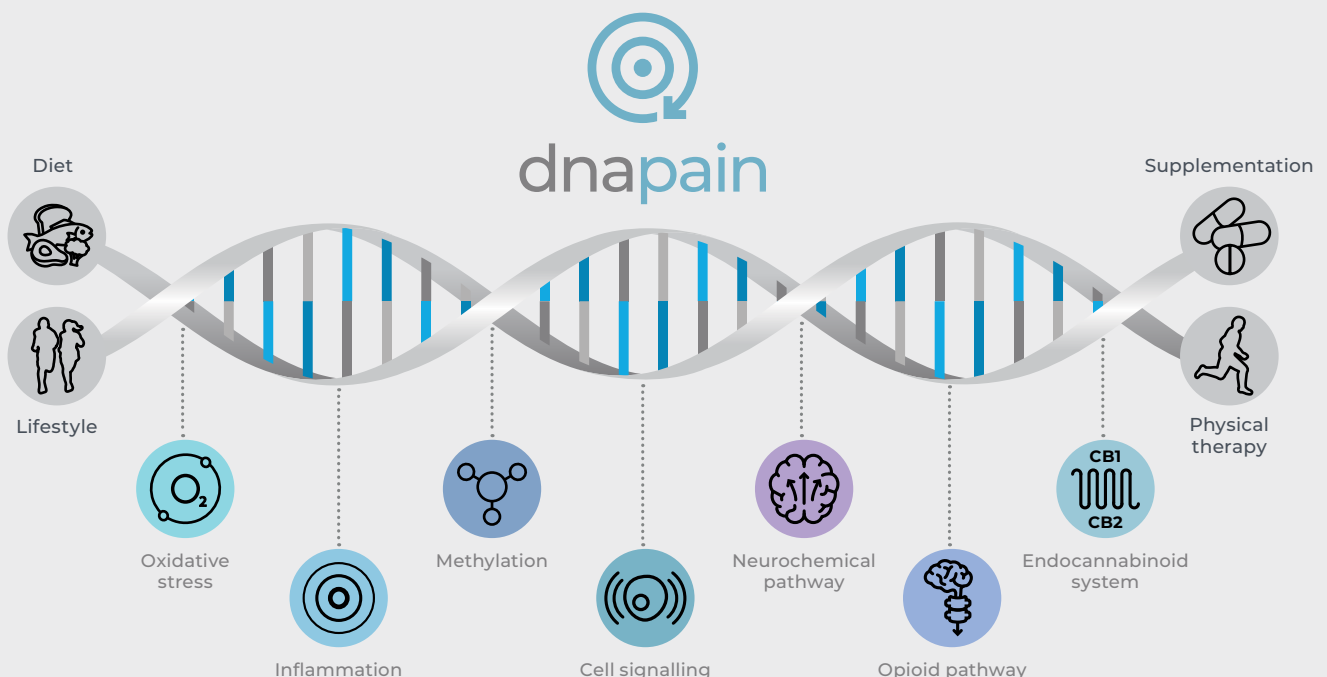
### VARIANT GENE

Genotype resulting in an increased risk for chronic pain and need for personalisation

## Personalised medicine and chronic pain

Chronic pain is defined as any persistent or intermittent pain that lasts more than 3 months. Whilst injury or a disease may be the primary cause of chronic pain, only a small minority of those subjected to injury develop chronic pain. Research shows that chronic pain is highly heritable, meaning there is a strong genetic component.

This report tests for genetic variations associated with changes in key biological pathways known to modulate susceptibility to chronic pain. Weaknesses in these pathways, together with environmental factors, can increase risk for the development of chronic pain. This report provides valuable insights into individual priority areas that should be considered for successful and sustained chronic pain management outcomes with a focus on personalised diet, nutraceutical, exercise, and lifestyle interventions.

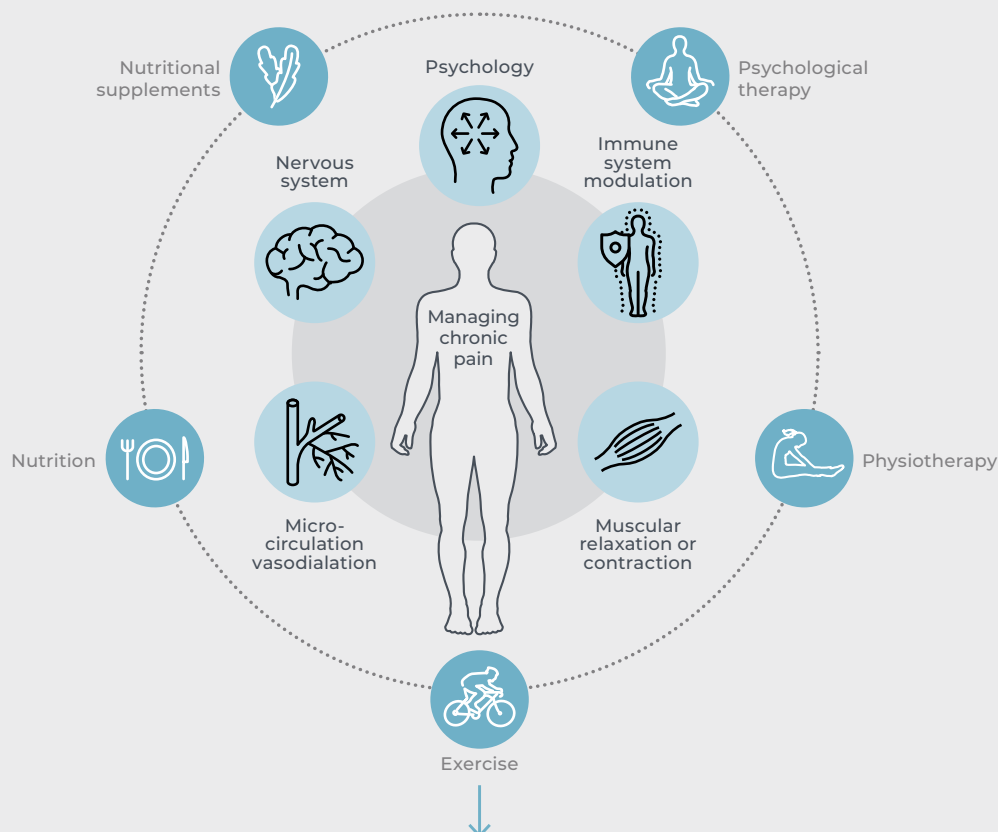


## Understanding chronic pain

Chronic pain affects 1 in 5 people globally, and features prominently in the top 10 causes of disability. It is a complex multifactorial disease that is the result of an interplay between an individual's environment, lifestyle, and genetic make-up which influence the duration, intensity, perception and effects (physical, psychological, social & emotional) of chronic pain. Evidence shows that genetic variants associated with chronic pain can influence the function of various biological pathways. In addition, those suffering from chronic pain are at a higher risk of comorbid conditions such as anxiety or depression which can exacerbate pain perception because of their shared biological pathways and overlapping pathophysiology.

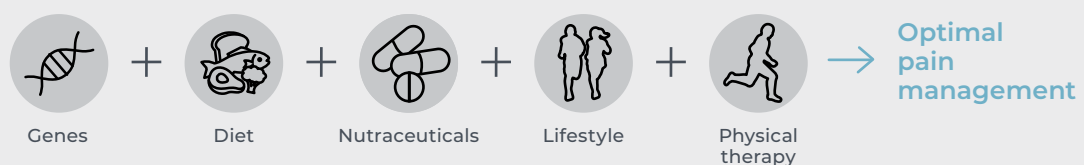
Current chronic pain management treatments are associated with negative side-effects and display variable effectiveness at the population level (attributed to interindividual variability in pharmacokinetic and pharmacodynamic properties of analgesic medications). Evidence-based non-pharmacological treatment approaches including nutritional/dietary modification, physical training exercises, and cognitive & behavioural mind/body techniques are now becoming more widely used. These approaches have improved morbidity and function in patients with chronic pain, and simultaneously reduced the risks and impact of common comorbidities. They also have reduced risk of adverse events and addiction liability. The knowledge gained from this test supports the implementation of a holistic and personalised approach to managing chronic pain.

### DNA PAIN PROVIDES INSIGHTS INTO KEY BIOLOGICAL PATHWAYS FOR IMPROVED & SUSTAINABLE MANAGEMENT OF CHRONIC PAIN








#### To improve motivation, compliance & sustainable outcomes:

identify and implement a personalised approach to chronic pain management



## Result summary

Each biological area, influencing chronic pain, has been allocated a priority rating of either low, moderate, or high priority, for you to understand where your focus areas should be. Based on the genes tested, a low priority biological area means that there is no need for increased support compared to standard health recommendations. A moderate or high priority biological area means that the particular area will require increased support with regards to appropriate diet, exercise and lifestyle interventions to off-set the imbalances in that pathway caused by the genetic variants you carry. Detailed information on each biological area is provided in the body of this report.

BIOLOGICAL AREA	PRIORITY
 Oxidative stress	
 Inflammation	
 Methylation	
 Cell signalling	
 Neurochemical pathway	
 Serotonin	
 Catecholamines	
 Opioid pathway	
 Endocannabinoid system	










## Summary recommendations

Based on your priority area outcomes, we have provided summary recommendations for the key area's you should be focusing on for successful and sustained chronic pain management. Personalised recommendations for diet, supplementation, exercise, and lifestyle, to support your priority areas, are summarised below.

**DIET****NUTRACEUTICAL****EXERCISE****LIFESTYLE**

## Genotype results

No Impact
  Low Impact
  Moderate Impact
  High Impact
  Beneficial Impact

BIOLOGICAL AREA	GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
 Oxidative stress	FAM173B	T>C	TT	
 Inflammation	IL-1A	-889 C>T	TC	
	IL-1RN	-87 G>A	GG	
	IL-6	-174 G>C	CC	
	TNFA	-308 G>A	GG	
 Methylation	MTHFR	677 C>T	CT	
	MTHFR	1298 A>C	AA	
	MTR	2756 A>G	AG	
 Cell signalling	KCNS1	A>G	GG	
 Neurochemical pathway	NPY	-399 C>T	CC	
	BDNF	Val66Met	TT	
 Serotonin	HTR2A	-1438G>A	GG	
 Catecholamines	ANKK1 (DRD2)	Taq1A/2A (C>T)	TC	
	COMT	Val158Met	GG	
 Opioid pathway	OPRM1	118 G>A	GG	
 Endocannabinoid system	FAAH	Pro129Thr	AC	

## Gene results per biological area with personalised recommendations



### Oxidative stress

Reactive oxygen species (ROS) play an essential role in several biological processes and are natural products of oxygen metabolism. Under certain environmental pressures, ROS levels can increase and overwhelm the antioxidant system. The resulting imbalance causes a state of oxidative stress which leads to lipid, protein and DNA damage at the cellular and tissue level. Altered ROS levels can also initiate proinflammatory cascades and activate microglia in the central nervous system resulting in chronic pain development.



### Oxidative stress results

#### Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
FAM173B	T>C	TT	

## Gene and genotype specific information



### FAM173B

FAM173B encodes a unique class of mitochondrial lysine-specific methyltransferases and promotes reactive oxygen species (ROS) production in neurons after transient peripheral inflammation, leading to persistent inflammatory and chronic pain.

### Result: TT

No variant was detected at this FAM173B locus.







## Inflammation

Inflammation is the body's immune response to pathogens, injury, or contaminants. All pain states – nociceptive, neuropathic, and mixed pain – are associated with inflammation. An increase in pro-inflammatory cytokines is linked to the maintenance and induction of neuropathic pain, and these cytokines and free radicals produced at the site of injury may be involved with nociceptor sensitization and maintenance of nerve-injury-induced pain. In the absence of injury, nerve inflammation causes neuropathic-like pain and induces spontaneous activity away from the generation site. Genetic variations in inflammation genes have been shown to alter their expressions or functions and thus may be associated with an altered risk for pain severity and a poorly regulated inflammatory response. One might experience this heightened inflammation as an 'all-over' or non-specific body pain.



### Inflammation results

#### Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
IL-1A	-889 C>T	TC	
IL-1RN	-87 C>T	GG	
IL-6	-174 G>C	CC	
TNFA	-308 G>A	GG	

## Gene and genotype specific information



### IL-1A

IL-1A, a pro-inflammatory cytokine and member of the IL-1 family. IL-1 has been increasingly implicated as an important leverage point in the inflammatory cascade, and IL-1 expression is therefore key in the pathogenesis of several chronic diseases.

Certain genetic variations in IL-1A can lead to a more active inflammatory response, and have been associated with increased risk for a number of chronic diseases including chronic pain.

### Result: TC

The T allele is associated with an enhanced promoter activity resulting in increased gene expression. Individuals with CT genotype have slightly enhanced levels of IL-1A, resulting in an increased activation of IL-1 receptors and a more pronounced inflammatory response. These individuals may experience increased pain intensity and have reduced pressure pain thresholds, especially following disk herniation. The effect is much more pronounced if individuals with a T allele, have an A allele at the IL-1RN -87 G>A locus. Address inflammation through implementation of a Mediterranean style diet, weight management, daily intake of anthocyanin-rich foods (blueberries) and omega 3 fatty acids. Promote collagen health and consider nutrients including hydrolysed collagen and vitamin C. Ensure adequate levels of iron and vitamin D. Engage in regular, guided physical therapy and practice mindfulness. Aquatic exercise (2/week) and core-stability exercises (3-5/week) have shown significant benefit.



### IL-1RN

IL-1RN, encodes the IL-1 receptor antagonist (IL-1Ra), which is a negative regulator of the pro-inflammatory response. This antagonist binds to the same cell receptors as IL-1 and blocks its inflammatory actions. Genetic variations in the IL-1RN gene can negatively affect IL-1Ra resulting in uncontrolled IL-1-induced systemic inflammation.

### Result: GG

No variant was detected at the -87 G>A locus.



## IL-6

Interleukin 6 (IL-6) is a pro-inflammatory cytokine that plays a crucial role in inflammation and regulates expression of C-reactive protein (CRP). IL-6 plays a pivotal role in the pathophysiology of pain sensitization with higher IL-6 levels associated with the incidence of developing neuropathic pain.

## Result: CC

Carriers of the CC genotype may be predisposed to dyslipidaemia and other chronic diseases of lifestyle, especially in the presence of a Modern Western diet, with a high saturated fat intake and high omega6:omega3 ratio. These individuals show strong and positive gene-environment interactions by following a Mediterranean style diet, limiting saturated fat and refined carbohydrates, and ensuring adequate omega 3 fat intake.



## TNFA

Tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ), a pro-inflammatory cytokine, is involved in both acute and chronic inflammation and has the ability to drive production of other types of cytokines. It is produced by various immune cells but mainly secreted by macrophages in the periphery and microglia in the central nervous system, where it can influence neuronal networks in order to modulate pain signalling.

## Result: GG

No variant was detected at the -308 G>A locus.





## Methylation

Methylation involves the process of creating methyl groups that can be added to a molecule, or substrate, and plays an essential role in the production of neurotransmitters. In order for methylation reactions to be completed, specific amounts of B-vitamins are required. B-vitamins are nutrients that are derived from the diet. Poor methylation function due to enzymatic deficiencies as well as low levels of B-vitamins have been associated with an increased risk of mood disorders.



### Methylation results

#### Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
MTHFR	677 C>T	CT	
MTHFR	1298 A>C	AA	
MTR	2756 A>G	AG	

## Gene and genotype specific information



### MTHFR

Methylene tetrahydrofolate reductase, the enzyme encoded by MTHFR, catalyses the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, which is a co-substrate for homocysteine remethylation to methionine. Reduced enzyme activity, due to function-reducing polymorphisms, results in the impairment of homocysteine metabolism and the folate cycle, leading to a decreased ability to synthesise important neurotransmitters.

### Result: CT

The T allele results in a 30% reduction in enzyme function and is associated with risk of elevated homocysteine levels and a decreased ability to synthesise neurotransmitters. Individuals with the CT genotype are at an increased risk of developing mood disorders, including depressive disorder. Increase intake of vitamin B-rich foods (dark green leafy vegetables, lentils, salmon) and, if necessary, supplement with a B-complex vitamin that includes methylated folate.

### Result: AA

No variant was detected at this locus, and the AA genotype does not alter the MTHFR enzyme activity.



### MTR

MTR encodes methionine synthase, which is responsible for the regeneration of methionine from homocysteine, using 5-methyltetrahydrofolate as its essential co-factor. This enzyme is dependent on methylcobalamin, and forms part of the S-adenosylmethionine (SAMe) biosynthesis and regeneration cycle.

### Result: AG

The G allele is associated with altered methionine synthase enzymatic capacity, resulting in increased levels of homocysteine. Individuals carrying the G allele have increased susceptibility for depressive disorder especially when there is low vitamin B12 status. Increase intake of vitamin B12 foods (eggs, clams) and supplement if necessary.





## Cell signalling

Injuries to peripheral nerves, either through trauma or disease, can lead to neuropathic pain. In both situations, inflammatory mediators are released and trigger alterations in primary sensory neurons, resulting in hyperexcitability, axonal conduction alterations and increased neurotransmitter release. This altered activity can also result from changes in the properties and/or expression of various types of voltage-gated potassium (K<sup>+</sup>) channels, suggesting that these K<sup>+</sup> channels play a vital role in regulating neuronal excitability.



### Cell signalling results

#### Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
KCNST	A>G	GG	

## Gene and genotype specific information



### KCNS1

The KCNS1 gene encodes a potassium channel alpha subunit and is involved in neuronal excitability. It is constitutively expressed in sensory neurons, with expression being markedly downregulated following nerve injury.

### Result: GG

There is evidence that people with the G allele are at an increased risk of developing neuropathic pain, following nerve injury and are prone to chronic postsurgical pain. Such individuals require special effort to avoid nerve damage at surgery, as well as aggressive early treatment in the presence of an unavoidable nerve lesion, to prevent a transition from acute to chronic pain. Participating in a physical therapist-guided pre-operative exercise programme may assist with healing time and improve quality of life post-surgery. Continued physiotherapy, mindfulness, and a phytonutrient-rich diet combined with caloric restriction may show added benefit.





## Neurochemical pathway

The neurochemical pathway plays a key role in neurogenesis by supporting the differentiation, maturation, and survival of neurons in the nervous system. The neuropeptides and neurotrophins in this pathway exert neuroprotective effects by regulating calcium homeostasis, attenuating neuroinflammation and the toxic effects of activated microglia, rendering neuronal cells resilient to neurodegeneration. Any alterations in this pathway, could result in a homeostatic imbalance, leading to mood disorders and inflammatory diseases.



### Neurochemical pathway results

#### Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
NPY	-399 C>T	CC	
BDNF	Val66Met	TT	



## Gene and genotype specific information



### NPY

NPY protects against stress-induced depression, and anxiety, and helps one to perform better mentally and physically under pressure. It is also involved in pain reduction by counteracting the primary stress hormones (cortisol and adrenaline).

### Result: CC

Individuals with the C allele may be more prone to anxiety in stressful situations, which results in low mood and depression as well as physical pain. These individuals also have a higher susceptibility to stress related inflammatory conditions. Incorporate anti-inflammatory interventions, from diet to physical therapy. Make use of a good quality probiotic daily, and increase vagal tone through deep breathing and cold water immersion.



### BDNF

BDNF, encoding brain derived neurotrophic factor, is a member of the nerve growth factor family of proteins. It is believed to promote many aspects of brain development, such as neuronal cell survival, differentiation, migration, dendritic arborization, synaptogenesis, and plasticity. It is proposed that this gene may take part in the regulation of the stress response and in the biology of neurodegenerative and mood disorders.

### Result: TT

The presence of the met (T) allele results in a 25% reduction in activity-dependent secretion of BDNF in the central nervous system (CNS). The T allele also predisposes to mood disorders such as depressive disorder and anxiety related disorders, especially after psycho-social stress exposure. Encourage adequate time outdoors, achieve optimal vitamin D levels, and ensure a daily physical activity routine to increase expression of BDNF.





## Serotonin

Serotonin, or 5-hydroxytryptamine, is a monoamine neurotransmitter that is derived from tryptophan. It is primarily found in the gastrointestinal tract, as well as blood platelets, and the central nervous system (CNS). Serotonin plays a key role in regulation of mood, appetite, sleep, cognitive functions, and pain perception. Serotonin receptor genes, mainly acting at post-synaptic neurons, regulate the serotonin levels in the brain. Genetic variations in these genes are known to regulate gene expression by affecting receptor binding potentials, resulting in either inhibition or excitation at post-synaptic neurons.



### Serotonin results

#### Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
HTR2A	-1438G>A	GG	

## Gene and genotype specific information



### HTR2A

5-hydroxytryptamine (serotonin) receptor 2A (HTR2A) is a G protein-coupled receptor that is encoded by the HTR2A gene. HTR2A not only plays a pronociceptive role resulting in increased spinal nociceptive transmission and central sensitisation but is also known to modulate mood and behaviour.

### Result: GG

The GG genotype is associated with normal HTR2A receptor function and expression.





## Catecholamines

Catecholamines act both as neurotransmitters and hormones vital to the maintenance of homeostasis. Dopamine is the most abundant catecholaminergic neurotransmitter that is synthesized in the brain and plays a critical role in the regulation of emotions, motivation, reward and reinforcement behavior, through the mesocorticolimbic pathway. Alterations to catecholaminergic neurotransmitters may result in an increased susceptibility to cognitive decline, altered mood regulation and pain sensitivity.



### Catecholamine results

#### Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
ANKK1 (DRD2)	Taq1A/2A (C>T)	TC	
COMT	Val158Met	GG	

## Gene and genotype specific information



### DRD2

DRD2 encodes the D2 subtype of the dopamine receptor, which is integral in the reward-circuitry pathway. The gene has been linked to co-morbid conditions associated with chronic pain, such as mood disorders and addictive behaviour disorders.

### Result: TC

The T allele is associated with a reduced number of dopamine binding sites in the brain. Individuals with the CT genotype are at an increased risk of developing mood disorders, such as depression, especially with previous traumatic exposures. Regular massage therapy and intake of vitamin D, omega 3 fatty acids and tyrosine may assist with balancing dopamine levels.



### COMT

COMT, encoding the catechol-O-methyl transferase enzyme, metabolizes catecholamines and thus modulates adrenergic, noradrenergic and dopaminergic signalling in the central nervous system and in the peripheral tissue. Given the number and nature of the neurotransmitters metabolized by COMT, this enzyme has been found to play a role in pain sensitivity and susceptibility as well as mood and other psychological outcomes.

### Result: GG

The COMT GG genotype is associated with faster COMT activity and thus accelerated breakdown of excitatory catecholamines including dopamine.





## Opioid pathway

The endogenous opioid system is widely distributed throughout the descending pain pathway, and plays an important role in various physiological functions including regulation of pain, emotion and the response to stress. The opioid system consists of the opioid peptides, which act as neurotransmitters and neuromodulators and exert their influence by activating opioid receptors. This causes a cascade of intracellular events which ultimately suppresses excitatory neurotransmitter release, culminating in analgesia and reduced perception of pain. Alterations to the opioid pathway can result in greater sensitivity to pain, altered analgesic responses to opioid administration and depressive-like symptoms. Opioid therapy has a place in pain management, but is only part of the solution, and some individuals see reduced responsiveness, as well as increased risk for addiction to opioid therapy. All patients should be screened using the Opioid Risk Tool (ORT) for risk for addiction.



### Opioid pathway results

#### Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
OPRM1	G>A	GG	

## Gene and genotype specific information



### OPRM1

OPRM1 encodes the mu opioid receptor (MOR), which is the principal target of endogenous opioid peptides and opioid analgesic agents such as beta-endorphin and enkephalins. The peptides exert their influence by activating opioid receptors, causing a cascade of intracellular events which ultimately suppresses excitatory neurotransmitter release, culminating in analgesia and reduced perception of pain.

### Result: GG

The OPRM1 GG genotype is associated with lower expression of mu opioid receptors, resulting in greater sensitivity to pain and depressive-like symptoms. Individuals carrying the G allele have a reduced response to morphine and other opioids. This is important to keep in mind when prescribing the type and dose of pain medication and provides insight in managing expectations. Recommend tai-chi (60 min, 2 times/week) as part of an exercise regime.





## Endocannabinoid system

The endocannabinoid system is thought to participate in the regulation of fear and anxiety responses, the immune system, and pain perception. The system consists of the cannabinoid receptors, their naturally occurring endogenous ligands, and the enzymes involved in their biosynthesis and degradation. Genetic variation in a key enzyme has shown a robust gene-environment interaction. Understanding this interaction could prove useful in the management of chronic pain.



### Endocannabinoid system results

#### Genotype result table:

GENE NAME	GENE VARIATION	RESULT	GENE IMPACT
FAAH	Pro129Thr	AC	



## Gene and genotype specific information



### FAAH

FAAH encodes Fatty Acid Amide Hydrolase, an enzyme that is expressed in the brain and liver. It deactivates N-arachidonoyl-ethanolamine (AEA), an endogenous central cannabinoid 1 agonist. FAAH plays an important role in pain, depression, appetite, and anxiety, and has been shown to be associated with risk for substance abuse.

### Result: AC

The AC genotype is not associated with any significant change in enzyme function.



# A lifetime of optimal health awaits you

Your genes do not change, which means our laboratories will only ever need one sample\* from you. Throughout your life, as your health goals and priorities change, we can continue to provide valuable health insights from this single sample\* to support your unique health journey.

*\*Requires finger prick blood spot sample collection*

## Our Commitment

**DNALYSIS Biotechnology** is continuously developing new tests with the highest standards of scientific rigour. Our commitment to ensuring the ethical and appropriate use of genetic tests in practice means that gene variants are only included in panels once there is sound motivation for their clinical utility and their impact on health outcomes.

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**ADVANCED** | **ACTIONABLE** | **APPROPRIATE**  
technology | interventions | use in practice

From the laboratories of:

**DNALYSIS**  
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### Risks and Limitations:

DNALYSIS Biotechnology has a laboratory with standard and effective procedures in place for handling samples and effective protocols in place to protect against technical and operational problems. However as with all laboratories, laboratory error can occur; examples include, but are not limited to, sample or DNA mislabelling or contamination, failure to obtain an interpretable report, or other operational laboratory errors. Occasionally due to circumstances beyond DNALYSIS Biotechnology's control it may not be possible to obtain SNP specific results.