Use genetics to personalize your clinical decision making — and find the best path sooner

Finding the right treatment takes time

Despite the availability of effective treatments for many psychiatric illnesses, including mood and anxiety disorders, arriving at the best treatment can still take weeks or months. Patients can become discouraged, discontinue treatments and experience prolonged suffering.

An estimated two-thirds of patients with depression will not respond to first-line treatment, and more than one-third will become treatment-resistant.[1-3]

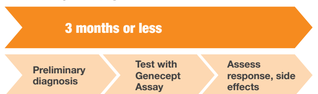
2/3
of patients don't respond to first-line treatment for depression[1-3]

The Genecept Assay® can shorten the path to finding effective treatments

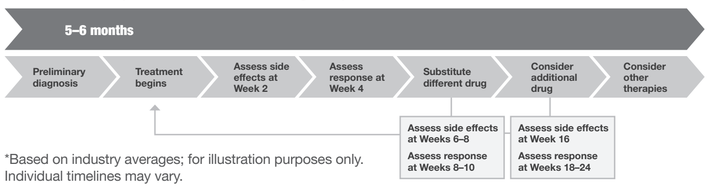
The Genecept Assay is a genetic test designed to help clinicians optimize treatment decisions and choose medications more likely to be safe and effective.

- Identifies variations in 18 key genes relevant to psychiatric treatment that indicate which therapies are likely to work as intended and not result in unwanted side effects or adverse events
- Easily administered as a cheek swab test
- Every result report includes a complimentary individualized consultation with an expert

Treatment for depression: guided by the Genecept Assay[4]



Treatment for depression: conventional drug trial process*



*Based on industry averages; for illustration purposes only. Individual timelines may vary.

The Genecept Assay covers a wide range of psychiatric disorders

Candidates for testing include:

- Patients living with depression, anxiety, OCD, ADHD, bipolar disorder, PTSD, autism, schizophrenia, chronic pain and substance abuse
- Any patient **without** optimal treatment response: previously failed treatment trials, poor response or adverse events
- Patients with polypharmacy
- Patients with psychiatric and medical comorbidities
- Patients with medication adherence issues

The Genecept Assay reports are easy to read, understand and share

Three types of test results are possible:

- A **positive or clinically significant** gene result
- A **negative or non-clinically significant** gene result (normal)
- An **indeterminate** gene result (may trigger a retest), or a gene variation of uncertain clinical significance – this result type is rare

The Genecept Assay report walks you through the genetic results and their treatment implications in detail. The report is easy to explain to patients, and the results help you have productive consultations about treatment with patients and families to improve adherence.

Complimentary consultation service

With each Genecept Assay report, Dynacare includes an optional and complimentary expert consultation service, enabling you to consult with a physician or pharmacist to help determine optimal treatment.

Case example: SLC6A4 in the treatment of intractable depression

A 30-year-old Caucasian female presented with intractable depression and severe anxiety along with a history of failures to a number of SSRIs.

Genecept Assay result

Genetic testing revealed the patient to carry a variant in the *SLC6A4* gene that plays a role in inhibiting serotonin reuptake and increases risk for failure with SSRIs. This result was consistent with the patient's previous medication history, having failed multiple SSRI trials over 15 years. Also found was an MTHFR gene variant, C677T, that may reduce production of methylfolate, which is needed for the synthesis of neurotransmitters.

Treatment change

The antidepressant mirtazapine (15 mg) was initiated at bedtime and then titrated up to 45 mg. Mirtazapine was chosen for serotonergic modulation via an alternative mechanism from the serotonin transporter.

Treatment also included continuing clonazepam for anxiety, adding L-methylfolate and discontinuing risperidone, which had been prescribed for a questionable diagnosis of bipolar type II disorder.

Outcome

On this regimen developed using the Genecept Assay results, the patient reported improved mood and has been able to attend work consistently and exercise daily. Her affect and energy both improved. In addition, her Global Assessment of Functioning (GAF) increased from 20 to 60.

The Genecept Assay can shorten the path to effective treatment, offering new hope for your patients.

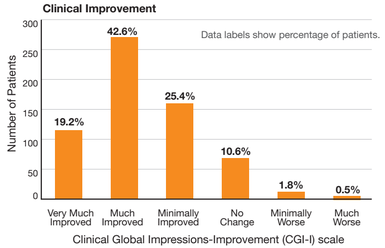
Clinical trial results

Studies have shown that using the Genecept Assay has resulted in significant improvements in clinical and economic outcomes.

Measurable clinical improvement, physician-reported[4]

In a naturalistic study of 685 patients, clinician-rated data using the Clinician Global Impression Improvement scale (CGI-I) showed that:

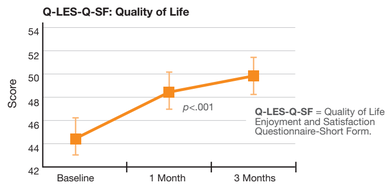
- **87%** of patients demonstrated a clinically measurable improvement
- **62%** of patients showed a significant clinical improvement (rated *much improved* or *very much improved*)
- Of the 69% of patients reported as treatment resistant, **91%** demonstrated a clinically measurable improvement



Measurable patient improvement, patient-reported[4]

In the same study, patients reported significant:

- Decreases in depression
- Decreases in anxiety
- Decreases in medication side effects
- Increases in quality of life



Improved patient adherence[5]

In a retrospective analysis of health claims data, individuals with Genecept Assay-guided treatment were significantly more medication adherent (a 6% increase) than patients with standard treatment.

An expanded panel for greater insight

The Genecept Assay includes:

- 18 well-characterized, well-annotated genes, extensively supported in peer-reviewed publications to affect treatment for psychiatric conditions
- A report with more than 195 citations to the literature
- 12 pharmacodynamic genes, 6 pharmacokinetic genes

The Genecept Assay analyzes two types of genes to inform proper treatment

Pharmacodynamic genes indicate the effect a drug has on the body and inform drug candidate selection.

Pharmacokinetic genes indicate the effect the body has on the drug via metabolism and inform drug dosage.

	Gene	Physiological Role	Impact of Mutation	Treatment Impact
Pharmacodynamic	**Serotonin Transporter (SLC6A4)**	Protein responsible for reuptake of serotonin from the synapse	Inhibition of this protein by SSRIs, which may lead to increased risk for non-response/side effects	Use caution with SSRIs; atypical antidepressants or SNRIs may be used if clinically indicated
	Calcium Channel (CACNA1C)	Subunit of the calcium channel, which mediates excitatory signaling	Associated with conditions characterized by mood instability/lability	Atypical antipsychotics, mood stabilizers and/or omega-3 fatty acids, which may help to reduce excitatory signaling, may be used if clinically indicated
	Sodium Channel (ANK3)	Protein that plays a role in sodium channel function and regulation of excitatory signaling	Associated with conditions characterized by mood instability/lability	Mood stabilizers and/or omega-3 fatty acids, which may help to reduce excitatory signaling, may be used if clinically indicated
	Serotonin Receptor 2C (5HT2C)	Receptor involved in regulation of satiety	Blocked by atypical antipsychotics, resulting in metabolic side effects	Use caution with atypical antipsychotics; inositol may be used to mitigate risk for weight gain if clinically indicated
	Melanocortin 4 Receptor (MC4R)	Receptor that plays a role in the control of food intake	Increased risk for weight gain and higher BMI, which is exacerbated by atypical antipsychotics	Use caution with atypical antipsychotics
	Dopamine 2 Receptor (DRD2)	Receptor affected by dopamine in the brain	Blocked by antipsychotic medications and is associated with risk for non-response/side effects	Use caution with antipsychotics
	Catechol-O-Methyltransferase (COMT)	Enzyme primarily responsible for the degradation of dopamine in the frontal lobes of the brain	Altered dopamine states can have emotional/behavioral effects and impact response to dopaminergic agents	Dopaminergic agents or TMS may be used if clinically indicated for **Val/Val patients** Use caution with dopaminergic agents in **Met/Met patients**
	Alpha-2A Adrenergic Receptor (ADRA2A)	Receptor involved in neurotransmitter release	Associated with improved response to stimulant agents	Stimulant agents may be used if clinically indicated
	Methylenetetrahydrofolate Reductase (MTHFR) • **A1298C** • **C677T**	Predominant enzyme that converts folic acid/folate to its active form (methylfolate), needed for synthesis of serotonin, dopamine and norepinephrine	Associated with varied activity and conversion of folic acid/folate to methylfolate	Supplementation with L-methylfolate may be used if clinically indicated
	Brain-derived Neurotrophic Factor (BDNF)	Important for proper neuronal development and neural plasticity	Impaired BDNF secretion, which may be associated with altered SSRI response in Caucasians	Increased physical activity/exercise may be beneficial for **Met carriers** if clinically indicated
	μ-Opioid Receptor (OPRM1)	Opioid receptor affected by natural and synthetic compounds	Activated by opioids and associated with varied analgesic response, dosage and abuse/addiction risk	Use caution with opioids; non-opioid analgesics may be used if clinically indicated
	Glutamate Receptor (GRIK1)	Excitatory neurotransmitter receptor in the brain	Associated with response to topiramate for alcohol abuse	Topiramate may be used for treatment of alcohol abuse if clinically indicated
Pharmacokinetic (CYP450s)	**CYP1A2** **CYP2B6** **CYP2C9** **CYP2C19** **CYP2D6** **CYP3A4/5**	Enzymes that metabolize medications in the liver	Large number of psychiatric medications are metabolized by CYP450s	Dose adjustment (an increase or decrease) may be required

Results in 5 to 8 business days from sample receipt

Ordering the Genecept Assay is simple:

1. Use the supplied collection kit to obtain a cheek (buccal) swab specimen from your patient.
2. Your patient's specimen will be tested upon receipt of the sample at our laboratory, and you will receive a results report within 5 to 8 business days from sample receipt.

1. Souery D, Papakostas GI, Trivedi MH. Treatment-resistant depression. *J Clin Psychiatry*. 2006;67(suppl 6):16–22.
2. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: Results from the national comorbidity survey replication (ncs-r). *JAMA*. 2003;289(23):3095–3105.
3. Warden D, Rush AJ, Trivedi MH, Fava M, Wisniewski SR. The STAR*D project results: A comprehensive review of findings. *Curr Psychiatry Rep*. 2007;9:449–459.
4. Brennan FX et al. A naturalistic study of the effectiveness of pharmacogenetics testing to guide treatment in psychiatric patients with mood and anxiety disorders. *Prim Care Companion CNS Disord*. 2015;17(2).
5. Fagerness J et al. Pharmacogenetic-guided psychiatric intervention associated with increased adherence and cost savings. *Am J Manag Care*. 2014;20(5):e146–e156.

Dynacare®

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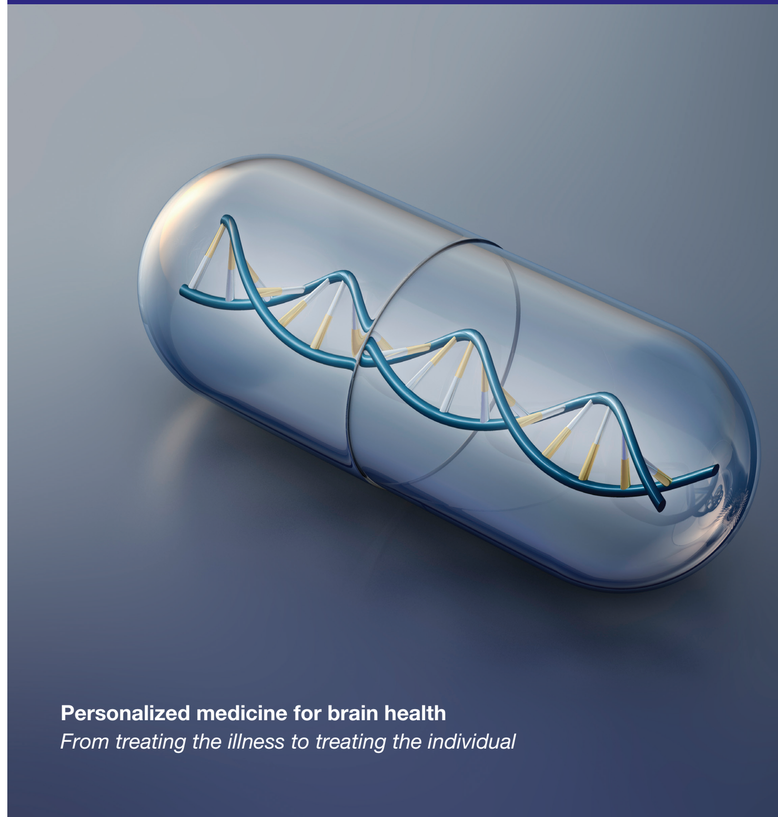
Dynacare® GENOMIND®

Find the right treatment faster

Genetic Testing with the Genecept Assay®



Personalized medicine for brain health

From treating the illness to treating the individual