LordsPath
Lab wahi jiski report sahi!

OneDNA
Discover.Empower.Transform.

Pharmacogenomic Approach to

GLP-1 Therapy Optimisation

Semaglutide Response Through Genetics

Why Semaglutide
works differently across patients?

A closer look at the genetic, metabolic, and physiological factors shaping treatment response variability.

Semaglutide, a **GLP-1** receptor agonist, is widely used for obesity and type 2 diabetes due to its proven efficacy in improving glycemic control and promoting weight loss. However, real world studies suggest that up to **~20–30% of patients** may experience suboptimal weight loss response, with emerging evidence indicating that genetic variability in pathways such as **GLP1R, MC4R, and FTO** contributes in part to this inter individual difference, alongside metabolic and environmental factors.

Why does it matter?

- Predicted Response to Semaglutide
- Understanding Genetics of Weight Loss
- Expected Treatment Outcomes
- Optimising Treatment Success

Comprehensive Test Overview

- **Pharmacogenomics analysis**
  Tests the key genes linked to GLP-1 response (GLP1R, TCF7L2, KCNQ1, ADRB3, FTO, MC4R, RET, and others)
- **Pharmacokinetics**
  Evaluates kidney function, body composition, and medication profile are unlikely to significantly affect semaglutide exposure or absorption.
- **Pharmacodynamics**
  Evaluates diabetes and marked insulin resistance suggest reduced beta cell reserve, which may limit the overall therapeutic response.
- **Lifestyle and Environmental Modifiers**
  Evaluates accelerated biological aging, chronic inflammation, and vitamin D deficiency may adversely influence metabolic health and treatment effectiveness.
- **Safety Profile and Comorbidity Index**
  Evaluates underlying health conditions and safety related factors that may influence treatment suitability, tolerability, and long term outcomes.

PREDICTED TREATMENT OUTCOMES AT 6 MONTHS		
GLYCAEMIC RESPONSE	**WEIGHT RESPONSE**	**COMPOSITE SPRA SCORE**
Expected HbA1c Reduction	**Expected Weight Loss**	**Semaglutide Predicted Response Assessment**
1.2 – 1.6%	**3.5 – 5.0 kg**	**62 / 100**
(from 8.6% to ~7.0–7.4%)	(3.7–5.3% body weight)	**MODERATE-GOOD RESPONSE**
Attenuated vs SUSTAIN trial mean (1.5%) due to TCF7L2 / KCNQ1 genotype	*Below trial mean (4–6 kg) due to ADRB3 Trp64Arg variant and sedentary lifestyle*	*Score accounts for genetics, epigenetics, PK/PD, lifestyle, and comorbidities. Score >60 indicates therapy is likely beneficial; optimise modifiable factors to push toward >75.*

Your genes are the reason Semaglutide hits differently for everyone

Diabetes risk factors and body composition differ significantly from Western populations. Providing treatment insights that are more relevant for Indian patients.

OneDNA analyses 7 critical genes that directly influence metabolism of semaglutide.

Gene	Clinical Relevance
GLP1R	Primary drug target determines receptor sensitivity and overall efficacy
TCF7L2	Regulates incretin response and insulin secretion
KCNQ1	Influences pancreatic beta cell function and insulin release
ADRB3	Impacts fat metabolism and thermogenesis linked to weight loss variability
FTO	Associated with appetite regulation and pathways responsible for obesity
MC4R	Regulates appetite control and satiety signalling; may influence weight loss response to semaglutide
RET	Influences thyroid C-cell signalling and safety considerations during GLP-1 receptor agonist treatment

Importance of PGx testing

Clinical response to Semaglutide varies considerably:

Super-responders	Typical responders	Non-responders
Achieve >20% weight loss (~32–40%)	Achieve 5–20% weight loss	Achieve <5% weight loss (~10-17%)

Genetic variations particularly in **GLP1R** have also been linked to increased risk of **gastrointestinal side effects** such as nausea and vomiting.

Key Insights Provided by the Test

SPRA™ Response Score	Treatment Outcome Prediction	Safety Risk Stratification	Lifestyle & Metabolic Optimization Plan
SPRA Score combining genetic, metabolic, and lifestyle inputs	outcomes for weight loss, HbA1c, and metabolic improvement over 3, 6, and 12 months	Risk profiling for side effects with preventive guidance and Personalized dosing and monitoring recommendations	Tailored diet, exercise, and behavioral support.

Test Specifications

Technique	Platform	Sample Type	Turn Around Time
Allele Specific PCR	Multiplex PCR Assay	Saliva	10 Days

Who can take this test?

1. **Initiating Semaglutide Therapy**
   PGx analysis of GLP1R and metabolic response genes helps predict efficacy, tolerability, and the likelihood of achieving meaningful weight loss and glycaemic outcomes.

2. **Suboptimal Response to Semaglutide**
   For patients who fail to achieve weight loss or HbA1c reduction despite adequate semaglutide therapy, PGx insights can help differentiate potential genetic non-response from modifiable factors such as adherence, lifestyle, or dosing, enabling more targeted treatment optimization.

3. **Strong Family History of Type 2 Diabetes or Obesity**
   Variants in genes such as TCF7L2, KCNQ1, FTO, and GLP1R may influence treatment response, providing valuable guidance before therapy initiation.

4. **Individuals concerned about drug related side effects**
   PGx testing provides insights into genetic factors that may influence drug response and tolerability, supporting more personalised treatment decisions.

5. **Complex or Resistant Metabolic Disease**
   PGx profiling provides deeper insight into metabolic pathways, helping clinicians personalise therapy in challenging treatment scenarios.

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