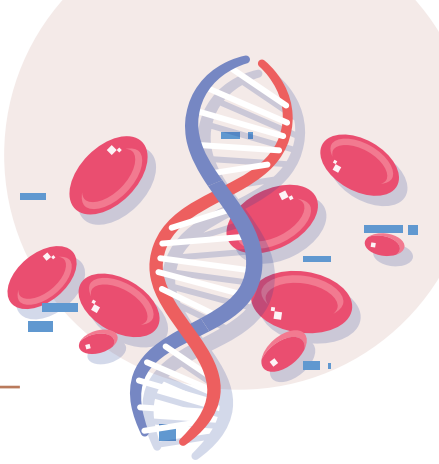
PRIME PATH LAB

DIABETES

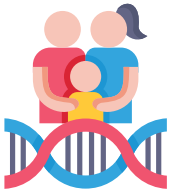
ETIOLOGY & DRUG RESPONSE

GENOMIC PANEL



Three Questions, One Panel

What Kind of Diabetes Is This?



Where Did It Come From?

Which Drug Is Safe?

Not all diabetes is type 1 or type 2. As many as 8 in 10 cases of monogenic diabetes are misclassified, and a smaller but consistently missed group is maternally inherited — passed down a line of relatives who were each labeled "type 2." This panel does three jobs from a single sample: it reclassifies the diabetes by reading its genetic cause, it traces mitochondrial (maternally inherited) diabetes that hides behind a routine diagnosis, and it profiles the pharmacogenomics that govern drug safety in patients who are almost never on just one medication.

Why it matters

A correct molecular diagnosis can move a patient off insulin and onto a low-dose pill — or stop unnecessary treatment entirely. But the longer a monogenic or mitochondrial case stays mislabeled, the more entrenched the wrong therapy becomes, and the harder the transition. Etiology and drug response are read together, once, from one buccal swab.

Pillar 1 - Reclassify the diabetes (monogenic / MODY)

The genotype rewrites the prescription. Identifying the gene tells you not just what to call the diabetes, but how to treat it:

- HNF1A (MODY 3) and HNF4A (MODY 1) : typically respond to low-dose sulfonylureas, often allowing patients to come off insulin entirely.
- GCK (MODY 2) : mild, stable fasting hyperglycemia that usually needs no treatment — a positive result can justify stopping therapy and reassuring the patient.
- HNF1B (MODY 5) : diabetes with renal cysts and genitourinary anomalies — a result that prompts renal evaluation, not just glucose control.
- WFS1 (Wolfram syndrome) : diabetes with optic atrophy and deafness — one of several syndromic causes this panel uncovers.

Pillar 2 - Follow the maternal line (MIDD / mitochondrial diabetes)

Maternally Inherited Diabetes and Deafness (MIDD) accounts for roughly 1% of all diabetes and is routinely mislabeled type 1 or type 2. It is caused by the mitochondrial m.3243A>G variant — the same variant behind MELAS — and it breaks every rule of nuclear inheritance: it passes only down the maternal line, never from fathers, and its severity tracks with heteroplasmy. The clue is in the history: diabetes paired with sensorineural hearing loss, often across affected mothers, siblings, and maternal aunts and uncles. The panel begins with targeted m.3243A>G sequencing and reflexes to whole mitochondrial-genome analysis with deletion/duplication testing when the targeted test is negative — so a clean first pass does not close the door on a mitochondrial cause.

Clinical pearl — the diabetic patient with hearing loss

Confirming MIDD changes management immediately, in three ways most "type 2" workups never reach:

1. Inheritance counseling flips. Children of an affected man are not at risk; every child of an affected woman is the opposite of the 50% autosomal-dominant math that applies to MODY.

2. The default drug may be wrong. Metformin is generally avoided in mitochondrial disease because of lactic-acidosis risk — so the reflexive first-line choice can be the unsafe one.

3. It is more than diabetes. MIDD carries cardiomyopathy, renal disease, retinal dystrophy, and progressive hearing loss, each warranting its own surveillance.

And MIDD is not the only "diabetes + deafness" diagnosis on this panel — WFS1 (Wolfram) and SLC19A2 (thiamine-responsive megaloblastic anemia) also pair the two. Unexplained hearing loss in a person with diabetes is, by itself, a reason to test.

Pillar 3 — Personalize the prescription (pharmacogenomics)

Patients with diabetes are rarely on a single drug. This profile reads the metabolizer genes that govern the medications they actually take. CYP2C9 influences sulfonylurea exposure and hypoglycemia risk. SLCO1B1 flags statin-associated myopathy — and most patients with diabetes are on a statin. CYP2C19 governs clopidogrel response, the antiplatelet many will eventually need. CYP2D6, CYP2B6, CYP3A4, CYP3A5, and CYP1A2 cover antidepressants, opioids, and other common comorbidity medications; G6PD flags oxidative-hemolysis risk; and HLA-B flags serious drug-hypersensitivity risk.

Who should be tested

- Diabetes before about age 35 without type 1 features (autoantibody-negative, detectable C-peptide, no ketoacidosis at onset)..
- "Type 1" with persistent C-peptide years after diagnosis, or young-onset "type 2" with a strong family history and without marked obesity or insulin resistance.
- Diabetes with sensorineural hearing loss, or a maternal-line pattern of diabetes screen for MIDD.
- Diabetes with syndromic features renal cysts, optic atrophy, congenital anomalies, or severe insulin resistance.
- Mild, stable, incidentally found fasting hyperglycemia (including in pregnancy) consider GCK.
- A known familial variant, or any patient for whom medication selection would benefit from pharmacogenomic guidance

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