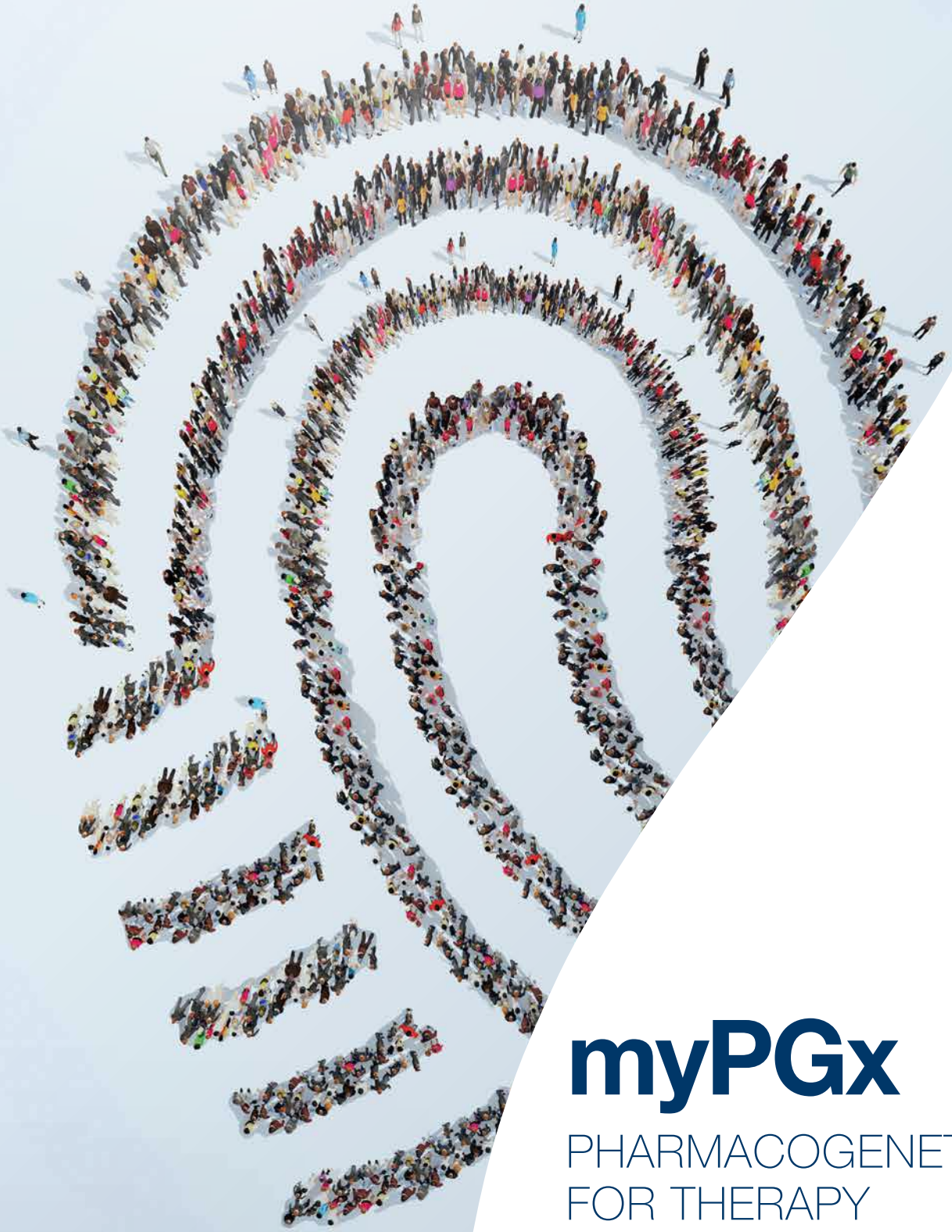
SYNLAB



myPGx

PHARMACOGENETICS FOR THERAPY OPTIMISATION

Genetic test to predict life-long individual drug compatibility

www.synlab.com

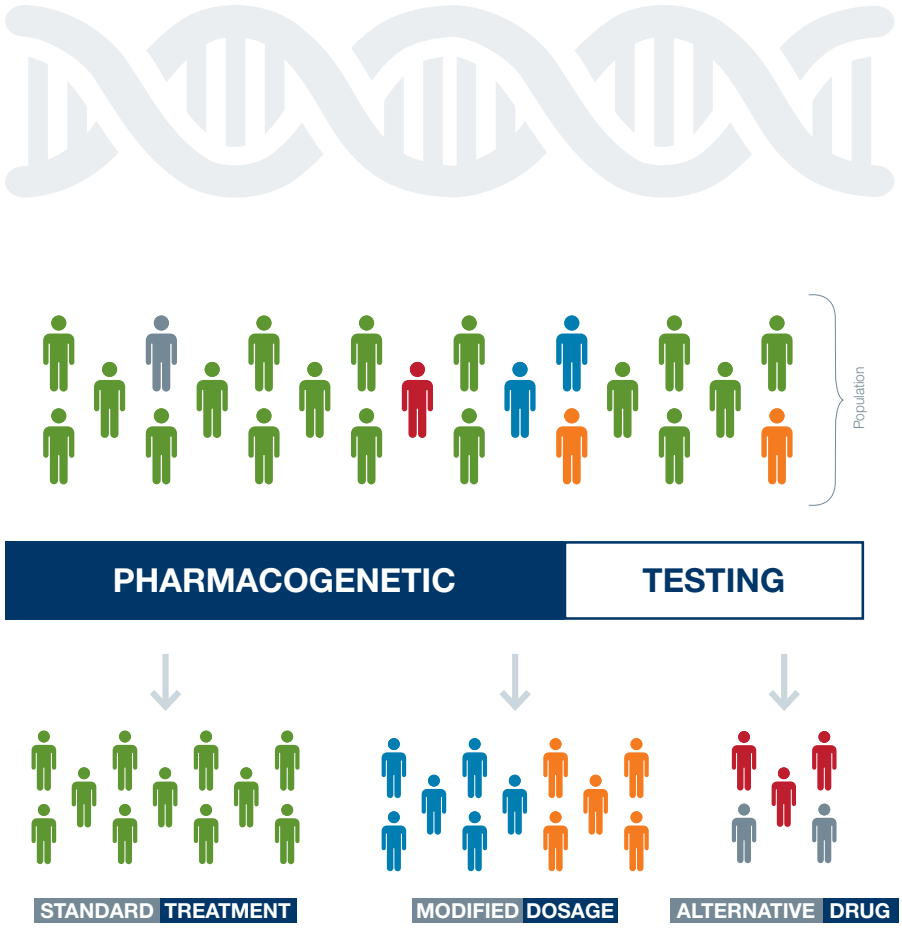
PERSONAL **PHARMACOGENETIC PROFILE**

THE **RIGHT DRUG**, AT THE **RIGHT DOSE**, FROM THE START

Over 95% of people have genetic variations affecting proteins involved in drug activation, transport and elimination. Studies from Europe found that up to 20% of ambulatory patients experience adverse drug reactions (ADRs) and 10% - 20% of inpatients will have at least one ADR during their hospital stay, as do around 8% of the general population.

Pharmacogenetics provides a tool to examine the individual genetic profile of the patient, identify significant pharmacogenetic variants and personalise the choice and dosage of drugs to increase the likelihood of successful therapy and reduce the risk of dangerous side effects.

Knowing the patient's pharmacogenetic profile allows the doctor to quickly and accurately prescribe the appropriate drug in a tailored dose.

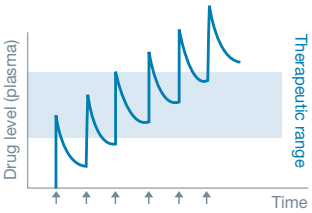


PHARMACOGENETIC

CLASSIFICATION GROUPS

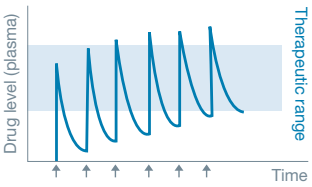
For each gene and drug family, patients are classified into one of three groups.

INACTIVE / REDUCED ACTIVITY

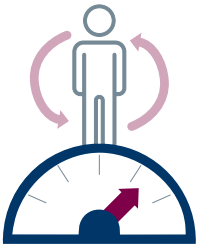


Change drug or adapt dose

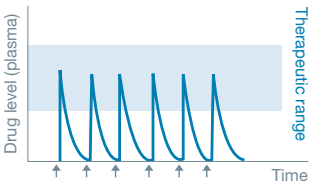
NORMAL ACTIVITY



Standard dosage of drugs and prodrugs



INCREASED ACTIVITY



Change drug or adapt dose

	SLOW/INTERMEDIATE METABOLISER	NORMAL METABOLISER	ULTRARAPID METABOLISER
	Genetic changes in genes related to drug metabolism can reduce therapeutic effect or increase the risk of side-effects (adverse drug reactions).		
POSSIBLE EFFECTS	Reduced clearance: increased drug concentration, risk of side effects.	Use and monitor according to standard instructions	Increased clearance: drug concentration too low, reduced therapeutic effects.
	Reduced prodrug activation: decreased drug concentration, reduced therapeutic effect.		Increased prodrug activation: risk of overdose effects.
ACTION	Alternative drug or adapted dosage		Alternative drug or adapted dosage

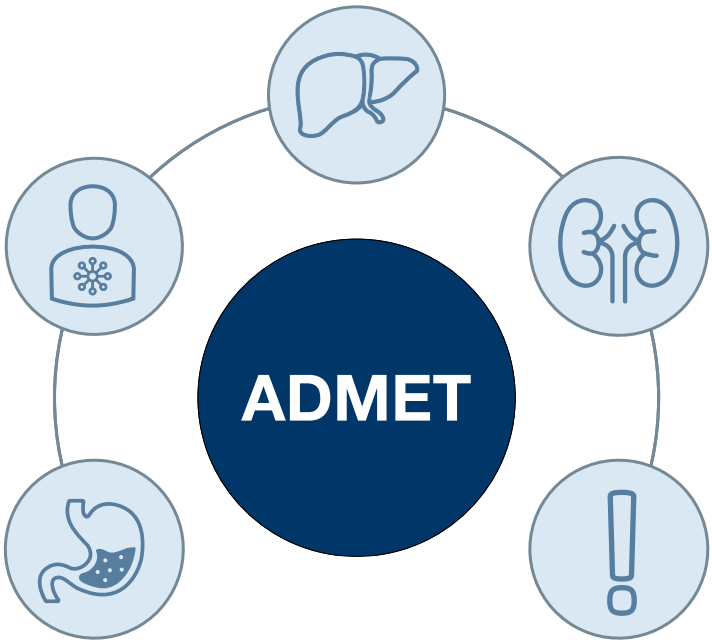
PHARMACOGENETIC TESTING

Pharmacogenetics is the genetics of ADMET: the study of variants affecting how drugs are **A**bsorbed, **D**istributed, **M**etabolised and **E**xcreted, as well as their eventual **T**oxicity. Most genetic variation is due to single-nucleotide variants (SNVs, formerly known as single-nucleotide polymorphisms or SNPs).

The genes most commonly affected are those coding cytochrome enzymes (CYP) involved in drug metabolism, phase II enzymes involved in drug conjugation before excretion, and proteins transporting drugs into or out of hepatocytes or target organs.

METABOLISM
Chemical modification of prodrugs and drugs, notably activation and degradation by hepatic CYP enzymes

DISTRIBUTION
Passage of a drug from the bloodstream to the tissues, especially target organs and liver



EXCRETION
Enzymatic and physical processes for removing drugs and metabolites from the body

ABSORPTION
Movement of drugs from the delivery site (e.g. the intestine) into the bloodstream

TOXICITY
Harmful effects of drugs and their metabolites

The targets of pharmacogenetic tests are based on medical evidence of utility, expert recommendations and publications from professional groups including CPIC, DPWG, EMA, FDA and others.

CPIC – Clinical Pharmacogenetics Implementation Consortium, DPWG – Dutch Pharmacogenetics Working Group, EMA – European Medicines Agency, FDA – Food and Drug Administration (U.S.)

myPGx

PHARMACOGENETIC TESTS*

- **Pre-emptive panels** currently analyse over 80 genetic variants in between 16 and 40 pharmacogenes
- Smaller **Specialised panels**, specific for particular medical disciplines, are available (for example, **myPGx**PSY, **myPGx**CARDIO).
- SYNLAB also provides highly-targeted, guideline-based **Companion diagnostic testing** for specific drug-gene interactions, for example 5-fluorouracil / DPYD or Clopidogrel / CYP2C19.

TARGETED GENE-DRUG PAIRS

GUIDELINE-BASED PHARMACOGENETIC MARKERS

- 5-fluorouracil → DPYD
- Irinotecan → UGT1A1
- Azathioprine → TPMT + NUDT15
- Clopidogrel → CYP2C19
- Warfarin → VKORC + CYP2C9
- Mavacamten → CYP2C19
- Statins → SLCO1B1
- Siponimod → CYP2C9
- Carbamazepine → HLA-B*15:02

MULTIGENE PANELS

PRE-EMPTIVE AND SPECIALTY-SPECIFIC PANELS

SYNLAB myPGx:

- ✔ Multidisciplinary pre-emptive panel
- ✔ Over 300 prescription drugs across multiple disciplines

myPGx Specialised panels

- ✔ Psychiatry | **myPGx**PSY
- ✔ Cardiology | **myPGx**CARDIO
- ✔ Gastroenterology | **myPGx**GASTRO
- ✔ Rheumatology and pain | **myPGx**RHEUMA

** exact content may vary between countries*

The majority
of people have genetic variations in proteins involved in drug activation, transport and elimination

Up to **20%**
of ambulatory patients experience ADRs

10% - 20%
of inpatients will have at least one ADR during their hospital stay

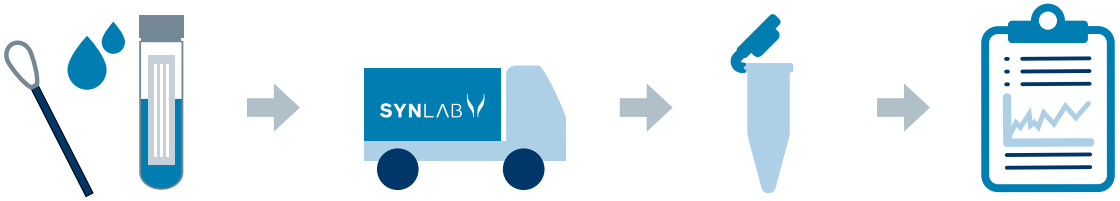
IMPROVED **QUALITY OF CARE** AND REDUCED **THERAPEUTIC COSTS**

BENEFITS OF PHARMACOGENETICS

Through knowledge of the patient's pharmacogenetic profile, the doctor can target and quickly prescribe the appropriate medication for the patient in the appropriate dosage. The consideration of individual response to medication can be recommended for all medical specialties. Pharmacogenetics is particularly valuable with the following classes of medication:

- Analgesics / NSAIDs
- Antibiotics / Antivirals / Antimycotics
- Antidepressants / Antipsychotics
- Antihypertensives
- Anticoagulants / Anti-platelet
- Cytostatics
- Proton pump inhibitors
- Statins

HOW IT WORKS



SAMPLE	DELIVERY	TEST	REPORT
• EDTA blood (2-6 ml) • Cheek swab • FTA card + Test request form	• Pick-up • Post • Partner laboratory	• SYNLAB expert laboratory • Genotype analysis of PGx panel	• Predicted phenotypes • Gene-drug effects • Detailed report with prescribing recommendations

Want to know more? Visit
www.synlab.com/mypgx

GOALS OF PHARMACOGENETICS

- Reducing the risk and severity of Adverse Drug Reactions (ADRs)
- Replacing traditional drug choice and dosage trial-and-error treatment plans
- Personalising the chosen drug to select the most effective medication
- Decreasing overall healthcare costs

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2. Miguel et al 2012, Pharmacoepidemiol Drug Saf, 21: 1139-1154
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