FAST FACTS:
OPTIMISING PAIN MANAGEMENT THROUGH PHARMACOGENOMIC TESTING

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INTRODUCTION

Pain is a common and complex clinical symptom with patients often showing high variability in their responses to standard analgesics. Traditional empiric prescribing fails to account for heritable differences in drug metabolism and receptor sensitivity. Pharmacogenomic testing (PGx) offers a more personalised approach by using genetic information to guide analgesic selection, dosing, and monitoring. For selected analgesics (notably codeine, tramadol and certain NSAIDs), pharmacogenomic testing can reduce predictable toxicity and treatment failure, supporting safer, more individualised prescribing.

IMPORTANT PHARMACOGENES IN PAIN MANAGEMENT

Genetic variation in drug-metabolizing enzymes, transporters, and receptors shapes an individual's pharmacokinetic and pharmacodynamic profile. Five pharmacogenes have been shown to play a role in pain management (see figure below).

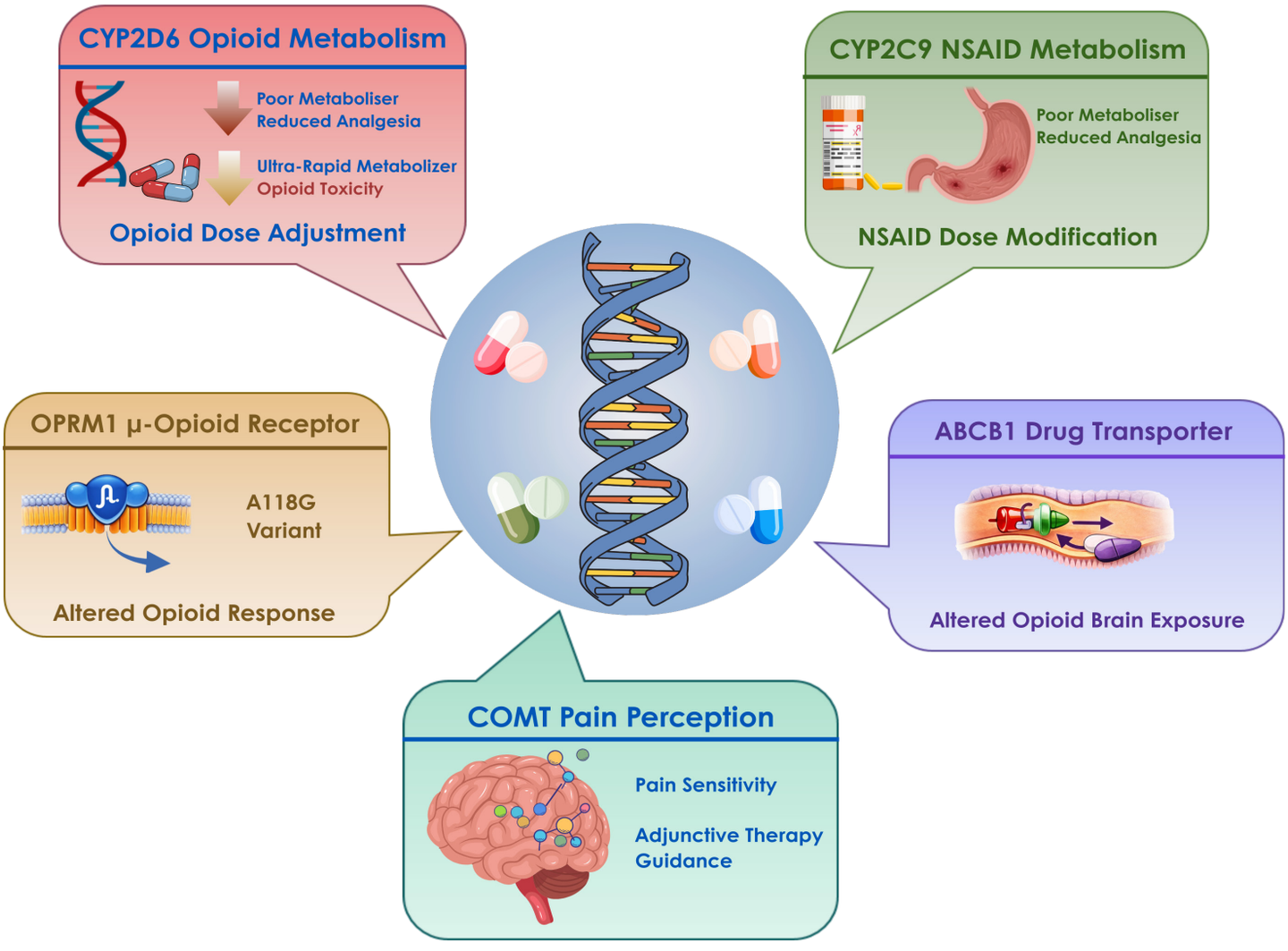

Figure: Five pharmacogenomic targets in analgesic therapy

WHICH PATIENTS SHOULD BE TESTED?

PGx testing may be helpful for many patients; the highest clinical utility is typically seen in the following scenarios:

- prior opioid failure / adverse effects
- need for codeine/tramadol
- recurrent NSAID intolerance
- polypharmacy / complex comorbidity

CLINICALLY ACTIONABLE PHARMACOGENOMIC VARIANTS

Pharmacogenomic variants differ in their associated clinical implications and the strength of evidence supporting these associations. The table below highlights some commonly prescribed pain medications with recommendations based on high quality clinical evidence.

Medication	Pharmacogene	Metaboliser status	Clinical implication (Source www.clinpgx.com)
Codeine	CYP2D6	Ultrarapid metaboliser	↑ Morphine formation → toxicity risk. Avoid codeine. Use alternative opioid (non-tramadol).
		Poor metaboliser	Minimal morphine formation → poor analgesia. Avoid codeine. Use alternative opioid.
Tramadol	CYP2D6	Ultrarapid metaboliser	↑ Active metabolite → toxicity risk. Avoid tramadol. Use alternative opioid (non-codeine).
		Poor metaboliser	Reduced active metabolite → poor analgesia. Avoid tramadol. Use alternative opioid.
Celecoxib	CYP2C9	Poor metaboliser	Markedly reduced metabolism → ↑ toxicity risk. Start at 25–50% usual dose OR consider alternative NSAID.
		Intermediate metaboliser	Reduced metabolism → ↑ exposure. Start at lowest recommended dose; titrate cautiously.
Ibuprofen	CYP2C9	Poor metaboliser	Markedly reduced metabolism → ↑ toxicity risk. Start at 25–50% usual dose OR consider alternative NSAID.
		Intermediate metaboliser	Reduced metabolism → ↑ exposure. Start at lowest recommended dose; titrate cautiously.
Melaxicam	CYP2C9	Poor metaboliser	Significantly prolonged half-life. Consider alternative NSAID (prefer shorter half-life agent).
Piroxicam	CYP2C9	Poor metaboliser	Significantly prolonged half-life. Consider alternative NSAID.

CYP: Cytochrome P450; GI: gastrointestinal; NSAID: non-steroidal anti-inflammatory drugs

CONCLUSION

Pharmacogenomic testing for CYP2D6 and CYP2C9 (as well as OPRM1 and COMT) is available at Ampath Laboratories as part of our PGx250 panel, with results made available within 4 weeks.

For more information, contact **pgx@ampath.co.za**