Pharmacogenomics and the Path Towards Personalized Medicine

Nicole Li ’27

Pain is a universal experience, yet pain management continues to be a very difficult and imprecise area of medicine today. Affecting more individuals than diabetes or heart disease, chronic pain is the leading cause of disability in the United States (Darnall, 2018). Around 11% of adults experience chronic pain in the U.S. (Wolters Kluwer, 2023). Despite chronic pain being so prevalent and the widespread use of opioids to combat the condition, one-third of patients on long-term opioids for non-cancer chronic pain find the medicine ineffective (Darnall, 2018). This urgent problem stems from the problematic trial-and-error strategy that fails to personally address each person’s problems and genetic profile. Pharmacogenomics has emerged as a promising solution, personalyzing pain therapy and analyzing the effect of genetic variation on drug metabolism. Over 90% of people universally have at least one genetic variant that can alter their response to a medication (Wolters Kluwer, 2023). Pain management is not a one-size-fits-all situation due to each person’s differing responses to medication. Therefore, precise and personalized medicine is imperative in pain care.

A clinically significant gene family in pharmacogenomics is the cytochrome P450 (CYP450) enzyme family, particularly the CYP2D6 gene. The CYP2D6 gene is responsible for the metabolism of many commonly prescribed opioids, including codeine, tramadol, oxycodone, and hydrocodone (Wolters Kluwer, 2023). Variations of CYP2D6 can have profound consequences. Poor metabolizers convert less of the drug into its active form, resulting in inadequate pain relief. On the other hand, ultrarapid metabolizers convert too much of the drug too quickly, leading to an extremely high amount of active metabolites, the small molecules remaining after metabolic reactions. This can cause severe side effects and toxicity, such as

vomiting, nausea, respiratory depression, and even death. In some tragic cases, children who received standard doses of codeine after a surgery experienced extreme side effects and passed away because their genetic information expressed ultrarapid metabolizers (Wolters Kluwer, 2023). According to the Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines, genotyping patients for CYP2D6 can aid in informing the type or amount of opioid to prescribe to the patient (Relling & Klein, 2011). For example, suppose a patient is known to be a poor or ultrarapid metabolizer. In that case, the doctor may use a non-CYP2D6 metabolized medication or a non-opioid such as celecoxib or tricyclic antidepressants.

There are a plethora of benefits to personalized pain management. Personalized therapy using genetic testing can significantly reduce the likelihood of adverse drug effects. Studies show that around 80% of patients who experience adverse drug effects have impaired CYP2D6 metabolisms (Hicks et al., 2009). In addition, using pharmacogenomics can improve drug efficacy, lower toxicity risks, and increase safer opioid prescribing in an era when addictions and overdose rates to prescribed opioids are rapidly skyrocketing (Smith et. al., 2018). By implementing genomic data, pain management can become more preventative rather than reactive. Clinicians in the future can avoid prescribing ineffective or harmful drugs and instead focus on medication tailored to each patient's genetic makeup.

While the potential and efficacy of pharmacogenomics are very promising, there are a handful of challenges that hinder the widespread adoption of this tactic. These include a lack of standardized testing methods, variability in lab results, and limited decision support tools (Wolters Kluwer, 2023). Additionally, there is insufficient education among primary care providers and pain specialists as most are not aware of pharmacogenomics or how to properly interpret its findings. Testing accessibility and insurance coverage also remains inconsistent.

Several factors, including a patient's age, use of other drugs at the same time, or medical history, can indicate a benefit from genomic testing. However, guidelines for routine screening have not yet been fully adopted.

As costs of genetic testing decline and digital health technologies improve, pharmacogenomic data will undoubtedly become increasingly integrated into electronic health records. This could lead to quick, real-time clinical decision-making and further personalized treatments. Furthermore, researchers are exploring non-opioids that could avoid going through the CYP metabolism entirely, but these drugs are all still in early stages of development and present a plethora of challenges to overcome. For example, drugs must effectively penetrate the blood brain barrier. Drugs that do not go through the CYP metabolism must still access the central nervous system sufficiently. Additionally, they must avoid accumulation and toxicity and be cleared effectively. Global health systems and schools must invest in training, research, public awareness programs, and education for the world to fully and effectively implement pharmacogenomic-guided pain management.

Pharmacogenomics has the evident potential to revolutionize pain management by transforming the traditional trial-and-error strategy with precise, data-driven, and personalized care. With innovative tools to analyze genetic differences in patients such as CYP2D6, clinicians can optimize drug selection, reduce toxicity and adverse effects, and prevent the burden of chronic pain and opioid abuse. As medicine and research advance, the future of pain management is in the heart of pharmacogenomics: individualized and effective treatment.

References

Darnall, B. (2018). Chronic pain: The science of relief. *Nature*, 557(7703), S13–S13. https://doi.org/10.1038/d41586-018-04994-5

Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther. 2017 Jul;102(1):37-44. doi: 10.1002/cpt.597. Epub 2017 Feb 13. PMID: 27997040; PMCID: PMC5478479.

Smith, D. M., Weitzel, K. W., Cavallari, L. H., Elsey, A. R., & Schmidt, S. O. (2018). Clinical Application of Pharmacogenetics in Pain Management. *Personalized Medicine*, *15*(2), 117–126. https://doi.org/10.2217/pme-2017-0032.

Relling, M. V., & Klein, T. E. (2011). CPIC: Clinical pharmacogenetics implementation consortium of the pharmacogenomics research network. *Clinical Pharmacology & Therapeutics*, 89(3), 464–467. https://doi.org/10.1038/clpt.2010.279

Schuft, K. (2018, June). *Pharmacogenomics: Effect of gene variability on pain management*. Wolters Kluwer. Retrieved April 21, 2025, from https://www.wolterskluwer.com/en/expert-insights/pharmacogenomics-effect-of-gene-variability-on-pain-management.