Practical applications of precision medicine in Psoriasis

Gaurav Pathak*; Samavia Khan; Prem Vyas; Rohan Shah; Babar Rao

*Corresponding Author: Gaurav Pathak

Robert Wood Johnson Medical School, 125 Paterson Street, Plainsboro NJ, 08536.

Tel: 609-647-8607; Email: Gnp28@rwjms.rutgers.edu

Letter to Editor

The high prevalence of psoriasis creates a significant barrier for the global healthcare system, affecting nearly 7.4 million US adults with direct treatment costs accumulating to over $12 billion annually [1]. Biologic drugs have become a major component of psoriasis management, with anti-TNF inhibitors, IL-17 inhibitors, IL-12, TYK 2 inhibitors, and other medications becoming integral to a patient's psoriasis treatment regimen [1,2]. However, given the ubiquitous use of biologics in psoriasis management, the response to these medications is not homogenous, with differences in patient genomics contributing to nearly 70% of the inter-individual drug response differences [2]. Pharmacogenetics provides dermatologists with more targeted treatment modalities to illicit the best response in psoriasis patients with minimal adverse effects. Given the costly nature of biologic medications, identifying the optimal drug for each patient may reduce annual healthcare expenditures.

Biologic treatment for psoriasis is largely a "trial-and-error" process with most dermatologists changing the biologic agents for 10-30% of their patients in the first year and an intra-class switch of at least 50% of treatment-nonresponsive patients [3]. A retrospective claims analysis indicated that 46% of psoriasis patients discontinued their biologic within 12 months and only 38% of patients were adherent to treatment [4]. Adherence to clinical guidelines such as the Clinical Pharmacogenetics Implementation Consortium (CPIC) regarding drug-gene interactions which may guide individual drug-dose therapy including making dose adjustments, identifying efficacious medications, and monitoring drug events. Genomic datasets are being developed that allow dermatologists to search for cell lines of interest and evaluate genotype data to predict dose-response data for various biologics (Table 1). These datasets along with pharmacogenetic testing can be utilized by physicians to aid in optimal biologic agent selection to minimize the "trial and error" process and associated costs. Additionally, other machine learning based

Pathak G

tests, use dermal biomarker patches to collect patient RNA and predict therapeutic response to commonly used psoriasis agents. Community dermatologists view pharmacogenetic testing applications favorably; 93% of respondents would use this technology to determine first line therapy even if it differed from initial choice. All the survey respondents stated that they would use such services if it was part of the prior authorization process and 98% stated that it would improve patient outcomes [3].

Various clinical trials are underway to evaluate the utility of genomic databases in guiding agent selection. Although pharmacogenetics is a useful tool in predicting a patient's response, environmental factors (epigenetics) and polygenic considerations may complicate predicting individual-drug responses [5]. Additionally, formularies may impact a physician's agent selection as their preferred agent may not align with formulary constrictions. Future studies should aim at identifying pharmacogenetic parameters and predictive biomarkers in larger cohort studies. In dermatology, precision medicine may personalize patient treatment regimens, reduce healthcare costs, and minimize adverse effects through ensuring optimal agent selection.

Table 1: Utility of selected genomic online datasets in dermatology.

Resources	Information available	Practical use for the dermatologist
PharmGKB/CPIC https://www.pharmgkb.org/	Clinical guidelines regarding genetic variants-drug interactions and actionable drug therapy modifications	Recommendations regarding optimizing drug therapy with medications included. Appropriate drug adjustments, and monitoring
PharmacoDB https://pharmacodb.ca/	Compilation of datasets allowing user to search for cell line of interest and dose-response data	Search for cell lines of interest and compare dose-response data
OMIM https://www.omim.org/	Online catalog of human genes and genetic disorders. Links to DNA and protein sequence	Understanding mutations associated with genetic conditions to guide therapeutic decision making
GARD https://rarediseases.info.nih.gov/	Important clinical trial information and clinical trials of rare diseases and genetic testing resources	An educational resource for physicians in treating rare genetic diseases and important information regarding genetic testing.
PACdb http://www.pacdb.org/	Pharmacogenetics database collecting genotypes, gene expression and pharmacology related information	Genotype data with response to treatment agents
CYP 450 drug interaction table https://drug-interactions.medicine.iu.edu/MainTable.aspx	CYP450 alleles and associated genotypes/phenotypes	CYP450 isoforms associated with altered enzyme activity, guiding agent and dose selection

Abbreviations: Pharm GKB: Pharmacogenomics Knowledgebase; CPIC: Clinical Pharmacogenetics Implementation Consortium; Pharmaco DB: Pharmaco-database; OMIM: Online Mendelian Inheritance in Men; GARD: Genetic and Rare Diseases; PACdb: Pharmacogenomics and Cell Database; CYP450: Cytochrome P450; SNPs: Single Nucleotide polymorphisms.

References

1. Feldman SR, et al. The Challenge of Managing Psoriasis: Unmet Medical Needs and Stakeholder Perspectives. Am Health Drug Benefits. 2016; 9: 504-513.

2. Munoz-Aceituno E, et al. Pharmacogenetics Update on Biologic Therapy in Psoriasis. Medicina (Kaunas). 2020; 56.

3. Strober B, et al. A Survey of Community Dermatologists Reveals the Unnecessary Impact of Trial-and-Error Behavior on the Psoriasis Biologic Treatment Paradigm. Dermatol Ther (Heidelb). 2021; 11: 1851-1860.

4. Doshi JA, et al. Biologic therapy adherence, discontinuation, switching, and restarting among patients with psoriasis in the US Medicare population. J Am Acad Dermatol. 2016; 74: 1057-1065 e4.

5. Bogdanos DP, et al. Twin studies in autoimmune disease: genetics, gender and environment. J Autoimmun, 2012; 38: J156-69.

Authors Information: Gaurav Pathak[1]*; Samavia Khan[1]; Prem Vyas[1]; Rohan Shah[2]; Babar Rao[1]
[1]Department of Dermatology, Rutgers Robert Wood Johnson Medical School, Somerset NJ, USA.
[2]Department of Dermatology, Rutgers New Jersey Medical School, Newark NJ, USA.

About the Journal: Open Journal of Clinical and Medical Case Reports is an international, open access, peer reviewed Journal focusing exclusively on case reports covering all areas of clinical & medical sciences.
Visit the journal website at www.jclinmedcasereports.com
For reprints and other information, contact info@jclinmedcasereports.com