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PGx: Personalized Cancer Therapy, Minimizing Adverse Effects

Sung-ho Kim*

Department of Cancer Systems Biology, Seoul National University, Seoul 08826, South Korea

Introduction

The field of pharmacogenomics (PGx) stands as a critical area in modern oncology, dedicated to understanding how an individual's genetic makeup dictates their response to drug therapies, influences potential toxicities, and ultimately impacts treatment efficacy. A thorough review of the current landscape of PGx in oncology emphasizes its clinical utility across a spectrum of cancer types. It also highlights the inherent challenges in its widespread implementation and points towards exciting future directions, including the sophisticated integration of multi-omics data and advanced Artificial Intelligence to forge even more personalized cancer treatment strategies [1].

Delving deeper into specific cancer types, PGx offers invaluable insights for lung cancer treatment. This area of study focuses on how both germline and somatic genetic variations play a crucial role in determining the effectiveness and potential adverse effects of targeted therapies and immunotherapies. The research provides a comprehensive overview of clinically actionable pharmacogenomic markers, particularly relevant for both Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC), underscoring their vital role in shaping individualized treatment plans [2].

In the context of colorectal cancer (CRC), the utility of pharmacogenomic markers is paramount for optimizing therapeutic outcomes. Studies review how specific genetic polymorphisms can significantly affect the pharmacokinetics and pharmacodynamics of essential chemotherapy agents, such as fluoropyrimidines and irinotecan, alongside various biological therapies. The overarching goal here is to precisely tailor treatment, thereby minimizing toxicity while simultaneously improving patient response rates through highly personalized approaches [3]. Similarly, the role of pharmacogenomics in personalizing targeted therapies for breast cancer is an actively researched area. Investigations explore genetic variants that impact the efficacy and toxicity of critical drugs, including trastuzumab, pertuzumab, lapatinib, and cyclin-dependent kinase 4/6 inhibitors. This work offers crucial insights into biomarker-driven treatment selection and precise dose adjustments, all designed to enhance patient outcomes [4].

Pharmacogenomics extends its reach beyond primary cancer therapies to address significant treatment-related complications. For instance, research delves into the pharmacogenomic factors that govern an individual's response to antiemetic drugs, which are vital for managing chemotherapy-induced nausea and vomiting (CINV). This work identifies genetic polymorphisms in drug-metabolizing enzymes and receptors that can reliably predict the effectiveness and potential side effects of antiemetics, paving the way for personalized strategies to optimize CINV prevention in cancer patients [5]. Another debilitating side effect, chemotherapy-induced peripheral neuropathy (CIPN), is also a focus of PGx studies. A comprehensive review in this area identifies specific genetic variants strongly associated with an increased risk or severity of CIPN across various chemotherapeutic agents. Such insights are crucial for developing potential biomarkers to predict and ultimately prevent this condition, further personalizing treatment to alleviate patient burden [10].

The expanding role of pharmacogenomics is clearly evident in the treatment of Acute Myeloid Leukemia (AML). Detailed reviews highlight how comprehensive genomic profiling, encompassing both tumor and germline DNA, can accurately predict a patient's response to standard chemotherapy, various targeted agents, and emerging novel therapies. This innovative application aims to significantly improve treatment efficacy and markedly reduce toxicity for AML patients, aligning perfectly with personalized medicine paradigms [6]. Furthermore, the burgeoning field of pharmacogenomics in cancer immunotherapy is transforming how clinicians approach treatment. Studies explore how both germline and somatic genetic variations can predict an individual's response to, and even resistance against, immune checkpoint inhibitors and other immunomodulatory agents. The ultimate objective is to pinpoint specific biomarkers for patient stratification and to develop more effective, highly personalized immunotherapeutic strategies [7].

A particularly sensitive application of PGx involves pediatric oncology, where unique aspects and challenges are thoroughly examined. This area focuses on how genetic variations distinctly affect drug metabolism and overall response in children diagnosed with cancer. The emphasis here is on the critical need for age-specific dosing guidelines and meticulously tailored treatment approaches to mitigate toxicity and enhance outcomes within this particularly vulnerable patient demographic [8]. Finally, the utility of pharmacogenomics and precision medicine is also extensively discussed in the management of ovarian cancer. Research reviews critical genomic biomarkers that predict patient response to chemotherapy, PARP inhibitors, and other targeted agents. The goal remains steadfast: to effectively guide treatment selection and overcome issues of drug resistance, thereby ensuring truly personalized care for ovarian cancer patients [9].

Description

Pharmacogenomics (PGx) has emerged as a cornerstone in modern oncology, providing a framework to understand how an individual's unique genetic variations profoundly influence their response to cancer drugs, the incidence of adverse toxicities, and the overall effectiveness of therapy. Recent comprehensive reviews

have thoroughly explored the current landscape, detailing the extensive clinical utility of PGx testing across numerous cancer types. These reviews also candidly address the existing challenges in integrating PGx into routine clinical practice, while simultaneously mapping out future directions. This includes sophisticated strategies like the integration of multi-omics data and cutting-edge Artificial Intelligence to further refine and personalize cancer treatment approaches, promising a new era of precision medicine for patients [1].

The application of PGx is particularly impactful across various specific cancer diagnoses. For lung cancer patients, a narrative review highlights the critical importance of germline and somatic genetic variations in modulating the efficacy and toxicity of both targeted therapies and immunotherapies. This work provides a valuable overview of clinically actionable pharmacogenomic markers relevant to both Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC), emphasizing their indispensable role in guiding tailored treatment strategies that can significantly improve patient outcomes [2]. Similarly, in colorectal cancer (CRC), PGx markers prove instrumental in optimizing therapeutic regimens. Research meticulously examines how genetic polymorphisms impact the pharmacokinetics and pharmacodynamics of foundational chemotherapy agents, such as fluoropyrimidines and irinotecan, alongside newer biological therapies. The primary objective remains to minimize drug-related toxicity while simultaneously maximizing response rates through individualized treatment plans [3]. Furthermore, for breast cancer, PGx is key to personalizing targeted therapies. This involves investigating genetic variants that influence the efficacy and toxicity of vital drugs like trastuzumab, pertuzumab, lapatinib, and cyclin-dependent kinase 4/6 inhibitors. Such insights are crucial for biomarker-driven treatment selection and precise dose adjustments, ultimately leading to improved patient outcomes [4].

Beyond modulating the direct anti-cancer effects, pharmacogenomics plays a significant role in mitigating the adverse side effects often associated with rigorous cancer treatments. For instance, studies into chemotherapy-induced nausea and vomiting (CINV) investigate the pharmacogenomic factors that influence a patient's response to antiemetic drugs. By reviewing genetic polymorphisms in drug-metabolizing enzymes and receptors, researchers can predict the effectiveness and potential side effects of these crucial supportive care agents. This knowledge facilitates personalized strategies designed to optimize CINV prevention, thereby enhancing patient comfort and treatment adherence [5]. Another severe and debilitating side effect, chemotherapy-induced peripheral neuropathy (CIPN), is also a major focus. A thorough review identifies genetic variants linked to an elevated risk or increased severity of CIPN when using various chemotherapeutic agents. These findings offer critical insights into potential biomarkers for predicting and preventing this condition, allowing for personalized interventions that reduce the patient's burden [10].

The role of pharmacogenomics is also rapidly expanding into hematological malignancies and advanced immunotherapeutic strategies. In Acute Myeloid Leukemia (AML), for example, comprehensive reviews detail how genomic profiling of both tumor and germline DNA can effectively predict a patient's response to standard chemotherapy, targeted agents, and novel therapies. This predictive capacity is aimed squarely at improving treatment efficacy and significantly reducing toxicity for AML patients through highly personalized medicine approaches [6]. Concurrently, the burgeoning field of pharmacogenomics in cancer immunotherapy explores how both germline and somatic genetic variations can predict a patient's response to, or even resistance against, immune checkpoint inhibitors and other immunomodulatory agents. The overarching goal is to precisely identify biomarkers for patient stratification, ultimately developing more effective and truly personalized immunotherapeutic strategies to combat cancer [7].

Finally, pharmacogenomics addresses unique patient populations and challenging disease contexts. A dedicated review highlights the specific aspects and inherent challenges of applying PGx in pediatric oncology. This area delves into how genetic variations uniquely affect drug metabolism and response in children battling cancer, underscoring the vital need for age-specific dosing guidelines and meticulously tailored treatment approaches. These efforts are crucial for minimizing toxicity and improving overall outcomes in this particularly vulnerable patient population [8]. Furthermore, the utility of pharmacogenomics and precision medicine is widely discussed in the nuanced management of ovarian cancer. This includes reviewing critical genomic biomarkers that can predict a patient's response to chemotherapy, PARP inhibitors, and other targeted agents. The aim is to effectively guide treatment selection and strategically overcome drug resistance, ensuring truly personalized care for ovarian cancer patients [9].

Conclusion

Pharmacogenomics (PGx) plays a pivotal role in personalizing cancer therapy across various malignancies by elucidating how individual genetic variations influence drug response, toxicity, and treatment efficacy. This approach is fundamental to improving patient outcomes and minimizing adverse effects. For instance, comprehensive reviews highlight the clinical utility of PGx testing in general oncology, detailing its integration with multi-omics data and Artificial Intelligence to create more personalized treatment plans [1].

Specifically, PGx guides personalized strategies in lung cancer, identifying germline and somatic genetic variations that affect targeted therapies and immunotherapies for both Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC) [2]. In colorectal cancer (CRC), PGx markers optimize treatment by examining how genetic polymorphisms influence chemotherapy agents like fluoropyrimidines and irinotecan, aiming to reduce toxicity and enhance response rates [3]. Breast cancer also benefits, with PGx identifying genetic variants impacting targeted therapies such as trastuzumab and cyclin-dependent kinase 4/6 inhibitors, enabling biomarker-driven drug selection and dose adjustments [4].

Beyond direct cancer treatment, pharmacogenomics addresses debilitating side effects. It helps predict the effectiveness and side effects of antiemetic drugs for chemotherapy-induced nausea and vomiting (CINV) [5]. Similarly, PGx identifies genetic variants linked to an increased risk or severity of chemotherapy-induced peripheral neuropathy (CIPN), offering insights for prediction and prevention [10]. The expanding role of PGx also extends to Acute Myeloid Leukemia (AML), where genomic profiling predicts treatment response to various therapies, enhancing efficacy [6]. It is also critical in cancer immunotherapy, identifying genetic variations that predict response and resistance to immune checkpoint inhibitors, thus developing more effective personalized strategies [7]. Unique challenges in pediatric oncology are addressed by PGx, focusing on age-specific dosing and tailored treatments to minimize toxicity in children [8]. Lastly, in ovarian cancer, PGx and precision medicine utilize genomic biomarkers to guide treatment selection for chemotherapy and PARP inhibitors, working to overcome drug resistance [9]. This collective evidence underscores PGx as an essential tool for advancing personalized medicine in oncology.

Acknowledgement

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Conflict of Interest

None.

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Address for Correspondence: Sung-ho, Kim, Department of Cancer Systems Biology, Seoul National University, *Seoul* 08826, South Korea, E-mail: sungho.kim@snu.ac.kr

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