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Editorial

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A Comprehensive Review of Anticancer Medications Approved by the FDA

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Abstract

Development of new anticancer medications is essential for both patient care and pharmaceutical research and development. One approach to achieving this crucial objective is to repurpose current medications that might have unintended side effects as possible candidates. A methodical analysis of effective anticancer medications could offer insightful information about trends in the discovery of anticancer medications, which might aid in the systematic discovery of novel anticancer medications. In this study, we offered an extensive data source, which included anticancer medications and their targets, and we carried out a thorough analysis in terms of historical tendency and networks. The data gathered in this study showed promise to be a fundamental for the development and repurposing of anticancer drugs when it was used to find novel drug-cancer connections.

Keywords: Anticancer drugs; Drug-cancer network; Cancer-drug-target network; Drug repurposing.

Introduction

From understanding cancer mechanisms to patient therapy, the last 50 years have seen a number of outstanding advancements in the fight against cancer. However, cancer continues to be one of the world's leading causes of death, placing a significant burden on healthcare systems and society. Cancer covers more than 100 different diseases with a variety of risk factors and epidemiologist and involves abnormal cell proliferation with the potential to infiltrate or spread to other parts of the body. The development of contemporary molecular biology techniques, high-throughput screening, structure-based drug design, combinatorial and parallel chemistry, and the sequencing of human genomes are just a few examples of the technological and scientific developments that have revolutionized drug discovery over the past 50 years [1]. For the pharmaceutical industry and patient healthcare, particularly cancer, however, the rising costs of developing new drugs and the declining number of truly effective medications approved by the US Food and Drug Administration (FDA) create unprecedented problems. Drug repurposing and network pharmacology are two of the many methods that have been suggested to speed up the drug development process and drastically reduce expenses in light of the growing number of FDA-approved medications and quantitative biological data from the human genome project.

More than 100 anticancer medications have been found and FDA-approved thanks to advancements in anticancer drug research and development during the past few decades. Based on their modes of action, these medications can be generally divided into two basic categories: cytotoxic and targeted agents. By concentrating on mitotic and/or DNA replication pathway components, cytotoxic chemicals can destroy rapidly dividing cells. By interacting with molecular targets implicated in the relevant pathways for cancer growth, progression, and spread, the targeted therapies prevent the growth and spread of the disease. These effective treatments and the data they are associated with could offer important hints for further identifying new therapeutic targets, finding new anticancer drug combinations, repurposing existing medications, and computational pharmacology. A historical overview of these medications has been offered in several publications, which highlighted the patterns of an increasing use of targeted agents, particularly monoclonal antibodies. Recently, network pharmacology has been successfully used in a variety of domains, including target discovery, side effect prediction, and research into general drug action patterns [2]. Therefore, analysis of drug-disease/target networks will significantly increase our understanding of the molecular mechanisms underlying drug actions and provide invaluable clues for drug discovery in addition to updating the FDA-approved anticancer drugs.

Therefore, for this study, we first thoroughly compiled the FDA-approved anticancer drugs as of the end of 2014 and then curated their related data, such as initial approval years, action mechanisms, indications, delivery methods, and targets from various data sources. We divided them into two groups: cytotoxic and targeted medicines based on their modes of action. We then examined these data to identify the various tendencies that existed between the two groups. In addition, we looked into the subcellular locations, functional divisions, and genetic mutations of the pharmacological targets. Finally, we created anticancer drug-disease and drug-target networks to identify the common anticancer drugs used to treat various cancer types and to demonstrate the strength of the drug-target interactions [3]. The network-assisted inquiry gives us fresh perspectives on the connections between anticancer medications and illness, or between medications and targets, which could be useful knowledge for further understanding anticancer medications and the creation of more effective therapies.

Discussion

We gathered anticancer medications that the FDA had approved from 1949 to the end of 2014 from various data sources. The National Cancer Institute (NCI) drug information, MediLexicon's cancer medicine list, and NavigatingCancer are a few websites where we first gathered information about anticancer medications. Then, we used the new natural language processing system MedEx-UIMA to retrieve the generic names of these medications. We looked for the FDA labels on Drug@FDA using the generic names. For those whose labels weren't in drugs@FDA, we got them via Dailymed or DrugBank. We manually extracted each drug's initial approval year, action mechanism, target, distribution method, and indication from the label [4]. To find the drug targets, we searched additional sources including MyCancerGenome,

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DrugBank, and numerous articles. To categorize the medications as cytotoxic or targeted agents, we manually evaluated ChemoCare. We excluded drugs used to treat drug side effects, cancer pain, other illnesses, or cancer prevention from our selected drug list. We gathered the targets for these targeted agents from MyCancerGenome, DrugBank, and FDA medication labels. The primary effect-mediating targets for each medication were then manually selected. In order to find the subcellular localization and family classes of the genes, we further retrieved the gene annotation from Ingenuity Pathway Analysis (IPA). For the purpose of data analysis, we first gathered the detail information for the indication from FDA drug labels before manually classifying them into higher-level classes. According to FDA labeling, the medication idelalisib, for instance, can be used to treat relapsed Chronic Lymphocytic Leukemia (CLL), follicular B-cell non-Hodgkin lymphoma (FL), and Small Lymphocytic Lymphoma (SLL). We identified leukemia and lymphoma as the therapeutic classes for the medication in our data analysis.

On the basis of our carefully selected data, we created the drug-cancer and drug-cancer-target networks. The drug-cancer network has two different types of nodes that represent different drug or cancer types, as well as edges that recommend drugs as a recognized cancer treatment. The drug-cancer-target network has three different types of nodes representing different cancer types, drugs or drug targets, and edges denoting correlations between drugs and cancer or interactions between drugs and targets. The network degree, or the number of edges on each node in the network, is used to evaluate the topological feature of each cancer type and medication. We found novel drug-cancer connections using a common target-based methodology. It is one of the "guilt-by-association" tactics predicated on the understanding that the medications may or may not have shared common targets. It is very likely to be successful for medication A-cancer type D and drug B-cancer type C relationships if two drugs A and B share a same target, drug A is currently used to treat cancer type C, and drug B is used to treat cancer type D. Notably, we left out medications used to treat other illnesses, cancer pain, and adverse effects of cancer treatment from this analysis [5]. We divided them into two groups based on the Mechanism of Action (MOA): 89 targeted medicines and 61 cytotoxic medications. Alkylating compounds, anti-microtubule agents, and topoisomerase inhibitors make up the majority of cytotoxic medications, while signal transduction inhibitors, gene expression modulators, apoptosis inducers, hormone treatments, and monoclonal antibodies make up the majority of targeted medications.

Among 89 targeted drugs, 18 are antibodies, of which two (rituximab and trastuzumab) were approved in 1990, eight in the 2000s (gemtuzumab ozogamicin, alemtuzumab, ibritumomab tiuxetan, tositumomab and iodine I 131 tositumomab, bevacizumab, cetuximab, panitumumab, and ofatumumab) and seven from 2010 to 2014 (denosumab, brentuximab vedotin, ipilimumab, pertuzumab, ado-trastuzumab emtansine, obinutuzumab, and pembrolizumab). The pattern was in line with earlier findings, which showed that the period's enhanced molecular understanding of cancer had greatly influenced the creation of anticancer medications, particularly targeted ones. One drug can be classified as either a cancer single (individual) drug or a cancer combination drug depending on the drug delivery system used to supply the medication to the patient. A combination medicine is one that is used to treat cancer patients by combining multiple different medications. Although the study of their combined use with other targeted drugs or with cytotoxic drugs has gained promise for the development of an effective cancer treatment, targeted agents have become the main focus of therapeutic cancer research. The 150 anticancer FDA-approved medications in our curated data collection included 89 targeted therapies that could be used to treat 23 different forms of cancer and that functioned on 102 protein targets. We conducted a survey from the angles of subcellular localization, functional classification, and genetic alterations to thoroughly grasp the target functions and their genetic significance in cancer. These revelations could be helpful for deepening our understanding of the molecular causes of cancer and advancing cancer therapies [6].

We manually reviewed each target's subcellular information and function classification that we had obtained from IPA. The findings indicate that the majority of pharmacological targets (45, 44%) are found in the plasma membrane, followed by 27 (26%) in the cytoplasm, 23 (23%) in the cell nucleus, and just seven (7%) in the extracellular area. Twenty-one tyrosine kinases, twelve transmembrane receptors, five antigens, and five G-protein coupled receptors were among the 45 targets in the plasma membrane. 27 targets were found in the cytoplasm, of which 23 were enzymes and 4 were miscellaneous things. 13 enzymes and 10 receptors were among the nucleus' 23 targets. The finding suggests that the most effective anticancer medications to date target the plasma membrane proteins. The data set revealed that receptors were the second-biggest group of anticancer target proteins (27, 26%), whereas enzymes made up the greatest categories of pharmacological targets (58, 57%). 28 (27%) of these enzymes were tyrosine kinases, 8 (8%), serine/threonine kinases, 6 (6%), peptidases, and 5 (%) were enzymes involved in the regulation of epigenetic factors. 12 (12%) of these receptors were transmembrane, 10 (10) were ligand-dependent nuclear, and 5 (%) were G-protein coupled [7].

We also created a specialized network for targeted medications, their targets, and their indications in addition to the drug-cancer network. Based on the FDA-approved targeted drug-cancer relationships and targeted drug-target associations in our curated data, the network has 214 nodes (89 medications, 102 targets, and 23 cancer categories) and 313 edges (118 drug-cancer associations and 195 drug-target associations).

Conclusion

FDA-approved anticancer drugs are crucial to the development of new anticancer drugs as well as the success of cancer treatment. In this study, 150 FDA-approved anticancer medications were meticulously gathered from 1949 to 2014. We categorize them into two sets: cytotoxic and targeted agency, based on their modes of action. Then, we carried out a thorough analysis focusing on the relationships among drugs, drug indications, drug targets, and drugs themselves. We outlined the historical traits and delivery systems of medications. We investigated the cellular distribution, functional categorization, and genetic characteristics of the targets. To further explore these relationships, we used network approach. In this study, we offered a thorough data source, which included anticancer medications and their targets, and we carried out a thorough analysis in terms of historical tendency and networks. Its use to identify novel drug-cancer connections showed that the information gathered in this study is likely to be useful for the development and repurposing of anticancer drugs.

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