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Cancer: Drug Development

(Future Perspective)

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Abstract: Cancer is a complex disease that affects millions of people worldwide. Despite significant advances in cancer treatment over the past few decades, there is still a significant unmet need for effective therapies. The development of new drugs is critical to address this need. In this research paper, we will review the current state of drug development for cancer, highlighting recent advancements, challenges, and future perspectives.

INTRODUCTION

Cancer is a leading cause of death globally. According to the World Health Organization (WHO), there were approximately 10 million deaths from cancer in 2020. The development of new drugs for cancer treatment is critical to improve patient outcomes and reduce mortality rates. The process of drug development is complex and involves several stages, including target identification, lead compound discovery, preclinical testing, clinical trials, and regulatory approval.

Drug development follows a series of stages and people with different expertise {e.g. biochemists, cell biologists, chemists, clinicians} may carry out the different stages at different facilities.
Once a potential drug has been identified and prepared as a final product for in vivo delivery [drug formulation], subsequent studies can be divided into pre-clinical and clinical studies. Pre-clinical studies test a drug in animal models and gather data on safety and efficacy for proof of concept. These studies are required before administration of the drug to humans in clinical trials.
In order to develop a new targeted therapy, a three-step approach has been proposed for development of the drug before it goes to the clinic: identify the molecular targets/pathways that drive tumor growth; create a genetically equivalent, high-incidence animal model where tumors of interest develop in their correct anatomical locations and at a developmentally relevant time; and screen for, or design, inhibitors to block the molecular pathway and test their effects in the animal models (Romer and Curran, 2005).

CHALLENGES IN CANCER DRUG DEVELOPMENT

Despite the advancements in research, drug development for cancer remains challenging. One of the significant challenges is the high failure rate of clinical trials. According to a study by the Tufts Center for the Study of Drug Development, the success rate of oncology clinical trials is only 11.8%. This is primarily due to the complexity of cancer and the heterogeneity of tumors.
Another challenge is the development of drug resistance. Cancer cells can develop resistance to drugs, rendering them ineffective. This can occur through several mechanisms, including mutations, activation of alternative signaling pathways, and the development of efflux pumps that expel the drug from the cancer cell.

ADVANCEMENT IN CANCER DRUG DEVELOPMENT

Over the past few decades, there have been significant advancements in cancer drug development. The use of targeted therapies and immunotherapies has revolutionized cancer treatment. Targeted therapies are drugs that specifically target cancer cells or their microenvironment, while leaving healthy cells unaffected. Immunotherapies, on the other hand, stimulate the immune system to recognize and attack cancer cells.
One of the most significant advancements in cancer drug development is the use of monoclonal antibodies (mAbs). These are laboratory-made antibodies that can specifically bind to cancer cells, triggering an immune response against them. Several mAbs have been approved for the treatment of various types of cancer, including breast cancer, colorectal cancer, and leukemia.

There is difficulty in finding a cancer model that can reliably predict the effect of a new drug in human patients. A tumor is similar to an organ with tumor cells interacting with host cells, the immune system, blood vessels, and the extracellular matrix. The obvious difficulty in testing new drugs in cultured cells is that the system is far from replicating a true tumor environment. The next step up from cells in culture is the use of organ cultures and organotypic cultures, as these systems possess a three-dimensional aspect. Organ cultures are made of tissue slices.
Organotypic cultures are made of cells grown in a specific matrix to mimic the tissue of interest. The most common model systems used in drug discovery are in vivo mouse models. There are several approaches for using a mouse model system. Absence in healthy tissue

would also be expected. Strategies of Drug Development is older approach is to use high doses of a single carcinogen, often with little relationship to the etiology and/or molecular defect of the tumor of interest. The most widely used approach is the creation of human tumor xenografts.
Xenografts are generated by injecting human cancer cells under the skin of immunodeficient (nude) mice (the use of nude mice is necessary to avoid rejection of human cells by the immune system of the mouse). Disadvantages of this system are that reactions of the immune system cannot be monitored and that the environment, although in vivo, is foreign to the tumor.
An improvement to this model is to inject human cells into the organ of the mouse from which they were derived (orthotopic). Injecting tumor cells of mice into mice (syngeneic tumor) is another alternative.
The approach that offers a better alternative are genetically altered mice, created by transgenic, knock-out, or RNAi technologies. For example, the multiple intestinal neoplasia (min) mouse carries a germline truncation of the adenomatous polyposis coli gene.
The min mouse develops multiple adenomas and is used to study colon carcinogenesis. Tissue-specific and inducible promoters can be used in these models to better mimic the etiology/molecular defect of the disease and the anatomical and temporal characteristics of human cancer.

DRUG SCREENING

Drug screening High-throughput screening is a common approach to selecting lead compounds for drug development. It permits the testing of millions of compounds in a short period of time. Plates containing hundreds of wells of biological material (e.g. cells) are used to test various chemical compounds for a desired biological effect (e.g. apoptosis). Robotics can be deployed to prepare plates and to analyse up to 100,000 compounds per day. Many screening protocols use synthetic molecules synthesized via combinatorial chemistry—methodologies that rapidly and systematically assemble molecular entities to synthesize a large number of different but structurally related compounds. Note that many successful drugs are based on natural compounds that have also been used in screening procedures.
Another approach for selecting lead compounds for development is virtual screening. In this approach, computer analysis is used to select compounds that will bind to a molecular target based on the previously known three-dimensional structural information about the target (e.g. crystal structure). As this is an in-silico approach, consumables are not required and the compounds examined may not necessarily exist. Studies suggest that high-throughput screening and virtual screening are complementary approaches, each yielding potentially promising results.

PHARMACOGENOMICS

Pharmacogenomics is the study of the influence of the genome on an individual's response to a drug. Gene variability in both the individual and in the tumor may lead to differences in drug response among individuals

CAREER IN CANCER RESEARCH

The future of cancer drug development is promising. Advances in genomic technologies have enabled the identification of new targets for cancer therapy. The development of precision medicine, which uses genomic and other molecular information to guide treatment decisions, is a significant step towards personalized cancer therapy.
Another promising area is the use of combination therapies. Combining multiple drugs can increase the effectiveness of cancer treatment and reduce the development of drug resistance. The use of artificial intelligence (AI) in drug development is also gaining traction. AI can be used to predict drug efficacy, toxicity, and resistance, enabling more efficient drug development.
People are the most important asset in cancer research and drug discovery. There are several avenues to pursue for a career in cancer research. The road most often travelled is to obtain a PhD in an area that interests you. Interest is important for several reasons: first, you will be spending many hours reading and thinking about your subject; second, you will spend many hours in the laboratory conducting experiments which focus around your topic; third, one can never predict in which area a big breakthrough will occur, so there is no sense in trying to guess. Research can be frustrating at times because you are trying to figure out something that no one knows or has really done before and progress tends to be in small steps. However, many small steps made by many individuals drive the field.
Alternatively, cancer research can be pursued in a pharmaceutical company with entry levels at different stages of education. In fact, working in a research laboratory after obtaining a BSc degree is another valid path for a career in cancer research. Cancer research is expensive and requires appropriate facilities equipped with high-tech equipment.
These facilities are available in universities, research institutes, hospitals, and in biotechnology and pharmaceutical companies. The relationship between these types of research providers has recently grown to be symbiotic; a close association leads to mutual benefit. Several organizations and funding agencies create opportunities that help foster collaborations between universities and industry. Such organizations also provide commercial business training for academics. A career in cancer research promises to be interesting and rewarding.
You are guaranteed to meet and work with interesting, intelligent, and talented people!

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