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New Horizons and Challenges of Cancer Therapy

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Abstract

Cancer is one of the top causes of death, and a huge barrier for high-quality life globally [1]. In 2020 alone, there were 19.3 million new cases, of which close to 10 million were fatal [2]. It is estimated that cancer-related healthcare costs would amount to $232.9 billion between 2020 and 2030 [3]. Therefore, it is imperative to develop new and improved medicines for cancer therapy to enhance the patients' quality of life and to lower the mortality rates. Currently, an increasing number of prospective medicines and novel therapies are being tested in clinical trials, some of which have benefited the enrolled patients. Here, we will review the eve and challenges of cancer therapy, with particular focus on immunotherapy and targeted therapy.

Introduction

According to the WHO, cancer is among the top two causes of deaths before aged 70 in more than 60% of the countries [1]. Early diagnosis and treatment are critical to improving survival outcomes. The diagnosis of various types of cancers is currently dependent on a combination of biopsy, blood biomarkers, ultrasound, X-ray, CT or PETCT, MRI and other imaging technologies. However, due to the highly heterogeneous nature of cancers, even within the same organ type, the sensitivity and specificity of biomarkers remain low (e. g. the sensitivity of macrophage inhibitory factor is as low as 20% for ovarian cancer diagnosis [4]). Even when diagnostic methods are combined, sensitivity remains relatively low, with specific range from 30-76% [4]. As such, the development of new and more sensitive and specific biomarkers and imaging technologies are needed to improve the rate of early cancer diagnosis. Early diagnosis allows for timely interventions, which have shown to enhance patient survival in many cancer types. For example, the 5-year survival rate is >90% for ovarian cancer patients who received treatment intervention at the early stage 1 of the cancer, compared to only 5% if they were treated at the late stage IV [5,6]. Despite recent advances in cancer therapy, there remains relatively few approaches that are highly effective. Many cancers show a high recurrence rate; e. g., the recurrence rate of rectal cancer ranges from 20% to 50%, with advanced cancers having a higher recurrent rate [7]. Surgery, radiation therapy, and chemotherapy have been the mainstays of cancer therapy. More recently, immunotherapy and molecularly targeted therapy have emerged as promising new options. The main goal of cancer therapy is to eradicate all residual cancer cells after resection and treatment, or to suppress tumor growth if complete remission cannot be achieved.

Immunotherapy

Immunotherapy in general enhances the patient's immune system to fight the cancer. It is a wide field which includes checkpoint inhibitors, adoptive cell therapy, and other forms of manipulating the immune system [8].These therapies have been proven to benefit patients via generating a durable anti-tumor immune response in many solid and hematologic malignancies. Each year, more than 1,000 immunotherapy clinical trials are underway across the United States [9]. The main challenge of immunotherapy is to manage the potential side effects such as pain, swelling, soreness, redness, itchiness, rash, chills/fever, dizziness, nausea or vomiting, fatigue, trouble breathing, or more severe symptoms like organ inflammation and infection risk [8].

Targeted therapy

Targeted therapy, as part of precision medicine, specifically homes in on dysregulated proteins or genes of each cancer patient to limit tumor growth and/or metastasis. This can be achieved by finding specific inhibitors of dysregulated proteins, or inhibitors that regulate the transcription and translation of mutated genes.

Small molecules and monoclonal antibodies are typically used in targeted therapies. Successful examples include Gilteritinib, a small molecule inhibitor of receptor tyrosine kinases for the treatment of acute myeloid leukemia with FLT3 mutations [10]; and Vemurafenib, an inhibitor of B-Raf enzyme, which has been shown to directly inhibit tumor growth to significantly prolong overall survival in patients [11]. An advantage of using targeted therapy is that it can potentially be designed to inhibit targets that are considered to be undruggable by traditional means, such as targeting RAS, one of the most mutated gene families in cancer [12].

Other forms of therapies

More recently, novel types of therapies, including DNA and RNA therapies are being studied as promising approaches for cancer therapy [13]. Such therapies offer the advantage of targeting genes that do not transcribe to their protein products [14], which would limit our ability to manipulate the protein expressions and functions. Moreover, most of the encoded proteins are not amenable for targeting by traditional methods, as they may not have the conventional binding sites for small molecules [15]. In fact, only about 10% of total proteins are druggable by traditional means. Therefore, RNA therapies that are not limited by protein function and structure provide a potentially effective and affordable method for personalized therapy.

Conclusion

Many breakthroughs in cancer therapy have been achieved within the past decades. However, much remains to be done in the field of early diagnosis, so that we can identify and treat cancers when they are at their most curable and responsive stages. Personalized therapy currently comes at a high cost, which is not affordable for most patients, especially those in low-income countries, in which less than 15% patients have access to comprehensive treatment. In contrast, more than 90% of patients in high-income countries can afford these costly interventions [16]. While there are many ongoing clinical trials, these are only accessible to a very small part of patients. More resources should be put in to help patients and their families identify and enroll in these potentially beneficial trials. Most importantly, it remains critical to continue to develop new therapeutic approaches with enhanced efficacy while at the same time have tolerable side effects.

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