Editorial

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Precision medicine revolutionizes cancer diagnosis and treatment

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Nowadays, according to estimates from the World Health Organization (WHO), cancer still ranks as the top leading cause of death disease worldwide [1]. In case of the rapid growing of the cancer incidence and mortality, the global cancer burden is expected to increase about 50% in the next twenty years [1]. Considering the complexity of main risk factors for cancer, efforts to uncover the underlying mechanism of tumorigenesis and establish the molecular classification models for prevention are critical for global cancer control.

In 2015, Barack Obama, President of the United States, announced the launch of the Precision Medicine Initiative to address the challenge of public health issues and diseases treatment, emphasizing to deliver the right treatments, at the right time, every time to the right person [2]. Unlike the "one-size-fits-all" approaches that only work in some patients but not in others, Precision Medicine aims to create a data ecosystem for individual patient's disease by collecting and analyzing individual data, including environment, lifestyle, genetic and biomarker informations [3]. Up to now, multibillion dollar investments related to Precision Medicine approaches that contribute to improving the diseases diagnosis and treatment, especially in cancer immunotherapy. This already placed cancer research and treatment at the forefront of medical priorities worldwide.

In the current issue, several outstanding reviews collaboratively summarize the advance of Precision Medicine approaches in cancer treatment, especially the cancer immunotherapy. Although focused on distinct research topics, most of these reviews underline the promising prospects of Precision Medicine in the cancer targeted therapy and immunotherapy.

Precision medicine guides cancer targeted therapy

As the most typical representative of Precision Medicine approaches, targeted therapy functions to interfere with the critical molecules involved in the development of cancer [4]. Althrough chemotherapy works by killing the highly proliferated cells, more frequent tumor cells, chemotherapy could also suppress the proliferation of normal cells and induce systemic toxicity. Moreover, phagocytized tumor cells could provoke the antitumor immunity by promoting the expansion of tumor-specific T cells, which could be attenuated by chemo drugs treatment [5]. Unlikely, targeted therapy needs first to collect the patients' abnormal genomic information or the expression level of specific cancer driver genes. This helps to determine the mutated or abnormal genes, and use specific drugs to target the specific cancer-driving molecules and suppress its oncogenic function [4]. Since the cancer-drivers is more specific in tumor tissues than normal tissues; therefore, targeted therapy, in most case, could specifically limited the tumor development with tolerable side effect [6].

There are two main types of targeted therapy drugs, protein-based drugs and small molecule drugs. Protein-based drugs, especially antibodies, preferred to recognize membrane protein in tumor tissues. The most famous protein-based targeted drugs is Herceptin that is the human epidermal growth factor receptor 2 (Her-2) specific antibody. The Her-2, promoting cell growth and division, expresses significantly higher in some tumor tissues than normal tissues; therefore, Herceptin could specifically target tumor cells to block the Her-2 receptor function and in turn prevent tumor development [7]. Besides, antibody could be also conjugated with chemo or immunostimulatory drugs to specifically target tumor tissues [8]. Although some nanobodies also successfully target intracellular proteins [9], small molecule drugs are much easier to infiltrate through the cell membrane or barriers in tumor tissues to target molecules inside the cell. Currently, an increasing of small-molecule targeted drugs has been developed for cancer treatment and more than ninety as such drugs have been approved for cancer treatment in clinic [10].

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Unignorably, patients always initially respond well to targeted therapy; however, the emergence of resistance through mutations and other multiple mechanisms commonly lead to relapse [11]. Therefore, Precision Medicine approaches are vital to identify the genomic and proteomic information and determine how tumor escapes the initial targeted therapy. However, given the high heterogeneity of tumor microenvironment, it is critical to collect the genomic information as comprehensive as possible from relapse tumors, metastasized tumors and blood, and further analyze the change of tumor drivers by combining the multiple-omics approaches to determine molecular classification the appropriate treatment strategies by inhibiting tumor cell proliferation or awaking antitumor immunity.

Precision medicine accelerates personalized cancer immunotherapy

Impressively, in the past decade, the success of tumor immunotherapies, especially the immune-checkpoint blockade (ICB) and chimeric antigen receptor (CAR) T cell therapy, has revolutionized the cancer treatment [12]. However, similar as other cancer treatment, including targeted therapy, radiotherapy and chemotherapy, only minority of patients responds to the immunotherapy [13], indicating the great potentials for Precision Medicine to continually improve the cancer diagnosis and treatment.

From the Coley's toxins to the current tumor immunotherapy approaches, tumor immunotherapy has been more and more fitted to the concept of Precision Medicine. More than a century ago, William Coley observed that about half of patient responded to the injection of heat-killed *Streptococcus pyogenes* and *Serratia marcescens*. Regrettably, such strategy was not adopted during Coley's lifetime because of the inconsistency of his results and the idea far ahead of his time [14]. Ultimately, the bacterium Bacillus Calmette-Guérin (BCG) vaccine was approved by the FDA at the late twentieth century. The Coley's observation finally encourages the entire immunology society to realize the critical role of stimulating the patients' own immune system to destroy the malignant tumors. By now, multiple more personalized immunotherapies, such as tumor vaccine, ICB, CAR-T and immune stimulatory drugs, were providing fundamental evidence for utility in redirecting the immune system to target cancer, and open up a new opera for tumor immunotherapy.

Nowadays, hundreds immunotherapy strategies, including the bispecific antibodies, are validated in clinical trials, aiming at redirecting the host immune system to specifically target tumor cells [15]. In the current issue, Chen reviews the advance of tumor-specific antibody based immunotherapy [16]; Cai comments on the two-sword effect of the STING agonists to antitumor tumor immunity [17]. Notably, although we have made remarkable achievement in provoking the immune response for against certain cancers, with the low response rate to immunotherapy there is still a long way to fully uncover the complexities of the immune system for cancer diseases.

In summary, the rapid development of single-cell sequencing and multi-omics technologies has accelerated the application of Precision Medicine approaches in cancer treatment. Furthermore, it will be also necessary to combine big-data with Precision Medicine approaches and futher comprehensively analyze the personalized responses and resistance patterns to develop synergistic strategies and maximize therapeutic responses for patients. Impressively, emerging evidence indicate that Precision Medicine will continually go further to drive personalized tumor targeted therapies forward to develop more safe and effective treatments for each patient.

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