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Prospects of medical disruptive technologies

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Abstract: With the integration of the modern information, material, and other technologies, the development of medical science and technology has been greatly enhanced, and disease diagnosis and modes of treatment have undergone revolutionary changes. In this paper, we analyze and evaluate the progress of five technologies viz., tumor immunotherapy, gene-editing technology, medical artificial intelligence, synthetic biology, and stem cell and translational medicine. We draw upon the existing academic literature, think-tank reports, and published expert opinions to explore the directions along which medical science and technology is being developed. We also provide policy and planning recommendations.
Keywords: medical technology; disruptive technology; tumor immunotherapy; gene editing

1 Introduction

Integration of inventions in modern information, material, and medical technologies has greatly promoted the development of the field of medicine. Recent developments in medical technology, such as in the fields of genomics, synthetic biology, tissue engineering, and stem-cell technology, have led to the invention of new applications for use in the clinic that are revolutionizing disease diagnosis and treatment. Since the 18th National Congress of the Communist Party of China, significant progress has been made in the fields of medical research and health sciences, including basic research, disease prevention and control, and drug discovery. The effects of technological innovations in the development of medical science are becoming apparent [1]. Innovation in medical science and technology should serve as the core driving force for improving the health prospects of the Chinese population and for promoting it as a country with formidable science and technology.

The term ‘disruptive technology’ refers to a major breakthrough in performance or the introduction of a new functionality. The disruption is brought about by either a new technology or the innovative application of an existing technology. Disruptive technologies can bring revolutionary changes in one or more related industries, causing major changes in social production structures and the lives of the people. Disruptive technologies in medicine arise from the application of new principles and new discoveries made in the field of biology. Such technologies integrate existing advanced technologies such as medical, information, and telecommunication technologies. The invention of new disruptive technologies by China in the field of medicine could not only extend human life span and affect our life style, but it would also promote the biomedical and medical-device industries as strategic industries for our nation.

Every major breakthrough in the field of medicine may lead to the expounding of new theories, the establishment of new methods, or to the transformation of medical treatment. An ongoing scientific and technological revolution in medical science and technology has spawned a series of new ideas and concepts, such as translational medicine, systemic medicine, precision medicine, individualized medicine, and smart medicine. These innovations have become indispensable for disease prevention and health management.

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2 Developmental trends of disruptive technologies in medicine

Technological breakthroughs based on artificial intelligence (AI), big data, genomics, synthetic biotechnology, gene editing (CRISPR/Cas9), and tumor immunotherapy have led to profound reforms in medical science and technology.

2.1 Tumor immunotherapy

A deeper understanding of the microenvironment of tumorigenesis and tumor-escape mechanisms has led to the development of new therapies for modulating the immune system to resist tumor formation. Immune checkpoint suppression, immune checkpoint blockade, and immunocyte therapy are areas of intense research in oncology. Internationally available drugs such as the PD-1/PD-L1 inhibitor and CTLA-4 monoclonal antibody that modulate the immune system are being used to treat more than ten types of tumors [2]. The Nobel Prize in Physiology or Medicine announced in October 2018, was awarded to immunologists from the United States and Japan “for their discovery of cancer therapy by inhibition of negative immune regulation”.

The year 2017 saw tumor immunotherapy reach a milestone in when the US Food and Drug Administration (FDA) approved two chimeric antigen receptor cell (CAR-T) therapies targeting the CD19 antigen. The main principle behind CAR-T is to isolate T lymphocytes from a patient, genetically modify their receptor genes to allow them to identify the CD19 antigen, and then transfer the amplified CAR-T cells back into the patient. This therapy has demonstrated excellent clinical efficacy in patients treated for refractory B-cell malignancies.

According to the website clinicaltrials.gov, as of September 30, 2018, the number of clinical trials of CAR-T enlisted for locations in the United States was 243, whereas that number of for locations in China was 195 (205 for locations in East Asia). The number of trials enlisted for locations in China was much higher than for locations in other Asian (six enlisted in Japan) or EU countries (98 trials). According to the data available in the Pharmacy Database, at present more than 19 CAR-T based products developed by domestic biopharmaceutical companies have been reported to the Drug Evaluation Center of the State Food and Drug Administration of China for clinical application.

2.2 Gene-editing technology

Gene-editing technology can be used to perform fixed-point modification of genomes and their transcripts. Such efficient and precise genetic engineering could prove valuable for the development of gene therapy, nucleic acid-based diagnostics, and for establishment of cell and animal disease models for biological research. This technology could bring revolutionary changes to biological research and medical treatment. CRISPR/Cas9 technology has attracted worldwide attention and has been named as one of the “top 10 scientific breakthroughs of the year” twice by the journal *Science*.

CRISPR/Cas9 based gene-editing has undergone the first phase of clinical trials in the United States, China, and Europe. Chinese scientists launched human clinical trials of CRISPR gene-editing technology as early as October 2016. This Phase I clinical trial was led by Sichuan University and it was aimed at patients with advanced non-small cell lung cancer. In January 2018, the University of Pennsylvania announced its Phase I clinical trial of CRISPR technology for editing several key genes in T cells, including programmed death receptor-1 (PD-1), in patients with melanoma. The goal of the trial was to determine the safety and feasibility of genetically modifying T cells.

In 2015, a team led by Professor Huang Jun of Sun Yat-sen University [3] used the CRISPR/Cas9 system to knock out the genes related to thalassemia in human embryos. In 2016, a team led by Dr. Fan Yong from Guangzhou Medical University [4] used the CRISPR/Cas9 system to genetically edit fertilized human eggs to prevent HIV infection. In 2017, the journal *Nature* published a report from the United States about of first genetically-edited human embryo [5]. This study, which was conducted at the Oregon Health and Science University, used the CRISPR/Cas9 technology to repair mutant genes associated with cardiac hypertrophy in early human embryos. Although gene-editing technology is extremely valuable for scientific and medical advancement, it is also associated with potential risks and ethical controversies. A lengthy and arduous way lies ahead for all the involved parties for solving the medico-ethical problems related to gene-editing technology.

2.3 Artificial intelligence in medicine

Artificial intelligence algorithms trained on large amounts of data can optimize the implementation of medical

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services. The application of AI in the field of medicine can transform models of medical service [6]. There has been a surge in the use of AI for addressing problems related to the distribution of scarce medical resources.. Overcoming the shortage of medical resources will be a fundamental goal for AI. AI is already being used for applications such as remote medical assistance, medical imaging, drug mining, dietetics, hospital management, health management, diagnosis of mental illness, monitoring of data from wearable devices, risk management, diagnosis of pathology, and other clinical care activities.

The *2017 Artificial Intelligence-Enhanced Medical Industry Research Report* shows that [7] there were 131 AI companies in China focusing on medicine and healthcare, as of August 2017. A few such enterprises that originated in China include Alibaba, Tencent, Baidu, Keda Xunfei, and Huada Gene, while a few of those that originated overseas include IBM, Google, Apple, Microsoft, and Amazon. The presence of conducive policies in China has also led to the establishment of several collaborative centers for research and development in AI. These include the Chinese Academy of Medical Sciences−Keda Xunfei Medical Artificial Intelligence Research Center, Huaxi−Xi's Medical Artificial Intelligence R & D Center, and Zhejiang University Rui Medical Artificial Intelligence Research Center. In April 2018, the first fully autonomous AI diagnostic system, called IDx-DR, was approved by the FDA. It diagnoses diabetic retinopathy, by viewing retinal photographs, without the involvement of a professional clinician. The approval of IDx-DR enables ordinary people to undergo routine diagnostic tests more quickly, while also keeping their medical data private. This is only one example of why the present era is witnessing an explosion in the development of AI diagnostic technology.

2.4 Synthetic biology

Synthetic biology, a technology which involves the design and synthesis of new genomes, can trigger a third revolution in biotechnology, following the discovery of the DNA double-helix and the human genome project. The core idea behind synthetic biology is the design and construction of new biological components, networks, and systems based on the knowledge drawn from systems biology and engineering to ultimately create artificial living organisms.

Synthetic biology has the potential to make major breakthroughs in genetic engineering, *in vitro* and *in vivo* diagnostics, the development of new vaccines, and even in the synthesis of eukaryotes. In recent times, synthetic biology has made significant progress in the screening of anticancer drugs, the design of tumor immunotherapy, and specific binding of tumor cell engineered bacteria (engineered microorganisms). Scientists are also working on extending the use of synthetic biology to provide new therapeutic strategies for treating autoimmune, metabolic, and infectious diseases. In addition, synthetic biology has also been used to produce complex small molecules new protein drugs, such as precursors for anti-malarial drugs or vaccine against this disease.

In 2010, American scientists created the world's first artificial life-form, a prokaryotic mycoplasma, which caused a worldwide sensation. In 2017, *Science* reported the synthesis of five additional chromosomes, as part of the Synthetic Yeast Genome Project, four of which were completed by Chinese scholars Yuan Yingjin, Yang Huanming, and Dai Junyi. In 2018, a research team from the Chinese Academy of Sciences [8] cooperated with domestic organizations to create a simple artificial eukaryotic cell that did not exist in nature—a feat attempted for the first time in the world. This achievement marks a significant breakthrough in the field of synthetic biology.

2.5 Stem cells and translational medicine

Stem cells are cells that possess the capacities of self-replication and renewal. They can differentiate into multiple types of functional cells under specific conditions to replace damaged cells and repair organs. Tissue engineering, induced pluripotent stem cell (iPSc) technology, stem-cell therapy for cancer, and stem cell-based gene therapy promise to revolutionize disease treatment [9].

The Japanese government considers investment in regenerative medicine to be an important pillar of its new economic growth strategy. It is committed to achieving the popularization of stem cell-based regenerative medicine by 2030. In March 2018, the European Union approved the use of a therapeutic agent comprised of stem cells, called Alofisel, for the treatment of complex perianal fistula in adults inactive or mild Crohn's disease. This was the first example of allogeneic stem cell therapy approved by the European Union. In China, the *13th Five-Year National Strategic Emerging Industry Development Plan*, the *13th Five-Year Plan for Biotechnology Innovation*, the *13th Five-Year Plan for Health and Health Science and Technology Innovation*, and other policy and regulatory documents, have proposed the development of the stem cell industry. In 2018, the Stem Cell and Transformation Research Project was proposed. It focuses on 30 projects that will receive a total of 585 million

yuan from the central government for the design, cultivation, and isolation of stem cells and organelles. The policy support and funding provided by the state has played a crucial role in the development of stem cell technology.

3 Prospects for the development of medical science and technology

In the next decade or so, the medical field will be revolutionized by a number of technological breakthroughs (Fig. 1). With technological advancements, tumor immunotherapy will be used to treat for more types of tumors. The use of polypeptides and synthetic viruses for use as vaccines will also experience a reduction in cost and increase in safety. The end result of all these efforts would be an improvement in the prognosis of cancer patients. The development of genomics will lead to personalized medicine, which is expected to improve the treatment of cancer, cardiovascular diseases, Alzheimer's disease, and other genetic diseases. In the future, gene-editing technologies are expected to control and block the spread of infectious diseases by the engineering of the causative agents. Synthetic biology will drive the development of new vaccines, as well as rapid and sensitive diagnostic reagents and *in vitro* diagnostic systems. Artificial organs developed from an individual's own stem cell samples would be used for transplantation, greatly reducing the waiting-time for procuring matched organs and reducing the risk of host rejection. New prosthesis capable of being connected to the nervous system with the help of bio-based sensors will provide an almost normal sensation of touch. Advances in AI in medicine and biomedical engineering will enable prosthetics to fully mimic the ability of natural limbs. Nanobots will be able to deliver drugs and perform minimally invasive surgeries [10].

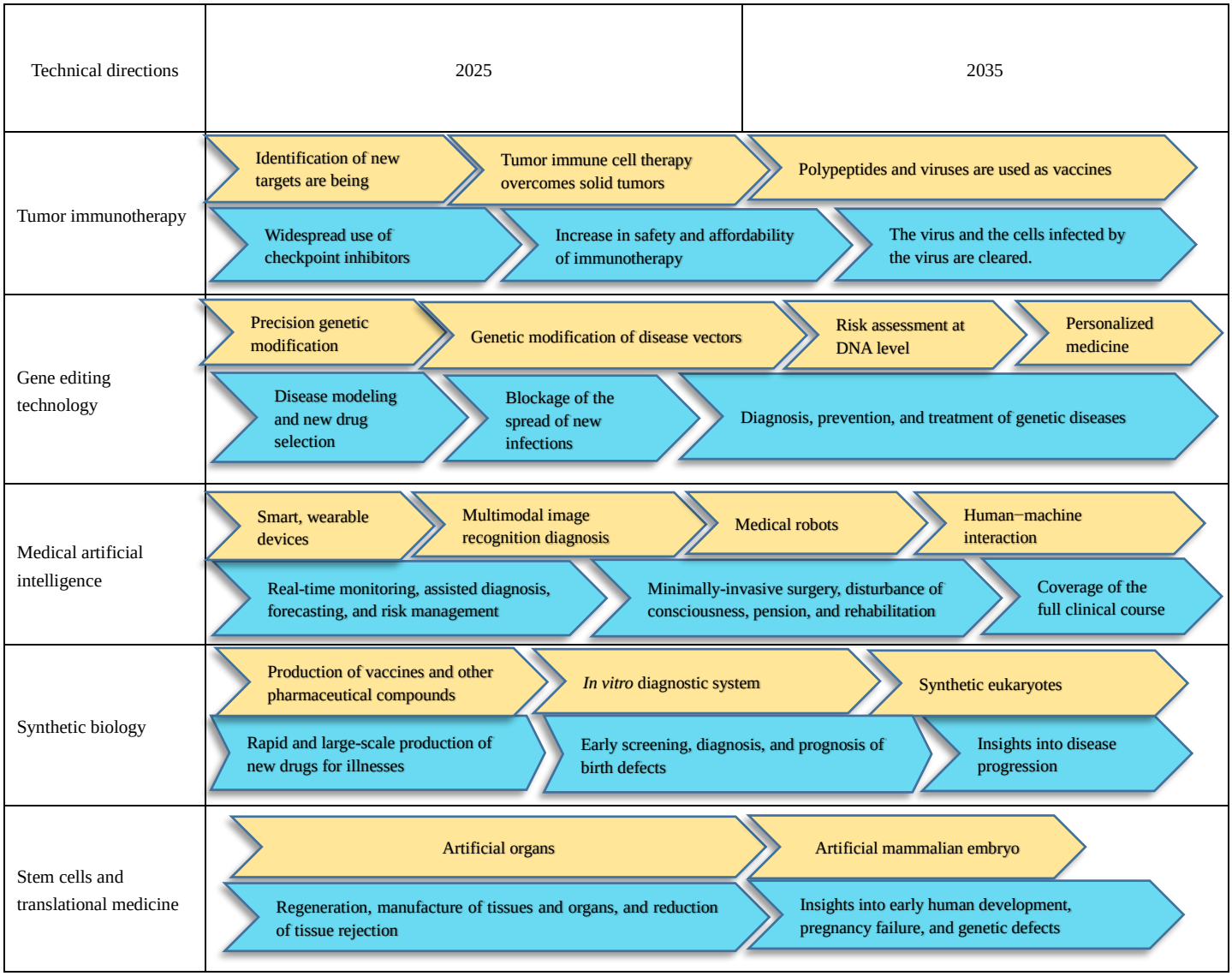

Fig. 1. Possible directions of development of the five major medical technologies discussed in this paper.

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4 Policy suggestions

4.1 Emphasize investment in basic medical research and encourage technological innovation

Discoveries in basic science are the source of improvement in healthcare productivity, and they lead to technology transfer and product innovation. An original innovation frequently involves the use of knowledge from the basic sciences for its development and mass production so that it can become a disruptive technology. In other words, it is the integration of basic science research with innovative thinking that serves as the crucible for the invention of disruptive technologies. We reiterate that the promotion of basic research, especially in the fields of information technology, life sciences, and material sciences, would help lead to the invention of new technologies [11]. Therefore, the advance allocation of human, financial, and material resources for research in these basic sciences would be conducive to the cultivation of disruptive technologies.

4.2 Optimize the top-level design and focus on integration of medical science with emerging technology

Advances in medicine are dependent on innovations in science and technology, as well as on their cross-disciplinary integration into cutting-edge technologies. Developments in the field of medical science and technology have been achieved by the integration of different branches of medical science with labor management, life science, optics, electronics, materials science, information science, and other technologies. Progress in medical science and technology requires that multiple cutting-edge discoveries be integrated together. Moreover, the field of medicine can itself provide an avenue for the further transformation of various cutting-edge technologies. We hope that the prioritization of cutting-edge research in life science, data science, nanotechnology, artificial intelligence, and their integration with medical technology will produce technological results with disruptive effects.

4.3 Improve policy and regulatory systems and reduce technical risks

Technological development is often accompanied by side effects. For example, gene editing has made it possible to introduce heritable changes into the germline. Thus, failure to standardize the techniques for altering genetic traits may not only lead to the emergence of enormous societal ethical issues, but it may also threaten our safety. Thus, the relevant technical guidelines for maintaining experimental safety need to be developed as soon as possible. It is necessary to establish standard technical guidelines and national-level regulations for the safe use of genetic editing, artificial intelligence, synthetic biology, and the stem-cell technology. Furthermore, we must reform the relevant macroeconomic policies, laws, regulations, and standards, as well as strengthen the supervision of technological research and application.

References

[1] Cao X T. Establishing the core base of medical science and technology innovation system [N]. People's Daily, 2017-11-21 (13). Chinese.

[2] Qiu Z M, Wang L, Fu Y Y. Treatment progress in malignant tumors with immune checkpoint PD-1/PD-L1 inhibitor [J]. The Practical Journal of Cancer, 2018, 33(5): 868–870. Chinese.

[3] Liang P, Xu Y, Zhang X, et al. CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes [J]. Protein & Cell, 2015, 6(5):363–372.

[4] Kang X, He W, Huang Y, et al. Introducing precise genetic modifications into human 3PN embryos by CRISPR/Cas-mediated genome editing [J]. Journal of Assisted Reproduction and Genetics,2016, 33(5): 581–588.

[5] Ma H, Marti-Gutierrez N, Park S W, et al. Correction of a pathogenicgene mutation in human embryos [J]. Nature, 2017, 548(7668): 413–419.

[6] Wang H X, Tian X Q, You M, et al. Application status, problemsand suggestions of artificial intelligence in medical field [J]. Soft Science of Health, 2018, 32(5): 3–5. Chinese.

[7] Iyiou Think Tank. Research report on artificial intelligence enablingmedical industry (2017) [R]. Beijing: Iyiou Think Tank, 2017. Chinese.

[8] Shao Y, Lu N, Wu Z, et al. Creating a functional single-chromosome yeast [J]. Nature, 2018, 560(7718): 331–335.

[9] Wang Y, Xu L, Shi H L. On development and trends of stem cells technology from perspective of patent [J]. Competitive Intelligence, 2017, 13(3): 43–50. Chinese.

[10] Augustyn J. Emerging science and technology trends: 2016—2045.A synthesis of leading forecasts [R]. USA: Office of the Deputy Assistant Secretary of the Army (Research & Technology), 2016.

[11] Li Z, Liu C P, Luo H. Elementary analysis the connotation and cultivation of disruptive technology—Focus on basic scientific research behind disruptive technologies [J]. Global Science, Technology and Economy Outlook, 2016, 31(10): 53–61. Chinese.