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PERSPECTIVES

Clinical translation of biomedical materials and the key factors towards product registration

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Summary Biomedical materials have been developed for facilitating tissue regeneration and healing enhancement. Although research on biomedical materials has made great progress in material innovation and preclinical testing, the bottleneck is their translation from research and development to clinical applications; that is, the current rate of product registration and industrialization is low, which directly affects their clinical applications. In this paper, we introduce the basic features of biomedical materials towards the making of medical products and the experiences of our group in research and clinical translation of biomaterials for bone-tissue regeneration in the last few years. Based on our experience, we propose that the translational medicine platform (TMP) is an effective route to facilitate the progress of biomedical materials from bench to bedside. Moreover, from the viewpoints of scientific technology and management, the functions of TMP were also addressed. Relationships among TMP, research institution, enterprise, and government were also explored from the viewpoints of technological innovation, chemical engineering integration, fund raising, and management. This paper provides a theoretical and practical reference for clinical translation of biomedical materials.

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Introduction

Biomedical materials are a group of special functional materials that aid in the diagnosis, treatment, recovery or replacement of diseased or damaged tissues or organs, and promoting functions of physiological systems. The use of medical materials not only saves the lives of many patients and significantly decreases the death rate of patients with various medical conditions, such as wounds and cancers, but also plays an important role in improving the quality of life and health of patients. Health issues have become a great challenge worldwide. Because of the more frequent occurrence of diseases, natural disasters, traffic accidents, and population ageing, the requirement for biomedical materials in clinical applications is rapidly growing, and biomedical instruments are predicted as a new growth point in the world economy [1,2].

There are 60 million physically challenged people out of the 1.3 billion people living in China. According to available statistical data, there are 70 million patients with osteoporosis, more than 0.3 billion people with various dental problems, 0.15 million patients undergoing joint replacement surgery annually, millions of people undertaking cosmetic surgery, and more than 20 million with coronary heart disease or cardiovascular disease. Therefore, the demand for biomedical materials is very high, which is expected to increase with the further development of rural markets [2,3]. Unfortunately, in China, less than 5% of biomaterials and medical instruments are manufactured domestically. In addition, the availability of products required for making these biomaterials is often limited and some products may result in less satisfactory treatment outcome. Meanwhile, huge financial profits and market potential have greatly attracted overseas' companies into domestic markets, and thus the percentage of high-level products supplied by domestic enterprises are significantly reduced. Consequently, domestic enterprises are experiencing great frustration and the cost for medical treatment is subsequently increasing. To solve these problems completely, independent research and development (R&D) of high-performance biomedical materials is urgently needed.

R&D of biomedical materials towards clinical translations

Translational medicine in orthopaedics has become a focus of local and international medical communities, especially in the development of biomedical materials [4–6]. Biomedical materials have been developed in China for more than 20 years. However, both fundamental research and technological development are far behind that of the developed countries. In the past few years, under the support of National Natural Science Foundation of China, National Basic Research Programme of China (973 Programme), and National High Technology Research and Development Programme (863 Programme), the research of biomedical materials in China has made great progress from low-level repetition to programme-oriented and cutting-edge development in some aspects of this discipline.

For many years, the biomaterials research group of the East China University of Science and Technology (ECUST) has focused on the clinical demand-driven development and R&D of bone-tissue-repair materials. We also have tried our best to promote our research outcomes towards industrializations and clinical applications. For example, based on the biology of wound healing and the self-repairing potential of the human body, we have proposed and developed a bioreactor that possesses the function of *in situ*-guided tissue regeneration by synergistic effects of biomaterials and growth factors. In this reactor, tissue cells can adhere, grow, and differentiate on the scaffold surface, thereby promoting new bone formation accompanied by the degradation of the scaffold materials [7,8].

Our group is the first to study calcium phosphate cement (CPC) in China [9–11]. Based on the theories and methodologies in chemical engineering, the transformation mechanisms of specific kinds of ultrafine calcium phosphates in liquid–solid systems were thoroughly investigated. We successfully prepared CPC with high purity and high activity by a series of processes, including micromixing, heterogeneous nucleation, heat treatment, pore formation at room temperature, and control of the degradation rate to meet biological and physiological needs in bone-defect repair. In addition, our group systematically investigated the hydrating and hardening mechanisms of CPC. Based on these basic studies, osseointegration characteristics and degradation mechanisms of the prepared CPC were confirmed by *in vivo* animal experiments. With the superior properties of self-setting, easily shaped capability, biocompatibility, and biodegradability, we have successfully obtained the first product registration for CPC materials certified by the State Food and Drug Administration (SFDA). Our CPC has been applied in more than 500 hospitals and in over 240,000 patients in big cities such as Beijing and Shanghai. Furthermore, a series of CPC-based bone-tissue-repair materials, including drug-loaded CPC, injectable CPC, and porous CPC, has been developed (Fig. 1).

To further improve the therapeutic efficacy, especially for patients with large or critical bone defects and for elderly patients with poor bone-regeneration potential, recombinant human bone morphogenetic protein-2 (rhBMP-2)-loaded bone-tissue scaffold has been developed [12,13]. Using genetic engineering technology, rhBMP-2 with high purity and high bioactivity has been successfully prepared by optimization of *Escherichia coli* expression system, construction of engineering bacteria, and expression and purifying technologies and has been patented in the United States [12]. In addition, the scale up (30 mg/batch) of rhBMP-2 was achieved as well. Based on these results, we have systematically studied the effects of the chemical composition, surface/interface structure of the materials, and other small molecular medicines on microstructure, presentation, and bioactivity of rhBMP-2. Based on these fundamental studies, we have fabricated rhBMP-2/CPC scaffold with enhanced osteogeneration potential [13]. Up to now, we have applied this new rhBMP-2/CPC scaffold for 68 patients with limb fractures and vertebral fusion. Our CPC has shown great clinical efficacy in enhancing bone regeneration. The rhBMP-2/CPC has also been authorized by the SFDA [armed (2013) No. 3460199].