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Research review paper

Prospects for translational regenerative medicine

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ABSTRACT

Translational medicine is an evolutional concept that encompasses the rapid translation of basic research for use in clinical disease diagnosis, prevention and treatment. It follows the idea "from bench to bedside and back", and hence relies on cooperation between laboratory research and clinical care. In the past decade, translational medicine has received unprecedented attention from scientists and clinicians and its fundamental principles have penetrated throughout biomedicine, offering a sign post that guides modern medical research toward a patient-centered focus. Translational regenerative medicine is still in its infancy, and significant basic research investment has not yet achieved satisfactory clinical outcomes for patients. In particular, there are many challenges associated with the use of cell- and tissue-based products for clinical therapies. This review summarizes the transformation and global progress in translational medicine over the past decade. The current obstacles and opportunities in translational regenerative medicine are outlined in the context of stem cell therapy and tissue engineering for the safe and effective regeneration of functional tissue. This review highlights the requirement for multi-disciplinary and inter-disciplinary cooperation to ensure the development of the best possible regenerative therapies within the shortest timeframe possible for the greatest patient benefit.

Contents

1. Introduction

Over recent years, there has been increasing interest in funding opportunities for initiatives that aim to bridge the 'translational gap' between

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basic and clinical research. As an emerging trend of medical practice and interventional epidemiology, translational medicine has now been established as a research platform in biomedical science. It acts as a bidirectional link between research and application to promote the rapid clinical translation and feedback of basic research results (Humes, 2005; Mankoff et al., 2004). Meanwhile, as an evolutional concept, translational medicine promotes cross-disciplinary integration and focuses medical research on the treatment or prevention of clinical diseases, where biomedical research has led to "patient-oriented" care (Petrou et al., 2009).

Basic research and clinical research have developed rapidly since the start of the 21st century. In parallel, barriers and gaps have become increasingly significant between clinical and basic research—a common perception is that the new discoveries generally fail to be efficiently translated into clinical research and ultimately into clinical practice (Katz, 2008; Mao, 2009; Newnham and Page, 2010; Tesio, 2004). More scientific researchers and government departments have realized that the gap between research and application will be a stumbling block for the continued rapid development of the life sciences. Many important discoveries lay dormant, leading to an imbalance between investments in basic biomedical research and rewards from treating human disease (Fig. 1). With the progressive advancements in life sciences, basic research has now penetrated into all fields of clinical medicine, rendering the rapid translation of knowledge and results acquired in the laboratory into techniques and therapeutics for clinical diagnosis and treatment a possibility. For example, stem cells grown in the laboratory have been the source of many breakthroughs in the treatment of heart disease (Perin et al., 2004; Segers and Lee, 2008; Stamm et al., 2004), graft-*versus*-host disease (GVHD) (Jacobsohn et al., 2004) and systemic lupus erythematosus (SLE) (Sun et al., 2009) in human beings. In 1998, the U.S. Food and Drug Administration (FDA) approved tissue-engineered skin called TransCyte® for clinical use, and numerous patients have received this treatment thus far. Recent advances in biomedical research and biotechnologies have offered new promises for the development of advanced therapies for human diseases (Cuende and Izeta, 2010), which may greatly improve patients' expectance of cures, patients' quality of life and public health. However, a substantial amount of basic medical research has not yet been translated to the bedside for routine clinical use (Belardelli et al., 2011). In this context, translational medicine has received increased attention and hence, has been popularized in the scientific arena (Milne and Kaitin, 2009; Valdespino Gómez, 2010). As a platform for communication between basic medicine, drug discovery and clinical disciplines, the importance of translational medicine in medical research and the health industry has significantly increased in recent years.

Fig. 1. Schematic depiction of the imbalance between investments in basic biomedical research and rewards from treating human disease. Potential new regenerative therapies are reported so frequently that one might predict a complete regeneration of multiple human tissues/organs in the next few years. However, most of these exciting discoveries never go beyond the laboratory bench. Obviously, some basic biomedical research in regenerative medicine is valuable even if it is not translated into a therapy. However, too many important discoveries are not further developed, with little research effort directed toward their potential for clinical translation, resulting in unrealized dividends from our investments in basic biomedical research.

Alongside recent positive developments in stem cell biology, regenerative medicine has enabled the development of new biotechnologies that exploit effective biological methods to promote self-repair and regeneration, such as the construction of new tissues to improve or restore the function of injured or destroyed tissues and organs (Gurtner et al., 2007). Although the challenges of introducing these therapies into widespread healthcare are still substantial, including significant biological, technical, clinical and regulatory hurdles, the potential benefits to patients would be profound (Chen and Jin, 2010; Chen et al., 2010a; Dutta and Dutta, 2010; Ruff and Fehlings, 2010; Vilquin and Rosset, 2006). Therefore, strengthening research on translational regenerative medicine may promote the application of new clinical therapeutic strategies and supply effective therapeutic measures for the treatment of severe tissue or organ deficits, and ultimately produce profound innovations that may drive the future of regenerative and engineering technology (Feuerstein and Ruffolo, 2007; Feuerstein et al., 2008; Shah et al., 2009).

The primary purpose of this review is to inform the reader of the current state of knowledge on translational regenerative medicine. We provide a conceptual description of translational medicine and a general introduction to current developments, with a particular emphasis on the status of research in regenerative medicine and the urgent need to translate advanced therapies from bench to bedside. This review utilizes a traditional approach rather than a systematic approach to provide a broad overview of the global translational medicine trends. This review is not meant to be exhaustive but aims to outline how stem cells and tissue engineering can provide a breakthrough in future reconstructive surgery, highlighting the orthopedic surgeons and oral health researchers remaining at the forefront of the movement to bring together clinicians, research scientists and industry partners to accelerate the pace of the clinical translation of medical research.

2. The concept of translational medicine

The pursuit of translational medicine was a priority of the scientific community at the beginning of the 21st century. Translational medicine encompasses the continuum of activities that extend from the conception of an idea to advanced preclinical and clinical testing and, ultimately, to the development of new therapeutics for patients (Mao, 2009; Newnham and Page, 2010). The concept of translational medicine has garnered wide attention and acceptance by the scientific community, but its precise definition has not been fully established thus far. With the increasing complexity and rigor of clinical research, the barrier between clinical and basic research is high, which limits the translation of new knowledge into clinical research and the subsequent feedback to basic research (Katz, 2008; Tesio, 2004). Translational medicine is increasingly important in the healthcare industry as it facilitates the movement of advanced therapies from a laboratory discovery to pre-clinical testing, early clinical trials, and late confirmatory studies that may lead to regulatory approval of therapeutics for use in patients (Belardelli et al., 2011; Schmidt, 2007). The goals of translational medicine are to break down the barriers between basic medicine, drug research and clinical medicine, to strengthen the integration between research and applications (Kreeger, 2003; Marincola, 2003; Moore, 2008). On the one hand, the knowledge and results obtained by basic scientists can be transformed into clinical applications to provide more advanced concepts, techniques, tools and methods related to disease diagnosis, treatment and prevention (Kreeger, 2003). On the other hand, clinical researchers communicate with basic science researchers to amend deficiencies in proposed therapeutics in a timely fashion, thereby promoting the development of basic research. These relationships are the foundation of the so-called dual-channel modulation and "Bench-2-Bedside (B2B)"