Stem cells and Tissue Engineering – The Ultimate Combo for Clinical Therapy?

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Introduction

There is not a day that goes by without the media presenting some amazing news flash that stem cells can be used to cure and treat diseases ranging from simple bone fractures to complicated neurological disorders, such as Alzheimer’s disease. But what are stem cells? And can they or will they be able to cure every disease in the future? And how will tissue engineering fit into the equation? For many, stem cells did not exist in their mind until Thomson et al. landmark publication in Science in 1998 [1]. Following Thomson’s paper, publications containing the word “stem cell” in the title multiplied. When the phrase “stem cell” was typed into the PubMed database (http://www.ncbi.nlm.nih.gov/pubmed/10881762) in 1998, approximately 2100 publications appeared; while in 2012 the number of publications that include “stem cells” as a phrase are close to 11,900.

Then what are stem cells? The simplest definition of a stem cell is a cell that can self-renew and differentiate via asymmetric cell division and regenerate an entire tissue from a single cell. The only stem cell that has been shown to meet all those requirements is the hematopoietic stem cell. Stem cells are often split into two groups. Firstly, somatic stem cells (or adult stem cells) that can be found in all organs of the human body and have the role to maintain those organs as well as meet requirements for cell regeneration when organs are damaged due to trauma or disease. Secondly, embryonic stem cells that can be isolated from the inner cell mass of the blastocyst from a circa five day old embryo and have the potential to differentiate into cells of all three germ layers that make up the human body. Recently a third type of stem cells has entered the scene. In 2006, a group in Japan under the leadership of Yamanaka et al. [2] published a paper showing that pluripotent embryonic stem cell like-cells could be derived from a normal somatic cell (non-pluripotent), simply by inducing expression of four key genes that are only found in embryonic stem cells [2]. These cells have all the attributions of embryonic stem cells and may have great potential for use in research and clinical therapy in the future. In 2012, Yamanaka was awarded the noble prize in medicine for his discovery (along with John B, Gurdon).

How do we use stem cells and how can we use them in the future? Without doubt, stem cells hold great potential not only for clinical therapy but also as a tool for basic research and drug development. Today, there is only one recognized clinical therapy in standard use in the healthcare system. This is the use of hematopoietic stem cells as a therapy for patients undergoing high dose chemotherapy to treat blood cancers such as leukemia, multiple myeloma, and lymphoma. This type of treatment has been ongoing for more than five decades and much of what we know about stem cells today can be attributed to discoveries made during the development of this type of treatment. There are many interesting clinical therapy potentials on the horizon where stem cells will be used. However, today none of these can be considered “standard care” and still there is much that needs to be done to develop these types of therapies so that they can benefit patients with complex diseases and traumas. On the other hand, stem cells are currently widely used in research and have over the past ten years or so advanced our knowledge on e.g., how cells differentiate, how diseases can develop, and lately, how cancer may develop from what has been termed cancer stem cells [3].

The human body, unlike that of fish and amphibians, cannot functionally regenerate organs and tissues lost due to injury or ageing. In the human body, the main response to tissue injury is the induction of repair mechanisms aimed at restoring the tissue by scar formation, rather than regenerating function and structure [4]. The objectives of promoting the body’s self-healing capability, the restoration of normal cell function, and the possibility to recreate complex organs “at the bench”, are the main objectives of the interdisciplinary fields of tissue engineering and regenerative medicine.

Regeneration is by no means a spontaneous process, and approaches aimed at replicating normal tissue function need to provide the essential microenvironment-be it cells, biomaterials, or signaling molecules, to support a body’s self-healing capabilities. While the field of regenerative medicine relies on cues from stem cell biology to promote innate regeneration processes, tissue engineering is focused at solving the technical aspects: i.e., the support and restoration of function by using a structural support matrix, a.k.a., biomaterials [5]. A biomaterial per definition can be any implantable construct or scaffold intended to provide the microenvironment necessary to promote the replication of natural tissue function. Ultimately, only a combination of the two approaches can succeed to fulfill the promise of recreating a process as complex as genuine regeneration.

Tissue engineering and regenerative medicine are by no means new concepts; in fact, they have been around for the better part of 20 years. Despite the substantial effort, both in labor force and financially, allocated to the development and integration of these concepts, tissue engineering and regenerative medicine strategies are far from being an integral part of today’s clinical treatment options. Where did we go wrong? There is no single answer to this question and our intention is not to find a scapegoat or point fingers. The theoretical concept of tissue engineering and regenerative medicine is brilliant and has the potential to revolutionize the current clinical treatment for a number of diseases and injuries, as well as solve the issue of donor organ shortage. The hope and confidence put into the accomplishment of this breakthrough are tremendous. In our opinion, this is where the problem lies. Hope and
confidence are well and good, but are we really technologically advanced enough to accomplish a feat as complex as genuine regeneration, which is nothing less than what we expect tissue engineering and regenerative medicine to solve. The achievement of ex vivo tissue generation and in vivo regeneration of function is not only a matter of choosing the right cell type, a suitable biomaterial as support matrix and adding a cocktail of signaling molecules for good measure. How can we assure that it is our tissue-of-interest that will be generated? How do we control the process once tissue generation is accomplished? Will the final tissue really be functional and an appropriate replacement? These questions are only the tip of the iceberg when it comes to the problems and challenges faced in tissue engineering and regenerative medicine. Scientists in the field do not only deal with the issues of combining the necessary skills in sterile cell culture techniques, the knowledge in engineering and materials science for development and production of suitable biomaterials, the understanding of molecular biology, immunology and the ability to appropriately interpret biological results; they are also required to address the regulations posed by governing bodies, while providing an elegantly-designed, high-quality, yet low-cost strategy intended for clinical application. And these obstacles do not even take into account the consideration of ethical guidelines and the lack of sufficient funding. We personally think that we are not ready yet to face all these challenges. Our knowledge about the human body and the (re)-generation of tissues is, despite all efforts, still limited and without first addressing the issues that researchers in the field have to deal with, the success of tissue engineering and regenerative medicine strategies is questionable. We do not doubt that one day we will be able to satisfy the hope and confidence placed in these efforts, but before we can achieve this, we need to refocus our strategies on better understanding what we are really dealing with. We cannot dive into creating a tissue without understanding how we can control the process or which parameters are essential for its success.

Stem cells and tissue engineering hold a great promise. However the hurdles along the way will be many, not only in the scientific arena but also dealing with irresponsible "scientists" that will promise cure using stem cells as long as you line their pockets with silver. Stem cells and tissue engineering are still in their infancy, but if we foster the field, and give scientist and physician the opportunity to advance the field using proper scientific and clinical standards, then a combo of stem cells and tissue engineering will pave the future as key therapeutic option for various diseases and traumas.

References