

Prospects and Potential of Regenerative Medicine



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Abstract

Regenerative medicine concept is advancement in biomedical application which is based on the principles of stem cell technology and tissue engineering in order to restore human tissue and organ's functions. This novel scientific approach is opening to represent a valuable treatment option for acute injuries, chronic diseases and congenital dysfunctions. This mini review is to express the state of art in regenerative medicine used strategies and burning problems to solve in the future.

Introduction

The every multi-cellular organism survival depends on the balanced cell division and cell death. Regenerative medicine (RM) involves the replacement or regeneration of human cells, tissue or organs, to re-establish their normal functions. RM is considered a novel front line of medical research, but the idea of creating artificial organs is not so recent [1]. The regeneration of body parts is a rather common phenomenon in nature; a salamander can regenerate an amputated limb in several days. Humans have this ability as well, but they lose it over the years: a severed fingertip can regenerate until 11 years of age. The human regeneration potential was well-known also in ancient times, as demonstrated by the myth of Prometheus: his liver was eaten by an eagle during the day and it completely regenerated itself overnight.

The medical and pharmaceutical sciences gained many success, but there are still many situations requires the resection of lesions or repair with autologous tissue or allograft. Tissue or organ rejection after transplantation was very common due to immunological responses, but the advent of cyclosporine (Immunosuppressive agent) the risk of rejection could be reduced [2]. There are two drawbacks of organ transplantation i.e. life-long immunosuppressive agents showed many side effects and the shortage of similar donors, not being able to meet increasing demand of organs.

Present Strategies of Regenerative Medicine

Following approaches trail the objective of RM

- Cell based therapy
- Immobilized biological or synthetic material to lead repair and growth
- Implantation of scaffolds seed with cells

Cell based therapy

However, all cells come down from one exclusive cell, called zygote. During development, cells differentiate gradually and acquire more and more specific tasks, while they lose their capacity for differentiating into other cells. The ability to differentiate into other cell types is defined as "cell potency" (Table 1). Cell therapy consists of injecting novel and healthy cells (differentiated endogenous or undifferentiated stem) in diseased tissues, which can differentiate depending on meticulous circumstances (Table 2).

Table 1: Types of cellular potency.

Totipotency	The ability of a single cell to produce all cells (potency possessed until 16-cell stage during blastocyst phase)
Pluripotency	The ability to differentiate into a cell of all three germ layers (e.g. embryonic stem cells)
Multipotency	Gene activation limits these cells to differentiate into multiple, but limited cell types (e.g. hematopoietic stem cells can differentiate into all blood cells: erythrocytes, lymphoid cells, neutrophils, platelets, etc.)
Oligopotency	The ability to differentiate into limited cell types (e.g. lymphoid stem cells become either B cells or T cells)
Unipotency	Ability to differentiate into one single cell type (e.g. precursor cell)

Table 2: Merits and demerits of cell types used in RM.

Cell Types	Merits	Demerits
Differentiated endogenous primary cells	No tissue rejections, Reduced inflammatory response	Difficult expansion because in vitro short lifespan Difficulty in getting healthy cells in diseased organs
Adult stem cells (ASCs)	No tissue rejection, No ethical problems, No tumors, Easy isolation In some cases easy access (e.g. apheresis and subcutaneous fat)	Low number in each tissue Difficult in-vitro expansion without differentiation
Embryonic stem cells (ESCs)	Unlimited ability to self-renew Potential to differentiate into many specialized cells from all the three germ layers	Ethical and political problems Tumorigenicity Need for feeder cell layers (risk of xeno-contamination when mouse fibroblasts are used)
Induced pluripotent stem cells (iPSCs)	Similar as ESCs Easier generation than ESCs No ethical problems	Tumorigenicity
Amniotic fluid-derived stem cells (AFSCs)	Great ability to proliferate without feeder cells, No tumorigenic, No ethical problems, Possibility of preservation as lifelong autologous stem cells together with other perinatal stem cells (umbilical cord placenta and amnion membrane-derived stem cells) Possibility of antenatal collection by amniocentesis or chorionicvillous sampling	Further research is needed (being the latest discovery)

Immobilized biomaterials

Tissues generally consist of cells and extracellular matrix (ECM). Biomaterials usually serve as ECM, giving both structural and functional support. During the last few years, ECM has been shown to play a key role in different functions, such as gene expression, survival, death, proliferation, migration, differentiation. Therefore, all of them should be reproduced by biomaterials enriched with bioactive factors, such as growth factors and cytokines. The materials used in RM (Table 3) can be classified as natural or synthetic with different advantages and disadvantages.

Table 3: Biomaterials used in RM.

Origin	Example
Natural materials	Collagen, fibrin, chitosan, dextran, alginate, gelatin, cellulose, hyaluronic acid (HA), silk fibroin
A cellular tissue Matrix	Bladder a cellular matrix (BAM), small intestinal submucosa (SIS), bowel a cellular tissue matrix (ATM), bovine pericardium (BPV), human placental membrane (HPM)
Synthetic polymers	Polyglycolic acid (PGA), polylactic acid (PLA), poly(lactic-co-glycolic acid (PLGA), polycaprolactone (PCL), poly(copalactone-co-ethyl ethylene phosphate) (PCLEEP), polydioxane (PDS), polyethylene glycol (PGE), poly-N-(2-hydroxyethyl) metacrylamide (PHEMA), poly-N-(2-hydroxypropyl) methacrylamide (PHPMA)

The ideal biomaterial should be biocompatible and biodegradable at the same rate as regeneration process without leaving toxic end-products, interfering with regeneration process and causing inflammation and/or obstruction. A technology, called dynamic optical projection stereolithography, complex 3D microstructures, like blood vessels, can be printed within few seconds. Without vasculature printing, essential for distributing nutrients and oxygen, tissue-engineered organs, such as liver or kidney, are useless in clinical practice. The bio-fabrication technique grounds on a photo-induced solidification process, which uses soft biocompatible hydro-gel containing living cells and forms one layer of solid structure at a time, but in a continuous fashion, by shining light on a selected area of a solution containing photo-sensitive biopolymers and cells.

Implantation of scaffolds seed with cells

This is a combination move toward of previous two techniques. In 2006, Atala et al. [3] reported autologous engineered bladder constructs could be used in patients suffering from myelomeningocele needing augmentation cystoplasty. The synthetic scaffold was made up of collagen and PGA and seeded with patient’s urothelial and smooth muscle cells, respectively on the endoluminal and abluminal side [4-7]. These cells were obtained through a patient’s biopsy and expanded in vitro before scaffold seeding.

Conclusion

RM opened new avenues for curative patients with difficult-to-treat diseases and physically impaired tissues. Despite many successes, RM is still unfamiliar to many scientists and clinicians [8]. This poses a great limit, as tissue engineering and regenerative medicine could overcome the unsolvable problems of the current medical treatments. In order to resort to RM in the clinical setting on a daily basis, it is mandatory to obtain important financial investments from different sources including governments and industries that are oriented toward research and medical innovation [9,10]. There is a considerable

need for long-term vision and support for RM to accelerate the development of novel therapies and to promote the stability of collaborations around the world. The crucial point of this revolution is transforming the current numerous scientific discoveries into novel and viable therapies: from bench to bedside.

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