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MINI-REVIEW

Stem Cells' Future: Toward Organ Bioprinting

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ABSTRACT

Organ Bioprinting is a new approach in the field of regenerative medicine that try to make a whole intact functionally active organ from tissue specific cells. Providing such organs are very important because every year many patients need to organ transplantation but the number of donors are so limited. Organs made from different tissue with different kinds of cell types and for Organ Bioprinting first we need to provide these cell types. Currently, with regards to advances in stem cell biology specially invention of easy methods for isolation mesenchymal stem cells (MSCs) as one the appropriate cell type for regeneration purpose and also due to their unique properties including lack of immune-rejection in allograft, MSCs have gained attention for using in organ production. MSCs can isolate from many tissues of adults and differentiate in a targeted manner into cells of interest; provide a main material of tissue engineering triangle (i.e. cells, biomaterial and growth factors) for 3D bioprinting of human organs on a substrate. Printers have the ability of designing tissues and organs with fusing living tissue specific cells and extracellular matrix in layers to produce 3D biologically functional new organ. It is conceivable that in the near future, stem cells will play their predicted role; i.e. whole organ production.

Keywords: Organ printing, Stem cells, Tissue engineering, Regenerative medicine, Mesenchymal Stem Cells (MSCs).

More than three decades have passed since the discovery of stem cells [1]. Stem cells possess ability of self-renewal and capability to differentiate to other types of cells as well [2]. These cells can be isolated from different tissues and be used for many applications [3, 4]. The most important prospect of stem cells applications can be regeneration of perfect organs and tissues in laboratory using their potentials [5, 6]. For this aim, stem cells should be easily isolated from tissue of origin and then expand in culture medium, in next step using differentiation methods tissue specific cell lines produce from stem cells and finally target tissue can be prepared for transplantation to patient [7, 8].

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But for printing an organ the steps are more complicated in compare with tissue and need additional sophisticated techniques as well as check point to make a functional organ. Either tissue or organ printing had many problem to come true and fortunately during recent years many problems have been solved [9]. Among these problems, culture difficulty, precise identification and printing of the cells, targeted control of stemness, and differentiation potential are noteworthy [5]. Although simple culture of stem cells in laboratory was an important milestone in regenerative researches but making tissue and then perfect organs such as heart and kidney need more scientific and technical knowledge [10].

Since tissue engineering was born, it made stem cells closer to clinic more than ever [11]. Golden triangle of stem cell, scaffold and growth factor/s always have been main foundations of this field researches and so far outstanding works have been done in tissue engineering [12]. Though in practice, tissue engineering has been suitable and effective in clinic and perfect regeneration, but it required further development like patient-specific utilization of stem cells. However, production of first cellular printer opened new view to stem cells researches and for the first time in history, mechanic and electronic technology along with cellular technology made conceivable production of natural organ [13, 14]. In this method, multiple tissue-specific cells were placed on each other layer by layer based on patterning of body's original tissue [15]. At the beginning, cellular print was done as 2D fashion, but after further inventions and using thermosensitive gels it is being possible to do 3D printing using with different kinds of printer including selective laser sintering (SLS), thermal inkjet (TIJ) printing and fused deposition modeling (FDM) [16-18]. This technology can be promising regarding to increasing number of patient who need an organ for transplantation every year, the limit number of organ donors and urgent need of patients who can't be alive anymore without new healthy organ [10]. Generation of perfect organ in laboratory has been a great dream of researchers in health area and nowadays due to development of technology, patients are more hopeful to have such a healthy organs [19]. So far prototypes of some organs have been produced and these organs possess full capillary system and are so precise [20]. Accurate Scan along with high resolution can print and produce new organ [21]. However, to generate better functional organs for patients more improvement in the field of accurate scan with high resolution, correct differentiation of stem cells to cells of interest, production of more reliable ECM-mimic scaffolds as well as producing more advanced printer are necessary [20-22]. Although the problem of organ rejection should be solved through using patient's own stem cells as autograft transplant but the produced organ must has stability and suitable physiological efficiency to best durability and operation in patient's body [23]. Interestingly, among different kinds of stem cells, mesenchymal stem cells (MSCs) have ten unique properties including immune-privilege and immunomodulatory properties can be uses as allograft clinical settings [24]. Therefore, MSCs can be promising cells for producing off-the-shelf organ products. According to recent development of tissue engineering, it can be predictable bright future in production of full organ and treatment of many disabilities and abnormalities in the human body [11].

Conclusion

Although by using the advanced 3D printers, producing full organ in laboratory is possible but there are still some ambiguities in this field. Among these ambiguities, tissue/organ immunocompatibility can be mentioned. The question is whether the *in vitro* produced organ can nicely adapt to niche of the body? On the other words, this means whether cells of created organ have properly trained to communicate each other and their niche as well? For instance, whether surface markers and other indicators of the cells are similar to natural organ? In addition, whether this technology does not conflict to ethical principles of different societies and beyond that, different religions? All these issues should be answered concerning organ printing; finally would determine future of *in vitro*-made organ application.

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