Neo-Bioartificial Whole Functional Organ Development Using Decellularization and Stem Cells Repopulation Technology: Cutting Edge Strategy for Humanized Organ Development

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Editorial

Shortage of available organs for organ transplantation in end stage organ failure is a major challenge. Annually >10,00,000 patients die for the want of the functional organ. Demand of donating organ for the treatment of end stages organ failure has increased tremendously in recent years. The knowledge of stem cells has proved its potential for the treatment of various fatal diseases. Stem cells are known to regenerate injured tissues or to replace the lost cells in a very effective manner. Whole organ development requires not only the stem cells but also the contiguous stem cell niche or microenvironment and extracellular matrix with complete vasculature and integrity. Adding up to the cell replacement therapy stem cells-based organ regeneration has been successfully accomplished in clinics for organ failure of the liver or kidney. Generation of biological or semi-biological organs using stem cells could be an alternative approach to solve the shortage of donor organs. Particularly, researchers have been looking for ways to establish a whole organ using stem cells. Stem cells from various sources have been tried to regenerate the damages organ system still which stem cell type is used, it remains a challenge to reliably generate large quantities of well-differentiated cells.

The recent breakthroughs and one specific trial in particular, provide much closer evidence for clinical practice. Recently, the first human tissue-engineered organ using stem cells was created and transplanted successfully into a patient. In the first reported instance of using stem cells to bioengineer a functional humanized organ, Paolo Macchiarini and his colleagues used a patient's own stem cells to generate bronchus, and successfully grafted it into the patient to replace her damaged bronchus. Macchiarini's group bypassed the problem of immune rejection by using allogenic stem cells [1,2]. Other tissue regeneration efforts using stem cells have also been recently made lots of breakthroughs, emphasizing the possibilities of using stem cells in future tissue/organ transplants.

In recent year's decellularization and recellularization approach for whole organ construction has been emerged as exceptionally promising technology [3]. Few landmark studies on complex organs development, such as liver, heart, kidney and lung have provided a better insight into the supremacy of the methodology. Encouraging results from animal model studies have emerged a potential hope to get the whole personalized functional organ for the end stage organ failure patients. These bio-artificial organs provide micro vascular structure for efficient supply of nutrient and oxygen to each and every cell and solve the problem of availability of 3D-natural architecture and organ scaffold, immune rejection and others.

Seeding of specific type of cells with high proliferation and controlled differentiation potential is necessary to repopulate the decellularized organ scaffold (a process called repopulation/recellularization). Although, a variety of organs have been used for decellularization and recellularization to generate the functional organ. None of them have proved their absolute potential to replace the damaged organ/tissue. Liver becomes a more convenient organ in terms of repopulation of decellularized organ because the major population of cells is of parenchymal. Functionally this organ performs more towards the detoxification and synthetic function. Hence, the desired cells can be used as per the requirement of the organ. As in the acute liver failure short-term support is needed to the failing liver. This concept becomes more viable as extra-corporeal organ support using xenogenic liver scaffolds repopulated with human hepatic stem cells [4,5]. Still there are certain complications and issues which need to be considered and solved before its clinical applications such as type of organ scaffold, sterilization of the scaffold, integrity of the vasculature and natural architecture within the scaffold, assessment of immunological barriers, type of cells/tissue to regenerate functional aspects of the regenerated organ, type of cells for infusion, route of cell delivery, required induction factors and assessment of long-term cell survival and engraftment.

Further studies are needed to determine the role of biological, structural and mechanical factors responsible for the generation of natural ECM with functional recovery. Petersen et al., and Ott et al. for the first time demonstrated transplant survival for few hours of repopulated lung scaffold into rats with adequate oxygen and CO2 exchange and appropriate pressure/volume relationships [6,7]. However the rat was died because of pulmonary oedema and/or haemorrhage resulting in respiratory failure. This approach provided a clue for the development of new organ by recellularization of decellularized organ scaffolds. Following to the above study Song et al., generated a bioartificial rat kidney by decellularization and recellularization approach using human umbilical cord blood derived endothelial cells and showed urine production along with slight macromolecular sieving and reabsorption potential.

Very recently our group has demonstrated the development of bioartificial organ from goat using decellularization technology [4,5-9]. This model provides more appropriate xenogenic source to plug the gap between the shortages of available donor organs due to the similarity in organ size and complexity and most importantly it has very low risk of zoonosis. This model represents most accepted choice for better understanding of whole organ regeneration and shows promise for a suitable organ donor for the recipients waiting for organ transplantation.
In summary, the concept of decellularization and recellularization has provided a new dimension for the development of bioartificial organs which can find its clinical applications after further advancements (Figure 1). However, development of bioartificial functional organs based on the decellularization and recellularization technology still remains challenging. Further vital research is needed for the prediction of functional outcome ex vivo and in vivo such as long-term survival, engraftment and cost effectiveness.

References