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Case Report

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Decellularization of renal fibrosis by cyclic hydrostatic pressure to restore renal function

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Introduction

Natural extracellular matrices (ECM) are currently being studied as an alternative source for organ transplantation or as new solutions to treat end-stage renal disease. As the gap between donors and patients in need of an organ transplant continues to widen, research in regenerative medicine seeks to provide different strategies for treatment Tissue and organ failure is currently one of the biggest health issues our society faces [1]. Arising from disease or trauma, complete treatment typically requires the repair or replace the affected organ However, the unavailability of adequate organs for transplantation to meet the existing demand has resulted in major organ shortage crisis. As a result, there has been a major increase in the number of patients [2]. The stem cell therapy fails because of the toxic environment in the organ, the implanted cells unable to regenerate. Afterwards researchers are trying to prepare the lab made artificial organ in the laboratory with the help of artificial scaffold and the tissue specific stem cells. Then tried for the transplantation of animal organs. To overcome this organ shortage challenge is the use of organ-derived scaffolds obtained via decellularization techniques by removing all viable cells from native tissues and retaining 3D structure of natural extracellular matrix (ECM) and vascular network for regeneration. This is the most adequate method where scaffold thoroughly decellularizes, free of endotoxin or bacterial contamination. An appropriate macro and microstructure to support physiological function, intact vascular tree, specific location cues.

Transplantation is the only curative treatment option available for patients suffering from end-stage organ failure, improving their quality of life and long-term survival. However, because of organ scarcity, only a small number of these patients actually benefit from transplantation [2]. Because of the complexity of the cell microenvironment; there has been increasing interest in utilizing the naturally derived extracellular matrix (ECM) itself rather than the synthetic scaffold. The regeneration of whole organs with a decellularized extracellular matrix (dECM) has remained a goal. Recently, decellularization techniques have been widely used in producing scaffolds that are appropriate for regenerating [3].

Bridging the gap between donors and patients in need of transplants through bio scaffold tissue, since current methods are usually limited to small tissues. Decellularized tissue is a superior scaffold that is preserving the microstructure of the organ or tissues. There is risk while removing the cells including denaturation of ECM or destruction due to high hydrostatic pressure. This tissue has several advantages over the manmade artificial scaffold with polymer hydrogel. It is a much more accurately structured ECM in which cells live in vivo and even incorporate some chemical and mechanical signals, which leads the cells in a “realistic way”. They are in their native cellular microenvironment it is a popular technique, which obtains a cellular scaffold, and their derivatives (hydrogel) which retains tissue specific components critical structures and functional proteins that gives the advantage to stimulating the sensitive repair mechanism in damaged tissues. In decellularized process, organ cells removed leaving behind the entire “Blueprint” in the form of architectural scaffold and cues for cell presentation and homeostasis.to form remoulded functional organ. The ECM obtained with close to “Intact” details and composition [4]. In the field of regenerative medicine, various regenerative technologies have lately been developed using various biomaterials to address these limitations. Decellularized scaffolds, derived mainly from various non-autologous organs, have been proved a regenerative capability [5].

ECM of mammalian organs and tissue used as substitutes scaffolds to restore or reconstruction of several tissues ECM is a non-cellular structure that regulates almost all of the cellular functions.. Researchers are able to take the tissue from a donor or cadaver. lyse and kill the cells within the tissue without damaging the extracellular components and immunogenic antibodies from donors tissue removed which will produce natural ECM scaffold. (6) A natural ECM scaffold provides the necessary physical and biochemical environment to recellularized with potent stem cells. The natural extracellular matrix (ECM), its specific properties, ensures an optimal microenvironment for homeostatic and regenerative cell development. In the context of regenerative medicine, ECM is a lair for residual and infiltrative cells. The composition and structure of kidney ECM is herein associated with its intrinsic capacity of remodelling and repair after insult

A variety of methods has been evaluating the decellularization process in terms of cell removal efficiency, in order to enhance the efficacy of decellularization methods Physical, chemical, and biological methods utilized to produce acellular scaffolds, by either perfusion- or immersion/agitation-based systems, or even a combination. Decellularization techniques differ in terms of applied materials and the routes used to deliver the main reagent, namely vascular, airway, or both to form acellular scaffolds. Recellularization is defined as the repopulation of acellular ECM scaffolds of tissues or organs with organ-specific cell types or stem cells aiming to reconstitute the micro-anatomy of the organ and thereby recreate the organ-specific function [7]. The cells used for recellularization need guidance for their rearrangement and maturation, Recellularization of the scaffold, providing a suitable biochemical and physical environment boost its regeneration ability in host tissues. The main principle in all methods is removing cellular material and leaving the ECM ultrastructure unchanged in the tissue. Direct force of pressure to a tissue will guarantee disruption of the ECM structure, so pressure is commonly used. Pressure decellularization involves the controlled use of hydrostatic pressure applied to a tissue or organ.. Which has become an increasingly popular technique used to obtain acellular scaffolds, and their derivatives (hydrogels, etc.), which retain tissue-specific components, including critical structural and functional proteins. These advantageous characteristics make this approach for creating materials capable of stimulating the sensitive repair mechanisms and the maintenance of ultrastructure of ECM.

Whole organ dECM technique widely used producing scaffolds to regenerate damaged organs. Scaffolds formed are much more accurate structures in which cells live with chemical and mechanical signals. In chronic kidney disease the renal failure occurs due to the renal fibrosis The transplantation of cadaver or donors organs after the decellularization is not the solution because for growing solid organs like kidney liver needs dozens of cells, exact right position of the cells, proper vascular network, sterile tissue for transplant, able to grow and repair themselves and most important they have to work life time. Also contaminated with dead cells and infection, such scaffolds cannot be transplanted into human beings as a replacement of organs Body organs are complex structures, mostly composed of various collections of tissues, made up of various extracellular matrixes and cellular components. Every organ has different types of cells because they have different functions. Even the cell's position should also be perfect otherwise; it affects function of the organ. Cells have a life span, and can repopulated cells be able to regenerate new young cells when they die? Nobody can give guarantees about life of the repopulated cells and its work for lifetime. Uncertainty about the viability and functionality of cells after organ grafting these are the main problems regarding decellularized donors or cadaveric organs to transplant in the organ failure patients. For small tissues like blood vessels, trachea, bladder and stomach and for skin grafting the decellularized ECM scaffold or their hydrogels in the form of powder, sheet or tube which are biological tissues so no chance of rejection. The current application, limited to tissue level an anatomically simple organ, ultimately provides the foundation for complex functioning organs regeneration in future.

In renal failure patients, the normal renal parenchyma is replaced by the fibrosis. In early stages patients treated with anti-inflammatory and anti-fibrotic drugs for prolonging their life but not curing the disease. In let stage disease treated with dialysis or renal transplant. Renal cells in the renal parenchyma as far as the function is concerned are dead due to the fibrosis. Cyclic HHP established a novel decellularized method where ECM proteins are removed from organs without altering mechanical properties and reducing inflammation. Decellularization technique developed with exclusive use of hydrostatic pressure, it is an easily accessible and low-cost technique How to apply the decellularization technique in-patient who is suffering from chronic kidney disease to restore renal function in situ. The applied material is patient's urine and route to deliver of device is the ureter. Left kidney used for decellularization, the device passed through left ureteric way to block the PUJ (Pelvi Ureteric Junction) to stop the drainage of urine flow and collect the urine in pelvis of the kidney and creates artificial hydronephrosis as the volume of urine increase day by day depending up on the urinary output. Urinary volume around 1 to 1.5 litters of urine collected in the pelvis produces a sufficient amount of Luminal hydrostatic pressure Which can effectively force decellularization through dense fibrotic tissues and drive cell residues out of the ECM. The decellularization through ureter provides a wide contact area for the fibrosed parenchymal cells. HHP, which is direct action, gives best removal of fibrotic cells, fibroblast and excessive collagen fibres and keeping the renal scaffold intact. Without damaging the natural renal scaffold, blood vessels capillaries, which are essential for the regeneration. Ureteral decellularization is more effective, efficient and forms a uniform decellularized scaffold. Natural pressure created due to blockage at PUJ, which is increasing slowly. Use of ultrasound and MRI can help to monitor pressure. There is no pressure side effect over surrounding kidney tissue and will not disturb patients due to pain.. If the patient fills any discomfort, the kidney can be decompressed by removing an artificial block at PUJ to drain the urine .This method of decellularization gives a purified sterile clean natural scaffold with vascular network, which is best for in situ regeneration. There is no necessity to carry recellularization or repopulation of stem cells; it happens automatically once the microenvironment becomes healthy.

This decellularized technique changes the cellular microenvironment by removal of fibrotic cells by cyclic hydrostatic pressure and creates the suitable environment to restore capillary blood supply to anoxic renal tissue, which stimulates the regeneration with the help of healthy stem cells present at the site of injury in the sub capsular region and normalise the renal function by regeneration. The host tissue response of these scaffold materials is dependent upon the efficacy of decellularization and removal of cell remnants' to regenerate complex organ function, which requires extensive decellularization and reconstruction technique mainly the ultrastructure, and vascular network. Recellularization is more important which needs to distribute proper cell type uniformly through decellularized tissue with sufficient blood supply [7]. For self-organ regeneration the patients body's regenerative capabilities and biological supply of stem cells in to renal dECM to generate a functional and viable renal tissues .To restore renal function the early diagnosis and proper decellularization treatment is required in chronic renal failure patient. Tissue or organ specific dECM becoming a more feasible option to carry out regeneration in failed organs. This decellurization procedure is more effective in the early stage of disease (1st and 2second stage)when fibrosis is less but as the renal disease progresses further the fibrosis becomes solid it will be difficult to dcellularize to form natural scaffold.

This left ureteral route decellularization done with cyclic hydrostatic pressure will eliminate the renal fibrosis, creates a healthy cellular microenvironment, and stimulates the in situ regeneration. This method is a less expensive, non-invasive, simple and quick procedure, which gives good results to restore renal function in chronic renal failure patients.

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