Archives of Medicine©
14 (12) 2022 : 001-002 • PERSPECTIVE

Developing human renal epithelial cells for transplant in regenerative medicine

Rebecca Motta*
Department of Nephrology, Leiden University Medical Centre, Leiden, The Netherlands

INTRODUCTION

By supplying a local source of trophic factors that encourage regeneration or by replacing damaged cells, cellular transplantation may be used to treat a number of human diseases. As a model cell, we used cadaveric donor-isolated human renal epithelial cells (hRECs). We looked at a novel encapsulation method for immunoisolating hRECs and lentiviral transduction of the Green Fluorescent Protein (GFP) as a model gene for genetically engineering hRECs to secrete the desired trophic factors in order to use hRECs effectively in the treatment of kidney diseases. In particular, we investigated the possibility of preserving cell viability and trophic factor secretion by encapsulating hRECs using conformal coating or GFP transduction. In order to accomplish this, we optimized hREC culture conditions and demonstrated that aggregation in three-dimensional spheroids significantly preserved cell viability, proliferation, and secretion of trophic factors. Through our fluid dynamic platform, we also demonstrated that both GFP-engineered and wild-type hRECs could be effectively encapsulated within conformal hydrogel coatings, enhancing cell viability and trophic factor secretion. The transplantation of genetically engineered human primary cells for the treatment of kidney-related and possibly other tissue-related diseases could be based on our findings in future therapies [1].

DESCRIPTION

Several human diseases could be treated with cellular transplantation. Acute kidney injury and chronic kidney disease are two of the most common conditions, and their high cardiovascular morbidity and mortality are linked to rising healthcare costs. There is a pressing need for strategies that can either slow the progression of chronic kidney disease or speed up the recovery process from acute kidney injury.

The use of various therapeutic methods is being investigated. These include transplanting cells that are derived from damaged or dysfunctional tissues, either by themselves or as helper cells. The latter may aid in tissue regeneration through the recruitment of cells with regenerative potential or the local secretion of cytoprotective factors. The microenvironment's influence on phenotypic changes and plasticity determine the fate of implanted cells. When compared to standard two-dimensional culture, the majority of cells have been shown to be better preserved in three-dimensional (3D) scaffolds [2].

Address for correspondence:

Rebecca Motta
Department of Nephrology, Leiden University Medical Centre, Leiden, The Netherlands
Email: rebeccamotta@gmail.com

Word count: 1070 **Tables:** 00 **Figures:** 00 **References:** 05

Received: 01.12.2022, Manuscript No. ipaom-22-13363; **Editor assigned:** 03.12.2022, PreQC No. P-13363; **Reviewed:** 15.12.2022, QC No. Q-13363; **Revised:** 20.12.2022, Manuscript No. R-13363; **Published:** 27. 12.2022

The immune system of the host does not reject autologous cells, so they may integrate into the remodeling tissue. Sadly, recovering healthy cells from damaged tissue may be limited by not being able to achieve a satisfactory yield. Another option for treatment is autologous somatic cells, also known as skin cells, that have been "reprogrammed" in vitro. However, these cells require expansion, which presents a significant obstacle. In addition, in the event of acute organ failure, prompt use may not be possible. In addition, gene therapy is required before using autologous cells if the cause of organ dysfunction is genetic. Because they can be cultured and stored to be readily available for the treatment of acute medical conditions, allogeneic cells may also be a viable option for regenerative and tissue repair therapies. Allogeneic cells' vulnerability to immune rejection after implantation is their primary drawback. Their use necessitates the simultaneous administration of immunosuppressive medications with undesirable side effects. Immunosuppression may also disrupt cell replication and function, potentially altering the implanted cells' regenerative properties [3].

Immunoisolation through the encapsulation of allogeneic cells and cell clusters may be an appealing strategy to prevent immune rejection without requiring lifelong immunosuppression as an alternative that has the potential to overcome these limitations. The production of capsules with a constant diameter of 500 to 1500 m is the foundation of conventional cell microencapsulation. The maximum distance between a cell and the blood supply that permits the proper diffusion of nutrients and oxygen has been determined to be 150 millimeters, according to experimental and computational studies. Due to their large size, conventional microcapsules can lead to central hypoxia of enclosed cell clusters, accumulation of cellular waste, and delayed trophic factor secretion. Additionally, the intraperitoneal cavity is the only option for transplant due to the large volume of capsule material. A novel method for conformal coating encapsulation (CCE) of cell clusters based on fluid dynamic principles has recently been developed by us to overcome these limitations. This interaction permits 'shrivel wrapping' of cell groups with a dainty (scarcely any many microns) layer of biocompatible polyethylene glycol (Stake) and alginate (ALG) hydrogel without influencing cell practicality or usefulness of the epitomized cells. In this study we utilized recently portrayed human renal epithelial cells (hRECs) as a model for showing practicality of a phone designing methodology that permits long haul ex vivo culture, immunoisolation and hereditary control of the cells while protecting suitability and discharge of trophic variables engaged with tissue recovery [4].

Following institutional protocol approval, unsuitable transplantable tissue was obtained through the National Disease Research Interchange (Philadelphia, PA). Kidneys were washed in Dulbecco's modified Eagle's medium (DMEM, Life Technologies) to remove blood cells and debris. The kidney cortex was the site of the tissue dissection. After that, the tissues were mechanically dissociated in tissue culture plates and digested with good manufacturing practice-grade enzyme mixtures containing 2.5 units/mL dispase II and 0.25 units/mL 4-phenylazobenzyloxycarbonyl activity/mL collagenase (NB6, Serva Electrophoresis GmbH). Renal epithelial growth medium (REGM, Lonza) was added to the enzyme mixture. After the digestion step, the conical tubes containing the tissue, medium, and digestion enzymes were incubated at 37°C for 2 hours in an orbital shaker at 225 rpm. If large pieces of tissue were still present, gravity sedimentation or slow centrifugation were used to remove them. After that, the suspended cells in the supernatant were transferred to a new 50 mL tube and centrifuged. For cytological evaluations, cells were resuspended in REGM, plated on gelatin-coated tissue culture flasks, and cultured at 37°C in normal atmospheric conditions. Up to six passages of human renal epithelial cells (hRECs) revealed 88% viability and a normal 46 XY karyotype. The characterization of cells has already been published. All of the experiments shown here were carried out using hRECs [5].

CONCLUSION

Human renal epithelial cells hRECs at section 4 and ~70% confluency were transduced at variety of contamination (MOI) somewhere in the range of 1 and 10 with a pRRLsinPPT-EGFP lentivirus given by the viral vector center office at the College of Miami. Fluorescence microscopy and flow cytometry using the LSRII machine (BD Biosciences) confirmed GFP positivity five days after transduction. The expansion of GFP+ cells occurred from passage 4 to passage 6. Two weeks after transduction, an HIV-1 p24 antigen ELISA was carried out in accordance with the manufacturer's instructions (Zeptometrix) to ensure that no viral proteins remained in the cell supernatant.

REFERENCES

1. **Nakatsuji S, Yamate J, Sakuma S.** Macrophages, myofibroblasts, and extracellular matrix accumulation in interstitial fibrosis of chronic progressive nephropathy in aged rats. *Vet Pathol* 1998;35(5):352-60.
2. **Mauro Vieira Jr J, Mantovani E, Tavares Rodrigues L, et al.** Simvastatin attenuates renal inflammation, tubular transdifferentiation and interstitial fibrosis in rats with unilateral ureteral obstruction. *Nephrol Dial Transplant* 2005;20(8):1582-91.
3. **Lei W, Zhang K, Pan X, et al.** Histone deacetylase 1 is required for transforming growth factor-β1-induced epithelial–mesenchymal transition. *Int J Biochem Cell Biol*. 2010;42(9):1489-97.
4. **Sousa AM, Liu T, Guevara O, et al.** Smooth muscle α-actin expression and myofibroblast differentiation by TGFβ are dependent upon MK2. *J Cell Biochem*. 2007;100(6):1581-92.
5. **Choi SY, Ryu Y, Kee HJ, et al.** Tubastatin A suppresses renal fibrosis via regulation of epigenetic histone modification and Smad3-dependent fibrotic genes. *Curr Vasc Pharmacol*. 2015;72:130-40.