

Isolation and Characterisation of a Novel Stem Cell Population from Human Umbilical Cord

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Stem cells have tremendous regenerative ability and have the potential to treat an enormous range of diseases. Most of the clinical applications of stem cells have been using adult stem cells. However, there are limitations with its use because of its limited proliferative ability and the difficulty culturing these cells outside the body. Embryonic stem cells (ESC) and Induced pluripotent stem cells (iPSC) are also potential stem cell sources but there are major issues relating to their use, such as the ethical concerns of ESC and the tendency to form tumours in ESC and iPSC.

Umbilical cord tissue and cord blood are promising alternative stem cells sources. Cord blood stem cells are rich in haematopoietic (*blood*) cells, but lack sufficient mesenchymal and epithelial stem cells for regenerating solid organs in the body.

We hypothesized that human umbilical cord harbors many cell types, which could be effectively isolated for treating various diseases. These may overcome the limitations associated with the use of adult stem cells, ESC and iPSC. The aims of our study are to isolate a novel stem cell population from umbilical cord and to be able to inducing these cells to differentiate into an epithelial cell type that could be used for tissue regeneration.

We surgically dissected the umbilical cord lining membrane from the Wharton's jelly and other internal structures. The cord lining cells were cultured in a specialized PTTe-1 culture medium. We successfully isolated and characterized a novel cell type expressing MUCIN1 (CD227) (Fig. 1) from human umbilical cord lining which we termed MUCIN-expressing Cord Lining Epithelial Cell (CLEC-muc).

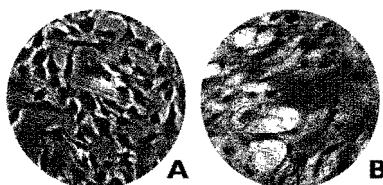


Fig 1. Features of CLEC-muc
A. Appearance of CLEC-muc
B. DAB staining showing abundant expression of Mucin1 (CD227).

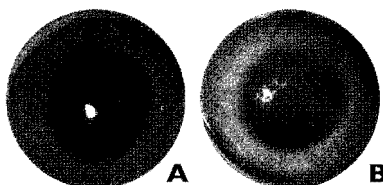


Fig 3. Transplantation of cultured CLEC-muc onto damaged rabbit eyes
A. CLEC-muc transplanted eye showing a clear and smooth cornea surface
B. No CLEC-muc

CLECs-muc differed from other known stem cells in terms of their appearance and cellular characteristics. These cells were highly proliferative and possessed both epithelial and mesenchymal stem cell characteristics. The cells exhibited both embryonic and adult stem cell properties with expression of embryonic (*Oct-4*, *Nanog*, *Sox2*, *Rex1*, *SSEA-4*) and adult (*p63*, *ABCG2*) stem cell markers. The cells were found to be less immunogenic, meaning that the risk of graft rejection was lower.

We subsequently induced these cells to differentiate into a highly specialised cornea-like epithelium which expressed cornea-specific cytokeratins CK3/CK12 (Fig. 2). To evaluate the in vivo regenerative ability of these cells, we transplanted cultured CLEC-muc sheets onto rabbit eyes that were devoid of cornea epithelium and cornea stem cells. We found that the transplanted cells

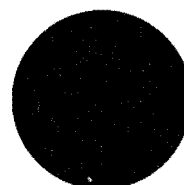


Fig 2. CLEC-muc were induced to form a cornea-like epithelial sheet expressing CK3/CK12 (red staining)

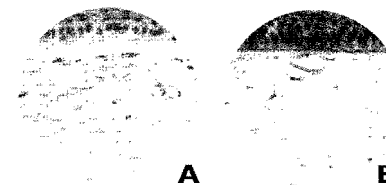


Fig 4. Histological appearance of transplanted cultured CLEC-muc was similar to normal in vivo cornea epithelium
A. Transplanted CLEC-muc sheet
B. Normal cornea

were able to successfully regenerate a smooth and clear corneal surface (Figs. 3 and 4). CLECs-muc were found to be non-tumorigenic.

In summary, we successfully isolated a novel stem cell population, CLEC-muc, that exhibited mesenchymal and epithelial stem cell characteristics. CLEC-muc has advantages over other stem cell sources (such as adult stem cells, ESC and iPSC), because it is easily obtainable, has no ethical issues related to its use, is highly proliferative, and does not form tumours.

CLEC-muc may serve as a readily available source of stem cells that may prove to be a better and safer stem cell source. These novel stem cells have potentially important clinical applications for use in regenerative medicine and tissue replacement for treating various diseases.