Pressure ulcer treatment: Elevation on injectable cell-loaded hydrogels for regeneration of soft tissue

Dr W.Y.Ip[1], Y.F Lui[1]

[1]*Department of Orthopaedics and Traumatology, The University of Hong Kong*

INTRODUCTION:

In our study, an artificial designed system for soft tissue regeneration is under investigation. One method for faster tissue generation in ulcer is by transplantation of additional cells into the wound. Rather than simply transplant the cells to the location, how to maintain the survivability and facilitate the differentiation of transplanted cells is also an important issue. In this case, injectable hydrogel can offer a reservoir for nutrients and growth factor during the transplantation operation to ensure cell survivability and cell differentiation. In the study, three types of common hydrogel have undergone investigation on their ability in acting as a carrier for adipose tissue derived stem cells for in transplantation.

METHODS:

Three types of hydrogel, which includes cross-linked gelatin, methylcellulose and the matrix gel Geltrex™ was selected for investigation. Reason for choosing the above three candidates is they can all undergo gelation at specific requirements to form a rigid matrix under human body temperature. This requirement is essential for large volume tissue regeneration, such as in supportive tissue such as granular or fat tissue to prevent rapid loss in cells.

All the gels are synthesized with the incorporation of DMEM supplemented with 10% FBS replacing the original water portion. 3T3-L1 cells are loaded into the gel and cultured under 37°C in 0.5% CO_2 for more than 7 days. In later part of investigation, the cell loaded hydrogel was also exposed to differentiation medium compose of isobutyl-methylxanthine, dexamethasone and insulin for cell differentiation evaluation.

RESULTS:

Despite from the fact that gelatin is a highly biocompatible material; cell survivability of cells loaded in gelatin was extremely low. Cells are not able to survive in gelatin gel unless the concentration of gelatin is lower that 7% by mass. All crosslinking reagents also proven to be too hazard to living cells even at minimum dosage.

On the other hand, Cells are able to survive and proliferate in high viscosity methylcellulose gel and concentrated matrix gel. For methylcellulose, only the cells in contact with the base of culture well are able to proliferate, while the survivability of suspending cells is unknown. For the matrix gel, cells are able to proliferate in a 3 dimension manner. Layers of cells can be observed under light microscope.

Fig. 1: Cells loaded Gelatin after 48hours of culture. No surviving cells can be found inside gelatin with concentration higher than 7%

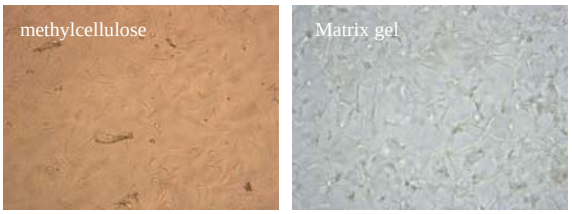

Fig. 2&3: 2) Cells loaded methylcellulose and, 3) Cells loaded in matrix gel after 48hours of culture. Cells proliferate in a 2-D manner only on the surface of culture plate in methylcellulose, while multiple layers of cells can be found inside the gel.

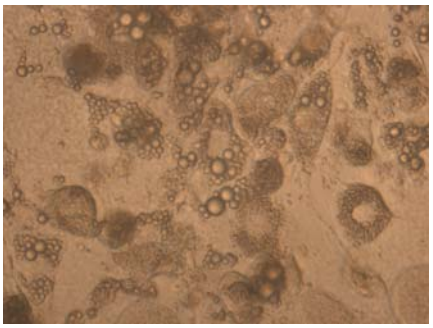

Fig. 4: Differentiated adipocyte can be found inside the matrix gel after exposed to differentiation medium for 14 days. Fatty acid can be found in form of droplets inside differentiated cells.

DISCUSSION & CONCLUSIONS:

In the study we have demonstrate that specific injectable hydrogel can act as a cell carrier to provide nutrient support or even facilitate differentiation to the loaded cells. Compare to direct transplantation of cells, this nutrient self-support system may achieve a higher cell survivability ratio as well as a faster formation of targeted tissue during early stage of transplantation. This can provide a better and faster rate of healing in conical wound in soft tissue such as pressure ulcer to replace the lost volume of tissue. In future study, the gel will be further supported by a soft degradable elastomer scaffold to provide a more stable environment for tissue formation