REGENERATION OF DEGENERATED INTERVERTEBRAL DISC USING ALLOGENEIC MESENCHYMAL STEM CELLS ENCAPSULATED IN SELF-ASSEMBLING PEPTIDE HYDROGEL

INTRODUCTION:

Low back pain is associated with the degeneration of intervertebral disc (IVD). Disc degeneration is an irreversible process and the precipitating cause of the degeneration is thought to be multi-factorial. The therapeutic effect of autogenic mesenchymal stem cells (MSCs) on disc degeneration has been previously reported and the effect is dependent on the stage of degeneration. However, autogenic transplantation may have limitations. Autogenic cells lack on-shelf availability in practice and may carry intrinsic factors, such as genetic predispositions, that cause the degeneration. In view of the immune-privileged environment in IVD and the ability of MSCs to escape from alloimmune recognition, we hypothesize that allogeneic MSCs can be effective in rejuvenating the degenerated IVD, with the use of self-assembling oligo-peptide hydrogel as a carrier for transplantation.

METHODS:

Degeneration of lumbar IVD (L2/L3 and L4/L5) was induced by annulus puncture with a 19G needle through an anterolateral retroperitoneal approach in New Zealand White rabbits. One month after, MSCs derived from femur bone marrow of Chinchilla Bastard rabbits were encapsulated in 0.25% PuraMatrix™ peptide hydrogel (BD Bioscience) at 0.5x10^6 cells/10ul and then injected into the nucleus pulposus of the degenerated discs. PBS or hydrogel only injection was performed separately as controls (6 discs per group). Disc hydration was evaluated at 1 or 3-month intervals post-injection by T2-weighted STIR 3T magnetic resonance imaging (MRI) using deuterium oxide/water mixtures as standards. Hydration values (H2O) of IVD were measured to calculate the percentage change of total mean hydration and the percentage change of maximum hydration [%ΔH2O = 100% × (H2OInjected/H2ONormal)]. Disc height was also determined from radiographs to calculate the disc height index (%DHI). The discs were assigned to mild (%ΔH2O less than -30%) or severe (%ΔH2O more than -30%) degeneration group by the time of injection. All animal experiments were performed under the approval of local institution and government review boards.

RESULTS:

By comparing to the control groups at both mild and severe degenerative stages, allogeneic MSCs were able to arrest the continual loss of total hydration in the discs at one month post-injection and gradually increase the hydration afterwards (Fig 1a, b). In the mildly degenerated discs, MSCs implantation also maintained the maximum hydration (Fig 2a) as well as the disc height index (Fig 3a), suggesting a focal hydration core in the nucleus pulposus was preserved and the collapse of disc height was prevented. Self-assembling peptide hydrogel on its own could also facilitate disc rehydration to some extent (Fig 1a) and effectively arrest disc height collapse (Fig 3a). In addition, it promoted the re-establishment of hydration core (Fig 2a). The effects of hydrogel were observed only at mild but not severe stage (Fig 2b, 3b) of degeneration.

DISCUSSION:

Base on the correlation of disc height and hydration with degenerative status of IVD, our data indicates that allogeneic MSCs can effectively arrest disc degeneration and regenerate the disc in a progressive manner. The regeneration effect of MSCs is more prominent at mild degenerative stage in which the hydration and disc height have been largely preserved. Interestingly, self-assembling peptide hydrogel can serve not only as a cell carrier, but also appears to facilitate the establishment of a hydrophilic core and to provide mechanical support, likely in a nano-scale, for resisting disc height collapse in degenerated IVD. Our data further suggests that a low quantity of allogeneic MSCs (~5000 cells) suffices for provoking a regenerative effect in degenerated IVD. Different quantity of MSCs and hydrogel concentration shall be tested in future to enhance the regeneration, particularly at severe stage of degeneration.

REFERENCES:

4. Leung, V. Y. L.; Tsui, Y K; *Li, L C; *Lee, M K; *Huang, S C; ****Lo, G G; *Wu, E X; *Luk, K D K; **Chan, D; *Cheung K M C

This study is funded by the Research Grants Council of Hong Kong.

53rd Annual Meeting of the Orthopaedic Research Society
Poster No: 1079