Effect of mesenchymal stem cell-derived exosome on tendon healing in rat cuff repair model

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INTRODUCTION:

After surgical repair of chronic rotator cuff tears, healing of the repaired tendons often fails. Our purpose was to explore the effects of mesenchymal stem cell (MSC) -derived exosome on tendon healing in a chronic rotator cuff tear model using a rat infraspinatus.

METHODS: Bone marrow harvested from both femurs of six 10 weeks old SD male rat. Exosome was extracted from MSC selected from the bone marrow. Forty 10 weeks old SD male rats were randomly assigned to the following two groups (20 rats per group: 6 for histological evaluation, 6 for biochemical study and 8 for mechanical testing): PBS+repair (Control), exosome+repair (Study). Four weeks after detaching the infraspinatus, the torn tendon was repaired. The right shoulder underwent infraspinatus repair, and the left underwent sham operation. PBS and exosome were applied to the repair sites. Histological, biochemical and mechanical evaluation were performed at 4 weeks after repair (Fig 1).

RESULTS:

Four weeks after repair, the study groups had a higher mean continuity of collagen fiber than the control group. The study group showed a higher mean load to failure than the control group, which did not reach a statistical significance. On western blot analysis, the mean amount of type 1 collagen and Matrix metalloproteinase 9 (MMP 9) in the study group significantly increased compared with those in the control group ($p=0.027$ and $p=0.004$) (Fig 2). Through a small RNA sequencing in exosome, a miRNA of miR-21-5p associated with elevated type 1 collagen and MMP 9 was found.

DISCUSSION AND CONCLUSION:

MSC-derived exosome might improve tendon healing after cuff repair. The miR-21-5p activates TGF-β and therefore stimulates a conversion of type 3 collagen to type 1 collagen. And this miRNA increases MMP 9 and decreases tissue inhibitor of metalloproteinase 3. A further study about miR-21-5p will be needed.

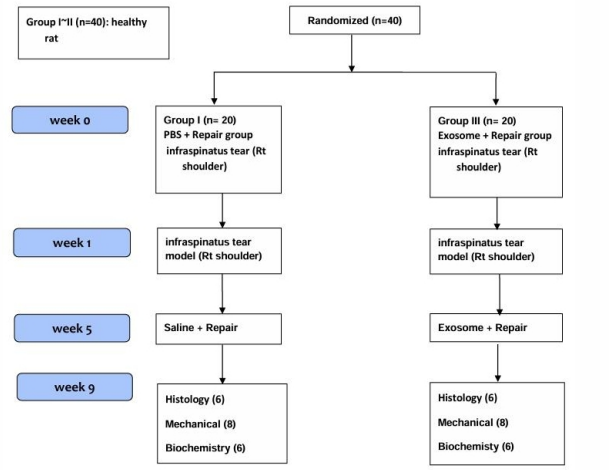

Fig 1. Flow diagram of the present study. PBS: phosphate buffered saline, Exosome: MSC-derived exosome.

Fig 2. Western blot analysis of infraspinatus. COL1: type 1 collagen, MMP9: Matrix metalloproteinase 9, Con: control group, Exo: study group. Right: right shoulder(repair), Left: left shoulder(sham operation). Asterisk indicates a significant difference ($P<0.05$).