Effect of Adipose stem cells derived mitochondria transplantation to the chronic injured anterior cruciate ligament cells

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INTRODUCTION: Mitochondria transplantation had been proposed to treat the injured ligament tissue. The effect of mitochondria transplantation to the chronic injured ACL cells is need to investigate. We hypothesize that the ACL cells' activity declined as longer injured time, and the mitochondria transplantation would improve the activity of chronic injured ACL cells.

METHODS: In this study, we perform two experiments (Figure 1). In the first experiment, we harvested the ACL injured tissue from rabbit after ACL transected 2(acute), 4(medium), and 8(chronic) weeks under IACUC approved. We investigate the cell proliferation, migration, and gene expression of collage synthesis, VEGF, TGFβ in injured ACL cells at different injured time points. In the secondary experiment, we isolated the mitochondria from the human adipose stem cells (hADSCs), and examined the cell activity change at chronic injured (8 weeks) ACL cells after mitochondria transplantation.

RESULTS: After injury, the ACL cells activity decrease at 2 weeks compared to non-injured ACL cells. The highest cell activity was expressed at 4 weeks injured ACL cells, and declined from 4 to 8 weeks after ACL injury (Figure 2). After hADSCs-mitochondria transplantation, the 8 weeks injured ACL cells' activity was significantly improved compared to that without mitochondria treatment group, and achieve the level of injured 4 weeks cells (Figure 3).

DISCUSSION: The study result showed that injured 4 weeks ACL cells presented highest cell activity which provide evidence of optimal time of ACL reconstruction. After injury more than 8 weeks, the ACL cells' activity declined significantly. The injured 8 weeks ACL cells could uptake and internalize the hADSCs-mitochondria with subsequently improve the cell viability, migration and expression of collagen synthesis, VEGF gene to the level of injured 4 weeks cells. The mitochondria transplantation improves the regeneration capability of chronic injured ACL cells, which indicated the possibility of mitochondria therapy to improve chronic injured ACL cells' regeneration capability to enhance graft maturation.

SIGNIFICANCE/CLINICAL RELEVANCE: The inferior cell viability, migration rate, and gene expression of collagen synthesis, VEGF and TGFβ was found in the chronic injured ACL cells. The mitochondria transplantation could be an effective biologic to improved injured ACL cells' activity with subsequently enhancing graft maturation in ACL reconstruction at chronic stage.

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Figure 1 **Study Design**

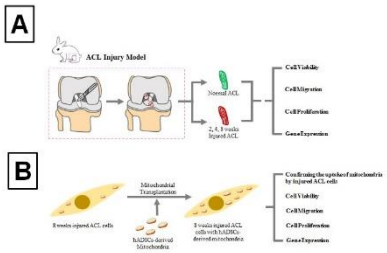


Figure 2
Cell activity and gene expression change of ACL cells at different injured time points

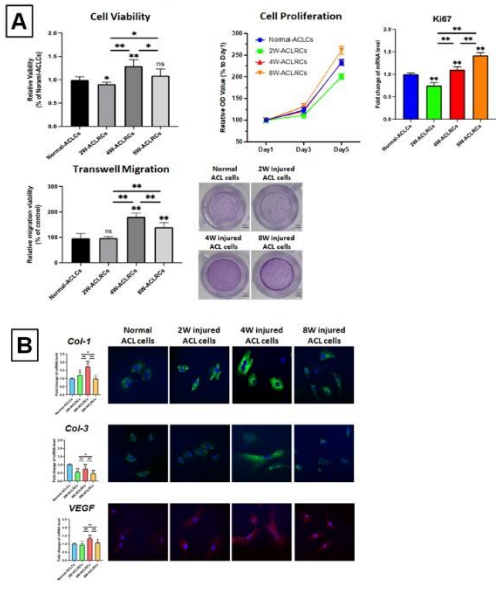
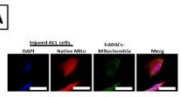


Figure 3
Mitochondria uptake by injured ACL cells



Cell activity and gene expression change of chronic injured ACL cells after Mitochondria transplantation