Bone Marrow-Derived Mesenchymal Stem Cells (MSC) and Its Conditioned Medium (CM) Attenuate Fibrosis in an Irreversible Model of Unilateral Ureteral Obstruction.

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Introduction and aim: The therapeutic potential of MSCs and its conditioned medium is an important target of recent researches. It is known about their ability to repair tissue and reduce local inflammation. A renal tubule interstitial inflammation can lead to develop a chronic damage, resulting in kidney fibrosis. In this study we evaluated factors influenced by the administration of MSC or its CM.

Results:

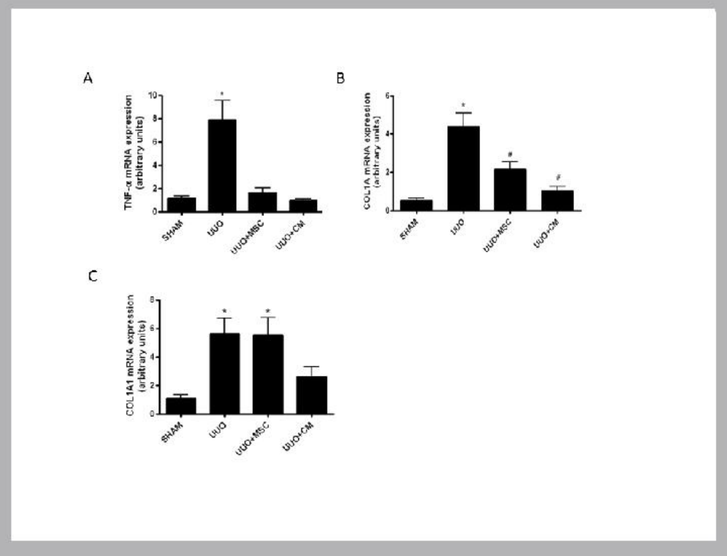

Figure 1. Real-Time PCR for *TNF-α* and *Col1A1* mRNA expression. A) TNF-α gene expression after 7 days of UUO. * *vs* all groups, p □ 0.05. **B)** Col1A1 gene expression after 7 days of UUO. * *vs* all groups, # vs UUO, p □ 0.05. **C)** Col1A1 gene expression of 14 dyas of UUO. * *vs* SHAM, p □ 0.05.

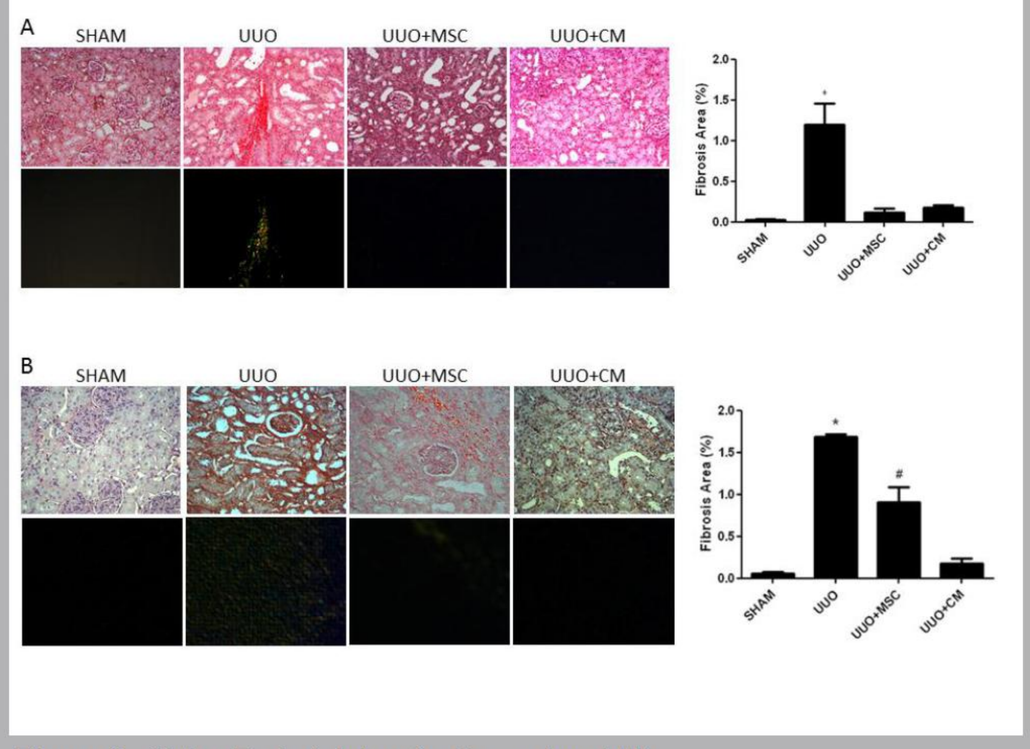

Figure 2. Sirius Red staining (collagen I and III).
A) Representative photographs of renal tissues staining with Sirius Red after 7 days of UUO and respective quantification. * *vs* all groups, p□ 0.05. **B)** Representative photographs of renal tissue staining with Sirius Red after 14 days of UUO and respective quantification. * *vs* all groups, # vs UUO+MSC vs UUO+CM, p □ 0.05.

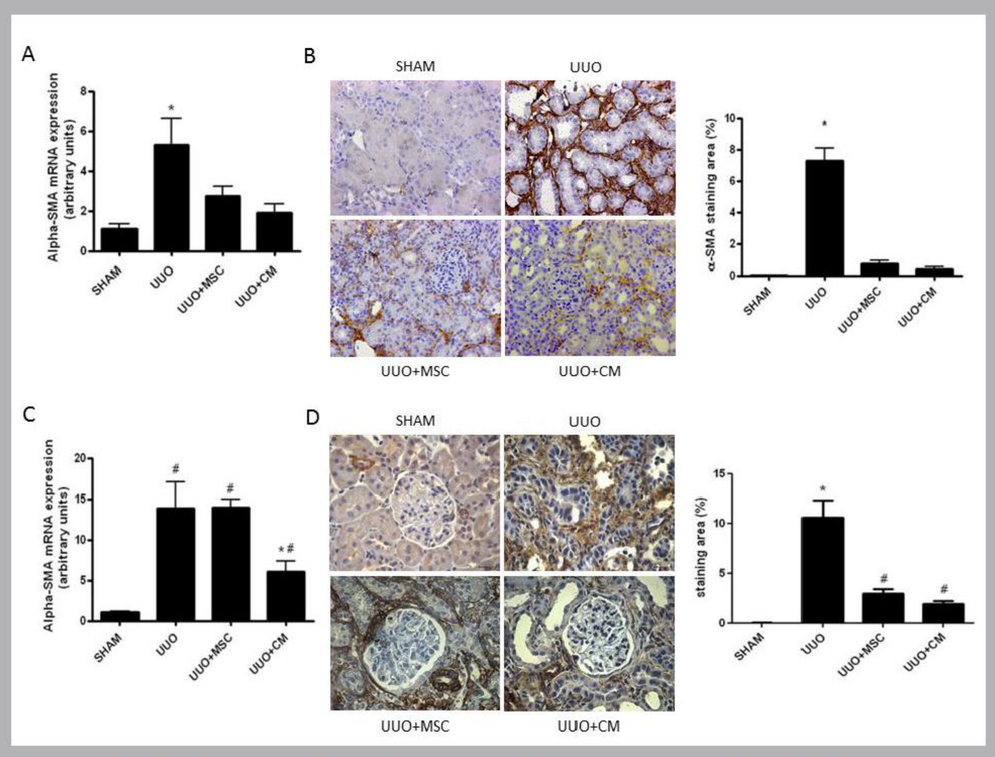

Figure 3. Real-time PCR and immunohistochemistry for α-SMA .
A) mRNA expression levels of α-SMA after 7 days of UUO. * *vs* all groups, p □ 0.05. **B)** Representative photographs of renal tissue staining with α-SMA antibody after 7 days of UUO and respective quantification. * *vs* all groups, p □ 0.05. **C)** mRNA expression levels of α-SMA after 14 days of UUO. * *vs* UUO, # *vs* SHAM, p □ 0.05. **D)** Representative photographs of renal tissue staining with α-SMA antibody after 14 days of UUO and respective quantification. * *vs* all groups, # *vs* SHAM, p □ 0.05.

Methods: MSC extracted from male rat's bone marrow were cultivated *in vitro* and characterized by flow cytometry and by cellular differentiation. Eight groups of female rats were used in *in vivo* experiments (n=7): SHAM, UUO, UUO+MSC and UUO+CM. The MSC or its CM were administered via abdominal vena cava after total ligation of the left ureter. After 7 and 14 days rats were sacrificed and their obstructed kidney collected. Collagen deposition and mRNA expression of different molecules were analyzed by real-time PCR. We also analyzed the amount of different proteins involved in Epithelial-Mesenchymal Transition (EMT), cell proliferation and apoptosis by immunohistochemical assays.

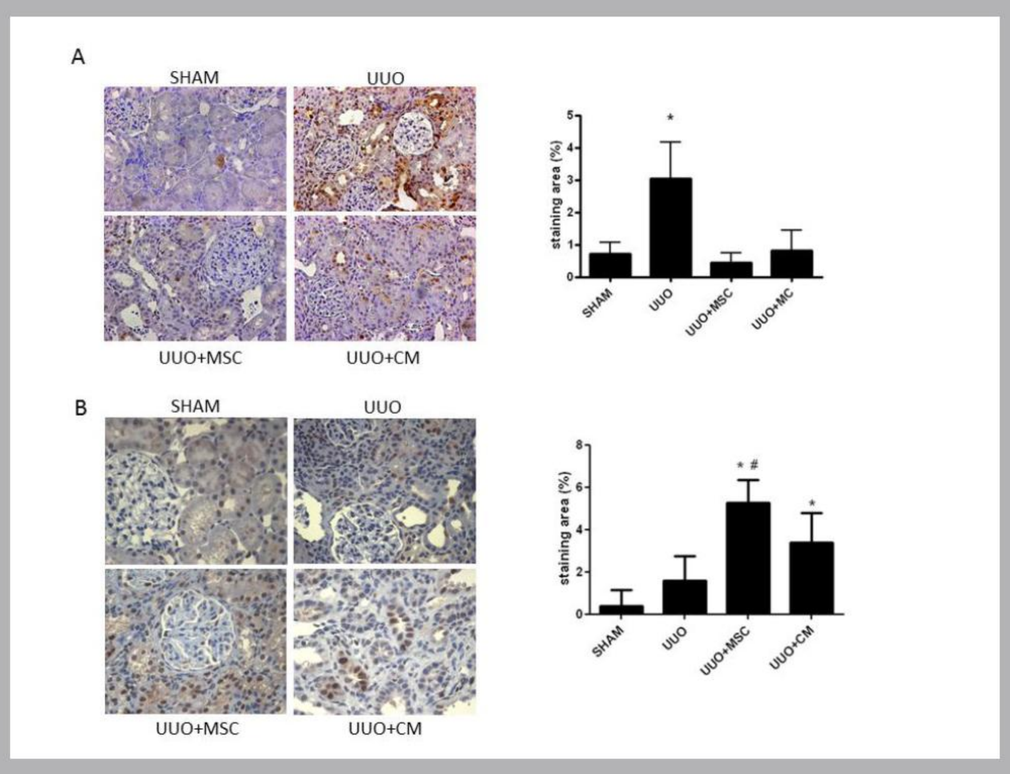

Figure 4. Immunohistochemistry for PCNA.
A) Representative photographs of renal tissue staining with PCNA antibody after 7 days of UUO and respective quantification. * *vs* all groups, p □ 0.05**.** **B)** Representative photographs of renal tissue staining with PCNA antibody after 14 days of UUO and respective quantification. * *vs* UUO, # *vs* UUO+CM, p □ 0.05.

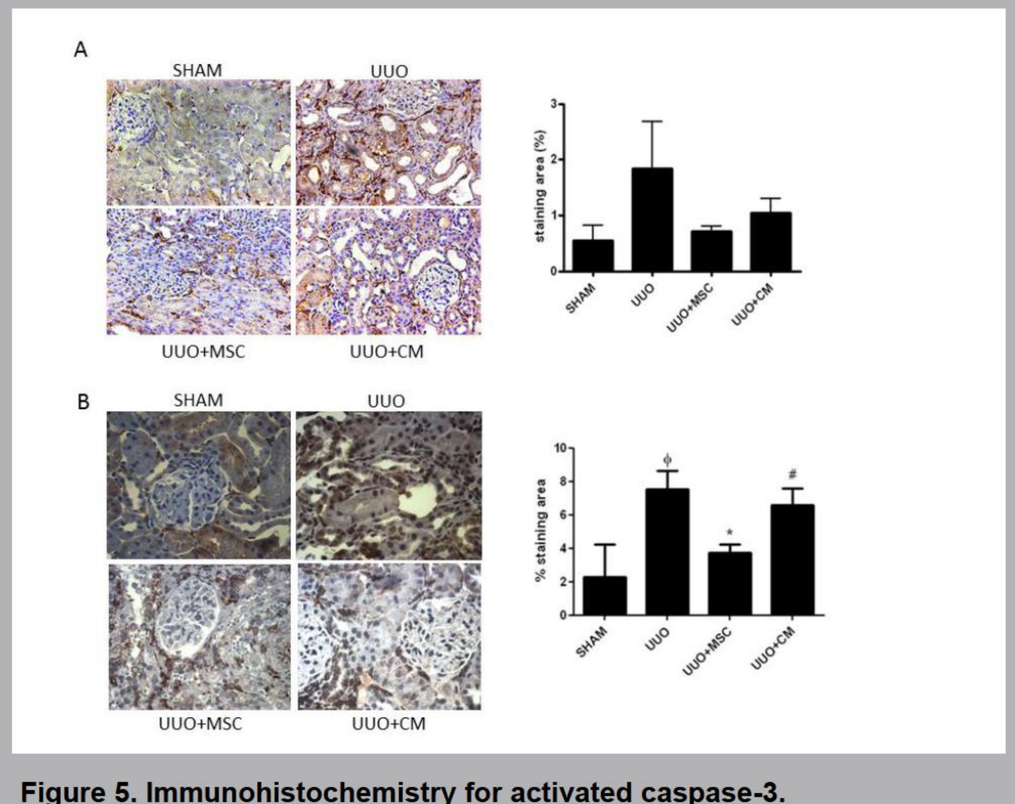

Figure 5. Immunohistochemistry for activated caspase-3.
A) Representative photographs of renal tissue staining with activated caspase-3 antibody after 7 days of UUO and respective quantification. Non-siginficant, p>0.05. **B)** Representative photographs of renal tissue staining with activated caspase-3 antibody after 14 days of UUO and respective quantification. * *vs* UUO, # *vs* UUO+MSC, φ *vs* SHAM, p □ 0.05.

Conclusions: Results suggest that the i.v. administration of MSCs or its CM improve fibrosis progression and modulate factors involved in apoptosis, inflammation, cell proliferation and Epithelial-Mesenchymal Transition (EMT) in Wistar rats subjected to UUO. These results indicate a potential treatment of this pathophysiological progressing and help us understand the mechanism of action of the MSCs.

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