EXOSOMES DERIVED FROM MESENCHYMAL STEM CELLS PREVENT FIBROSIS IN A MURINE MODEL OF UNILATERAL URETERAL OBSTRUCTION

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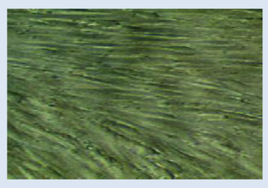
INTRODUCTION

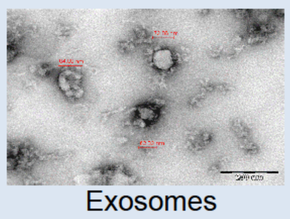
Immunomodulatory properties of mesenchymal stem cells (MSC) rendered them suitable for the prevention and/or the treatment of chronic inflammatory renal disease. However, the use of MSC could be associated with risks and constraints in particular due to chromosomic alterations.

AIMS



Mesenchymal stem cells

versus



Exosomes

The use of exosomes secreted by MSC which may display similar the properties to parental MSC could be an interesting alternative reducing previous concerns.

METHODS

We have investigated the effects of intravenously administered fetal mesenchymal stem cells (fl-MSC) or their exosomes on renal interstitial inflammation and fibrosis in the inflammatory nephropathy of Unilateral Ureteral Obstruction (UUO).

Male C57BL/6 mice underwent fl-MSC or exosomes injection immediately prior to left ureteral obstruction.

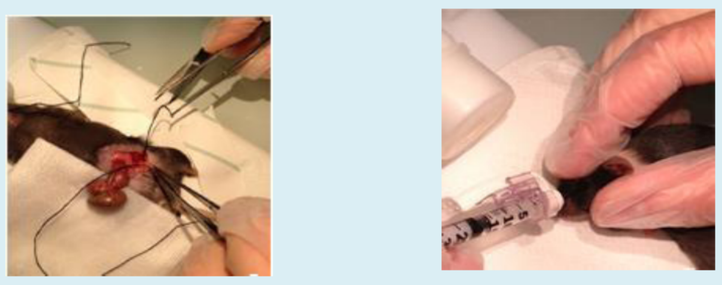


Fig 1: Ostruction of the left ureter and retroorbital injections.

One week later, the renal cortex was analyzed using a systematic and quantitative scanning of slides for fibrosis (Rouge Sirius staining), for infiltration by inflammatory cells (lymphocytes (CD3) and macrophages (F4/80)) and epithelial-mesenchymal transition (EMT) as evidenced by S100A4 expression.

RESULTS

In Both fl-MSC and exosomes groups, lower Red Sirius scores and decreased macrophage infiltration were observed compared to the PBS group.

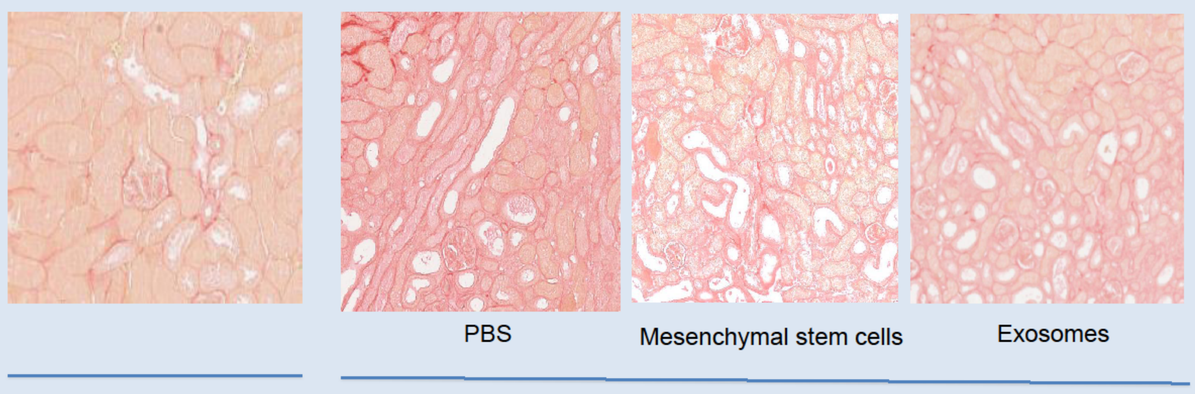
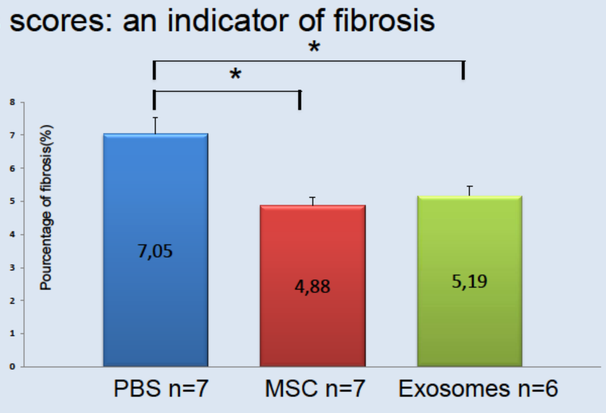


Fig 2: Red Sirius scores: an indicator of fibrosis



P<0,05
Mann Whitney's test

Fig 3: Difference of fibrosis depending on the treatment in obstructed kidney

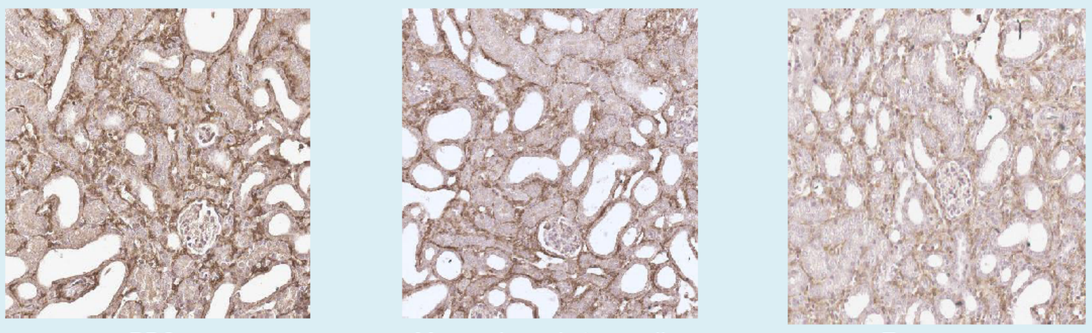
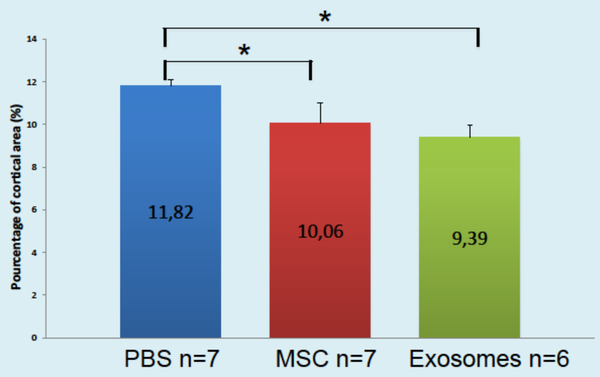


Fig 4: Macrophagic infiltration evaluated by Immunohistochemistry (F4/80)



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Mann Whitney's test

Fig 5: Difference of macrophagic infiltration depending on the treatment in obstructed kidney

No quantitative differences were noted for the CD3+ population.

A phenotype of sub population of lymphocyte T cells is in process as well as the quantification of extracellular matrix deposition (Western Blot) and expression of cytokines and chemokines (luminex).

CONCLUSION

Exosomes of MSC isolated from foetal liver share similar anti-inflammatory properties with MSC and prevent fibrosis in the early stage of UUO. They can be considered as an alternative strategy to MSC for the prevention of inflammation and fibrosis in inflammatory nephritis.

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