Proteomic Profiling of Exosomes Derived from Immortal Human Bone marrow Alpha-1 Antitrypsin Overexpressing Mesenchymal Stromal Cells and Their Protective Effects

Sara Shoeibi PhD, **Hua Wei** PhD, **Wenyu Gou** PhD, **Erica Green** PhD , **Charlie Strange** MD, **and Hongjun Wang** PhD

Departments of Surgery, Medical University of South Carolina, CRI 410, 173 Ashley Avenue, Charleston, SC 29425, USA

Background

Mesenchymal stem cell (MSC)-derived exosomes mediate therapeutic targets for cellular therapies.

However, basic and clinical research in this field is impaired by the **limited life span of primary MSCs** during culture expansion.

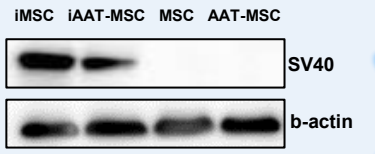
Generating human immortal MSCs (hiMSCs) and human immortal alpha-1 antitrypsin overexpressing (hiAAT)-MSCs may overcome this problem.

Objectives

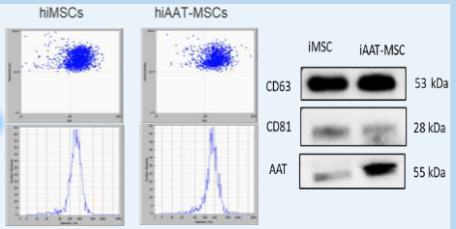
1. Comparison of proteomic profiles in exosomes of human immortal MSCs (hiMSCs) and human immortal AAT-MSCs (hiAAT-MSCs)
2. The Study of the protective effect of iMSCs and iAAT-MSCs

Results

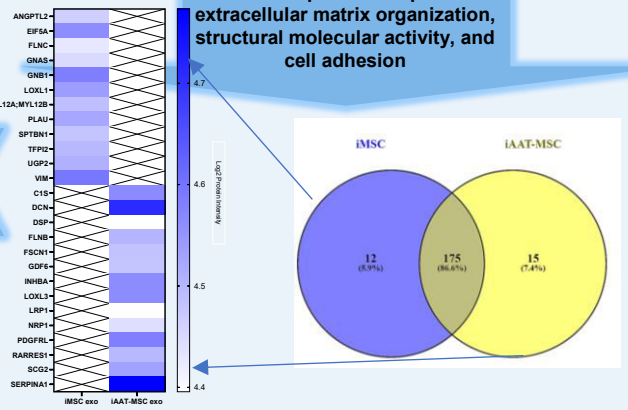
Immotirtalizaon MSCs and AAT-MSCs: detection of SV40



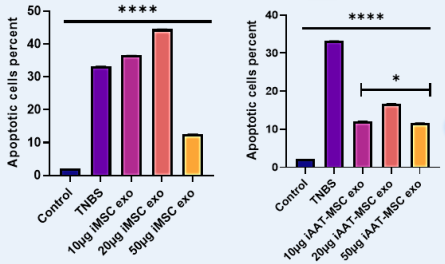
Isolation of exosomes and characterization: size and marker detection



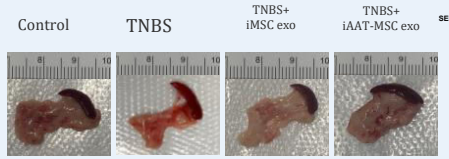
Proteomics: proteins important to extracellular matrix organization, structural molecular activity, and cell adhesion

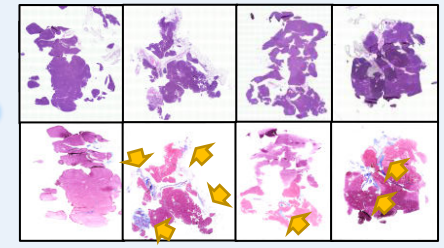


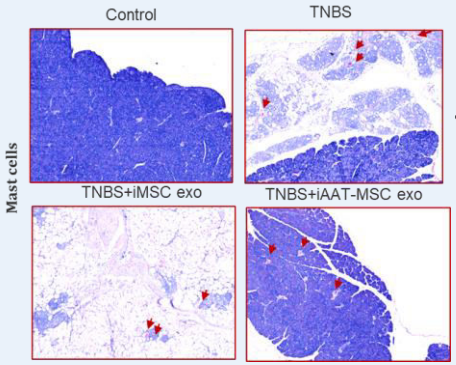
Protective effects of exosomes in induced TNBS-acinar cell line

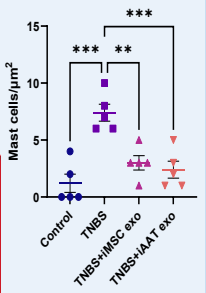


Exosomes and CP treatment in the mouse: low mast cell numbers and pancreatic damage









Methods

1) **Immortalization** MSCs and AAT-MSCs by transduction of simian virus 40 T antigen (SV40T).
2) **Isolation of exosomes** secreted bone marrow derived-iMSCs and iAAT-MSCs by ultracentrifugation
3) **Proteomics** analysis through liquid chromatography and mass spectrometry
4) Study the **protective effect** of iMSCs exosomes by culture rat acinar cell line with different concentrations of exosomes with TNBS
5) Study the effects of exosomes in chronic pancreatitis (CP) model in mouse

Conclusions

- ❑ hiAAT-MSCs exosome contains a different profile of paracrine markers with impacts on MSC differentiation, and protective cell/tissue activity.
- ❑ hiMSCs and specially hiAAT-MSCs exosomes could contribute to improving survival in TNBS-induced acinar cells.