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CD362+ mesenchymal stem cell treatment of kidney disease in type 2 diabetic LepR$^{db/db}$ mice

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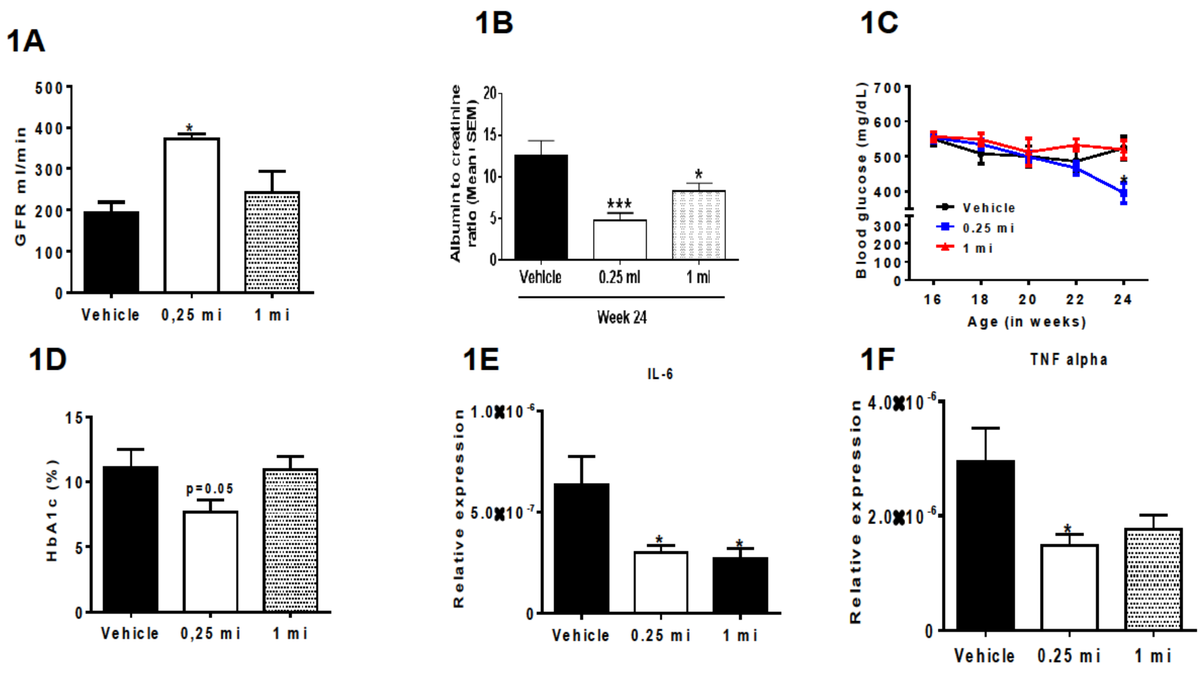
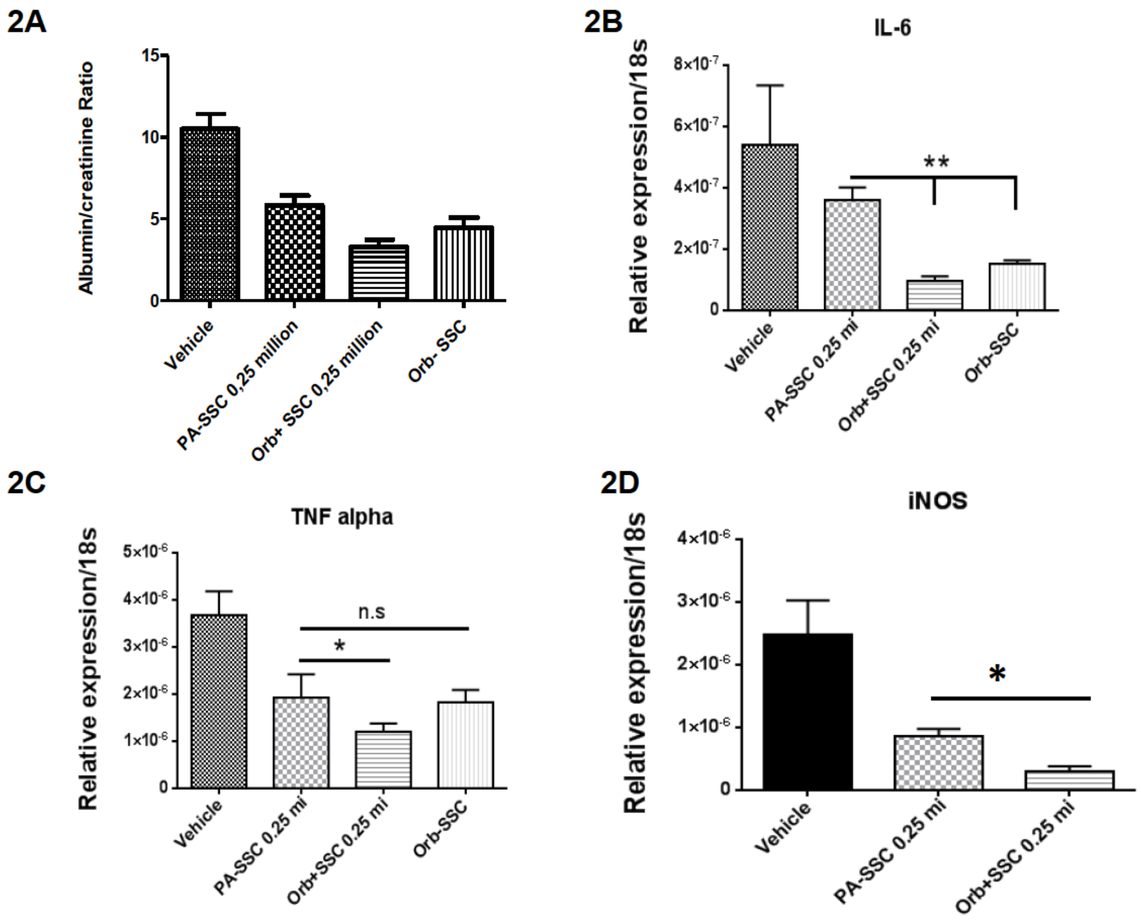
BACKGROUND
Mesenchymal stem cells (MSC) are extensively studied as potential therapeutic modulators of disease. CD362/Syndecan-2 is a heparan sulphate proteoglycan identified as a functional marker for MSC isolation and therapeutic development. These are present in both bone marrow derived MSC and umbilical cord stem cells. However, their therapeutic potential in diabetic nephropathy is yet unclear. We speculated that a single dose of CD362+ MSC could have benefits in diabetic kidney disease.

METHODS
LepR$^{db/db}$ type 2 diabetic male mice were procured from Taconic Biosciences (DK-8680 Ry, Denmark). Uninephroctomy was done at 6 weeks of age to accelerate diabetic kidney disease via increased hyperfiltration. At 16 weeks of age mice were randomized to either a single intravenous dose of 250,000 CD362+ MSC or saline. 56 days after injection all mice were sacrificed and kidneys were collected for immunostaining, flow cytometry, ELISA and RT-PCR. Proteinuria was assessed as albumin to creatinine ratio in spot urine samples. Also we evaluated the efficacy of CD362+umbilical cord derived mesenchymal stem cells (UCMSCs) in uninephroctomized mice treated with high fat diet to further aggravate diabetic kidney disease. Bio-distribution of MSC after injection was studied in various organs at various time points (0,6,12,24,48 hrs and 4, 14, 28, and 56 days) by detecting human DNA (ALU) sequences in mouse tissues.

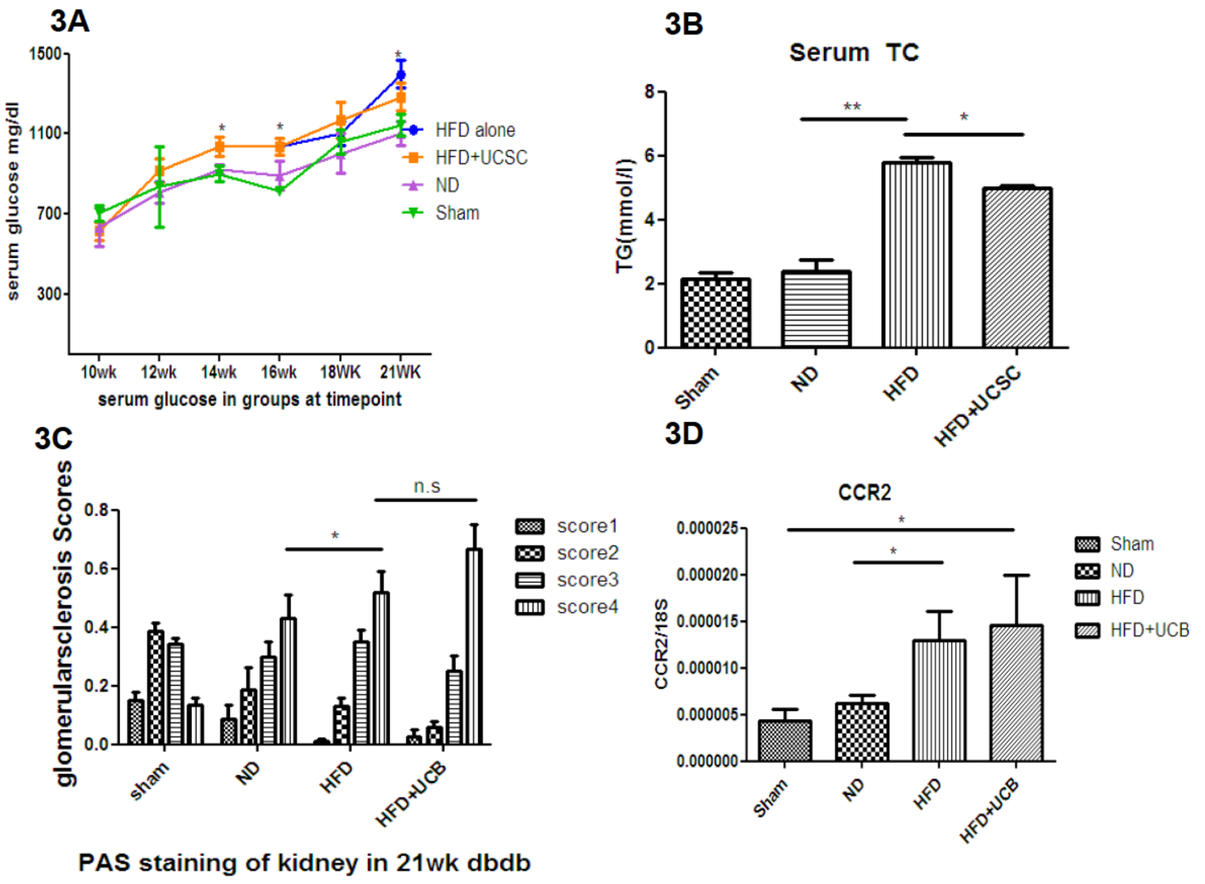
RESULTS
1) Low and high doses of hBMMSCs decreases blood glucose levels and protect mice from DN by reducing poteinuria and glomerulosclerosis and low dose of hBMMSCs seems to be more beneficial than the high dose .



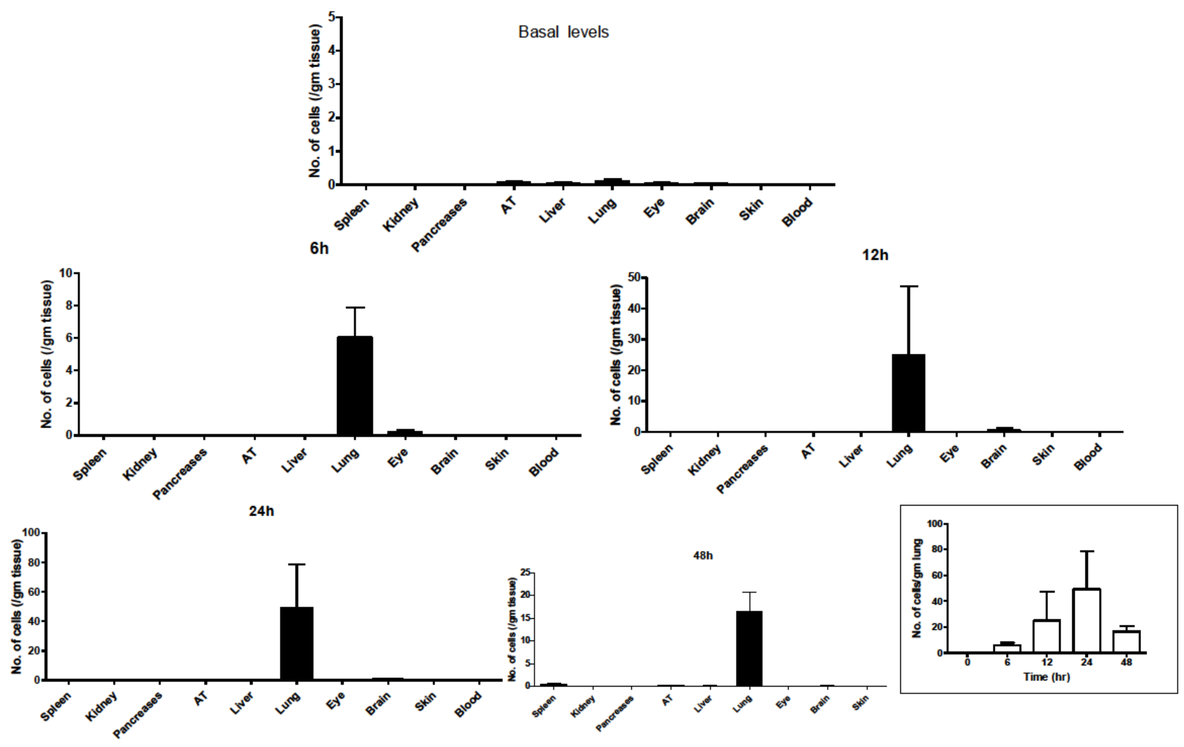
2) CD362+ hBMMSCs significantly reduces renal inflammatory cytokine gene expression compared to CD362- hBMMSCs.



3) High fat diet (HFD) significantly aggravate diabetic kidney disease and ttreatment of these mice with CD362+hUCMSCs shows elevated clinical and functional parameters remained unaffected in contrast to hBMMSCs.



4) Bio distribution studies demonstrated the presence of MSCs in lungs at an early time points 6hr to up-to 48hrs and then after went undetectable. In other organs MSCs are undetectable at all time points.



CONCLUSIONS
We conclude that CD362+ hBMMSCs are efficient for the treatment of DN, though the cell are not able to reach kidney, indicating a systemic effect of these stem cells after single dose injection.

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