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The use of Mesenchymal Stromal Cells to ameliorate Diabetic Kidney Disease in the BTBR$^{ob/ob}$ model

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The use of mesenchymal stromal cells (MSC) in diabetic models as a possible therapy to ameliorate diabetic kidney disease (DKD) is not new. Several researchers have conducted successful experiments reporting improvement on the course of DKD after MSC interventions. However, most of the research focuses on type-1 diabetes, particularly using Streptozotocin-induced rodents as model. In order to demonstrate the true potential of MSC as a therapeutic option for DKD, further studies must also expand the research on alternative diabetic models. In this study, we have evaluated the impact of two different human MSC on the BTBRob/ob mice model (a type-2 diabetes model, susceptible to hyperglycemia-associated kidney damage) that closely resembles the pathogenesis in humans.
Adipose-derived (hADSC) or dermis-derived (hABCB5+) MSC were administered intravenously to two independent cohorts of 12 weeks-old BTBRob/ob mice and followed-up until 24-26 weeks of age. Key parameters in which MSC showed amelioration by previous studies were observed, such as albuminuria and histology of glomerular lesions. Additionally, two new methodological approaches were implemented to better evaluate therapeutic efficacy and increase our understanding of functional and morphological changes in the BTBR: transcutaneous glomerular filtration rate and a semi-quantitative methodology based on tissue clearing and three-dimensional analysis.
Weak evidence of improvement by MSC on DKD was found at functional level by lowering albumin excretion in urine of diabetic treated groups in both cohorts. Although the observed changes were not significant, two independent experiments showed similar trends to what is reported in the literature. Still, this tendency was not transduced in improvement of conventional histology or transcutaneous measurements of glomerular filtration rate after its implementation.
Although the benefit of MSC could not be proven in this model, important findings were made after the successful implementation of the above-mentioned tissue clearing approach in terms of robust morphometrical analysis (glomerular size and afferent arteriole dilation), and glomerular perfusion patterns in DKD that seem to go along with mesangial proliferation and glomerulosclerosis.