Title of abstract: Human Mesenchymal Stem Cells and its Exosomes in Posthemorrhagic Hydrocephalus: A Focus on Edema and Ependymal Repair

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Background

Germinal matrix hemorrhages and intraventricular hemorrhages (GMH/IVH) often lead to posthemorrhagic hydrocephalus (PHH), a severe cause of morbidity and mortality in premature neonates. GMH/IVH is known to disrupt the ependyma, which forms a functional and physical barrier between the cerebrospinal fluid (CSF) and the brain tissue. Consequently, CSF circulation and physiology are severely affected; and thus, ependyma is a chiefly important target when it comes to designing PHH treatments. Bone marrow-derived mesenchymal stem cells (MSCs) are extremely effective anti-inflammatory agents which have already shown positive results regarding PHH treatment. However, there is no therapy to recover the ependyma in humans.

Methods

Human MSCs were cultured under inflammatory or non-inflammatory conditions to extract and purify their correspondent exosomal fraction through sequential centrifugation steps. The effect on the ependymal differentiation and ciliogenesis was tested *in* vivo and *in vitro*. Also, the effect on the parenchymal edema was assesed *in* vivo on a PHH surgical model. Conditioned and non-conditioned exosomes were used. Ventricular wall explants were analysed through confocal microscopy. The exosomes were functionally characterised through proteomics.

Results

Firstly, no rejection of the human MSCs nor of their exosomes is observed. Both MSCs and exosomes have a posititve effect on ciliogenesis and edema proportion and severiy. This also indicates that exosomes are able to partially reproduce the human MSCs therapeutical effect *in vitro* and *in* vivo. Functional enrichment of proteomics gives some insight on the mechanism that makes the therapy possible.

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