MULTICILIATED EPENDYMA RECOVERY THROUGH A SEQUENTIAL CELL THERAPY IN POSTHEMORRHAGIC HYDROCEPHALUS (D14)

Topic
AS03 Stem Cells, Organoids, Neural Injury Neurotoxicity and Repair

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Abstract Body
Posthemorrhagic hydrocephalus (PHH) is a significant cause for premature children's morbidity, mortality, and peri/postnatal neurodevelopmental impairment. PHH is mainly triggered by germinal matrix hemorrhages (GMH) and causes germinal matrix and ependyma disfunction. Ependyma constitutes a relevant tissue barrier with roles in cerebrospinal fluid homeostasis, circulation, and neurogenesis, hence situating ependyma as a main target when treating PHH. Clinical treatments are directed to eliminate immediate inflammatory condition triggered by the bleeding, to drain excess of CSF if needed, but not to treat or recover ependyma structure. Ependymal progenitors were obtained from P0 mice. Cells were cultured under specific conditions to enhance either ependymal proliferation or differentiation status. Different GMH/IVH neuroinflammatory conditions were mimed in the ependyma cultures, different stem cell therapies tested and effect on the ependymal differentiation measured. Additionally, ventricular wall explants from mice with induced PHH were obtained and cultured as ex-vivo system of PHH. A combination of stem cells was applied on the tissue to probe its regenerative capabilities on the multiciliated ependyma. All samples were analyzed through immunofluorescence and laser confocal microscopy and quantified. Results show that (i) ependymal progenitors' maturation is hindered under neuroinflammatory conditions, showing no multiciliated ependyma and (ii) the tested stem cell combination promotes ependymal progenitors' survival albeit does not alter the differentiation of the selfsame. In summary, it can be stated that the final differentiation of the ependyma is disrupted by the molecular conditions triggered by GMH/IVH, which our proposed cell therapy is able to counteract through increased survival and differentiation in a murine model of experimental PHH. Funding: Junta de Andalucia (UMA18-FEDERJA-277) and Instituto de Salud Carlos III (PI19/00778), Spain; co-financed by FEDER funds from the European Union, Spain. Also, II-PPITD, Universidad de Malaga, Spain (to JL-dSS); and I-PPITD, Universidad de Málaga, Spain (to LMR-P)