

## Long-time effects of an experimental therapy with mesenchymal stem cells in congenital hydrocephalus

María García-Bonilla<sup>1,3</sup>, Betsaida Ojeda<sup>1</sup>, Kirill Shumilov<sup>1,3</sup>, Javier Vitorica<sup>2</sup>, Antonia Gutiérrez<sup>1,3</sup>, Patricia Páez-González<sup>1,3</sup>, Antonio J. Jiménez<sup>1,3</sup>

1 Department of Cell Biology, Genetics, and Physiology, University of Malaga, 29071, Spain

2 Department of Molecular Biology and Biochemistry, University of Seville, 41004, Spain

3 IBIMA, Malaga, Spain

mgbonilla@uma.es

### Introduction

Bone marrow-derived mesenchymal stem cells (BM-MSK) are a potential therapeutic tool due to their ability for migrating and producing neuroprotector factors when they are transplanted in other neurodegenerative diseases. Moreover, some investigations have shown that BM-MSK are able to modulate astrocyte activation and neuroprotector factor production. The aim of this study was to evaluate the long-time effects of a BM-MSK experimental therapy in the hyh mouse model of congenital hydrocephalus.

### Methods

BM-MSK were characterized in vitro and then transplanted into the ventricles of young hydrocephalic hyh mice, before they develop the severe hydrocephalus. Non-hydrocephalic normal mice (wt) and hydrocephalic hyh mice sham-injected (sterile saline serum) were used as controls. Samples were studied by analyzing and comparing mRNA, protein level expressions and immunoreaction related with the progression and severity of hydrocephalus.

### Results

Fourteen days after transplantation, hydrocephalic hyh mice with BM-MSK showed lower ventriculomegaly. In these animals, BM-MSK were found undifferentiated and spread into the periventricular astrocyte reaction. There, BM-MSK were detected producing several neuroprotector factors (BDNF, GDNF, NGF, VEGF), in the same way as reactive astrocytes. Total neocortical levels of NGF, TGF- $\beta$  and VEGF were found increased in hydrocephalic hyh mice transplanted with BM-MSK. Furthermore, astrocytes showed increased expressions of aquaporin-4 (water channel protein) and Slit-2 (neuroprotective and anti-inflammatory molecule).

### Conclusions

BM-MSK seem to lead to recovery of the severe neurodegenerative conditions associated to congenital hydrocephalus mediated by reactive astrocytes.