

**Title of abstract:** Testing exosomes as a treatment for posthemorrhagic hydrocephalus

**Authors:** Javier Lopez-de San Sebastian \* [1], Luis Manuel Rodriguez-Perez [1,2,3], Alba Anguita-Guardia [1], Antonio Jesús Jimenez [1,2], Patricia Paez-Gonzalez [1,2].

1 Departamento de Biología Celular, Genética y Fisiología Animal. Universidad de Málaga. 29071, Spain

2 Instituto de Investigación Biomedica de Málaga - IBIMA -. 29010, Spain

3 Departamento de Fisiología Humana, Histología Humana, Anatomía Patológica y Educación Física y Deportiva. Universidad de Málaga. 29010, Spain

Presenting author: Javier Lopez-de San Sebastian. [jls@uma.es](mailto:jls@uma.es) +34 659443348

## **Background**

Germinal matrix hemorrhages and intraventricular hemorrhages (GMH/IVH) lead to posthemorrhagic hydrocephalus (PHH), a severe cause of morbidity and mortality in premature neonates. GMH/IVH disrupts the ependyma, which forms a physical and functional barrier between the brain parenchyma and the cerebrospinal fluid (CSF). CSF circulation and physiology is also affected by ependyma disruption. Thus, ependyma is a key target when designing PHH treatments. Despite this, hydrocephalus treatments are surgical and focused on alleviating ventricular pressure by draining CSF. No therapy is currently aimed to recover the ependyma. Nevertheless, bone marrow derived mesenchymal stem cells (MSCs) are known to be great agents when dealing with inflammation. Also, exosomes have proven to be promising tools when designing anti-inflammatory treatments. Therefore, gaining insight in the treating capabilities of MSCs exosomes in PHH can be valuable.

## **Materials and Methods**

MSCs were cultured under inflammatory or non-inflammatory conditions to extract and purify their correspondent exosomal fraction through sequential centrifugation steps. Characterization of the exosomes was performed.

To test their effect on the ependymal differentiation, both types of exosomes were applied on a primary culture of ependyma which had been previously subject to neuroinflammatory conditions. Additionally, exosomes were transplanted on *ex vivo* explants obtained from surgically induced PHH mice to determine the effect on the severity of edema. All samples were analyzed through confocal microscopy.

## **Results**

Differential effects in edema progression and ependymal cells ciliogenesis are found when analyzing treatments with conditioned and non-conditioned exosomes in moderate PHH and severe PHH.

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