

## Poster

## Impact of maternal dietary supplementation in the prevention of neuropediatric diseases



Noelia Sola Idígora, José Manuel Caro Vega(1), María Irene Ayuso Fernández(2), Rafael Gonzalo Gobernado(2), Patricia Ybot González(1).

(1) Grupo de Neurodesarrollo, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío, Av. Manuel Siurot, s/n, 41013 Sevilla, España.

(2) Grupo de Neurovascular, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío, Av. Manuel Siurot, s/n, 41013 Sevilla, España.

**Keywords:** Dietary supplementation; Neural tube defects; Neonatal hypoxia-ischemia brain injury; D-chiro-inositol; Omega-3

### ABSTRACT

**Motivation:** A balanced maternal diet during pregnancy is crucial for the proper development of the embryo. In this project, we will study the impact of maternal dietary supplementation in the prevention of the development of neonatal strokes and neural tube defects (NTDs) using two mouse models.

1. Neonatal stroke is a pathology with a heterogeneous etiology, leading to important sequelae. Currently, hypothermia is the only clinical intervention used in full-term newborns with perinatal asphyxia. However, the influence of diet has recently begun to be considered relevant in reducing brain damage in possible future injuries. Thus, maternal diet supplementation with omega-3 fatty acids as a tool for neuroprotection has been proposed. In order to test this, we will start with the development of a neonatal mouse model of hypoxia-ischemia (HI) and characterize the type and severity of brain injury.

2. Neurulation refers to the neural tube formation process. When neural tube fails to close completely, NTDs are originated, including craniorachischisis or spina bifida. While 70% of NTDs can be prevented with folic acid supplementation during pregnancy, the rest remains resistant. Loop-tail mouse is a folic acid resistant model of NTDs who carries a mutation for the *Vangl2* gene (which is involved in the Wnt-PCP pathway). Previous studies have shown that inositol prevents NTDs in folate-resistant models. Preliminary studies of our group have suggested that maternal supplementation with D-chiro-inositol during embryonic days (E)8.5-E10.5 has a positive effect on the dorsal fusion of the neural folds and on the distribution of actin present in these. Therefore, we propose to extend the period of supplementation (E1.5-E11.5) to determine whether such effect is more pronounced.

**Methods:** We used the Rice-Vannucci model of HI modified to postnatal day (P)8 CD1 mice. Pups were subjected to unilateral left carotid artery ligation and subsequently exposed to 9% O<sub>2</sub> for 45'. Infarct size measurement was done 24h post HI, evaluation of brain damage was done 3 days post-HI and behavioural outcomes were assessed at P8, P9 and P12. To assess the impact of maternal dietary supplementation in the prevention of NTD we provided water supplemented with D-chiro-inositol to pregnant mice *Vangl2*<sup>+/Lp</sup> from E1.5 to E11.5. Embryos were obtained and genotyped at E12.5 for later phenotype analysis. In addition, in situ hybridization studies and fluorescent phalloidin stainings were performed

### REFERENCES

- Rice, J.E., Vanucci, R.C., Brierley, J.B. (1981) The influence of immaturity on hypoxia-ischemic brain damage in the rat. *Annals of Neurology*, **9**(2), 131–141.
- Ayuso, M.I., Gonzalo-Gobernado, R., Montaner, J. (2017). Neuroprotective diets for stroke. *Annals of Neurology*, *Annals of Neurology*, 107, 4–10.
- Greene, N.D., Leung, K., Copp, A.J. (2017). Inositol, neural tube closure and the prevention of neural tube defects. *Birth Defects Research*, 109(2), 68-80.
- Nikolopoulou, E., Galea, G.L., Rolo, A., Greene, N.D., Copp, A.J. (2017). Neural tube closure: cellular, molecular and biomechanical mechanisms. *Development*, 144(4), 552-566.

