Effects of Methylmercury on cell death, proliferation and cellular phenotypic specification of human neural stem cells

J. Lli[1,2], L. Sandoval[1,2], M.C. González[2], M. Motas[2] and I. Liste[1,*]

[1] Unidad de Regeneración Neural. Unidad Funcional de Investigación de Enfermedades Crónicas
[2] Toxicología ambiental, Centro Nacional Sanidad Ambiental. Instituto de Salud Carlos III, Carretera Majadahonda a Pozuelo km. 2 (28220), Madrid, Spain
E-mail: iliste@isciii.es

Methylmercury (MeHg) is a long-lasting organic pollutant that is mainly found in aquatic environments. The main source of MeHg human exposure is the MeHg- contaminated seafood. MeHg accumulates in various organs, however, the brain is its main target. The developing brain is particularly affected by MeHg although adult brain may also be vulnerable.

MeHg interacts with cysteine to go through the cysteine channels of the blood brain barrier. After that, it accumulates mainly in the cerebellum and the cerebral cortex. MeHg affects the cellular cytoskeleton and mitochondria, it affects the intracellular Ca^{2+} and extracellular glutamate concentrations and induces apoptosis.

Human neural stem cells (hNSCs) are the precursors of neurons and glia, these cells can differentiate into all neural cells of the Central Nervous System (CNS). hNSCs are valuable tool in neurotoxicology assays giving the opportunity to study early stages of neural development.

In the present investigation, we are using human neural stem cells as model. The neurotoxic assays are being performed in the cellular line hNS1 that is a clonal and multipotent cell line. To observe the effects of MeHg, we have exposed the hNS1 cells to different concentrations of MeHg and analyzed cell viability, proliferation and cell fate specification under proliferation and differentiation conditions.

The objective is to identify the key targets for developmental neurotoxicity (DNT) to obtain toxicity pathways and biomarkers that could be incorporated into testing strategies in DNT chemical assessment.