Unveiling cadmium's impact on neuronal differentiation by FTIR micro-spectroscopy and metabolic analyses

Alessandro Leta [a], Diletta Ami [a], Federica Bovio [a], Matilde Forcella [a], Paolo Mereghetti [b], Paola Fusi [a], Antonino Natalello [a]
E-mail: a.leta1@campus.unimib.it
[a] Department of Biotechnology and Biosciences, University of Milano-Bicocca, Piazza della Scienza, 2, 20126, Milano, Italy
[b] Bioinformatics Consultant, 15061, Arquata Scrivia, Italy

Keywords: cadmium, SH-SY5Y, neurotoxicity, FTIR, micro-spectroscopy

Abstract: Heavy metals, such as iron, zinc and copper, can be essential nutrients, but some others are poisonous and cause toxic effects on biological systems. Among them, cadmium (Cd) is a widespread environmental contaminant with 30000 tons/year released mainly by anthropogenic activities. This metal, with no biological role, accumulates inside human body with a half-life of 10-30 years and exerts its toxicity towards several organs, including the nervous system. In addition, more recently, Cd has been associated to neurodegenerative disorders such as amyotrophic lateral sclerosis and Parkinson's disease [1].
The goal of this study is to see whether cadmium can interfere with neuronal differentiation and for this purpose we employ, as a model system, the human neuroblastoma SH-SY5Y cell line, a widely used *in vitro* model for both neurotoxicity and neurodegeneration studies.
FTIR (micro-)spectroscopy is a powerful tool to monitor, in a non-destructive and label-free way, the global biochemical composition of whole intact cells through the absorption of electromagnetic radiation in the mid-infrared range (4000-600 cm^{-1}). This vibrational technique probes many molecules simultaneously and its sensitivity to structural and compositional changes makes it complementary to other biochemical methods [2].
Preliminary results have highlighted significant differences between the IR spectra of differentiated and undifferentiated SH-SY5Y cells, thus prompting us to investigate the IR absorption of Cd exposed SH-SY5Y cells, both differentiated and undifferentiated, at different time point.
Given the complexity of the resulting IR spectra, due to the overlapping absorptions of the main cell biomolecules, their interpretation will require a sophisticated multivariate analysis to pull out significant and non-redundant information [2].
In parallel, Seahorse analysis and specific enzymatic assays will be performed to investigate whether Cd exposure will affect the metabolic changes that normally occurs during the neural differentiation process.

[1] Forcella M, Lau P, Fabbri M, Fusi P, Oldani M, Melchioretto P, Gribaldo L, Urani C. "Is Cadmium Toxicity Tissue-Specific? Toxicogenomics Studies Reveal Common and Specific Pathways in Pulmonary, Hepatic, and Neuronal Cell Models". Int J Mol Sci. 2022 Feb 4;23(3):1768. doi: 10.3390/ijms23031768. PMID: 35163690; PMCID: PMC8836438.
[2] Ami D, Franco AR, Artusa V, Romerio A, Shaik MM, Italia A, Anguita J, Pasco S, Mereghetti P, Peri F, Natalello A. "Vibrational spectroscopy coupled with machine learning sheds light on the cellular effects induced by rationally designed TLR4 agonists". Talanta. 2024 Aug 1;275:126104. doi: 10.1016/j.talanta.2024.126104. Epub 2024 Apr 17. PMID: 38677166.