UNIVERSITÀ DEGLI STUDI DI MILANO-BICOCCA
DOTTORATO DI RICERCA IN Tecnologie Convergenti per i Sistemi Biomolecolari – XLII CICLO

Research Topic ID: XLII – 1.7

Project Tutor: Prof. Paola Coccetti

Project Supervisor/s: Prof. Paola Fusi

Project Title: A metabolic study of cadmium neurotoxicity

Scientific background & Objectives

Cadmium is a toxic heavy metal massively released into the environment by anthropogenic activities. Chronic assumption is very common, through contaminated air, food and water, as well as cigarette smoke. Once inside the human body, cadmium accumulates with a half-life of 26-30 years; recent data strongly suggest that it may contribute to the pathogenesis of different neurodegenerative diseases.

In our laboratory we have been studying cadmium neurotoxicity in human cell models, both neuronal and glial. In this project, cadmium toxicity will be investigated in human neuronal differentiated cells, as well as during cell differentiation and in glial cells, both in monocultures and cocultured with neuronal cells. Characterization of cadmium toxicity will involve: cells morphology, metabolism in live cells, oxidative stress, endoplasmic reticulum stress, mitochondria functionality, cell death mechanisms; metabolic rearrangements will also be investigated through Fourier Transform Infrared (FTIR) spectroscopy in a label free, untargeted, non-destructive approach.

Project's Networks, Sustainability & Mobility

a) the coherence of the suggested project with competences/tools of the hosting lab
b) intradepartmental or external collaborations
c) at least one pertinent research article published by the proposer/s
d) 1 (or more) putative foreign institutions for achieving the required ordinary mobility (6 months)

a) The project is coherent with the research carried out in my laboratory on cadmium toxicity. In past years we have investigated the molecular mechanisms and metabolic alterations induced by sublethal cadmium concentrations, leading to carcinogenesis. More recently we undertook the characterization of cadmium toxicity on neuronal cells, with the aim of understanding its possible role in neurodegenerative diseases' pathogenesis.

b) Intradepartmental collaborations: Prof. Antonino Natalello, Dr Diletta Ami, Prof. Daniela Ferrari, Prof. Marzia Lecchi
External collaborations: Prof. Chiara Urani (University of Milano-Bicocca) Prof. Stefano Porru (University of Verona), Prof. Giovanna Mazzoleni (University of Brescia) Prof. Stefan Schildknecht (Albstadt-Sigmaringen University, Germany)

c) Pertinent research articles:

   1. Bovio F, Sciandrone B, Urani C, Fusi P, Forcella M, Regonesi ME. Superoxide dismutase1 (SOD1) and cadmium: A three models approach

to the comprehension of its neurotoxic effects. Neurotoxicology. 2021 May;84:125-135. doi: 10.1016/j.neuro.2021.03.007. Epub 2021 Mar 24. PMID: 33774064.

2. Bovio F, Melchioretto P, Forcella M, Fusi P, Urani C. Cadmium promotes glycolysis upregulation and glutamine dependency in human neuronal cells. Neurochem Int. 2021 Oct;149:105144. doi: 10.1016/j.neuint.2021.105144. Epub 2021 Jul 23. PMID: 34303722.

3. Bovio F, Perciballi E, Melchioretto P, Ferrari D, Forcella M, Fusi P, Urani C. Morphological and metabolic changes in microglia exposed to cadmium: Cues on neurotoxic mechanisms. Environ Res. 2024 Jan 1;240(Pt 1):117470. doi: 10.1016/j.envres.2023.117470. Epub 2023 Oct 21. PMID: 37871786.

4. Ami D, Bovio F, Forcella M, Brioschi M, Mereghetti P, Fusi P, Natalello A. Identifying label-free and untargeted biomarkers of SH-SY5Y cell fate in ATRA-induced differentiation through FTIR spectroscopy and integrated omics. Talanta. 2026 Jan 1;296:128464. doi: 10.1016/j.talanta.2025.128464. Epub 2025 Jun 14. PMID: 40532461.

5. Bovio F, Ferrian M, Franceschi A, Melchioretto P, Porru S, Forcella M, Fusi P, Urani C. Cadmium accumulation in neuronal cells leads to essential metals imbalance and zinc transporters dysregulation. Toxicology. 2026 Jan;519:154319. doi: 10.1016/j.tox.2025.154319. Epub 2025 Oct 24. PMID: 41139003.

d) Prof. Stefan Schildknecht (Albstadt-Sigmaringen University, Germany)