"THE POTENTIAL OF APPLIED BIOLOGY IN LIMITING URBAN AIR POLLUTION AND PREVENTING ITS EFFECTS ON HUMAN HEALTH AND ON THE ENVIRONMENT"

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Project "DIPARTIMENTI DI ECCELLENZA"

My PhD project is part of AWAIR, a European project, that aims to define new indicators for air quality and to evaluate the effectiveness of measures applied during Severe Air Pollution Events (SAPEs), to achieve greater protection of the health of citizens. The project will be conducted as part of a co-tutorship agreement with Helmholtz Zentrum München, where I will spend half of the time of my PhD. Part of this project is to evaluate the effect of air pollution on human health, it's well known that the size of particles has been directly linked to their potential for causing health problems. The atmospheric aerosols ranging from several nanometers to approximately 100 μm in diameter and an important role is attributable to ultrafine (nanosized) particles. Nanomaterials (NMs) are available with a range of physicochemical characteristics, which allows a more systematic toxicological analysis, therefore, the study of NMs, provides an opportunity to identify plausible health effects for ultrafine particles (UFP,<100 nm in diameter) and to facilitate the understanding of the mechanism of toxicity of UFP. To this purpose, in my first year of PhD, I have analyzed the toxicity of CdS quantum dots (QDs), which is widely studied in our laboratory. Cd QDs is a nanomaterial with excellent optical properties used in different field as electronics, optoelectronics, in solar cells, pharmacy and nanomedicine for biomedical applications; chemical-physical properties of nanomaterial influence their behavior in the biological system, therefore we have compared the effects of cadmium in nanometric form (CdS QDs) and in ionic form Cd^{2+}, which is well known its toxicity. At this purpose, RNA sequencing (RNAseq) was performed in two different cell lines which represent different target and routes of exposure. Both cell lines, HepG2 (liver hepatocellular carcinoma), and THP-1 (peripheral blood monocyte), differentiated into macrophages, were respectively treated with subtoxic dose of CdS QDs and the equivalent dose of Cd^{2+}. Based on previous studies the subtoxic doses for the two cell lines were chosen and the exposure time was set at 24h. HepG2 were treated with 3 μg mL^{-1} of CdS QDs and the equivalent dose of Cd^{2+}. THP-1 were exposed to 50 μg mL^{-1} of CdS QDs but the equivalent dose of Cd^{2+} is lethal for the cells, therefore we chose, from literature data, to expose the cells also to 6.4 μg mL^{-1} of CdS QDs and to the equivalent dose of Cd^{2+}. The treatments highlight that HepG2 cells are more sensitive to CdS QDs respect THP-1, which are involved to defense against exogenous

substances. The transcriptomic data analysis was performed and the different genes modulation reveals a cell type specific response to the two treatments and further their implication in different biological processes. In HepG2 cells exposed to CdS QDs the 53% of genes are up-regulated and remaining 47% are down-regulated. Gene Ontology (GO) enrichment analysis for biological process show the involvement of genes in xenobiotic metabolic pathway, in inflammatory cellular response, cell-cycle and post-transcriptional process, for fold enrichment value. However, at subtoxic dose the normal cellular functions does not appear altered. Differently from CdS QDs, the Cd^{2+} exposure in HepG2 induced the down-regulation of 75% of the modulated genes and a preliminary GO analysis show the activation of biological process mostly related to oxidative stress and general cellular stress response.

RNAseq for THP-1 was performed, the transcriptomic data analysis is still under investigation and results will be compared with those obtained from HepG2. The results of this work will be compared with future toxicological studies with UFP, in order to achieve major understanding of biological mechanism.