miR-21 involvement in cobalt and zinc oxide nanoparticles-induced cell malignant transformation

I. Barguilla[1], S. Ballesteros[1], A. Corchero[1,*], L. Rubio[1], R. Marcos[1,2] and A. Hernández[1,2]

[1] Grup de Mutagènesi, Departament de Genètica i de Microbiologia, Facultat de Biociències, Universitat Autònoma de Barcelona, Bellaterra, Spain
[2] CIBER Epidemiología y Salud Pública, ISCIII, Spain
E-mail: adricorchero@gmail.com

The growing application of nanotechnology in industrial processes has increased the exposure to nanoparticulated material by the overall population. The few existing information on the properties of these nanoparticles, in terms of potential genotoxic risk, urge the scientific community to evaluate the adverse effects of these nanomaterials in order to correct negligence and mitigate damage to humans and environment. In this scenario, a new discipline has born: Nanotoxicology.

Recent studies, have shown dysregulation in the expression of micro RNAs resulting from exposure to nanomaterials. MicroRNA molecules (miRNAs) are non-coding RNAs with a length ranging from about 20 nucleotides in animals, and with a regulatory function. Their sequences are complementary to a target mRNA, and when hybridizes with it, it silences its translation into protein. As they contribute to the regulation of gene expression at the cellular level, their biogenesis is highly regulated both temporally and spatially. Alterations in this process of genesis and maturation triggers multiple diseases in humans, including cancer. Among them, miR-21 is particularly linked to the most common tumors in humans, such as breast, lung and prostate cancers. This fact leads us to think that miR-21 can be involved in the regulation of the expression of cellular Tumor Suppressors. That is the reason why we have focused our studies on this specific miRNA.

We cultured MEF cells long term exposed to sub-toxic doses of cobalt and zinc oxide nanoparticles. Different assays were performed weekly in order to determine the moment of transformation and tumoral phenotype acquisition. After weeks of treatment, the expression of miR-21 before and after cellular transformation was quantified reporting dysregulation. Simultaneously, we studied the relative expression of three tumor suppressors: PTEN, PDCD4 and TPM1. To confirm the trends shown in the qPCR analysis and stablish cause-effect relationships, we studied the expression of miR-21 and Tumor suppressors after exposing the cells to mimics and inhibitors of their expression.

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