Genotoxicity assessment of nanoparticles

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The current expansion of nanotechnology and the steady broadening of the range of its practical applications allow to predict, for the coming years, a very substantial increase in the levels of exposure (accidental or intentional) to nanoparticles of anthropogenic origin for humans (including especially sensitive population groups) and for the environment. It is, therefore, necessary to put the basis to be able to perform a risk assessment, preferably integrated, in both areas. This includes having in each case the relevant data of both exposure and toxicity (hazard).

Particles smaller than 100 nm have certain characteristics which distinguish its toxic potential compared to the material (of the same chemical composition) from which they originate. These small particles, among other features, have an increased absorption, especially by unusual ways such as inhalation or skin, are capable of crossing barriers impassable in other conditions (such as blood-brain or retinal), penetrate in organs or tissues hard to reach for other compounds (such as the prostate), or interact with subcellular organelles in special and poorly characterized conditions.

On the other hand, the same considerations apply when nanotechnology is used to vectorize and deliver drugs, despite these being, often, previously known and duly characterized products. The presentation of the same compound in a nano-scale can modulate its toxicity in a way that we cannot predict a priori. While it is expected that nanotechnology will enable us to achieve lower equipotent doses, and therefore obtain lower toxicity levels (as well as a more accurate vectorization should also help to reduce the deleterious effects), we cannot ignore the fact that the drug may reach new tissular, cellular or molecular targets, and it will do so in conditions that make their behaviour difficult to predict.

There is a relatively abundant literature on nanotoxicology. However, certain aspects are identified that still require significant efforts of reflection and experimentation, both in regard to methodological and theoretical considerations or to specific aspects of the toxicological evaluation which have been unsatisfactory or insufficiently addressed.

Among the latter are for example, the need for standardization of procedures in vitro, the lack of repeated dose toxicological data in vivo, and of genotoxicity or teratogenicity data. Because of the limited knowledge we have about the behaviour of these materials, the application of broad spectrum techniques such as toxicogenomics would be also of special interest. Equally important is research to adapt the ecotoxicity tests, especially in regard to forms of exposure. It appears also as especially relevant issue the study of the distribution of nanoparticles in the body and the dynamics of internalization into cells.

We will present our experiences in genotoxicity assessment of an array of nanoparticles, going from gold with or without coating to cobalt ferrite, magnetite, gadolinium/prussian blue complexes, ceria particles, zirconium oxide or graphene oxide. Specially worth of mention is the case of genotoxicity produced by eliciting red-ox reactions by particles sequestered within the lysosomes, ie., without reaching the nucleus.

Notas - Notes