EVALUATING *IN VIVO* TOXICITY OF NANOMATERIALS USING THE ZEBRAFISH EMBRYO MODEL

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Nanomaterials have unique physico-chemical properties that make them very attractive for their use in several applications (including medical), but could be injurious for the human health and environment (Colvin, 2006). Thereafter it is important for nanomaterial R&D projects to include toxicological and safety evaluations so that actual risks of nanomaterials are defined and adverse environmental consequences are minimized. Thus, there is an obvious need for the development of rapid, relevant and efficient testing strategies to evaluate the biological activity and toxic potential of novel nanomaterials.

Early developmental life stages are often uniquely sensitive to environmental insult, due in part to the enormous changes in cellular differentiation, proliferation and migration necessary to form required cell types, tissues and organs. Since molecular signalling underlies all of these processes and most toxic responses result from disruption of proper molecular signalling; early developmental life stages are perhaps the ideal life stage to determine if nanomaterials are potentially toxic.

The zebrafish embryo was originally used to study the genetics of development due to its transparency, quick embryonic development, easy collection in high numbers and similarity with human development. In fact

- The zebrafish embryo constitutes a complete, developing vertebrate organism, and it allows testing predictability for toxicity not only in the context of cellular function, but also at the level of organ and organism toxicity (Hill et al, 2005).
- The anatomic and genomic similarity with humans (80% genetic homology), foresee tests predictability for human toxicity (Carroll & Fitzgerald, 2003).
- There are more than 8.000 publications cited in PubMed using zebrafish as a model organism and this number grows exponentially.
- The zebrafish embryo (up to 3-4 days after hatching) is not considered an animal by current European legislation (directive 86/609/EEC) and therefore its use in research studies is coherent with trying to reduce & replace the use of rodents for this kind of studies.

Zebrafish embryos can be used as an *in vivo* model to reveal whether a nanomaterial is potentially toxic at multiple levels of biological organization (i.e. molecular, cellular, systems, organism) and it has the potential of being an effective and accurate tool for rapidly assessing nanomaterial toxicity at minimal cost. This model is also well-suited to identify areas of relative distribution of nanomaterials that are fluorescently labelled.

Finally it is worth commenting that information gained from preliminary toxicity studies with zebrafish can be useful as feedback for scientifics & engineers designing novel nanomaterials in a way that they can take into consideration potential toxicity and ensure the development of materials that have the least amount of toxic potential.

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