Poster

SIZE, ASPECT RATIO, AND FUNCTIONAL CONJUGATE EFFECTS OF SILICA AND CHALCOPYRITE NANOMATERIAL TOXICITY IN DEVELOPING ZEBRAFISH EMBRYOS.

Steve M Nelson[1], Tarek Mahmoud[3], and Pam Shapiro[3], Miles Beaux II[2], Dave McIlroy[2], Deborah L Stenkamp[1]. [1] Department of Biological Sciences, Neuroscience Graduate Program, University of Idaho, [2] Department of Physics, University of Idaho, [3] Department of Chemistry, University of Idaho, Moscow, ID, USA.
nels4115@vandals.uidaho.edu

Nanomaterials have recently emerged as a viable option for the targeted delivery of therapeutic molecules. Several types of nanomaterials can be functionalized and conjugated to biomolecules in order to facilitate cell entry (1), track particle distribution in an organism (6), or to effectively deliver therapeutic molecules (2-3) into specific cell populations. Recently, several researchers have proposed that silica dioxide derived nanomaterials and quantum dot chalcopyrites might be used as biological tags (5, 7) or as carriers for drug delivery.

One limitation of nanomaterial mediated drug delivery is the potential for undesired toxic effects. Of particular importance is the safe administration of such drug loaded nanomaterials to women who have recently become pregnant. *In vitro* studies suggest that silica dioxide derived nanomaterials are non-toxic to cell lines (2, 4). Chalcopyrites ($CuInS_2$), which have been primarily used in the development of photovoltaic components for solar cells (5), have not been extensively tested for toxicity in cell culture or otherwise. It remains unclear if silica nanomaterials or chalcopyrites are toxic to developing embryos.

Using the zebrafish as a model, we report the toxicity of silica nanoparticles (bare, amine functionalized, and fluorophore conjugated; 20-60 nm), silica nanowires (bare and FITC conjugated; 50 nm wide, variable lengths), and chalcopyrites (3 nm) in developing zebrafish embryos. Individual embryos received a microinjection volume of 3nl into the yolk of one of the following solutions: sterile nanopure water, 10ng/ml, 100ng/ml, or 1µg/ml of the nanomaterial being tested. Embryos were treated at the 1-2 cell stage or at 36 hours post-fertilization (hpf). In addition, several embryos from each clutch were not treated in order to establish a baseline for embryonic death per clutch. Embryos from each treatment category (including the untreated group) were placed individually in wells of a 96-well plate and embryo mortality and teratogenic effects were assessed at 4 hr intervals following treatment for the first day then again at 36, 60, 84, 108, and 132 hpf. Embryos treated at 36 hpf were assessed for mortality and teratogenic effects at the intervals of 60, 84, 108, and 132 hpf.

Our results indicate that there is a composition dependent toxic effect and aspect ratio dependent teratogenic effect of the nanomaterials we tested. Chalcopyrites were the most toxic of any material we tested. Of the silica dioxide derived materials, the nanowires were the most toxic and the only nanomaterial to exhibit teratogenic effects on developing zebrafish embryos. The presence of a fluorophore conjugate on the nanomaterials does not

appear to significantly affect embryo mortality. We conclude that, of the materials tested, the silica nanoparticles are the least toxic and best suited to be used for the delivery of drugs to developing zebrafish embryos and possibly other model systems. Finally, we also present preliminary data on silica and chalcopyrite nanomaterial distribution following microinjection in developing zebrafish embryos.

References

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