

## ***In vivo* evaluation of ultra-small non-magnetic iron oxide nanoparticles using *Drosophila melanogaster*: potential applications**

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Iron oxide nanoparticles (IONPs) are used in many different applications, including biomedical ones. Among this type of nanoparticles, the non-magnetic, ultra-small IONPs, composed of a ferrihydrite core covered with tartaric and adipic acids (FeAT-NPs), show special characteristics. In studies with human cultured cells, FeAT-NPs showed suitable properties for their use as an oral anemia treatment, and as a transporter of platinum drugs. However, *in vivo* evaluation is needed in order to assess their effectiveness and/or toxicity. These studies were carried out using *Drosophila melanogaster* as model organism.

The potential toxicity and genotoxicity of FeAT-NPs were evaluated, in two different conditions of the nucleotide excision repair system (NER; active and inactive), with the eye SMART assay, that detects induction of somatic mutation and recombination. To evaluate the effectiveness of FeAT-NPs as an anemia treatment, iron uptake was analyzed measuring Fe levels in *Drosophila* larvae using inductively coupled plasma mass spectrometry (ICP-MS). To test their role as drug carriers, FeAT-NPs were conjugated with the prodrug cisplatin (IV), and they were evaluated with the eye SMART assay. Treatments with cisplatin (II) and its prodrug, cisplatin (IV), were performed to compare the transport effectiveness. The SMART assay was carried out with surface treatments. The effectiveness of the transport was determined by ICP-MS, quantifying the levels of Pt on DNA.

Results show that FeAT-NPs are efficiently taken up by *Drosophila* larvae and increase their Fe levels. They show weak genotoxic activity at the highest tested concentrations, without any toxicity. Their conjugation with cisplatin (IV) prodrug show less genotoxicity than that of cisplatin (II) or cisplatin (IV), in both NER conditions. Levels of Pt on DNA are being determined. These results altogether show that FeAT-NPs might be a suitable oral anemia treatment, but their usefulness as chemotherapy treatment needs further analysis.