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## Zinc Oxide Nanoparticles as Support for Classical Anti-cancer Therapies

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Abstract: Recidivation of tumors and the development of resistances against the classical anti-tumor approaches represent a major challenge we face when treating cancer. In order to master this challenge, we are in desperate need of new treatment options beyond the beaten tracks. Zinc oxide nanoparticles (ZnO NPs) represent such an innovative approach. Zinc oxide is characterized by a high level of biocompatibility, concurrently ZnO NPs are able to exert anti-tumor effects. By concentration of the nanoparticles at the tumor site, tumor cells can specifically be exposed to the nanoparticles while low zinc concentrations at off-target sites are tolerated well and can be excreted easily. We evaluated the toxicity of ZnO NPs in vitro with the help of immortalized tumor cell lines and primary cells stemming from healthy tissue. Additionally, the Chorioallantoic Membrane Assay (CAM Assay) was employed to gain insights into the in vivo behavior of the nanoparticles. We could show that ZnO NPs interact with tumor cells as nanoparticulate matter. Furthermore, the extensive release of zinc ions from the nanoparticles nearby and within the tumor cells results in overload with zinc. Beyond that, ZnO NPs were found to further the generation of reactive oxygen species (ROS). We were able to show that tumor cells were more prone to the toxic effects of ZnO NPs at intermediate concentrations compared to fibroblasts. With the help of ZnO NPs covered by a silica shell in which FITC dye was incorporated, we were able to track ZnO NPs within tumor cells as well as within a whole organism in the CAM assay after injection into the bloodstream. Depending on the applied concentrations, selective tumor cell killing seems feasible. Furthermore, the combinational treatment of tumor cells with radiotherapy and ZnO NPs shows promising results. Still, further investigations are needed to gain a better understanding of the interaction between ZnO NPs and the human body to be able to pave the way for their application as an innovative anti-tumor agent in the clinics.

**Keywords:** metal oxide nanoparticles, nanomedicine, overcome resistances against classical treatment options, zinc oxide nanoparticles

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