Sono-formulation of anticancer drugs into nanodrugs

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The use of high frequency ultrasound, HFU, for reformulation of conventional anticancer drugs into more effective nanodrugs has a great potential, but still unexplored. Our recent research findings[1,2] have proven that ultrasonic technologies can be used to generate nanoparticles from small drug molecules containing phenol and quinone moieties, by a simple and versatile procedure. The delivery of drugs in a nanoparticle formulation, solely made of dimers and aggregates of the drug molecules, may potentially have several advantages over conventional formulations. In this research project, we sought to apply HFU to manipulate an anticancer drug, namely doxorubicin (DOX), at molecular level to obtain DOX nanoparticles (DOX NPs). The chemical, structural and biofunctional analysis performed on DOX NPs revealed the formation of dimeric products. Although DOX NPs showed comparable cytotoxicity to DOX, in different breast cancer cells such as MDA-MB-231, HCC-1143, HCC1937, we have found that a different mechanism of action is responsible for the NPs and dimers cytotoxicity. We employed a combination of Stochastic Optical Reconstruction Microscopy (STORM)[3], fluorescence correlation spectroscopy (FCS) and fluorescence lifetimes imaging (FLIM) to elucidate the endosomal escape and the mechanism of action of DOX NPs. We probed the different intracellular trafficking processes, with 20 nm lateral resolution, and visualised the localization of DOX NPs in mitochondria This allowed us to speculate on the mechanism of action of DOX NPs. We can anticipate the use of this synthesis approach to transform many other sono-reactive drugs into nano-formulations.

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3.Wojnilowicz, M., Glab, A., Bertucci, A., Caruso, F. and Cavalieri, F**.** *ACS Nano* **2019**, 13, 187-202.