Serena Mazzucchelli, J Pharm Drug Deliv Res 2017, 6:3 (Suppl)
http://dx.doi.org/10.4172/2325-9604.C1.017

Metronomic treatment of breast cancer with Doxorubicin-loaded ferritin nanocages prevents chemo resistance and cardio toxicity in comparison to liposomal Doxorubicin

Serena Mazzucchelli
University of Milan, Italy

Metronomic chemotherapy (LDM) is based on frequent drug administrations at lower doses, resulting in neovascularization inhibition and induction of tumor dormancy. LDM application in clinical practice is limited by low drug accumulation at tumor site, controversial effectiveness against chemo resistance in advanced metastatic cancers, and acquired resistance after prolonged treatment. Nanotechnology could offer groundbreaking solutions to improve the effectiveness of LDM chemotherapy, by taking advantage of the unique targeting efficiency of ferritin (HFn) nanocages. Here, we exploit the HFn mediated targeted delivery of Doxorubicin (DOX) in an aggressive breast cancer mouse model with DOX inducible chemo resistance. HFnDOX was recently demonstrated to overcome chemo resistance by actively promoting DOX nuclear translocation *in vitro* and was tested as a MTD treatment on a DOX sensitive tumor model with encouraging results. We find that LDM administration of HFnDOX strongly improves the antitumor potential of DOX chemotherapy arresting the tumor progression, demonstrating that HFn mediate the nuclear delivery of DOX and increase its accumulation both in tumor tissue and in cancer cell nuclei. Moreover, we find that HFnDOX antitumor effect is attributable to multiple nano drug actions beyond cell killing, including inhibition of tumor angiogenesis and avoidance of chemo resistance. Otherwise, although an even better reduction of tumor progression was achieved with liposomal DOX (plDOX), a five-fold increase in MDR1 positive cells has been displayed, suggesting that plDOX is not suitable in view of a protracted LDM treatment, due to the onset of chemo resistance. Multi-parametric assessment of hearts, including histology, ultra structural analysis of tissue morphology and measurement of markers of reactive oxygen species and hepatic/renal conditions, provided evidence that metronomic HFnDOX allowed us to overcome cardio toxicity contrary to what is observed with DOX and plDOX. Our results suggest that HFnDOX has tremendous potential for the development of nano metronomic chemotherapy toward safe and tailored oncological treatments.

Biography

Serena Mazzucchelli is a Research Associate at University of Milan (UNIMI). She completed her Bachelor Degree in Biological Sciences (2004), Degree in Biology (2006) and PhD in Biological Sciences (2009) in Department of Biotechnology and Biosciences at University of Milan-Bicocca-Italy. From 2009 to 2012, she completed her Post-doc fellowship in Department of Biomedical and Clinical Sciences "L. Sacco" (DIBIC-UNIMI). Currently, she is a Research Associate carrying out her research focused on "The development of nano devices therapy of breast cancer" at DIBIC-UNIMI. She is an Author of 35 papers and a Reviewer.

mazzucchelli.serena@gmail.com

Notes: