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Detection of nanoparticle and drug-induced apoptosis in circulating cells *in vivo*

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The detection and enumeration of apoptotic and necrotic cells in response to nanoparticles (NPs) is important to control nanoparticle toxicity and efficiency of anti-tumor therapy. Previous studies recorded *in vitro* are not able to be effectively translated into *in vivo* conditions, as invasive extraction of cells from a living system may alter cell properties (e.g., morphology or marker expression), induce artifacts, or prevent the long-term study of cell-NP and cell–drug interactions in their biological environment. Another limitation is the low sensitivity in detecting rare circulating apoptotic tumor cells (CTCs) that are indicators of metastatic progression. Here we show that these limitations can be overcome by the use of *in vivo* flow cytometry (FC), which allows real-time monitoring of circulating normal blood cells and CTCs in response to NPs and anti-tumor drugs. We introduce high speed, multicolor *in vivo* FC that integrates photoacoustic (PA) fluorescence FC (PAFFC) to demonstrate a promising preliminary application of this unique technique for detection of rare circulating apoptotic cells in a mouse model. The verification of this approach was performed initially *in vitro* by the induction of apoptosis in cancer cells using a chemical apoptotic inductor (H2O2) and compared with apoptosis induced by graphene NPs followed by the injection of these cells in the circulatory system of a mouse. PA and fluorescence channels were used to detect cells with graphene and apoptotic cells in micro-vessels of the mouse's ear. The coincidence of PA and fluorescence signals indicated cells with graphene–induced apoptosis.

Biography

Jacqueline Nolan is a graduate student at the University of Arkansas for Medical Sciences in Little Rock, Arkansas. She is currently pursuing her Doctorate degree in Cancer Biology in Dr. Vladimir Zharov's laboratory.

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