Bona fide induction of apoptosis in transformed cells during photothermal therapy using gold nanoprisms

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Gold nanoparticles (NPs) are promising vehicles to specifically deliver drugs to cancer cells and in addition to their use in drug targeting, they can be used as "heaters" during photothermal therapy of solid carcinomas using near-infrared (NIR) laser light.[1,2] We have previously shown that functionalization of gold nanoprisms (NPRs) with glucose selectively enhances their cellular uptake in transformed cells.[3] During the last years several types of NPs have been used to kill tumoural cells, although in most cases the type of cell death (necrosis, apoptosis , autophagy, etc.) induced has not been clearly identified so far. Here we will present data that unequivocally show that apoptosis is really induced in transformed cells during photothermal therapy using gold NPRs. In addition, we will show for the first time the molecular mechanism of apoptosis during photothermal therapy in transformed cells following irradiation with NIR laser light.[4] To this aim we have established conditions to readily induce apoptosis on mouse embryonic fibroblast (MEF) cells transformed with the SV40 virus and analyzed the mechanism of apoptosis using MEFs from different knock out mice, which are deficient in proteins involved in the different routes of apoptosis (Bak and Bax, Bid, caspase-3 or caspase-9). Our results show that "hot" NPRs activate the intrinsic mitochondrial pathway of apoptosis mediated by Bak and Bax through the activation of the BH3-only protein Bid and that apoptosis and cell death is dependent on the presence of both caspase-9 and caspase-3. Our findings demonstrate how the functionalization and dose of NPRs, as well as laser power density and irradiation time exposure, must be regulated to specifically induce apoptotic cell death. Moreover the molecular mechanism presented here may help to predict the efficacy of NP-based photothermal therapy to treat cancer patients.

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