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Therapeutical Role of Copper Oxide Nanoparticles (CuO NPs) for Breast Cancer Therapy

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Abstract : Metal oxide nanoparticles are well known to generate oxidative stress and deregulate normal cellular activities. Among these, transition metals copper oxide nanoparticles (CuO NPs) are more compelling than others and able to modulate different cellular responses. In this work, we have synthesized and characterized CuO NPs by various biophysical methods. These CuO NPs (~30 nm) induce autophagy in human breast cancer cell line, MCF7 in a time and dose-dependent manner. Cellular autophagy was tested by MDC staining, induction of green fluorescent protein light chain 3 (GFP-LC3B) foci by confocal microscopy, transfection of pBABE-puro mCherry-EGFP-LC3B plasmid and western blotting of autophagy marker proteins LC3B, beclin1, and ATG5. Further, inhibition of autophagy by 3-Methyladenine (3-MA) decreased LD50 doses of CuO NPs. Such cell death was associated with the induction of apoptosis as revealed by FACS analysis, cleavage of PARP, dephosphorylation of Bad and increased cleavage product of caspase3. siRNA-mediated inhibition of autophagy-related gene beclin1 also demonstrated similar results. Finally, induction of apoptosis by 3-MA in CuO NPs treated cells were observed by TEM. This study indicates that CuO NPs are a potent inducer of autophagy which may be a cellular defense against the CuO NPs mediated toxicity and inhibition of autophagy switches the cellular response into apoptosis. A combination of CuO NPs with the autophagy inhibitor is essential to induce apoptosis in breast cancer cells. Acknowledgments: The authors would like to acknowledge for financial support for this research work to the Department of Biotechnology (No. BT/PR14661/NNT/28/494/2010), Government of India.

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