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PMMA nanoparticles promote the internalization of a survivin molecular beacon by endocytosis in human A549 cells: Fate of the nanoparticles and the theranostic agent

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Statement of the Problem: The development of effective drug delivery systems represents one of the main goals in nanomedicine. Data in literature demonstrate that, depending on the uptake pathways, the nanocarriers and their payloads can be trafficked into different organelles. In this context, the aim of the work was to evaluate: The ability of Polymethylmethacrylate Fluorescent Nanoparticles (PMMA-NPs) to promote, in human A549 cancer cells, the internalization of a Molecular Beacon (MB) specific for survivin mRNA as theranostic agent; the involvement of endocytosis in the NP uptake; the NP fate at different times of cell incubation to verify their localization in lysosomes; the MB localization in relation with the Endoplasmic Reticulum (ER) where the target mRNA is located.

Methodology: The PMMA-NP capability to promote the MB uptake by endocytosis and the NP and MB intracellular localization studies were realized by confocal microscopy using markers of endocytic process and organelles; the NP fate was also evaluated by fluorescence measurements.

Findings: PMMA-NPs promoted the MB uptake; significant increase of the number and the mean area of dextran filling endocytic vesicles in the presence of NPs after incubation of 30 days; strong co-localization of NP and lysosome tracker fluorescence after 2-48 hours of incubation (the cell culture medium fluorescence decreases in the 24-72 hour window and increases after 96 hours); co-localization of the MB fluorescence with the ER-marker signal after 90 days of incubation.

Conclusion & Significance: These data highlight the ability of the PMMA-NPs to promote the survivin-MB internalization and the involvement of endocytotic pathway in their uptake. These results demonstrate that the PMMA-NPs are an appropriate delivery system capable of being eliminated by the cells involved in the treatment; these evidences also contribute to consider the MB as an effective tool for the intracellular sensing.

Biography

Barbara Adinolfi has received Master's degree in Pharmaceutical Chemistry and Technology in 2000 from the University of Pisa, Italy. She has received PhD in Pharmacotoxicological, Pharmacognostical Sciences and Pharmacological Biotechnologies in 2005 from the University of Milan and with the specialization in Pharmacology in 2008 from the University of Pisa. She has worked from 2000 until 2013 in the Department of Pharmacy, University of Pisa. She has also worked in the Department of Biomedical Sciences, University of Copenhagen from 2009-2010. Presently, she is working in the CNR Institute of Applied Physics in Florence. Her research activity is focused on the evaluation of anticancer activity of natural and synthetic compounds, on the evaluation of the role of specific proteins as putative prognostic markers in cancer and on the activity of nanoparticles as intracellular delivery tools for oligonucleotide optical switches by confocal microscopy.

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