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Light-triggerable liposomes for enhanced endo/lysosomal escape and gene silencing in PC12 cells

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Liposomes are an effective gene/drug delivery system, widely used in biomedical applications including gene therapy and chemotherapy. Here we designed a photo-responsive liposome (lipVP) loaded with a photosensitizer verteporfin (VP). This photosensitizer is clinically approved for photodynamic therapy (PDT). LipVP was employed as a DNA carrier for pituitary adenyl cyclase-activating polypeptide (PACAP) receptor 1 (PAC1R) gene knockdown in PC12 cells. This has been done by incorporating *PAC1R* antisense oligonucleotides inside the lipVP cavity. Cells which have taken up the lipVP were exposed to light from a UV light source. As a result of this exposure, reactive oxygen species (ROS) were generated from VP, destabilizing the endo/lysosomal membranes and enhancing the liposomal release of antisense DNA into the cytoplasm. Endo/lysosomal escape of DNA was documented at different time points based on quantitative analysis of colocalization between fluorescently labeled DNA and endo/lysosomes. The released antisense oligonucleotides were found to silence *PAC1R* mRNA. The efficiency of this photo-induced gene silencing was demonstrated by a $74\pm 5\%$ decrease in *PAC1R* fluorescence intensity. Following the light-induced DNA transfer into cells, cell differentiation with exposure to two kinds of PACAP peptides was observed to determine the cell phenotypic change after *PAC1R* gene knockdown.

Biography

Wei Deng has received her PhD degree in Chemistry with nanotechnology background at Macquarie University, Australia in 2012. She was rewarded a highly competitive fellowship (Discovery Early Career Research Award) from the Australian Research Council in 2012. She is currently a Research Fellow in the Centre of Excellence in Nanoscale Biophotonics, Macquarie University. Her research fields were mainly focused on biomedical applications of liposomes and polymer nanoparticles, in particular, light (or X-ray)-controlled drug/gene delivery systems in cancer treatments.

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