

LOCALIZED OPTICALLY-ACTIVATED GENE RELEASE IN BREAST CANCER CELLS USING AU NANOPARTICLES AS CARRIERS

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Gene delivery at specific locations is highly desired for precise gene therapy. We describe a new photoactive, nanoscale gene delivery vehicle based on oligonucleotide-conjugated nanoparticles (NNP). Biomolecular activity has previously been triggered using chromophores and inductive coupling of a radio frequency (RF) magnetic field to metal nanocrystals; however, RF excitation lacks spatial controllability. In contrast, focused infrared (NIR) light, can be used to activate a more localized area down to 1 micron. Potentially, this method could activate the area (nm range) of one NNP. We present a new method that uses NIR light to optically activate oligonucleotides (ODN) conjugated to NNPs. We selectively release genes at desired locations of MCF7 breast cancer cells without disturbing surrounding areas.

We show this method can be used for the intracellular delivery of therapeutic genes. Conjugated NNPs are internalized by MCF-7 cells that overexpress membrane receptor protein HER-2. SYBR Green I staining is used to visualize double-stranded ODN (dsODN) attached to the internalized NNPs. A 10 mW laser (785 nm) is used to illuminate the cells at specific locations. Due to photothermal heating of NNPs, the dsODN denatures at a critical temperature. We show that after 1 minute, the fluorescence intensity decreases, indicating that the dsODN has denatured and the antisense HER-2 ODN has been released inside the cell to subsequently interfere with HER-2 mRNA translation. Time-lapsed immunofluorescence study shows the down regulation of HER-2 in the optically excited cells.

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