F*luc*-mRNA delivery to cervical cancer cells using Curcumin-Poly-L-lysine modified gold nanoparticles: A Proof of Principle Study

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Cervical cancer is one of the leading causes of female death in developing communities, with a mortality rate of 265 653 annually. This non-communicable disease shows immense complexity at the epigenetic, genetic and cellular levels, limiting conventional treatment. Nanotherapeutics hold a promising attribute in solving these limitations due to their localized delivery, low profile in bio-distribution, targeting, aqueous solubility, therapeutic index and oral bioavailability. Chemical and physical nanoparticle (NP) synthesis often use toxic and expensive reducing reagents, limiting upscaling production and harming the environment. Green chemistry using plant materials is a sustainable alternative for conventional reduction methods, which confer dual reducing and capping properties. Curcumin, a bio-active component isolated from the rhizome of *Curcuma longa*, offers additional advantages by exhibiting a wide range of pharmacological properties, enabling the NP to work synergistically to its therapeutic payload. Therefore, this study aims to elucidate the potential and antitumour properties of economical and eco-friendly curcumin synthesised and capped gold NPs for the localised delivery of mRNA to the tumour microenvironment of cervical cancer (HeLa) cells. Gold NPs were biologically synthesized and capped using varying concentrations of curcumin [0.25mM, 0.5mM, 0.75mM and 1mM]. The nanoparticle was further functionalised using poly-L-lysine (PLL) to enhance F*luc*-mRNA binding and stabilised by PEGylation. Nanocomplexes were characterised using UV-vis spectrophotometry, transmission electron microscopy (TEM), and nanoparticle tracking analysis (NTA). F*luc*-mRNA binding, compaction and nuclease protection was assessed using the band shift, dye displacement and nuclease digestion assays, respectively. The degree of cytotoxicity of the nanocomplexes in the HEK239 and HeLa cell lines were evaluated using the MTT assay, and transgene expression was assessed using the luciferase reporter gene assay. The gold NP-curcumin hybrids showed long term colloidal stability [19-38 mV], and were of an excellent size [64.7-120.4 nm] for gene therapy. Furthermore, the nanocomplexes exhibited low cytotoxicity [>88%] and significant transgene expression. Overall, these gold nanoparticles have shown great potential as a vehicle, which works synergistically with its payload facilitating additional selection pressure to eradicate cancer and further suggesting a potential for immunotherapeutic application. Further studies will be conducted to assess the potential of this mRNA-based delivery system to transport the cytokine, Interleukin-12 (IL-12), efficiently and safely to cervical cancer cells for immunotherapy.

Keywords: Biological synthesis; Cancer Therapy; Cervical cancer; Curcumin; Nanotherapeutics; Gold nanoparticles