Trastuzumab-functionalized piezoelectric nylon-11 nanovectors as an innovative tool in cancer therapy

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Nanotechnology suggests the exploitation of biocompatible and biodegradable nanovectors for the enhancement of bioavailability and targeting of drugs [1]. In this context, an innovative approach has been recently proposed in cancer nanomedicine based on the use of nanomaterials that can remotely respond to external stimuli such as ultrasound [2]. Piezoelectric nanomaterials, featuring the capability of converting mechanical energy into electricity, present great potential in cancer therapy. Nylon-11, a polyamide bioplastic, presents satisfactory piezoelectric properties [3] never exploited in biomedicine so far: here, we propose the use of trastuzumab-modified nylon-11 (Tmab-nylon-11) nanovectors to improve the therapeutic outcome in cancer neoangiogenesis treatment, by exploiting an indirect electric stimulation mediated by the mechanical excitation of the nanoparticles: this stimulation in fact affects cell fate by enhancing drug release or/and regulating the invasion and migration pathways [2,4].

Nylon-11 nanoparticles were prepared by a simple anti-solvent method. Trastuzumab (Tmab) was conjugated to the nanoparticles, after reducing the antibody molecule by using 1,4-dithiothreitol (DTT), by exploiting the cysteine residues of the antibody and the 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[maleimide(polyethylene glycol)-2000] (DSPE-PEG-Mal) on the particles. Successful binding was confirmed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and bicinchoninic acid (BCA) assay. The morphological characterization of the particles was assessed using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The biocompatibility of the Tmab-nylon-11 nanoparticles was tested on human brain capillary endothelial cells (HCMECs). Statistical analysis was carried out by using analysis of variance (ANOVA) followed by Fisher's *post-hoc* test.

SEM and TEM imaging suggest the formation of spherical-shaped nanoparticles. SDS-PAGE and BCA assay show the presence of the antibody on Tmab-nylon-11 nanoparticles. Dynamic light scattering (DLS) measurements show a size of nylon-11 and Tmab-nylon-11 nanoparticles of 193.9 ± 3.5 nm and 182.1 ± 0.9 nm, respectively (Figure 1A). After synthesis, the particles were stored at 4°C, and the long-term stability has been monitored using DLS and ζ-potential measurements. Finally, the biocompatibility data showed that the particles are well tolerated by HCMECs up to 250 µg/mL after 24 h of incubation (Figure 1B).

Concluding, piezoelectric nylon-11 nanoparticles were successfully synthesized by a simple anti-solvent method and decorated with trastuzumab to improve therapeutic efficiency. The obtainment of biocompatible, stable, and monodisperse polymeric piezoelectric nanoparticles is the first step towards innovative approaches in cancer nanomedicine.

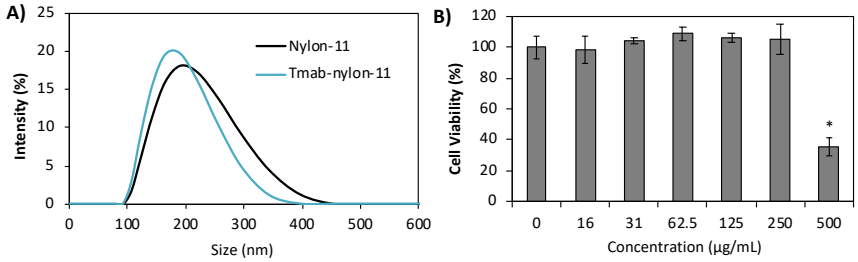

Figure 1: A) Size distribution of the nanoparticles. **B)** Biocompatibility results for Tmab-nylon-11.

References

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