Cell surface conjugation of Discoidal Polymeric Particles on Mesenchymal Stem Cells

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Abstract

The application of bioactive drugs is limited due to their low solubility, short exposure, and serious side effects on tissues off target. Therefore, various nanotechnological solutions have been developed to address these issues. One strategy is to use cell as carriers. The cargo of nanoparticles can be immobilized on the cell surface and can enable precise delivery across complex physiological barriers[1-2]. This study demonstrates the Mesenchymal Stem Cells (MSC) cells conjugated with 5µm discoidal Poly(lactic-co-glycolic acid)-Polyethylenimine-maleimide-PEG_{5000}-succinimidyl valerate (PLGA-PEI-PEG) as a cellular backpack immobilizing on the cell surface.

Background

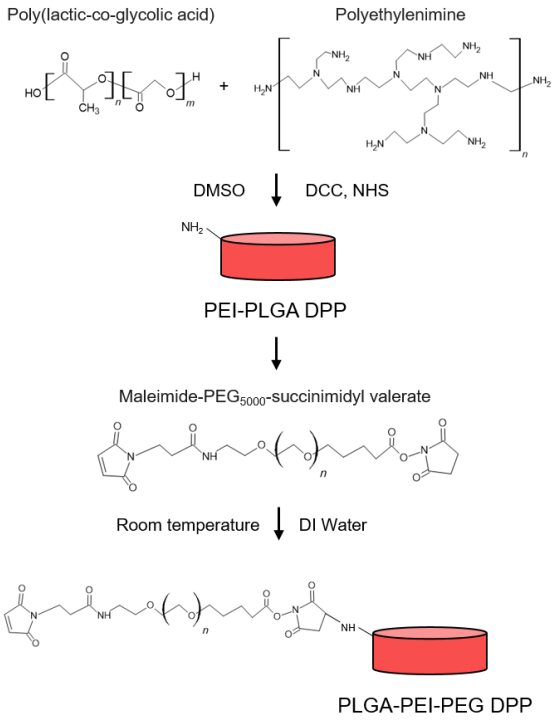
Cell based drug delivery systems involve the utilization of the cells biological functions. This study examines the feasibility of transporting 5µm PLGA-PEI-PEG DPPs using MSC stem cells. For covalent conjugation of nanoparticles to thiol groups on the cell surface, the PEG chains forming the nanoparticles corona were functionalized with maleimide groups. Confocal microscopy was used to examine the localization and distribution of DPPs on the cell surface.

Materials

Commercially available Polyvinyl alcohol (PVA), acid-terminated poly-lactide-co-glycolide (PLGA, lactide:glycolide = 50:50, M_w = 24000-38000 g/mol), dichloromethane (DCM), chloroform ($CHCl_3$), dimethyl sulfoxide (DMSO), N-Hydroxysuccinimide (NHS), N – Ethyl-N-(3-(dimethylamino)Propyl)carbodiimide Hydrochloride (EDC),polyethylenimine, Maleimide-PEG_{5000}-succinimidyl valerate and Sylgard 184 elastomer were utilized for synthesis. All reagents and solvents were used without further purification.

Methods

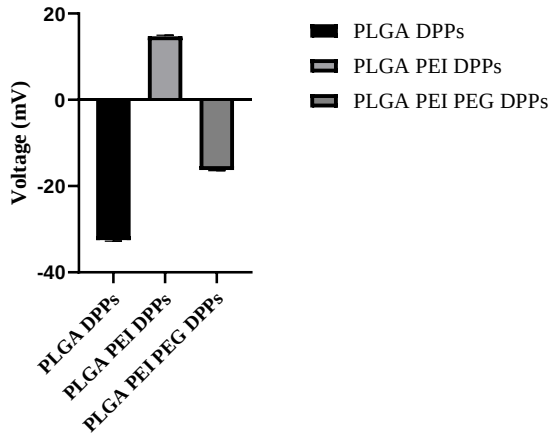
Firstly, PLGA was dissolved in DMSO and reacted with DCC and NHS. Then Branched PEI was added in PLGA Solution. The unreacted materials were removed by dialysis and lyophilized. PLGA-PEI DPPs were synthesized by top-down fabrication method using nanoimprint lithography technique as mentioned earlier[3]. After fabrication of PLGA-PEI DPPs, 1 mg of particles was mixed with 5 mg of maleimide-PEG_{5000}-succinimidyl valerate and dissolved in DI water. The reaction mixture was left on an orbital shaker at 300 RPM at room temperature for 60 min. Excess PEG was removed by centrifuge and particles were resuspended in DI water.



Results

The change in zeta potential confirmed the coating of PEG_{5000}-succinimidyl valerate. Zeta potential of PLGA – PEI DPPs was 14.5mV which was reduced to -16.2 mV after PEG_{5000}-succinimidyl valerate coating. Confocal microscopy confirmed that DPPs were attached and localized on the surface of the cells immediately after 6 hours.

(A)



(B)

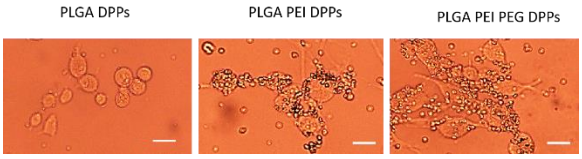


Fig.1 (A) Zeta potential of PLGA, PLGA- PEI and PLGA- PEI- PEG DPPs, (B) confocal microscopy of DPPs attached on MSC cell surface.

Conclusion

The attachment of PLGA DPPs to the MSC cell surface is least in comparison to PLGA–PEI and PLGA –PEI-PEG. Cell surface have a negative charge, as does PLGA. Therefore, charge- charge interaction couldn't took place. Since, PLGA-PEI DPPs has a positive charge, PLGA-PEI were able to attach to the cell surface. Even though PLGA- PEI-PEG DPPs had a negative charge, they were still able to attach to the cells surface. Thus we believe that PEG chains that form the DPPs corona when functionalized with maleimide groups allow the nanoparticles to be covalently conjugated to thiol groups on the surface of cells.

Acknowledgements

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