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Room/Aula: B016 - Rizzi

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Time 10:00

"Polyethylenimine-based nanoparticles for targeted plasmid DNA delivery"

Targeted delivery of polymer-based nanoparticles has been considered as an efficient approach to transfer genetic materials into cells. Considering the over expression of several specific receptors on desired cells, we hypothesized that the conjugation of small ligands to polyethylenimine (PEI) at different conjugation degrees might be an effective strategy for pDNA delivery into the cells over-expressing the receptors on their surfaces. In order to test the hypothesis, the conjugated PEI/plasmid DNA complexes were prepared using small molecules to target αvβ3 and Large Aminoacid Transporter-1 (LAT-1). Moreover, the conjugates were characterized with respect to plasmid DNA condensation ability, particle size and zeta potential as well as cell-induced toxicity, apoptotic effects and plasmid protection against DNase degradation. The results demonstrated that the majority of the conjugated derivatives of PEI were able to condense the plasmid and protect it against enzyme degradation. The results of dynamic light scattering (DLS) and atomic force microscopy (AFM) revealed that the formed nanoparticles were in the size range of 85-200 nm. The highest level of transgene expression was achieved by terac-conjugated PEIs at where they could increase the level of gene expression up to 4 fold in the cell lines over-expressing integrin $\alpha_V\beta_3$ receptor whereas no increase in the level of IL-12 expression in the cell lines lacking integrin receptors was observed. Also, the results of the competitive inhibition of the receptors demonstrated the specificity of transfection for the cells over expressing $\alpha_v\beta_3$ receptor. On the other hand, tetrac and L-thyroxine conjugation of PEI significantly reduced the polymer-induced apoptotic effects. Also, the results of in vivo imaging of the polyplexes revealed that ^{99m}Tc-labeled PEI/pDNA complexes accumulated in kidney and bladder 4 h post injection. The results obtained in this investigation suggest the potential of tetrac and L-thyroxine as small molecules mimicking the binding properties of integrin binding peptides (e.g., RGD) for targeted gene delivery.