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RGD Conjugated Dendritic Polylysine as an Adjuvant for Cellular Delivery of Antisense Oligonucleotide

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Extended Abstract

Dendritic polylysines (DPL) are highly branched and well-defined spherical polymer with positively charged primary amino groups on surface. This structural feature is useful for a delivery of antisense oligonucleotide or siRNA (Yamagata et al., 2011, Watanabe et al., 2009). In this study, we investigated integrin receptor-mediated antisense oligonucleotide delivery by preparing RGD (and iRGD)-conjugated dendritic poly-lysines (RGD-DPL and iRGD-DPL) (Kok et al., 2002). RGD (or iRGD) was conjugated onto DPL surface through bisulfide bond formation and the conjugation reaction was confirmed by monitoring the retention time in capillary zone electrophoresis and absorbance at UV-Vis spectroscopy. Cellular delivery by DPL-RGD (or iRGD)/antisense oligonucleotide complex was examined by antisense splicing correction assay on integrin alpha v / beta 3 positive A375B3 cells, which was stably transfected with plasmid pLuc/705. DPL-RGD (or -iRGD)/antisense oligonucleotide complexes exhibited integrin receptor mediated uptake on A375B3 cells without inducing cellular toxicity. In addition, the delivery of DPL-RGD (or –iRGD)/oligonucleotide complexes on both 2D cell culture and 3D cell clumps of A375B3 was integrin receptor-dependent with moderate effeciency. Notably, DPL-iRGD/oligonucleotide complexes showed moderately enhanced delivery activities on 3D cell clumps of A375B3 cells. Our data suggest that RGD (or -iRGD) conjugated DPL may have a potential use as an adjuvant for cellular derlivery of antisense oligonucleotide or siRNA. (No. R13-2008-010-00000-0)

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