EuroSciCon

3rd Edition of International Conference and Exhibition on

Polymer Chemistry

March 26-28, 2018
Vienna, Austria

Polym Sci, Volume 4
DOI: 10.4172/2471-9935-C1-009

HIGHLY BRANCHED POLY(β-AMINO ESTER)S AS NEW GENE DELIVERY VECTORS

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One of the main bottlenecks for clinical gene therapy is the lack of safe and efficient gene delivery vectors. Over the last decade, linear poly (β-amino ester)s (LPAEs) have emerged as a new class of gene vectors. However, their linear structure has severely limited the further improvement of their performance. In contrast, various dendritic polymers have demonstrated their great potential over their linear counterparts as gene delivery vectors due to their three-dimensional spatial structure with multiple terminal groups. Herein, a novel type of dendritic polymer, highly branched poly (β-amino ester)s (HPAEs), was developed as a new class of gene vector via "A2+B3+C2" type Michael addition from commercially available 4-amino-1-butanol, trimethylolpropane triacrylates and bisphenol A ethoxylate diacrylate. NMR (Nuclear magnetic resonance) and GPC (Gel Permeation Chromatography) results indicate that the composition and structure of HPAEs can be easily controlled and adjusted by simply varying the feed ratio of B2 to C3. HPAEs can effectively condense DNA to form small and stable polyplexes. HPAEs have shown very high gene transfection efficiency and low cytotoxicity over twelve different cell types including primary and neural cells, far more efficient and safe than the commercial transfection reagents SuperFect, Xfect and Lipofectamine 2000. Furthermore, ***in vivo*** transfection studies revealed that HPAEs can carry therapeutic COL7A1 cDNA to restore the expression of type VII collagen along the basement membrane zone in both recessive dystrophic epidermolysis bullosa (RDEB) knockout and human RDEB graft mouse models. HPAEs are highly efficient and safe gene vectors for gene delivery.

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