Modified PAMAM dendrimers with short oligo-peptides for early endosomal escape and enhanced gene delivery

Le Thi Thuy, Sudipta Mallick and Joon Sig Choi*

Department of Biochemistry, Chungnam National University, Gung-dong 220, Yuseong-gu, Daejeon 305-764, Republic of Korea

E-mail: joonsig@cnu.ac.kr

Recently, non-viral vectors have become a popular research topic in the field of gene therapy. In this study, we conjugated short oligopeptides to polyamidoamine-generation 4 (PAMAM G4) to achieve higher transfection efficiency. Previous reports have shown that the PAMAM G4-histidine (H)-arginine (R) dendrimer enhances gene delivery by improving cell penetration and internalization mechanisms. Therefore, we synthesized PAMAM G4-H phenylalanine (F) R, PAMAM G4-FHR and PAMAM G4-FR derivatives to determine the best gene carrier with the lowest toxicity. Physicochemical studies were performed to determine mean diameters and surface charge of PAMAM derivatives/pDNA polyplexes. DNA condensation was confirmed using a gel retardation assay. Cytotoxicity, cell uptake and transfection efficiency were analyzed using human cervical carcinoma (HeLa) and human liver carcinoma (HepG2) cells. Similar levels of transfection were achieved in both cell lines by using gold standard transfection reagent PEI 25kD. Therefore, our results show that these carriers are promising and may help achieve higher transfection with negligible cytotoxicity.

Confocal laser scanning microscopy image and flow cytometry analysis of HeLa cells incubated with polyplexes for 4 h. DNA was labeled by Alexa Flour 546 (red), polymer was labeled by Alexa flour 488 (green), Nucleus was stained by Hoechst 3342

References

