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Preparation and characterization of poly(ester amine) derivatives for lung cancer gene therapy

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Primary objectives of gene therapy are to correct the genetic defects that underlie a disease process and to provide supplemental therapeutic modality through genetic engineering. Over 75% of current gene therapy is performed using viruses as gene delivery vehicles. However, with viruses, there are serious concerns over the issues of toxicity, immunogenicity, payload gene size limitations, and difficulty in scale up for industrial production. Non-viral vectors therefore have attracted attention from academic and industrial point of view. Among the non-viral vectors, polymeric systems offer several important advantages. First, polymers are tremendously versatile and can provide physical, chemical, and biological properties that are necessary for gene delivery applications. Second, polymers can be synthesized in parallel synthesis pathways for high-throughput screening of biocompatibility and transfection efficiency. Third, various formulations, designs, and geometrics can be made from polymeric materials for specific types of gene delivery applications. Moreover, the surface chemistry of polymers can be easily modified with biological ligands for site specific targeting in the body. However, some non-degradable polymers accumulate in the body resulting in the cytotoxicity and thus the reduction in their gene transfer ability. Even though, low molecular weight polymers, which can be eliminated via kidney is an alternative choice, exhibits lower colloidal stability and DNA condensation due to their reduced number of electrostatic interactions thus reduced transfection efficiency.

As biodegradable polymers are designed to contain a combination of various functional components, it is likely that engineered systems for non-viral gene delivery, especially with the application of biodegradable ester linkage will eventually be constructed. This biodegradable linkage approach to vector development is giving way to a safety profile where low molecular weight polyethylenimines are couples with diacrylate linkers to yield high molecular weight poly(ester amine)s (PEAs) with reduced cytotoxicity and high transfection efficiency. For example, the initial emphasis on identifying materials that bind and condense nucleic acids may have underappreciated the importance of their subsequent cellular uptake; attention has now turned to vectors with a hydrophobic, biodegradable cross linker such as polycaprolactone diacrylate [1] or hydrophilic, biodegradable cross linkers such as glycerol dimethacrylate [2] and glycerol triacrylate [3] whose chemical structure with ester linkage allowed the controlled fashioned degradation with suitable nucleic acid condensation, following cellular uptake and thus gene delivery ability. The need for a safety and biocompatibility approach extends to in vitro investigations, as modifications intended for in vivo applicability can significantly affect both in vitro and in vivo performance.

Biography

Dr. Rohidas B. Arote has been studied with gene delivery for more than 7 years. He has been awarded as "Young Scientist" in the field of Gene Therapy. He published 35 international and 2 domestic papers related to non-viral gene delivery. Since 2007, he published more than 25 international publications on development of non-viral gene carrier. Recently he synthesized novel biodegradable poly (ester amine)s based on glycerol dimethacrylate and low molecular weight polyethylenmine and this polymer showed significant transfection efficiency in gene silencing activity in vitro as well in vivo for which he applied a patent in Korea. Currently he is a Assistant Professor at Seoul National University.

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