

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 geometries 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 or hydrophilic, biodegradable cross linkers such as glycerol dimethacrylate and glycerol triacrylate 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.

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Protocolization of a 10% reduction of the autoimmunity area global test reagent budget pursuing the lowest impact on the patient care quality

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L'Hospital Clínic de Barcelona (HCB) is a University Hospital of 855 beds and 4000 employees with an assigned health care area of 555.000 inhabitants of a part of Barcelona city, and the highest complexity health care level for the whole 7.200.000 Catalonia population. HCB attends annually 46328 admittances, 421.849 external medical advises, 161.824 emergencies and 18.785 chirurgical interventions, with a budget of 450.000.000 €.

Due to the economic impact of the financial crisis, the current Health Minister of the Catalan Government requested a 10% reduction of the health budget in 2011. Each public health care center was requested to ensure a 10% budget reduction. Along the previous years, the annual test volume of the Autoimmunity Area (AIA) of the Immunology Department was increasing every year around a 20%.

Therefore, we planned to decrease the current budget in a clinical protocol based way in agreement with the clinical staff of each clinical area, with the objective to minimize the effect on the clinical care quality. Accordingly, the global count of the test results show only a 1% reduction from January to June 2011 whereas we obtained a 33% reduction from July to December 2011 in comparison to 2010, and the mean annual reduction remains in a 13,67% reduction for 2011 in comparison to 2010. Further economical and technical data are been analyzed to be presented at the conference.

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