pBAE polymers: a new delivery platform of biologicals for nucleic acid-based therapies

Cristina Fornaguera, Maria Navalón-Lopez, Antoni Torres-Coll, Nil Gonzalez-Rios, Coral Garcia-Fernandez, Maria Stampa Lopez-Pinto, Yvette Rabadà, Elena Haro, Carles Bofill-Bonet, Patricia Gonzalez-Saez, Jennifer Fernandez-Alarcon, Marta Guerra-Rebollo, Jose Rodrigo Magaña, Salvador Borrós

Grup d'Enginyeria de Materials (Gemat), Institut Químic de Sarrià (IQS), Universitat Ramon Llull (URL)

Cristina.fornaguera@iqs.url.edu

Nucleic acid-based targeted therapies are becoming the next-generation standard of care therapeutics for many therapeutics devoted to treat current unmet medical needs, such as cancer and rare diseases. Although traditional small molecules could be used for these purposes, in the last days, there is no doubt on the enhanced performance that biologicals could bring to the field. Beyond the application of viral vectors for monogenic diseases treatment and mRNAs for infectious diseases prophylaxis, it is now the time nucleic acids can be used for therapeutics [1,2].

However, nucleic acids in vivo delivery has still some drawbacks to be overcome. Nucleic acids stability in biological environment is compromised by the presence of nucleases. In parallel, being bigger macromolecules as compared to small drugs, they are easier recognized by the immune system and prematurely cleared up from circulation. Thus, the use of a nanometric carrier system that can overcome both issues, while ensuring a safe and efficient selectively targeted therapy is an urgent need.

Among possible nanocarriers, polymeric nanoparticles, and specifically, our proprietary **oligopeptide end-modified poly (beta-aminoester) polymers (pBAE)** stood as promising carriers, not only for nucleic acids, but also for different type of viral vectors that can be used for tumor and muscular distrophies therapeutics, among others [3-5]. Thus, in here, we **aim** to present pBAE polymeric nanoparticles as a novel platform with demonstrated safety and efficacy for the direct in vivo delivery of nucleic acids for therapeutics of different diseases, such as lung cancer vaccination, Duchenne Muscular Dystrophy gene therapy and Aortic Aneurism reparation.
Through these different example applications, we have already demonstrated the possibility to *selectively target the polymers* and resulting nanosystems to different cells of interest [5,6]. For example, for tumor therapeutics, we can be selective in the tumor microenvironment cell type (i.e. cancer stem cells, antigen presenting cells). Also, we have shown how changing the administration route allows the control and tuning of the particles biodistribution, which could be advantageous for different applications. Additionally, we have demonstrated the potential efficacy of our technology for oncolytic virotherapy as well as for mRNA vaccination, among others [5,7].

In this communication we present and review different studies to demonstrate that our pBAE polymers family successfully deliver nucleic acids and coated viruses in a tunable way, for specific unmet medical needs such as tumor therapeutics. With these results in specific applications as proof-of-concept, we aim to demonstrate the application our pBAE polymers could have for any other disease requiring for the controlled delivery of nucleic acids.

References

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