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Harnessing the immunogenicity of viral proteins for designing novel cancer DNA vaccines

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Harnessing the power of the immune system to destroy or prevent cancers is a highly attractive strategy and a unique approach to cancer therapy. Competitive advantages of cancer vaccines are exquisite specificity, low toxicity, and the potential for a durable treatment effect due to immunologic memory, but their development is challenging due to the low immunogenicity of tumor antigens. As it is the case for cancer, a proper activation of cytotoxic T cells is necessary to clear infection by killing virus-infected cells. For that purpose, the immune system is able to detect and eliminate certain viral threats. We aim to investigate if the expression of specific viral proteins could similarly promote cancer immunization. DNA vaccine is a simple, versatile and clinically applicable method that could greatly benefit from such a strategy. We first demonstrated that the co-administration of a plasmid encoding the HIV-1 Gag viral capsid protein enhanced the efficacy of melanoma DNA vaccine. It favored antigen-specific Th1 immunity, delayed B16F10-OVA tumor growth and improved mouse survival in both prophylactic and therapeutic vaccination approaches. Similarly, a prophylactic DNA immunization against the melanoma-associated antigen gp100 was enhanced. Safety and immunogenicity of pGag have been demonstrated in human in the context of HIV vaccine development. Its use as a genetic adjuvant is thus of particular interest from a translational point of view. We then engineered the vesicular stomatitis virus G glycoprotein as permissive insertion sites allowed T-epitope insertions. Inclusion of either ovalbumin MHC class I or MHC class II restricted epitopes induced the proliferation of specific CD8+ and CD4+ T cells, respectively. The cytotoxic T-cell response was high when the two plasmids were co-delivered allowing a protective therapeutic effect against B16F10-OVA tumor. In conclusion, Gag and VSV-G proteins can be exploited for designing DNA vaccine strategies with promising therapeutic potential in cancer.

Recent Publications

- Lambricht L, Vanvarenberg K, De Beuckelaer A, Van Hoecke L, Grooten J et. al. (2016) Co-administration of a plasmid encoding HIV-1 Gag enhances the efficacy of cancer DNA vaccines. Molecular Therapy. 24(9):1686-1696.
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- Vandermeulen G, Athanasopoulos T, Trundley A, Foster K, Préat V, Yáñez Muñoz R J, Dickson G (2012) Highly potent delivery method of gp160 envelope vaccine combining lentivirus-like particles and DNA electrotransfer. Journal of Controlled Release. 159(3):376-83

Biography

Gaëlle Vandermeulen is a senior Postdoctoral Researcher at the University of Louvain. After completing a Master's degree in Pharmacy, she joined the Advanced Drug Delivery and Biomaterials group at the Louvain Drug Research Institute of the University of Louvain (UCL). Her PhD work was part of a European project and she spent several months at the Université Paris Descartes. She completed a PhD on skin DNA electroporation in 2008 and performed a Postdoctoral stay focused on HIV DNA vaccine at the Royal Holloway University of London. She aims to develop novel delivery systems for nucleic acid-based drugs, with a particular focus on DNA vaccines.

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