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Cell penetrating peptides: Potent delivery vehicles that enable the generation of cytotoxic T cells against an antigenic cargo

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Cytolytic T cells (CTLs) have a unique potential to destroy viral infected cells and cancer cells. Vaccination strategies that can elicit CTLs are thus actively pursued within the cancer and HIV immunotherapy field. Because induction of CTLs requires antigen to be processed in the cellular cytosol, conventional vaccines relying on the injection of recombinant protein antigens generally fail to evoke CTL responses. To acquire access to the cytosolic route of antigen presentation, we decided to use cell penetrating peptides (CPPs) as carriers for an antigenic cargo. CPPs are small peptide sequences inspired by the protein sequences viruses use to cross cellular membranes. CPPs typically contain multiple cationic amino-acid residues (lysines or arginines) and/or display an amphipatic 3-D organisation. Two different approaches were persued. In a first approach, we used a cationic, amphipathic CPP to deliver antigenic information to the immune system in the format of an mRNA encoding a model antigen. Through its cationic residues, the CPP condensed the mRNA into nanoparticles that allowed antigen expression inside the cytosol of dendritic cells. These CPP-mRNA nanoparticles were superior in evoking CTLs when compared to conventional lipid based mRNA vaccination. In a second approach, we used CPPs to deliver peptide epitopes to the immune system. Again, RNA was used as scaffold for nanoparticle assembly. In this case, the RNA did not encode an antigen, but potently activated innate immune responses. The thus obtained nanoparticles were extermely potent at inducing CTLs and inhibited tumor growth in a pre-clinical murine melanoma model.

Biography

Stefaan De Koker is a Bio-Engineer with a PhD in Biotechnology obtained at Ghent University. He has been leading a research team working on the design of novel vaccines that elicit potent cytotoxic T cell responses against cancer and HIV from 2012. Currently, he has coauthored over 45 A1 papers at the interface between Materials Sciences and Immunology. His research has been published in journals such as *Nanoletters, Angewandte Chemie, ACS Nano, Journal of Immunology* and *PNAS*.

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