

## DC targeting skin vaccines for improved cancer immunotherapy

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Cancer immunotherapy requires potent tumor-specific T cell responses, initiated by dendritic cells (DCs). Our aim is to develop a vaccine that targets antigens to antigen presenting cells such as DC and Langerhans cells (LC) *in vivo* in human skin and simultaneously induce maturation and migration of these cells to stimulate tumor specific CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses. We use glycans for DC and LC specific targeting of the vaccine. Moreover the glycans that target C-type-lectin receptors (CLRs) on these cells enhance the intracellular routing of antigen and MHC class I and II loading. Our strategy allows inclusion of multiple tumor antigens, as well as Toll-like receptor (TLR) ligands, directing the vaccine to specific skin DC and LC that simultaneously induce maturation and migration, and T cell priming. We have previously shown that targeting of the CLR DC-SIGN and Langerin, which are potent uptake receptors expressed on DCs and LC in human skin, using Lewis (Le) y-modified Melanoma antigen MART-1, resulted in increased binding and internalization by human monocyte-derived DCs (moDCs) as well as LCs, and led to enhanced antigen presentation to primary CD8<sup>+</sup> T cells. Injection of our vaccine in full thickness ex-vivo human skin, show a powerful mobilisation and antigen presentation of the skin resident antigen presenting cells, whereas conventional vaccines were not that efficient. Our data demonstrate the potency of DC and LC targeting glyco-vaccines for instructing both CD4<sup>+</sup> and CD8<sup>+</sup> antigen specific T cell responses. This may be a crucial step towards development of novel potent anti-cancer vaccine but may also have major implications in the development of new vaccines in the field of infectious diseases.

### Biography

Yvette van Kooyk completed her PhD at the University of Amsterdam, in 1993. She worked as Associate Professor at the Tumor Immunology Lab at the Radboud University Hospital in Nijmegen, The Netherlands. In 2001 she became Professor at the VU University Medical Centre in Amsterdam where she chairs the division Dendritic Cell Immunobiology. She has published 200 papers in scientific journals such as *Cell*, *Nature*, *Nature Immunology*, *J. Exp Med*, *Annual Rev Immunology*, is an inventor of 4 patent applications, and Chief Scientific Officer of the start-up biotech company DC4U.

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