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TriMix and antigen mRNA based vaccination

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Our immune system can detect and destroy cancer cells. However, growing cancer cells camouflage themselves as well as possible, blocking the attack of the immune system, or worse, they hijack certain cells of the immune system and turn them into cancer-promoting cells. In an attempt to stop this process, scientists want to boost the immune system. This can be done through cancer vaccination. The rationale is to provide the immune system with the identification card of cancer cells (tumor antigens) as well as an adjuvant to alarm the immune system. Several cancer vaccination strategies have been developed, among which the use of dendritic cells engineered in the laboratory using mRNA. We studied mRNA as a tool to deliver tumor antigens and immune modulating proteins, in particular, a mix of three mRNA molecules encoding the co-stimulatory molecule CD70 and two DC activation stimuli, CD40 ligand, and active TLR4 referred to as TriMix mRNA. Vaccination of stage III/IV melanoma patients with this dendritic cell vaccine have proven to be safe and well tolerated, to induce tumor antigen-specific immune responses and more importantly to induce objective clinical responses in over a quarter of patients. Although promising, ex vivo engineered cell-based vaccines are patient-specific and therefore time and money consuming. To generate a widely applicable cancer vaccine, it is important to immediately activate the dendritic cells in the patient's body. Therefore we studied several ways to deliver tumor antigen and/or TriMix mRNA to dendritic cells *in situ*. We studied several routes of delivery, including intranodal, intratumoral and intravenous. Linked to the systemic delivery of mRNA we studied several modes of mRNA encapsulation, including the use of lipids and polymers. The results of these studies will be presented and discussed in view of the current state-of-the-art.

Biography

Karine Breckpot has completed her PhD on genetically engineered dendritic cell vaccines in 2004 at the VUB (Belgium) and continued this line of research during her postdoctoral studies performed at VUB (Belgium) and the University College London (UK). She is a tenure track professor at the VUB, member of the faculty and research board, and president of the ethical committee for use of laboratory animals. She is a recognized expert in the field of immunotherapy as evidenced by her list of publications, patents, invited lectures, awards and presence in grant review committees.

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