

P2.06

Induction of a strong and persistent antitumor immune response using liposomal vaccines in the HPV-transformed orthotopic lung tumor model TC-1

C. Jacobberger-Foissac ¹, B. Frisch ¹, V. Flacher ², B. Heurtault ¹, S. Fournel ¹

¹Bio team, Laboratoire de Conception et Application de Molécules Bioactives, Illkirch, France

²Laboratory ICT - Immunology, Immunopathology and Therapeutic Chemistry, CNRS UPR 3572, Institut de Biologie Moléculaire et Cellulaire, Strasbourg, France

Background: Despite being quite effective, conventional cancer therapies have the major drawback of triggering numerous side effects. Currently, a challenging goal in this area is the development of innovative targeted antitumor immunotherapy with a long-term efficiency.

In this context, our team took advantage of liposomal nanoparticle properties for the conception of cancer vaccines, which contain all the elements needed for the induction of an efficient antitumor immune response i) a peptide able to activate CD4⁺ T helper cells ii) a tumor peptide expressed by the cancer cells, recognized by CD8⁺ T cytotoxic cells and iii) Toll or Nod-Like receptor (TLR and NLR) ligand which act as adjuvants for the activation of the innate immune response. The aim of our project is to conceive liposomal vaccines, which would be effective even against tumors in later stage.

Materials and methods: Different vaccines formulations containing the three types of components have been designed and compared for their capacity to induce a strong immune response associated with antitumor activity in vivo. C57BL/6J mice were injected in the tail vein with tumor cells (TC-1 cell line) expressing the E7 peptide, leading to the development of pulmonary tumor nodules. Then, injections of liposome-based vaccines were performed subcutaneously at different times after tumor implantation. One month later, lung tumor nodules are counted and the spleen and lymph nodes are harvested to perform an IFN- γ ELISpot assay against tumor cell epitopes to measure the number of tumor specific T cell.

Results: We compared the therapeutic potential of these three vaccinal candidates and analyzed the immunological mechanisms involved in their action. Liposomal vaccine containing MPLA as adjuvant (TLR4 liposomes), was the most effective treatment against TC-1. This vaccine induced a potent Th1-oriented antitumor immunity, which led to a significant reduction in tumor growth and a prolonged survival of mice, even when injected after pulmonary tumors apparition. TLR4 liposomes antitumor efficacy was dependent of CD8⁺ T cells presence, whereas CD4⁺ cell depletion enhanced its therapeutic impact. Subcutaneous injection of this treatment induced the migration of CD103 skin DCs to draining lymph nodes. We also observed unexpected differences between TLR and NLR agonists activity. In the same way as TLR4 liposomes, TLR2/6 liposomes induced a Th1-immune response but weak and not sufficient for a prolonged antitumor activity. Surprisingly, whereas NOD1 liposomes treatment resulted in the control of early tumor growth, they did not extend survival.

Conclusions: This study highlights the importance of immune monitoring of cancer vaccine therapy and shows that our modulable platform can be used for the strategical development of vaccines