Systemic DC activation modulates the tumor microenvironment and shapes the long-lived tumor-specific memory mediated by CD8+T cells

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Both innate and adaptive immunity are crucial for cancer immune surveillance, because tumors are often composed of a mixture of HLA class I+ and class I- cells. However, precise therapeutic equations to restore such surveillance in cancer patients have yet to be developed. Dendritic cells (DCs) are well-known to link the innate and adaptive immunity, and play a pivotal role in determining the character and magnitude of an immune response. However, ex vivo DC therapy requires the generation of large numbers of DCs from individual patients and the quality of the DCs will likely depend on the patient’s condition at the time of venipuncture to harvest DC precursors. We have studied the role of DCs in situ for tumor immunity by focusing on the link between innate and adaptive immunity. Initially, we tried to establish in vivo DC targeting strategy that exploits the pro-inflammatory potential of dying cells together with the adjuvant activity of NKT cells. Then, we have developed a strategy in murine models for the induction of antigen-specific T cell responses by using CD1d+allogeneic cells loaded with NKT cell ligand, i.e., α-galactosylceramide and transfected with antigen-encoding mRNA, which we call artificial adjuvant vector cells (aAVCs), thus combining the adjuvant effects of NKT cell activation with delivery of antigen to DCs in vivo. We have recently discovered two novel functions for this approach, showing that it efficiently expanded antigen-specific CD8+ T cell clones in the tumor. Additionally, aAVC therapy expanded specific Vβ-expressing anti-tumor T cell clones and led to formation of long-term memory T cells. These findings of this study help to inform a next-generation of platform for the efficacious vaccines.