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Dendritic Cell-Derived Exosomes Elicit Effective Anti-Tumor Immunity in Different Mouse Models of Hepatocellular Carcinoma

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Abstract

Hepatocellular carcinoma (HCC) presents as one of the most lethal malignancies worldwide owing to its aggressive nature, high mortality and low response rates to treatments in the clinic. Exosomes from DCs (DEXs) bear abundant signature proteins from their parental cells, such as major histocompatibility complex class I (MHC-I), class II (MHC-II) and co-stimulatory molecules, and thus have been employed as a cell-free alternative option to DC vaccines for cancer immunotherapy. Unlike DCs, DEXs are stable vesicles with long shelf-lives when frozen and can be tailor-manufactured from genetically modified cell lines. However, their potency in hepatocellular carcinoma (HCC), a life-threatening malignancy with limited treatment options in the clinic that responds poorly to immunotherapy, remains to be investigated. We investigate and monitor the tumor growth and microenvironment in three different HCC mouse models with the exosomes derived from a-fetoprotein (AFP)-expressing DCs (DEX_{AFP}) systemical therapy, especially,which could mediate effective tumor suppressor effect in autochthonous hepatocellular carcinoma mouse models.Our findings provide evidence that AFP-enriched DEXs can trigger potent antigen-specific antitumor immune responses and reshape the tumor microenvironment in HCC mice and thus provide a cell-free vaccine option for HCC immunotherapy and thus opens a new avenue for HCC immunotherapy. More importantly, the long shelf-life and availability of large amounts of DEXs affords practical advantages over DCs in clinical deployment of DC-based vaccines.

Keywords: Dendritic cells; Interferon; Interleukin; Carcinogen; Exosome; Hepatocellular carcinoma; Immunotherapy; Alpha-fetoprotein