Intraperitoneal administration of poly(I:C) with polyethylenimine leads to significant antitumor immunity against murine ovarian tumors

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Abstract

Ovarian cancer is currently the most lethal gynecologic cancer in the United States. There is an urgent need for the development of innovative therapies against ovarian cancer, such as immunotherapy. The toll-like receptor (TLR) 3 ligand, polyriboinosinic: polyribocytidylic acid (poly(I:C), has emerged as a promising adjuvant for activating the host immune responses for the control of tumors. We reasoned that a strategy to enhance the intracellular uptake of poly(I:C) will likely improve the poly(I:C) adjuvant effect. Since polyethylenimine (PEI) has been shown to increase the transfection efficiency of nucleic acids, we characterized the antitumor effects in mouse ovarian surface epithelial cells (MOSEC) tumor-bearing mice treated intraperitoneally with poly(I:C) and PEI. We observed that tumor-bearing mice treated with poly(I:C) and PEI generated significantly better therapeutic anti-tumor effects against MOSEC tumors compared to treatment with poly(I:C) alone. Furthermore, we found that NK cells play a significant role in the antitumor effects generated by treatment with poly(I:C) in combination with PEI. Intraperitoneal administration of poly(I:C) with PEI led to the uptake of poly(I:C) mainly by CD11b+ macrophages, resulting in the high expression of MHC class II and IL-12 (M1 phenotype). In addition, adoptive transfer of CD11b+ macrophages from mice treated with poly(I:C) and PEI was found to lead to increased number of activated NK cells in the recipient mice. Taken together, our data indicate that PEI can potentially be used to improve the uptake of poly(I:C) by CD11b+ macrophages, leading to activation of NK cells and the control of murine ovarian tumors.