Decoy receptor 3;upregulated by Epstein-Barr virus latent membrane protein 1;enhances nasopharyngeal carcinoma cell migration and invasion.

陳志榮

Ho CH;Chen CL;Lee WY;Chen CJ

摘要

Abstract

Decoy receptor 3 (DcR3), a member of tumor necrosis factor receptor superfamily, has been implicated in tumorigenesis through its abilities to modulate immune responses and induce angiogenesis. Epstein-Barr virus (EBV), a ubiquitous -herpesvirus, is associated with malignancies including nasopharyngeal carcinoma (NPC). Previous studies show that DcR3 is overexpressed in EBV-positive lymphomas and Rta, an EBV transcription activator, can upregulate DcR3 in Burkitt lymphoma cell lines. However, DcR3 expression has not been demonstrated in EBV-associated NPC nor have there been any EBV latent genes linked to DcR3 upregulation. Here, we showed DcR3 was overexpressed in NPC. Higher DcR3 expression score and DcR3-positive rate were found in metastatic NPC than in primary NPC tissues, suggesting DcR3 may enhance cell metastatic potential. This hypothesis is supported by our observation that NPC HONE-1 cells overexpressing DcR3 exhibited significant higher migration and invasion abilities in vitro. We found besides Rta, EBV latent membrane protein (LMP) 1 can upregulate DcR3 via nuclear factor-kappaB and phosphatidylinositol 3-kinase-signaling events. Approximate 75% of LMP1-positive NPC tissues overexpressed DcR3, suggesting LMP1 may enhance DcR3 expression in vivo. Data herein suggested that increasing DcR3 expression by LMP1 not only helps EBV-associated cancer cells gain survival advantage by preventing host immune detection but also increases the chance of cancer metastasis by enhancing cell migration and invasion. All these DcR3-mediated events facilitate normal cells to gain cancer hallmarks.