SUPPRESSED INNATE IMMUNE RESPONSE AGAINST MAMMARY CARCINOMA IN BALB/C MICE

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SUPRIMIRANI UROĐENI IMUNSKI ODGOVOR TUMORA DOJKE KOD BALB/C MIŠEVA

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ABSTRACT

Breast carcinoma is one of the leading causes of deaths among women worldwide. The immune response in breast cancer is mediated by innate and adaptive immune cells, including natural killer (NK) cells, dendritic cells (DCs) and T lymphocytes. The 4T1 mammary carcinoma line derived from BALB/c mice shares many characteristics with naturally occurring human breast cancer. We aimed to investigate the mechanisms of anti-tumour immunity using the experimental 4T1 breast cancer model in syngeneic BALB/c mice. After 12 days of tumour inoculation, mammary carcinoma-bearing mice had significantly decreased numbers of NKp46⁺ NK cells compared with healthy mice and lower cytotoxic activity of total splenocytes and NK cells in vitro. Additionally, significantly higher numbers of CD11c⁺ DCs were detected in the spleens of tumour-bearing mice, but the number of activated CD80⁺CD86⁺ dendritic cells was entwithsimilar to that in healthy mice, indicating an increased number of immature DCs in tumour-bearing mice. The data indicate that 4T1 mammary carcinoma progression in BALB/c mice is associated with suppressed innate anti-tumour immunity.

Keywords: *4T1 mammary carcinoma, BALB/c mice, NK cells, dendritic cells.*

APSTRAKT

Rak dojke je jedan od najčešćih uzroka smrti žena, širom sveta. Imunski odgovor na tumor dojke posredovan je ćelijama urođene i stečene imunosti, uključujući ćelije ubice (NK), dendritske ćelije (DCs) i T limfocite. 4T1 mišji karcinom dojke, dobijen iz BALB/C miša, deli mnoge karakteristike sa spontano nastalim humanim karcinomom dojke. Cilj istraživanja je bio ispitati mehanizme anti-tumorske imunosti koristeći 4T1 eksperimentalni model tumora dojke singen sa BALB/c miševima. Dvanaest dana nakon inokulacije tumora, miševi sa tumorom imali su značajno manji broj NKp46+ NK ćelija, u poređenju sa zdravim miševima kao i manju citotoksičnost ukupnih splenocita i NK ćelija, in vitro. Takođe, detektovan je značajno veći broj CD11c+ dendritskih ćelija u slezini miševa sa tumorom, dok se broj aktiviranih CD80+CD86+ dendritskih ćelija nije značajno razlikovao u poređenju sa zdravim miševima, ukazujući na povećan broj nezrelih dendritskih ćelija u miševa sa tumorom. Rezultati ukazuju da je progresija 4T1 karcinoma dojke povezana sa suprimiranim urođenim anti-tumorskim odgovorom.

Ključne reči: *4T1 karcinom dojke, BALB/c miševi, NK ćelije, dendritske ćelije.*

INTRODUCTION

Breast cancer is characterised by the development of metastasis in distant organs, such as the lungs, bones, liver and brain, and it is one of the leading causes of cancer deaths among women (1, 2). The role of innate immunity in breast cancer growth and progression remains unknown, but the role of the specific immune response has been extensively studied (3-4). The role of NK cells in immune surveillance as a first line of antitumor defence is well established (5-8). NK cell activity is variable during tumour progression and is related to clinical stage and disease outcome (4, 8-11). T cells are important effector cells against tumours, according to many studies on tumour models in mice (12-16). Cytotoxic CD8⁺ T cells kill tumour cells, while the anti-tumour immune response of CD4⁺ T cells can be polarised towards Th1, Th2 or Th17 type. The type-1 immune response is characterised by the secretion of interferon-gamma (IFN-γ), which contributes to tumour rejection by stimulating the cytotoxic activity of CD8⁺ T and NK cells (17-20). In contrast, in the type-2 anti-tumour immune response, *interleukin-4 (*IL-4), *interleukin-5 (*IL-5) and *interleukin-10 (*IL-10) suppress cellular immunity and therefore facilitate tumour growth and metastases (21-22). The role of the type-17 anti-tumour immune response has not been clarified. Interleukin-17 (IL-17), a hallmark Th17

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