INNATE LYMPHOID CELLS: ROLES IN TUMOUR GENESIS AND PROGRESSION

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UROĐENE LIMFOIDNE ĆELIJE- ULOGA U GENEZI I RASTU TUMORA

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ABSTRACT

Innate lymphoid cells (ILCs) represent the most recently identified members of the innate immune system. These cells play important roles in inflammation, tissue remodelling and metabolic disease. ILCs can be subdivided into three major groups according to their cytokine production. The role of ILCs in tumourigenesis and tumour progression is not completely clarified. In this review, we discuss whether and how ILCs are involved in tumour genesis, growth and metastasis.

Keywords: *Innate lymphoid cells, tumour, progression, antitumor immunity*

SAŽETAK

Urođene limfoidne ćelije (engl. Innate lymphoid cells- ILCs) predstavljaju populaciju nedavno opisanih ćelija urođene imunosti. Ove ćelije igraju značajnu ulogu u zapaljenju, obnavljanju tkiva i metaboličkim poremećajima. U zavisnosti od produkcije citokina, ILCs se mogu podeliti u tri glavne subpopulacije. Uloga ILCs u tumorogenezi i progresiji bolesti nije u potpunosti razjašnjena. U ovom preglednom članku, mi razmatramo da li i kako ILCs utiču na genezu, rast i metastaziranje tumora.

Ključne reči: *Urođene limfoidne ćelije, tumor, progresija, antitumorska imunost*

INNATE LYMPHOID CELLS

The innate immune response is important in combating various microbes during the early phases of infection. Innate lymphoid cells (ILCs) represent the most recently identified constituents of the innate immune system by playing a role in inflammation, tissue remodelling and metabolic disease (1). ILCs lack the known immune cell lineage markers. Unlike T and B lymphocytes, ILCs do not have antigen receptors and memory functions (2). ILCs are localized in intestinal and lung mucosae as well as the skin and are capable of rapidly switching on responses to pathogens, even upon first exposure (1). These cells can be subdivided into three major groups according to their cytokine production (Fig 1; 3-4). The ILC2 group represents the innate equivalent of Th2 cells. This group only includes ILC2 cells (e.g., nuocytes, natural helper cells, innate helper cells, and multipotent progenitor cells) that secrete IL-5 and IL-13 in response to IL-25, IL-33 and thymic stromal lymphopoietin (TSLP), and they mediate innate responses during helminth infections and allergies (1-2). The ILC1 group is composed of ILC1 cells and natural killer (NK) cells. They represent the innate equivalent of adaptive Th1 and cytotoxic T cells, respectively. While NK cells play well-known roles in antiviral and antitumour immunity, several additional ILC1s have recently been identified that produce IFN-γ. The ILC3 group includes ILC3 cells and lymphoid tissue inducer (LTi) cells (1, 5). These cells mainly secrete IL-17 and IL-22 in response to IL-23 and IL-1b, and they represent the innate equivalents of Th17 and Th22 cells, respectively. The development and differentiation as well as effector functions of the ILCs are dependent upon the transcription factor, GATA3 (1, 6).

The role of ILCs in inflammatory immune responses, tissue remodelling and metabolic disease are well documented (Fig 1; 1, 2, 7). Recent studies described the involvement of ILCs in tumour growth and progression (8-11). In this paper, we summarize the role of ILCs in tumour genesis and anti-tumour immunity modulation.

THE HISTORY OF INNATE LYMPHOID CELLS

Natural killer (NK) cells were the first discovered ILCs. Five years ago, a new type of innate lymphoid cells was described in fat-associated lymphoid clusters (FALCs). These cells did

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