LymphomaHub

HL

The role of the microenvironment and possible implications in clinical practice with the arrival of checkpoint inhibitors

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S. Vardhana and A. Younes of the MSKCC published a clinical review on the role of T-cells, B-cells and immune checkpoints in classical Hodgkin Lymphoma (cHL) in Haematologica in July 2016.

Here are the key take home messages from this review:

T- cells

The role of non-malignant T- cells in cHL is ambiguous. T- cells are thought to suppress the development and growth of lymphomas. However, the presence of multiple tumor-infiltrating T- cells "rosetting," but failing to eliminate malignant Reed-Sternberg (RS) cells has been well described in cHL.

B- cells

Less is known regarding the role of non-malignant B cells in cHL pathogenesis compared to T cells. In cHL, non-malignant B cells are also generally present in the microenvironment. However, their role in facilitating cHL growth is less established.

Immune checkpoints

Broadly speaking, immune checkpoints (PD-1, CTLA4 and LAG-3) are a diverse group of proteins with the function of restricting physiologic immune cell responses in order to limit damage to host tissues. Targeting checkpoints with anti-PD1 antibodies has resulted in significant clinical responses in cHL, with 15-20% CRR in R/R cHL. However the mechanism by which this occurs has not been fully elucidated and various questions remain unanswered: ultimate roles for T- and B- cells in promoting and restricting cHL growth, dominant checkpoint inhibitors and type of immune cells that serve as primary effectors for checkpoint blockade therapy. A better understanding of the role of the microenvironment on RS cells will help to define a rationale for combination strategies.

In conclusion, cHL remains a perplexing disease in which components of the microenvironment, including T- and B-cells, may help to nourish or to extinguish RS cell growth.

The immune microenvironment in Hodgkin Lymphoma: T-cells, B -cells, and immune checkpoints

Abstract

Classical Hodgkin Lymphoma is curable in the majority of cases with chemotherapy and/or radiation. However, 15-20% of patients ultimately relapse and succumb to their disease.

Pathologically, classical Hodgkin Lymphoma is characterized by rare tumor-initiating Reed-Sternberg (RS) cells surrounded by a dense immune microenvironment. However, the role of the immune microenvironment, particularly T- and B-cells, in either promoting or restricting classical Hodgkin Lymphoma growth remains undefined. Recent dramatic clinical responses

seen using monoclonal antibodies against PD-1, a cell surface receptor whose primary function is to restrict T-cell activation, have reignited questions regarding the function of the adaptive immune system in classical Hodgkin Lymphoma. This review summarizes what is known regarding T-cells, B-cells, and immune checkpoints in classical Hodgkin Lymphoma.

Reference:

1. S. Vardhana & A. Younes. The immune microenvironment in Hodgkin lymphoma: T- cells, B- cells, and immune checkpoints. *Haematologica*. 2016 Jul;101(7):794-802.
