Mini-Review

CLINICAL INVESTIGATION

Immunity regulation and bone marrow

Abstract

The primary hematopoietic organ is assumed to be bone marrow. However, evidence suggests that immune cells such as regulatory T cells, conventional T cells, B cells, dendritic cells, Natural Killer T (NKT) cells, neutrophils, myeloid-derived suppressor cells, and mesenchyme stem cells have active function and trafficking in the bone marrow. Furthermore, multiple human cancers have a preset metastatic site in bone marrow. The immunological network in the bone marrow is discussed in this review. We believe that bone marrow is an immune regulatory organ that can fine-tune immunity, and that it could be a therapeutic target for immunotherapy and immune vaccination.

Keywords: Bone marrow, Regulatory T cell, Tumor, Immunity, Memory T cell

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Introduction

The tissue that makes up the centre and epiphysis of bones is called bone marrow, and it's where new blood cells are made. Bone marrow has traditionally been considered a hematopoietic organ. B cells, on the other hand, are known to be generated and developed in the bone marrow. Antigen-specific antibody-producing plasma cells with a long lifespan are mostly located in the bone marrow. As a result, bone marrow plays a role in humoral immune responses. Bone marrow is a nest for function, migration, and selective retention of innate and adaptive immune cells, despite the absence of structured T- and B-cell regions in normal bone marrow. The immunological networks in the bone marrow are discussed in this review. We believe that bone marrow is an immune regulatory organ that can fine-tune immunity, and that it could be a therapeutic target for immunotherapy and immune vaccination [1].

The structure of the bone marrow

Cortical and trabecular bone, cartilage, hemopoetic and connective tissues make up the organ of bone. A lattice of fine bone plates packed with hematopoietic marrow, fat-containing marrow, or blood vessels makes up spongy or trabecular bone. Arterial arteries reach the marrow via the foramina nutricia and split into numerous arterioles. These veins' small arterioles and capillaries run throughout the bone marrow, supplying sinusoids that are joined by intersinusoidal capillaries. Endosteal, subendosteal, central, and perisinusoidal are the four zones of the bone marrow cavity in trabecular bone [2]. A hematopoietic component (parenchyma) and a vascular component make up bone marrow (stroma). Hematopoietic Stem Cells (HSCs) and hematopoietic progenitor cells are found in the parenchyma and are not randomly distributed in the bone marrow, but more near the endosteum of the bone and more around blood vessels. The stroma of the bone marrow contains multipotent non-hematopoietic progenitor cells that can differentiate into osteoblasts, endothelial cells, reticular cells, fibroblasts, and adipocytes, among other mesenchymal tissues. The microvasculature of the bone marrow produces a sinusoid, which is radially distributed around the draining central sinus and has a single layer endothelium. The vasculature acts as a barrier between the extralymphoid organ and the peripheral circulation, separating the bone marrow compartment as a functional and spatial entity. Individual leukocytes migrate into and out of the bone marrow, involving rolling/extravasations along the vascular endothelium, thanks to stromal cells, which include endothelial cells [3]. In contrast to other organ-specific endothelial cells, bone marrow-derived endothelial cells express cytokines and adhesion molecules such as vascular cell adhesion molecule 1 (VCAM-1 or CD106) and E-selectin on a continuous basis. Organ regeneration also depends on the existence of endothelial precursors in the grafted cell population, which enhances vascularization of injured tissues, or the secretion of pro-

angiopoietic substances by the infused cells. As a result, not only does the bone marrow microvasculature system play a role in stem cell mobilisation and development, but it also suggests that it is important for leukocyte migration and maintenance in the bone marrow environment.

In the bone marrow, there are immune cells

Immune responses are started and maintained in primary lymphoid organs and secondary lymphoid tissues, which are functionally compartmentalized. T-cell regions in secondary lymphoid organs have a distinct architecture and cellular composition that is thought to be necessary for primary T-cell responses. Bone marrow resembles a secondary lymphoid organ in structure and function, and contains follicle-like structures comparable to lymph nodes or spleen, however it lacks the structured T- and B-cell regions. In the absence of the thymus, the bone marrow microenvironment offers adequate support for T cell development. Infections, inflammation, and autoimmune increase the number of lymphoid follicles in the bone marrow.

$CD4^+$ T cell

In mice, bone marrow includes a high number of memory $CD4^+$ T cells, which express high amounts of CD44 and low levels of CD45RA in humans. $CD4^+$ memory T cells' basic homeostatic proliferation and survival are regulated by IL-7, the dominant cytokine, and IL-15, an accessory cytokine, similarly to $CD8^+$ T cells. Despite the fact that human $CD4^+$ memory T cells multiply in vitro in response to IL-7 and IL-15,18 investigations in mice revealed that acute homeostatic proliferation of'memory-phenotype' $CD4^+$ T cells is unaffected by IL-7 and IL-15 [4].

$CD8^+$ T cell

Memory $CD8^+$ T cells prefer to proliferate in the marrow of the bone marrow. 47 In the bone marrow, antigen-specific memory $CD8^+$ T lymphocytes get proliferative signals from IL-7 and/or IL-15. It suggests that the bone marrow serves as a 'niche' for antigen-independent memory CD8+ T cell proliferation. Memory $CD8^+$ T lymphocyte populations in bone marrow have a CD44-positive phenotype and a larger number of HLA-DR molecules, indicating that CD8+ T lymphocytes are activated. After an acute infection or tumor formation, large numbers of tumor-associated antigen-specific CD8+ T cells were shown to remain in the bone marrow for several months [5].

Conclusion

The primary hematopoietic organ, bone marrow, is well-known. Bone marrow, on the other hand, comprises a high number of immune cell types with crucial and distinct functions. It is clear that bone marrow can take the place of secondary lymphoid tissue as a primary or memory immune response site. Immune modulation takes place in the bone marrow microenvironment, either through cell–cell interaction or by soluble substances like cytokines. As a result, bone marrow is an immune regulatory organ that may have a significant impact on systemic immunity as well as the therapeutic efficacy of conventional and immune therapy/vaccination. As a result, learning about the immune regulatory mechanisms in the bone marrow microenvironment will help researchers better comprehend human bone biology and immunology. Given the distinct functions of bone marrow memory T cells, one might expect bone marrow to be an ideal source of immune cells for adoptive immunotherapy for both cancer and infectious illnesses.

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