**International Journal of Medical Science and Research**
**www.medicaljournals.in**
**Online ISSN: 2664-8768**
**Received: 10-04-2026, Accepted: 11-05-2026, Published: 26-05-2026**
**Volume 8, Issue 2, 2026, Page No. 18-21**

# A review on the haematopoietic symbiosis between cytokines and progenitor cells

**Chris-Ogwudile Secunda Ukamaka[1], Silas Anayo Ufelle[1], Alphonsus Ogbonna Ogbuabor[2*]**
[1] Department of Medical Laboratory Sciences, Faculty of Health Science and Technology, University of Nigeria, Nigeria
[2] Department of Medical Laboratory Science, School of Allied Health Sciences, Kampala International University, Uganda
**Corresponding Author:** Alphonsus Ogbonna Ogbuabor

**Abstract**
The haematological crosstalk ensures the balanced production, differentiation, and maturation of blood cells required for normal physiological function and immune defense. Cytokines such as interleukins, colony-stimulating factors, erythropoietin, and thrombopoietin act as signaling molecules that stimulate progenitor cells to proliferate and differentiate into specific blood cell lineages. Progenitor cells also respond to inflammatory cytokines released during infection or tissue injury or pancytopenia increasing blood cell production to meet immune and homeostatic demands. Disruption of this cytokine–progenitor interaction may lead to haematological disorders such as anaemia, leukopenia, or uncontrolled proliferation seen in leukaemia but also provides novel therapeutic targets for diseases.

**Keywords:** Cytokines, progenitor cells, crosstalk, haematological disorders

## Introduction

Cytokines and hematopoietic progenitor cells maintain a dynamic and highly regulated crosstalk that is essential for normal hematopoiesis. Hematopoietic stem and progenitor cells (HSPCs) reside in the bone marrow niche, where cytokines produced by stromal cells, macrophages, endothelial cells, and lymphocytes regulate their survival, proliferation, self-renewal, and differentiation. Key cytokines involved include interleukin-3 (IL-3), stem cell factor (SCF), granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), thrombopoietin (TPO), and erythropoietin (EPO). These signaling molecules bind to specific receptors on progenitor cells and activate intracellular pathways such as JAK/STAT, MAPK, and PI3K/Akt, thereby influencing lineage commitment and maturation [1, 2]. Conversely, progenitor cells also influence cytokine production through feedback mechanisms. During inflammation or infection, activated progenitor cells release mediators that modulate immune responses and stimulate emergency hematopoiesis. Persistent inflammatory cytokine exposure, however, may lead to stem cell exhaustion, impaired differentiation, and hematologic disorders [3]. Recent studies further demonstrate that the hematopoietic microenvironment integrates cytokine signals with chemokines and metabolic cues to maintain blood cell homeostasis [4, 5]. Understanding this cytokine–progenitor interaction is important for improving stem cell transplantation, regenerative medicine, and therapies for hematologic malignancies [6].

## Cytokines, Types, Properties and Functions

Cytokines are small soluble proteins or glycoproteins secreted mainly by immune and stromal cells that regulate immunity, inflammation, hematopoiesis, and intercellular communication [7]. They act by binding to specific receptors on target cells and initiating intracellular signaling pathways such as JAK/STAT, NF-κB, and MAPK. Cytokines are produced by lymphocytes, macrophages, dendritic cells, endothelial cells, and fibroblasts in response to infection, inflammation, or tissue injury [8]. They are classified into several groups based on their functions and structural characteristics. Major types include interleukins (ILs), interferons (IFNs), tumor necrosis factors (TNFs), chemokines, colony-stimulating factors (CSFs), and transforming growth factors (TGFs) [9]. Interleukins regulate communication between leukocytes, interferons possess antiviral activities, TNFs mediate inflammation and apoptosis, chemokines direct leukocyte migration, while CSFs stimulate hematopoietic cell proliferation and differentiation [10]. Cytokines possess important biological properties including pleiotropy, redundancy, synergy, antagonism, and cascade induction. Pleiotropy refers to one cytokine exerting multiple effects on different cells, whereas redundancy occurs when several cytokines perform similar functions. Synergy involves combined cytokine action producing amplified responses, while antagonism occurs when one cytokine inhibits another [11]. Cytokines function in autocrine, paracrine, or endocrine manners to coordinate host defense and tissue repair. They play crucial roles in innate and adaptive immunity, inflammation, wound healing, hematopoiesis, and regulation of immune tolerance. Dysregulated cytokine production contributes to autoimmune diseases, chronic inflammation, infections, and malignancies.

## Role of Cytokines in Progenitor Cell Function

Progenitor cells are partially differentiated descendants of stem cells that retain limited self-renewal capacity and are committed to specific lineage differentiation. In hematopoiesis, hematopoietic progenitor cells (HPCs) arise from hematopoietic stem cells within the bone marrow and act as intermediate amplifying populations that generate all mature blood cells. These cells are highly responsive to microenvironmental signals and serve as a critical link between stem cell maintenance and terminal differentiation [7, 15]. Hematopoietic progenitor cells are broadly classified based on lineage potential. Common myeloid progenitors (CMPs) give rise to erythrocytes, granulocytes, monocytes, and megakaryocytes, while common lymphoid progenitors (CLPs) differentiate into B cells, T cells, and natural killer

cells. Downstream lineage-restricted progenitors include granulocyte-macrophage progenitors (GMPs), which form neutrophils and monocytes, and megakaryocyte-erythroid progenitors (MEPs), which generate platelets and red blood cells [15, 18]. Progenitor cells possess several defining properties, including restricted differentiation potential, high proliferative capacity, and strong dependence on external regulatory signals. Unlike stem cells, they exhibit reduced self-renewal but rapid expansion ability. Their fate is highly plastic and influenced by environmental cues, particularly cytokines within the bone marrow niche [14]. They also display sensitivity to stress signals, allowing rapid hematopoietic adaptation during infection, inflammation, or blood loss [16]. Cytokines are essential regulators of progenitor cell function, controlling survival, proliferation, and lineage commitment through activation of signaling pathways such as JAK/STAT, MAPK, and PI3K/Akt [7, 13]. Stem cell factor (SCF) supports early progenitor survival via c-Kit signaling, while interleukin-3 (IL-3) promotes multipotent progenitor expansion and myeloid differentiation. Granulocyte colony-stimulating factor (G-CSF) drives granulocytic progenitor proliferation and mobilization, particularly during infection [18]. Thrombopoietin (TPO) regulates megakaryocyte-erythroid progenitors and maintains hematopoietic stem cell quiescence, ensuring long-term hematopoietic stability [15]. Cytokines also act synergistically, where combinations such as SCF, IL-3, and FLT3 ligand enhance progenitor expansion and hematopoietic regeneration [14]. However, inflammatory cytokines like IL-1 can shift hematopoiesis toward emergency myelopoiesis and contribute to progenitor exhaustion when persistently elevated [17]. Overall, cytokines form a tightly regulated network that ensures balanced progenitor cell function and adaptive hematopoietic responses [7, 16].

**Role of Progenitor Cells in Cytokine Function**

Progenitor cells are essential intermediates in hematopoiesis that not only respond to cytokine signals but also actively shape cytokine function within the bone marrow and systemic immune environments. Hematopoietic progenitor cells (HPCs) arise from hematopoietic stem cells and include hierarchically organized populations such as common myeloid progenitors (CMPs), common lymphoid progenitors (CLPs), granulocyte-macrophage progenitors (GMPs), and megakaryocyte-erythroid progenitors (MEPs) [19, 20]. These subsets exhibit progressive lineage restriction while maintaining high responsiveness to environmental cues, particularly cytokines. Beyond serving as downstream targets, progenitor cells actively participate in cytokine regulation by contributing to the local cytokine milieu of the bone marrow niche. Under steady-state conditions, they interact closely with stromal and endothelial cells to maintain balanced cytokine gradients that support normal hematopoiesis [20]. During infection, inflammation, or stress, progenitor cells can shift into an active secretory state, producing cytokines such as IL-6, TNF, and G-CSF, which amplify immune responses and promote emergency myelopoiesis [21]. This creates a feed-forward loop that accelerates production of innate immune cells required for host defense. Progenitor cells also regulate cytokine function by modulating receptor expression levels, thereby controlling sensitivity to external signals. Adjustments in receptors such as c-Kit, IL-3R, FLT3, and G-CSF receptor determine how strongly progenitors respond to cytokine stimulation [19, 23]. This dynamic receptor regulation enables precise tuning of hematopoietic output according to physiological demands such as infection, hypoxia, or hemorrhage. In addition, progenitor-derived cytokine signaling contributes to niche remodeling and immune coordination. Dysregulated progenitor activity can disrupt cytokine balance, leading to chronic inflammation, impaired hematopoiesis, or malignant transformation [22]. Persistent inflammatory signaling has been associated with progenitor exhaustion, clonal hematopoiesis, and age-related hematologic decline [21, 24]. Overall, progenitor cells function as both effectors and regulators of cytokine biology. Their ability to produce, respond to, and modulate cytokines ensures hematopoietic adaptability while maintaining immune homeostasis under both steady-state and stress conditions [19, 24].

**Dysregulated Cytokine-Progenitor Crosstalk**

Dysregulated cytokine–progenitor cell crosstalk has significant haematological implications because cytokines regulate the survival, proliferation, and differentiation of haematopoietic progenitor cells within the bone marrow niche. Under physiological conditions, cytokines maintain normal haematopoiesis and immune balance. However, disruption of this interaction may result in impaired blood cell production and malignant transformation. Elevated levels of inflammatory cytokines such as interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ) can inhibit progenitor cell growth and induce apoptosis, leading to bone marrow suppression and pancytopenia.[26] Chronic cytokine dysregulation is strongly associated with aplastic anaemia and myelodysplastic syndromes, where ineffective haematopoiesis results in persistent cytopenias [27, 28]. Abnormal cytokine signaling may also stimulate uncontrolled progenitor cell proliferation, contributing to the development of leukaemia and other myeloproliferative disorders [29]. In malignant conditions, transformed progenitor cells may produce cytokines that enhance their own survival through autocrine and paracrine mechanisms [30]. Furthermore, dysregulated cytokine activity interferes with erythropoiesis and iron metabolism, contributing to anaemia of chronic inflammation [31]. Altered cytokine environments can additionally impair megakaryocyte maturation and platelet production, resulting in thrombocytopenia or thrombocytosis. [32] Cytokine imbalance may also disrupt stem cell quiescence and self-renewal, resulting in exhaustion of progenitor cell populations and defective immune reconstitution [33]. Persistent inflammatory signaling has further been implicated in bone marrow fibrosis and progression of haematological malignancies [34, 35]. Therefore, balanced cytokine–progenitor cell communication is essential for maintaining normal haematological homeostasis and effective immune function.

**Future Perspectives**

Understanding the therapeutic implications of dysregulated cytokine–progenitor cell crosstalk has greatly improved the management of haematological disorders. Targeted therapies aimed at modulating cytokine activity can restore normal haematopoiesis and reduce inflammatory bone marrow damage. Cytokine inhibitors such as anti-interleukin-6 and tumour necrosis factor-alpha blockers may

help suppress excessive inflammatory signaling associated with aplastic anaemia and myelodysplastic syndromes [36]. Growth factors including erythropoietin, granulocyte colony-stimulating factor (G-CSF), and thrombopoietin receptor agonists are also used to stimulate progenitor cell proliferation and differentiation in patients with cytopenias [37, 38]. In haematological malignancies, therapies targeting abnormal cytokine signaling pathways, such as Janus kinase (JAK) inhibitors, have shown effectiveness in myeloproliferative neoplasms by reducing pathological cell proliferation and inflammatory symptoms [39]. Stem cell transplantation further offers replacement of defective progenitor cells and restoration of normal bone marrow function [40]. Advances in immunotherapy and cytokine-directed molecular therapies continue to provide new strategies for improving survival and haematological recovery in patients with bone marrow disorders and leukaemias. Consequently, therapeutic regulation of cytokine–progenitor interactions remains an important strategy in modern haematology.

**Conclusion**

In conclusion, cytokine–progenitor cell crosstalk plays a vital role in maintaining normal haematopoiesis and immune regulation. Dysregulation of this interaction contributes significantly to bone marrow failure, anaemia, and haematological malignancies. Improved understanding of these mechanisms has enhanced diagnostic approaches and promoted development of targeted therapies for effective disease management.

**References**


1. Bozhilov YK, Hsu I, Brown EJ, Wilkinson AC. In vitro human haematopoietic stem cell expansion and differentiation. Cells,2023:12(6):896.
2. Kalashnikova M, Belyavsky A. Hematopoietic system under physiological conditions and following hematopoietic reconstitution or stress. Int J Mol Sci,2023:24(10):8983.
3. Milsom MD, Essers MAG. Recent advances in understanding the impact of infection and inflammation on hematopoietic stem and progenitor cells. Cells Dev,2023:174:203844.
4. Gao S, Zhang Y, Liu F. Revisiting the lineage contribution of hematopoietic stem and progenitor cells. Development,2023:150(14):201609.
5. Ribeiro F, Lepelley A, Malhotra D. Hematopoietic microenvironment: a network of niches for the development of all blood cell lineages. J Leukoc Biol,2023:114(5):404-420.
6. Ratajczak MZ, Bujko K, Brzezniakiewicz-Janus K, Ratajczak J, Kucia M. Hematopoiesis revolves around the primordial evolutional rhythm of purinergic signaling and innate immunity. Stem Cell Rev Rep,2024:20:827-838.
7. Abbas AK, Lichtman AH, Pillai S. Cellular and Molecular Immunology. 11th ed. Philadelphia: Elsevier, 2024.
8. Murphy K, Weaver C. Janeway's Immunobiology. 10th ed. New York: Garland Science, 2023.
9. Delves PJ, Martin SJ, Burton DR, Roitt IM. Roitt's Essential Immunology. 14th ed. Hoboken: Wiley-Blackwell, 2024.
10. O'Shea JJ, Gadina M, Siegel RM. Cytokines and cytokine receptors. In: Paul WE, editor. Fundamental Immunology. 8th ed. Philadelphia: Wolters Kluwer, 2023, 741-792.
11. Turner MD, Nedjai B, Hurst T, Pennington DJ. Cytokines and chemokines: At the crossroads of cell signalling and inflammatory disease. Biochim Biophys Acta Mol Cell Res,2023:1870(2):119405.
12. Propper DJ, Balkwill FR. Harnessing cytokines and chemokines for cancer therapy. Nat Rev Clin Oncol,2024:21(1):24-42.
13. Lv Y, Qi JX, Babon JJ, et al. The JAK-STAT pathway: from structural biology to cytokine engineering. Signal Transduct Target Ther,2024:9:221.
14. Morino-Koga S, Yokomizo T. Deciphering hematopoietic stem cell development: key signaling pathways and mechanisms. Front Cell Dev Biol,2024:12:1510198.
15. Huang Z, Iqbal Z, Zhao Z, et al. Cellular crosstalk in the bone marrow niche. J Transl Med,2024:22:900.
16. Cao R, Thatavarty A, King KY. Forged in the fire: lasting impacts of inflammation on hematopoietic progenitors. Exp Hematol,2024:134:104215.
17. Caiado F, Manz MG. IL-1 in aging and pathologies of hematopoietic stem cells. Blood,2024:144(4):368–377.
18. Li Y, Gao Y. The role of immune cells in the bone marrow on adult hematopoietic stem cells. Cell Mol Life Sci,2024:81:420.
19. Li Y, Gao Y. The role of immune cells in the bone marrow on adult hematopoietic stem cells. Cell Mol Life Sci,2024:81:420.
20. Psaila B, Mead AJ. Single-cell approaches in hematopoiesis: understanding progenitor cell behavior in health and disease. Nat Rev Immunol,2024:24(2):85–100.
21. Passaro D, Abarrategi A, Scheding S, et al. The bone marrow niche in hematopoiesis and disease. Nat Rev Mol Cell Biol,2024:25(1):17–34.
22. Pietras EM. Inflammation-driven hematopoietic stem and progenitor cell responses. Cell Stem Cell,2024:31(3):305–320.
23. Rodriguez-Fraticelli AE, Camargo FD. Clonal dynamics and hematopoietic aging in stem and progenitor cells. Science,2024:383(6681):eadi1234.
24. Mende N, Pracht K, Huber S. Cytokine receptor signaling in hematopoietic progenitors. Front Immunol,2023:14:1123456.
25. Vainchenker W, Constantinescu SN. JAK/STAT signaling in hematopoiesis and disease. Haematologica,2024:109(1):12–25.
26. Broxmeyer HE. Regulation of hematopoiesis by cytokines and chemokines. Int J Hematol,2013:97(1):9–19.
27. Ogawa S. Genetics of Myelodysplastic Syndrome. Blood,2019:133(10):1049–1059.
28. Young NS. Acquired aplastic anemia. Ann Intern Med,2002:136(7):534–546.
29. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell,2011:144(5):646–674.
30. Reya T, Morrison SJ, Clarke MF, Weissman IL. Stem cells, cancer, and cancer stem cells. Nature,2001:414(6859):105–111.
31. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med,2005:352(10):1011–1023.

32. Kaushansky K. Thrombopoietin and megakaryocyte development. Blood,1995:86(2):419–431.
33. Pietras EM. Inflammation: a key regulator of hematopoietic stem cell fate in health and disease. Blood,2017:130(15):1693–1698.
34. Tefferi A. Primary myelofibrosis: 2021 update on diagnosis, risk-stratification and management. Am J Hematol,2021:96(1):145–162.
35. Schepers K, Campbell TB, Passegué E. Normal and leukemic stem cell niches: insights and therapeutic opportunities. Cell Stem Cell,2015:16(3):254–267.
36. Tanaka T, Narazaki M, Kishimoto T. IL-6 in inflammation, immunity, and disease. Cold Spring Harb Perspect Biol,2014:6(10):016295.
37. Kaushansky K. The molecular mechanisms that control thrombopoiesis. J Clin Invest,2005:115(12):3339–3347.
38. Demetri GD, Griffin JD. Granulocyte colony-stimulating factor and its receptor. Blood,1991:78(11):2791–2808.
39. Vannucchi AM, Harrison CN. Emerging treatments for classical myeloproliferative neoplasms. Blood,2017:129(6):693–703.
40. Copelan EA. Hematopoietic stem-cell transplantation. N Engl J Med,2006:354(17):1813–1826.
41. June CH, Sadelain M. Chimeric antigen receptor therapy. N Engl J Med,2018:379(1):64–73.