INOSR Experimental Sciences 14(1):16-20, 2024. ISSN: 2705-1692
©INOSR PUBLICATIONS INOSRES141.1620
International Network Organization for Scientific Research
https://doi.org/10.59298/INOSRES/2024/141.1620

Role of Eosinophils in Immunity, Allergy, and Inflammation: Friend or Foe

Nyiramana Mukamurera P.

Faculty of Medicine Kampala International University Uganda

ABSTRACT

Eosinophils are multifunctional granulocytes involved in both protective and pathological immune responses. Traditionally recognized for their role in host defense against parasitic infections, eosinophils have gained significant attention for their involvement in allergic diseases, such as asthma, allergic rhinitis, and atopic dermatitis, where they are often considered detrimental. Eosinophils contribute to tissue damage and inflammation by releasing cytotoxic granule proteins, cytokines, and chemokines, perpetuating chronic inflammation. In conditions such as eosinophilic gastrointestinal disorders and hypereosinophilic syndrome, eosinophils infiltrate tissues and exacerbate inflammation, leading to organ dysfunction. However, eosinophils also exhibit beneficial roles, including modulating immune responses, promoting tissue repair, and maintaining tissue homeostasis. Recent research has highlighted their regulatory functions, where they interact with other immune cells to mediate both pro- and anti-inflammatory responses. The dual nature of eosinophils—both as protectors in immunity and contributors to pathology—presents a complex challenge in understanding their full impact on health and disease. Advances in biologic therapies targeting eosinophil activity, such as IL-5 inhibitors, offer promising treatment options for eosinophil-associated disorders. This review explores the diverse roles of eosinophils in immunity, allergy, and inflammation, examining both their protective and harmful functions, while discussing therapeutic strategies aimed at modulating eosinophil activity in various diseases.

Keywords: Eosinophils, allergy, inflammation, immune regulation, IL-5 therapy

INTRODUCTION

Eosinophils are a type of white blood cell that play a multifaceted role in the immune system [1]. Known for their involvement in allergic reactions and parasitic infections, they are part of the body's immune response, releasing toxic proteins and cytokines to combat pathogens. While traditionally viewed as effector cells against parasitic helminths, eosinophils have emerged as key players in a broader range of immune functions, including responses to bacterial and viral infections [2, 3]. However, eosinophils are most often associated with pathological conditions, particularly in allergic diseases such as asthma, allergic rhinitis, and atopic dermatitis, where they contribute to chronic inflammation and tissue damage [4]. Eosinophils are recruited to sites of inflammation through the action of cytokines, especially interleukin-5 (IL-5), which drives their maturation and activation. Once activated, eosinophils release a variety of pro-inflammatory mediators that can either help protect the host or, in some cases, worsen disease conditions by promoting excessive inflammation [5, 6]. Recent research has revealed that eosinophils also play regulatory roles, helping to maintain tissue homeostasis and modulate immune responses. These findings challenge the conventional view of eosinophils solely as harmful agents in inflammation, suggesting they can act as both "friend" and "foe." Understanding these dual roles is critical for developing targeted therapies for eosinophil-related diseases.

Eosinophils are bone marrow-derived granulocytes that comprise a small percentage of circulating white blood cells (1-3% in healthy individuals) [7]. They are easily recognizable by their characteristic bilobed nucleus and the presence of cytoplasmic granules that contain a range of cytotoxic proteins, such as major basic protein (MBP), eosinophil peroxidase (EPO), and eosinophil cationic protein (ECP). Eosinophils are primarily found in the blood

but can migrate to tissues, particularly the gastrointestinal tract, lungs, and skin, where they mediate immune responses [8]. Despite their relatively low numbers, eosinophils play significant roles in immune defense and the modulation of inflammation. Historically, they were viewed primarily as effector cells in parasitic infections, but their roles have expanded to include immune regulation, participation in allergic diseases, and contributions to various inflammatory disorders [9]. Thus, understanding their biology and function is critical for addressing eosinophil-related diseases.

EOSINOPHILS IN HOST DEFENSE

Parasitic Infections

Eosinophils are well-known for their protective role against parasitic helminths (worms), such as schistosomes and filaria [10]. During parasitic infections, eosinophils are recruited to infection sites through signals from cytokines, primarily interleukin-5 (IL-5), IL-4, and IL-13, produced by T-helper type 2 (Th2) cells [12, 13]. Once at the site, eosinophils release their toxic granule proteins, including MBP and EPO, which damage the parasite's outer layer, leading to its destruction. Eosinophils also contribute to the clearance of immune complexes and the activation of other immune cells, including mast cells and basophils, further amplifying the host's defense against parasitic invaders[14]. In this context, eosinophils act as "friends," aiding in the resolution of parasitic infections and protecting the host from further invasion.

Bacterial and Viral Infections

While eosinophils are primarily associated with helminthic infections, they also participate in immune responses to bacterial and viral pathogens. Recent studies have shown that eosinophils possess the ability to directly kill bacteria, such as *Escherichia coli* and *Staphylococcus aureus*, by releasing extracellular DNA traps (eosinophil extracellular traps, or EETs). These traps immobilize and neutralize bacteria, preventing their spread [15, 16]. Additionally, eosinophils have been implicated in antiviral responses, particularly in the lungs, where they help control respiratory viral infections such as respiratory syncytial virus (RSV) [17]. Eosinophils produce antiviral mediators, including nitric oxide (NO) and reactive oxygen species (ROS), which contribute to viral clearance. However, excessive eosinophil activation in viral infections can also lead to tissue damage and exacerbate inflammation, highlighting their dual role.

Eosinophils in Allergic Reactions

Eosinophils are perhaps best known for their role in allergic diseases, including asthma, allergic rhinitis, atopic dermatitis, and eosinophilic esophagitis [18]. In these conditions, eosinophils are often considered "foes," contributing to tissue damage, inflammation, and the perpetuation of allergic responses.

Asthma

In allergic asthma, eosinophils are recruited to the lungs in response to allergen exposure and Th2 cytokines, especially IL-5 [19]. Upon activation, eosinophils release pro-inflammatory mediators, including cytokines, chemokines, and cytotoxic granule proteins, which lead to bronchoconstriction, airway hyperresponsiveness, mucus production, and airway remodeling. The chronic presence of eosinophils in the airways can exacerbate inflammation and contribute to disease severity [20]. Eosinophilic asthma, a subtype characterized by elevated eosinophil levels in the airways, is particularly resistant to standard therapies. However, biologic therapies targeting eosinophil-associated pathways, such as IL-5 (e.g., mepolizumab, reslizumab) and IL-4/IL-13 signaling (dupilumab), have shown promise in reducing eosinophil-driven inflammation and improving clinical outcomes [21, 22].

Allergic Rhinitis and Atopic Dermatitis

In allergic rhinitis and atopic dermatitis, eosinophils play a role in amplifying local inflammation and tissue damage. In allergic rhinitis, eosinophils contribute to nasal congestion, sneezing, and itching by releasing mediators that increase vascular permeability and attract other inflammatory cells [23]. Similarly, in atopic dermatitis, eosinophils infiltrate the skin and release pro-inflammatory cytokines and enzymes that damage skin cells, contributing to the chronicity of the condition.

Eosinophils in Inflammatory Disorders

Beyond allergies, eosinophils are implicated in several chronic inflammatory diseases, including eosinophilic gastrointestinal disorders (EGIDs), hypereosinophilic syndrome (HES), and certain autoimmune diseases [24].

Eosinophilic Gastrointestinal Disorders (EGIDs)

EGIDs, including eosinophilic esophagitis (EoE), are characterized by eosinophil infiltration of the gastrointestinal tract, leading to chronic inflammation and tissue damage [25]. In EoE, eosinophils accumulate in the esophagus in response to food allergens or environmental triggers, causing symptoms such as dysphagia, food impaction, and esophageal strictures. Targeting eosinophil activity through dietary management and biologics (e.g., anti-IL-5) has become a central therapeutic strategy for these disorders.

Hypereosinophilic Syndrome (HES)

HES is a group of disorders characterized by persistently elevated eosinophil levels and organ damage due to eosinophil infiltration [26]. Commonly affected organs include the heart, lungs, skin, and gastrointestinal tract. The pathogenic role of eosinophils in HES is attributed to their ability to release cytotoxic proteins and cytokines that cause tissue damage. Treatments for HES often include corticosteroids, cytotoxic agents, and targeted therapies like anti-IL-5 antibodies [27].

Autoimmune Diseases

Eosinophils have been implicated in the pathogenesis of autoimmune diseases such as eosinophilic granulomatosis with polyangiitis (EGPA, formerly known as Churg-Strauss syndrome). In EGPA, eosinophils contribute to vasculitis and tissue inflammation, affecting the lungs, kidneys, and peripheral nerves [28]. As with other eosinophil-driven conditions, biologic therapies targeting eosinophil-associated cytokines have shown efficacy in managing EGPA.

Regulatory Functions of Eosinophils: Beyond Inflammation

Recent research has revealed that eosinophils play regulatory roles beyond their well-known effector functions in immunity and inflammation [29]. These regulatory roles suggest that eosinophils may also act as "friends" in maintaining immune homeostasis and tissue repair.

Tissue Homeostasis and Repair

Eosinophils contribute to tissue homeostasis by promoting the resolution of inflammation and supporting tissue repair [30]. For example, in adipose tissue, eosinophils help maintain metabolic homeostasis by producing IL-4 and IL-13, which promote the polarization of anti-inflammatory M2 macrophages [31]. Similarly, eosinophils have been shown to play a role in tissue remodeling and repair following injury, particularly in the lungs and intestines.

Immune Regulation

Eosinophils can also modulate immune responses by influencing the activity of other immune cells. Through the release of cytokines and growth factors, eosinophils can regulate the functions of dendritic cells, T cells, and B cells, contributing to both pro-inflammatory and anti-inflammatory responses [32]. This immunoregulatory role highlights the complexity of eosinophil function in health and disease.

Therapeutic Targeting of Eosinophils

Given the dual role of eosinophils in both protective and pathological processes, therapeutic strategies have been developed to target eosinophil activity in diseases where they are detrimental. Biologic therapies that block IL-5 or IL-5Rα (e.g., mepolizumab, benralizumab) have shown success in reducing eosinophil levels and alleviating symptoms in eosinophil-driven diseases such as asthma, EoE, and HES [33]. Other emerging therapies targeting eosinophil trafficking and activation pathways hold promise for treating eosinophil-associated disorders [34].

CONCLUSION

Eosinophils are versatile immune cells that play complex roles in host defense, allergy, and inflammation. As "friends," they contribute to protection against parasites, tissue repair, and immune regulation. However, their role as "foes" in allergic diseases, chronic inflammation, and autoimmune disorders

REFERENCES

1. Kita, H. (2011). Eosinophils: multifaceted biological properties and roles in health and disease. *Immunological Reviews*, 242.
2. Ravin, K., & Loy, M. (2016). The Eosinophil in Infection. Clinical Reviews in Allergy & Immunology, 50, 214-227.
3. Ondari, E., Calvino-Sanles, E., First, N., &Gestal, M. (2021). Eosinophils and Bacteria, the Beginning of a Story. *International Journal of Molecular Sciences*, 22.
4. Desreumaux, P., & Capron, M. (1996). Eosinophils in allergic reactions. *Current opinion in immunology*, 8 6, 790-5.
5. Kita, H. (2011). Eosinophils: multifaceted biological properties and roles in health and disease. *Immunological Reviews*, 242.
6. Diny, N., Rose, N., & Čiháková, D. (2017). Eosinophils in Autoimmune Diseases. *Frontiers in Immunology*, 8.
7. Robinson, D. S., Kay, A. B., & Wardlaw, A. J. (2023). Eosinophils. *Inflammatory Mechanisms in Allergic Diseases*, 43-75.
8. Simon, D., Wardlaw, A., & Rothenberg, M. (2010). Organ-specific eosinophilic disorders of the skin, lung, and gastrointestinal tract. *The Journal of allergy and clinical immunology*, 126 1, 3-13; quiz 14-5.

9. Fulkerson, P., & Rothenberg, M. (2013). Targeting eosinophils in allergy, inflammation and beyond. *Nature Reviews Drug Discovery*, 12, 117-129.
10. Klion, A., &Nutman, T. (2004). The role of eosinophils in host defense against helminth parasites. *The Journal of allergy and clinical immunology*, 113 1, 30-7.
11. Zhu, J. (2015). T helper 2 (Th2) cell differentiation, type 2 innate lymphoid cell (ILC2) development and regulation of interleukin-4 (IL-4) and IL-13 production. *Cytokine*, 75 1, 14-24.
12. Dixon, H., Blanchard, C., Deschoolmeester, M., Yuill, N., Christie, J., Rothenberg, M., & Else, K. (2006). The role of Th2 cytokines, chemokines and parasite products in eosinophil recruitment to the gastrointestinal mucosa during helminth infection. *European Journal of Immunology*, 36.
13. Zhu, J. (2015). T helper 2 (Th2) cell differentiation, type 2 innate lymphoid cell (ILC2) development and regulation of interleukin-4 (IL-4) and IL-13 production. *Cytokine*, 75 1, 14-24.
14. Rigoni, A., Colombo, M., & Pucillo, C. (2018). Mast cells, basophils and eosinophils: From allergy to cancer. *Seminars in immunology*, 35, 29-34.
15. Köckritz-Blickwede, M., & Nizet, V. (2009). Innate immunity turned inside-out: antimicrobial defense by phagocyte extracellular traps. *Journal of Molecular Medicine (Berlin, Germany)*, 87, 775 - 783.
16. Barroso, M., Gropillo, I., Detoni, M., Thompson-Souza, G., Muniz, V., Vasconcelos, C., Figueiredo, R., Melo, R., & Neves, J. (2021). Structural and Signaling Events Driving Aspergillus fumigatus-Induced Human Eosinophil Extracellular Trap Release. *Frontiers in Microbiology*, 12.
17. Phipps, S., Lam, C., Mahalingam, S., Newhouse, M., Ramirez, R., Rosenberg, H., Foster, P., & Matthaei, K. (2007). Eosinophils contribute to innate antiviral immunity and promote clearance of respiratory syncytial virus. *Blood*, 110 5, 1578-86 .
18. Bélanger, É., Madore, A., Boucher-Lafleur, A., Simon, M., Kwan, T., Pastinen, T., & Laprise, C. (2020). Eosinophil microRNAs Play a Regulatory Role in Allergic Diseases Included in the Atopic March. *International Journal of Molecular Sciences*, 21.
19. Bélanger, É., Madore, A., Boucher-Lafleur, A., Simon, M., Kwan, T., Pastinen, T., & Laprise, C. (2020). Eosinophil microRNAs Play a Regulatory Role in Allergic Diseases Included in the Atopic March. *International Journal of Molecular Sciences*, 21.
20. Mormile, M., Mormile, I., Fuschillo, S., Rossi, F., Lamagna, L., Ambrosino, P., Paulis, A., & Maniscalco, M. (2023). Eosinophilic Airway Diseases: From Pathophysiological Mechanisms to Clinical Practice. *International Journal of Molecular Sciences*, 24.
21. Chikumoto, A., Oishi, K., Hamada, K., Hirano, T., Kakugawa, T., Kanesada, K., & Matsunaga, K. (2022). Sequential Biotherapy Targeting IL-5 and IL-4/13 in Patients with Eosinophilic Asthma with Sinusitis and Otitis Media. *Biomolecules*, 12.
22. Principe, S., Porsbjerg, C., Ditlev, S., Klein, D., Golebski, K., Dyhre-Petersen, N., Dijk, Y., Bragt, J., Dankelman, L., Dahlén, S., Brightling, C., Vijverberg, S., & Zee, A. (2021). Treating severe asthma: Targeting the IL-5 pathway. *Clinical and Experimental Allergy*, 51, 992 - 1005.
23. Erjefält, J., Greiff, L., Andersson, M., Matsson, E., Petersen, H., Linden, M., Ansari, T., Jeffery, P., & Persson, C. (1999). Allergen-induced eosinophil cytolysis is a primary mechanism for granule protein release in human upper airways. *American journal of respiratory and critical care medicine*, 160 1, 304-12.
24. Straumann, A. (2019). Eosinophil-Associated Gastrointestinal Disorders. In *Clinical Immunology* (pp. 633-640).
25. Gonsalves, N. (2019). Eosinophilic Gastrointestinal Disorders. *Clinical Reviews in Allergy & Immunology*, 1-14.
26. Lazzari, C., Yacoub, M., Campochiaro, C., Bulotta, A., Palumbo, D., Ogliari, F., Dagna, L., Marchesi, S., Ponzoni, M., & Gregorc, V. (2023). Case report: Successful use of mepolizumab for immune checkpoint inhibitors–induced hypereosinophilic syndrome in two patients with solid malignancies. *Frontiers in Oncology*, 13.
27. Busse, W., Ring, J., Huss-Marp, J., & Kahn, J. (2010). A review of treatment with mepolizumab, an anti-IL-5 mAb, in hypereosinophilic syndromes and asthma. *The Journal of allergy and clinical immunology*, 125 4, 803-13.

28. Fijołek, J., & Radzikowska, E. (2023). Eosinophilic granulomatosis with polyangiitis – Advances in pathogenesis, diagnosis, and treatment. *Frontiers in Medicine*, 10.
29. Shah, K., Ignacio, A., McCoy, K., & Harris, N. (2020). The emerging roles of eosinophils in mucosal homeostasis. *Mucosal Immunology*, 13, 574 - 583.
30. Aoki, A., Hirahara, K., Kiuchi, M., & Nakayama, T. (2020). Eosinophils: Cells known for over 140 years with broad and new functions. *Allergology international: official journal of the Japanese Society of Allergology*.
31. Stower, H. (2014). Metabolism: Eosinophils in energy homeostasis. *Nature Medicine*, 20, 714-714.
32. Wen, T., & Rothenberg, M. (2016). The Regulatory Function of Eosinophils. *Microbiology spectrum*, 4 5.
33. Nagase, H., Ueki, S., & Fujieda, S. (2020). The roles of IL-5 and anti-IL-5 treatment in eosinophilic diseases: Asthma, eosinophilic granulomatosis with polyangiitis, and eosinophilic chronic rhinosinusitis. *Allergology international: official journal of the Japanese Society of Allergology*.
34. Massironi, S., Mulinacci, G., Gallo, C., Elvevi, A., Danese, S., Invernizzi, P., & Vespa, E. (2023). Mechanistic Insights into Eosinophilic Esophagitis: Therapies Targeting Pathophysiological Mechanisms. *Cells*, 12.

CITE AS: Nyiramana Mukamurera P. (2024). Role of Eosinophils in Immunity, Allergy, and Inflammation: Friend or Foe. INOSR Experimental Sciences 14(1):16-20. https://doi.org/10.59298/INOSRES/2024/141.1620