MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Advances in Clinical Toxicology
ISSN: 2577-4328

Mechanism of Action of Nerve Growth Factor Induced Histamine Release from Mast Cells during the Inflammation Process

Ferjan I*

Institute of Pharmacology and Experimental Toxicology, Medical faculty of Ljubljana, Slovenia

***Corresponding author:** Ilonka Ferjan, Institute of Pharmacology and Experimental Toxicology, Medical faculty of Ljubljana, Korytkova ulica 2, 1000, Ljubljana, Slovenia, Email: ilonka.ferjan@mf.uni-lj.si

Review Article

Volume 8 Issue 1

Received Date: December 12, 2022

Published Date: January 23, 2023

DOI: 10.23880/act-16000255

Abstract

Mast cells and the biogenic amine, histamine, play a central role in inflammatory reactions. Nerve growth factor (NGF) is essetial for the survival of neurones and has significant role in inflammation and repair of tissues. It has been shown, that NGF induces degranulation of mast cells by interacting with tropomyosine-receptor kinase A (TrkA receptor). NGF can induce release of histamine and other mediators from mast cells or enhance secretion induced by different stimuli. The results of our and others previous studies show, that histamine release from mast cells induced by NGF is strongly dependent on the concentration of extracellular Na^+, Ca^{2+} ions. The extracellular Na^+ ions can affect the activity of Na^+/Ca^{2+} exchanger of mast cells. Na^+, Ca^{2+} exchange mechanisms could be important in secretory process of mast cells. The studies of different signaling molecules in NGF induced histamine relese have shown that tyrosine kinase, phosphatidylinositol-3-kinase, protein kinase C and phospholipase C are also involved in the signal transduction process responsible for NGF induced histamine secretion from mast cells. These data indicate that NGF may contribute in allergic reactions and many other inflammatory states.

Keywords: Nerve Growth Factor; Mast Cells; Histamine Release; Mechanism of Action

Abbreviations: NGF: Nerve Growth Factor; TrkA Receptor: Tyrosine Kinase A receptor.

Introduction

In the inflammation process, mast cells have a very important role. After the activation of mast cells, they release many mediators involved in the inflammation [1]. Biogenic amine, histamine, is one of the essential inlammatory mediator [2]. Nerve growth factor (NGF) is essetial for the survival of neurones and has a signifficant role in inflammation and repair of tissues [3-5]. It has been shown, that the extracellular ionic composition influences the secretion process of mast cells [6]. The existence of Na^+/Ca^{2+} exchanger on rat mast cell membrane has been demonstrated [7]. The action of Na^+/Ca^{2+} exchanger depends on the concentration of extracellular Na^+ and Ca^{2+} ions. $Na+/Ca^{2+}$ exchanger of mast cells has been shown to be involved in the secretion of the inflammatory mediators [8]. Our previos studies have further shown that many enzymes (Tyrosine kinase, phosphatidylinositol-3-kinase, protein kinase C and phospholipase C and phosphatidylinositol-3-kinase) could also play a signifficant role in the secretory process [8].

The Role of Extracellular Na^+ and Ca^{2+} Ions in HIstamine Release Process Induced by NGF

Extracellular Na^+ and Ca^{2+} ions play a crucial role in the secretion process of histamine induced by NGF) [6,8]. The response is dependent on the presence of extracellular Ca^{2+}

ions and is enhanced with increasing concentration of Ca^{2+} ions in the medium. However, lowering extracellular Na+ ions increases histamine release induced by NGF. In the medium containing low concentration of Ca^{2+} ions, removal of Na+ ions from the medium further potentiates histamine release induced by NGF (6).

The Involvement of Na+/Ca^{2+} Exchanger in the Degranulation Process of Mast Cell

On mast cell membrane Na^+Ca^{2+} exchanger has been demonstrated [7]. The extracellular Na+ ions can affect the activity of Na^+Ca^{2+} exchanger of mast cells. In physiological conditions the exchanger exchanges Ca^{2+} ions from the cell for Na+ ions from the medium [9]. In the medium containing low concentrations of Na^+ ions, the reverse action of the exchanger can be activated, resulting in influx of Ca^{2+} ions from the medium into the cell [9]. The increased concentration of intracellular free Ca^{2+} ions leads to enhanced histamine release.

Inhibitor of Na+/Ca^{2+} exchanger, amiloride, reduces the potentiated histamine release under these conditions [8]. These data further shows the involvement of Na+/Ca^{2+} exchanger in the secretion process of histamine from mast cells [7,8].

The Regulation of Histamine Release from Mast Cells by Tyrosine Kinase, Phosphatidylinositol-3-kinase, Protein Kinase C and Phospholipase C

Our previous results have shown that tyrosine kinase, phosphatidylinositol-3-kinase, protein kinase C, phospholipase C and phosphatidylinositol-3-kinase are involved in the regulation of the mechanism of histamine release from mast cells [8]. These enzymes play a signifficant role in the signal transduction pathway involved in the NGF induced histamine release [10]. These data indicate the importance of NGF in many states that are involved in mast cell activation. NGF may contribute in asthma and many other allergic reastions [11].

Conclusion

- Histamine release induced by NGF is dependent on the presence of extracellular Na^+ and Ca^{2+} ions [6,13].
- Extracellular Na^+ and Ca^{2+} ions regulate the activity of Na^+/Ca^{2+} exchanger of mast cells [7,8]. The influx of Ca^{2+} ions from the medium into the cell leads to the increased concentration of intracellular free Ca^{2+} ions which enhances histamine release from mast cells.
- Many enzymes (tyrosine kinase, phosphatidylinositol-3-kinase, protein kinase C, phospholipase C and phosphatidylinositol-3-kinase) are involved in the mechanism of histamine release induced by NGF [8,14].
- In addition to neurotrophic activity of NGF, it plays a crucial role in stimmulation of various inflammatory cells [12], including mast cells [14]. Therefore it can contribute to many allergic reactions and various other inflammatory states.

References

1. Mukai K, Tsai M, Saito H, Galli S (2018) Mast cells as sources of cytokines, chemokines and growth factors Immunol Rev 282(1): 121-150.

2. Moller A, Grabbe J, Czarnetzki BM (1991) Mast cell and their mediators in immediate and delayed immune reactions. Skin Pharmacol 4(1): 56-63.

3. Minnone G, Benedetti F, Bracci-Laudiero L (2017) NGF and its receptors in the regulation of inflammatory response Int J Mol Sci 18(5): 1028.

4. Frossard N, Freund V, Advenier C (2004) Nerve growth factor and its receptors in astma and inflammation. Eur J Pharmacol 500(1-3): 453-465.

5. Komi DEA, Khomtchouk K, Santa Maria PL (2020) A review of the contribution of mast cells in wound healing: involved molekular and cellular mechanisms Clin Rev Allergy Immunol 58(3): 298-312.

6. Štempelj M, Čarman-Kržan M, Ferjan I (2003) Regulatory role of extracellular Na^+ and Ca^{2+} ions in nerve growth factor induced histamine secretion from rat mast cells 52: 74-78.

7. Alfonso A, Lago J, Botana MA, Vieytes MR, Botana LM (1999) Characterization of the Na^+Ca^{2+} Exchanger on rat mast cells. Cell Physiol Biochem 9(2): 53-71.

8. Štempelj M, Ferjan I (2005) Signaling pathway in nerve growth factor induced histamine release from rat mast cells. Inflamm Res 54(8):344-349.

9. Matsuda T, Takuma K, Baba A (1997) Na^+Ca^{2+} Exchanger: Physiology and Pharmacology Jpn J Pharmacol 74(1): 1-20.

10. Minnone G, Benedetti FD, Bracci-Laudiero L (2017) NGF and its receptors in the regulation of inflammatory response Int J Mol Sci 18(5): 1028.

11. Skaper SD (2017) Nerve growth factor: a neuroimmune crosstalk mediator for all seasons. Immunology 151(1): 1-15.

12. Smith TF, Sanchez Legrand F, McKean LP, Kutner MH, Cragoe EJ, et al. (1992) Role of sodium in mediator

release from human basophils. J Allergy Clin Immunol 89(5): 978-986.

13. Kioussis D, Pachinis V (2009) Immune and nervous systems: More than just a superficial similarity. Immunity 31(5): 705-710.

14. Seebeck J, Westenberger K, Elgeti T, Ziegler A, Schutze S (2001) The exocytotic signaling pathway induced by nerve growth factor in the presence of lyso-phosphatidylserine in rat peritoneal mast cells involves a type D phospholipase Regul Pept 102(2-3): 93-99.