MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Advances in Clinical Toxicology
ISSN: 2577-4328

The Role of Nerve Growth Factor in Alergic Reactions and Healing Process of Tissues

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

Commentary

Volume 7 Issue 1

Received Date: March 30, 2022

Published Date: April 15, 2022

DOI: 10.23880/act-16000241

Abstract

Nerve growth factor is a protein which regulates the differentiation and survival of nerve system. It is produced in neurons and in several non-nervous cells which are involved in some inflammatory and immunological states. These cells include mast cells, lymphocytes, macrophages and fibroblasts. Mast cells play a crucial role in the inflammatory and allergic reactions. Inflammatory cells express specific receptors for binding NGF, tyrosine kinase (TrkA) receptor. Binding of nerve growth factor to this receptor activates the immune cells. Activation of the cells leads to secretion of many inflammatory mediators from them. The mediators (histamine, serotonin, tryptase and some interlevkines) are involved in the early response of inflammatory cells. The cytokines and growth factors produced later in the inflammatory process activate fibroblasts and other cells, which participate in healing process of tissues.

Keywords: Nerve Growth Factor; Mast Cells; Alergic Reactions; Healing Process

Abbreviations: TrkA: Tyrosine Kinase; NGF: Nerve growth factor; p75NTR: p75 Neurotrophin Receptor.

Introduction

Nerve growth factor (NGF) is a polypeptide essential for the survival, development, differentiation and function of peripheral and central neurons [1]. It is produced in neurons and in several non-nervous cells. It elicits several biological effects on neuronal and nonneuronal tissues [2]. Recently, it has been shown that NGF exerts several effects on the cells which are involved in some inflammatory and immunological states [3]. These cells include mast cells, lymphocytes, macrophages, neutrophils, epithelial cells and fibroblasts [4]. NGF is produced by different cell types (muscle cells, epithelial cells, fibroblasts, adipocytes and immune cells) at the site of inflammation. Inflammatory cells express specific receptors, tyrosine kinase TrkA NGF receptors [5,6]. Binding of nerve growth factor at these receptors activates inflammatory cells and induces the secretion of many inflammatory mediators from them.

NGF Receptors

Two classes of receptors for NGF binding were determined: neurotrophin Receptor (p75NTR) and tropomyosine-receptor kinase A (TrkA) [5,6]. The immune response is mediated by TrkA receptor activation, which is NGF specific receptor [5]. NGF binds at TrkA receptor selectively. The receptor is located on nervous cells [7] as well as on structural cells and on immune cells [5,6]. It comprices a tyrosine-kinase domain. After binding of NGF on the receptor, kinase activation and phosphorylation of proteins occur [5,6]. These modulate the cells activity and their functions.

NGF, Inflammation and Immune Response

Beside neurotrophic activity of NGF, it exerts several effects on the cells of immune system [8]. It is produced by several immune cells and involved in many inflammatory and immunological diseases [5].

Mast cells play a central role in the inflammatory and allergic reactions [9]. They are hematopoietic cells that represent a source of inflammatory mediators [10]. In response to immunologic stimuli they release a variety of inflammatory mediators, such as histamine, proteases, metabolites of arachidonic acid and cytokines [9]. NGF can regulate the secretion of many inflammatory mediators from mast cells, which can make the contributions to immediate and late allergic disorders [11]. The mediators (histamine, serotonin, tryptase and some interlevkines) are involved in the early response of inflammatory cells [11]. Since the activation of mast cells with NGF evokes rapid release of histamine within minutes, this indicates the role of NGF in early stage of allergic reactions. In the late phase of allergic reaction eosinophils and other inflammatory cells infiltration occurs [12]. The cytokines and growth factors produced by these cells later in the inflammatory process activates fibroblasts and other cells, which participate in healing and repair processes of tissues [10].

Early Response of Mast Cells

Elevated levels of mast cells and NGF have been indicated during inflammation. Numerous studies have reported elevated concentrations of NGF in biological fluids of patients with asthma and other allergic diseases [4-6]. NGF induces rapid release of some mediators (histamine, serotonin, tryptase and some interlevkines) from mast cells, which are involved in the early response of mast cells and some other inflammatory cells [5]. Some data show that NGF plays role in airway inflammation and bronchoconstriction in patients with asthma [6]. All these data indicate that NGF contributes in early phase of allergic inflammation.

Late Response of Mast Cells

Mast cells produce and secrete different cytokines and growth factors which play a crucial role in many late biological processes. These functions of mast cells, which are occurring in late response, include the contributions of mast cells in angiogenesis, fibrosis and wound healing [13,14]. Mast cells mediators including interleukin-4, interleukin-8, vascular endothelial growth factor, fibroblast growth factor and nerve growth factor contribute to fibroblast proliferation. This play the predominant role in repair process of tissues [13,14]. NGF and other mediators secreted from mast cells are involved in neoangiogenesis and reepithelization processes. All these events lead to repair process of tissues and improve wound healing and scar formation [15].

Conclusion

All these data indicate that NGF could regulate early and late response of inflammatory and immune cells. Rapid release of some mediators by mast cells is involved in astma and early phase of allergic reastions. Mediators secreted from mast cells in the late response, play an important role in tissue healing and repair processes of tissues.

References

1. Montalchini RL, Skaper SD, Toso RD, Petrelli L, Leon A (1996) Nerve growth factor: from neurotrophin to neurokine. Trends Neurosci 19(11): 514-520.

2. Yankner BA, Shooter EM (1982) The biology and mechanism of action of nerve growth factor. Annu Rev Biochem 51: 845-868.

3. 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.

4. Stephen DS (2017) Nerve growth factor: a neuroimmune crosstalk mediator for all seasons. Immunology 151(1): 1-15.

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

6. 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.

7. Patapoutian A, Reichardt LF (2001) Trk receptors: mediators of neurotrophin actions. Curr Opin Neurobiol 11(3): 272-280.

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

9. Stempelj M, Ferjan I (2005) Signaling pathway in nerve growth factor induced histamine release from rat mast cells. Inflamm Res 54(8): 344-34.

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

11. Micera A, Puxeddu I, Aloe l, Schaffer FL (2003) New insights on the involvement of Nerve Growth Factor in allergic inflammation and fibrosis. Cytokine Growth

Factor Rev 14(5): 369-374.

12. Komi DEA, Khomtchouk K, Maria PLS (2019) A review of the contribution of mast cells in wound healing: involved molekular and cellular mechanisms. Clin Rev Allergy Immunol 58(3): 298-312.

13. Kennelly R, Conneely JB, Hayes DB, Winter DC (2011) Mast cells in tissue healing: from skin to the gastrointestinal tract. Curr Pharm Des 17(34): 3772-3775.

14. Hinz B (2016) The role of myofibroblasts in wound healing. Curr Res Transl Med 64(4): 171-177.

15. Komi DEA, Khomtshouk K, Maria PLS (2019) A review of the contribution of mast cells in wound healing: involved molecular and cellular mechanisms. Clin Rev Allergy Immunol 58(3): 298-312.