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Short Communication

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Signal Transduction of Nerve Growth Factor Induced Histamine Secretion from Mast Cells

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Abstract

Mast cells play a central role in allergic reactions. In response to immunologic or non-immunologic stimuli they release many inflammatory mediators. Biogenic amine, histamine is one of the essential mediator, which is relesed from mast cells during inflammation reactions. Nerve growth factor (NGF) is essetial for the survival of various neurones and has significant role in inflammation and allergic reactions. Histamine release from mast cells induced by NGF is strongly dependent on the concentration of extracellular Na+and Ca2+ ions. The studies of the role of different enzymes in NGF induced histamine relese have shown that tyrosine kinase, phosphatidylinositol-3-kinase, protein kinase C and phospholipase C are involved in the signal transduction responsible for NGF induced histamine secretion from mast cells. The right ionic composition of the extracellular fluid and the exact signaling pathway involved in NGF induced histamin secretion indicate the importance of NGF in various inflammatory and allergic deseases.

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

Abbreviations

NGF: Nerve Growth Factor
TrKA Receptor: Tyrosine Kinase A Receptor

1. Introduction

Mast cells play a central role in allergic reactions. In response to immunologic or non-immunologic stimuli they release many inflammatory mediators [1]. Biogenic amine, histamine is one of the essential inflammatory mediator, which is released from mast cells during inflammation and allergic reactions. The stimmulation of histamine release from mast cells can be induced by an immunologic or non-immunologic stimuli. The mechanism of non-immunological induced histamine relese is different from that induced by the immunologic stimuli [2]. Nerve growth factor (NGF) is essential for the survival of several neurones and has a wide range of other effects [2,3]. Among these effects, NGF can induce degranulation of mast cells by interacting with its high-affinity receptor of a TrkA-type [2]. Since elevated levels of NGF in fluids of patients with allergic diseases have been reported, it can play an important role in allergic reactions [4]. Therefore, it is of interest to study the mechanism of the secretory process induced by NGF. Basic secretagogue, compound 48/80 is used as a standard for non-immunological trigger of secretion process from mast cells. The signal trunsduction pathway involved in histamine release from mast cells provoked by NGF can be compared with the secretion induced by basic secretagogue compound 48/80.

2. The Effect of Ionic Composition of the Medium in Histamine Relese Process Induced by Different Stimuli.

The secretion of mediators from mast cells induced by immunologic or by non-immunologic stimuli is strongly dependent on the presence of Ca2+ ions. Stimmulation of mast cells by an imunologic stimuli and by NGF require the presence of extracellular calcium to induce histamine release [5]. However, the relese induced by compound 48/80 is not strongly dependent on the presence of extracellular calcium [5]. These findings show that some different steps are involved in the secretion process induced either by NGF or by compound 48/80. Beside the importance of extracellular Ca2+ in the secretion process, extracellular Na+ ions play also an important role in the secretion of the inflammatory mediators [6].

Sodium-free medium potentiates NGF induced histamine relese [7]. Similar potentiation of histamine release in sodium free medium occurs also by stimmulation of mast cells either by compound 48/80 or by the immunologic stimuli [7,8]. Since, amiloride, an inhibitor of Na+Ca2+ exchanger abolish this effect, Na+Ca2+ exchanger might have a role in changing the concentration of Na+ and Ca2+ ions [5]. In the medium containing low concentratins of Na + ions, Na+Ca2+ exchanger of mast cells exchanges extracellular Ca2+ ions for intracellular Na+ ions [7]. Therefore the influx of Ca2+ ions in the cell occurs [9]. Conseqvently, the increased intracellular free calcium concentration leads to the potentiation of histamine release induced by various stimuli [10].

3. The Regulation of Histamine Release by Various Enzymes

Various enzymes are required in the signal transduction of histamine secretion induced by NGF and compound 48/80. Tyrosine kinase, phospholipase C and proteinkinase C are involved in the signal trunduction pathway induced by both secretagogues [10]. However, phosphatidylinositol-3-kinase is activated only in NGF mediated degranulation process [10]. This indicates that NGF triggers histamine secretion by a specific mechanism, which differs from that induced by compound 48/80. However, the same enzymes are needed in the secretory process induced either by NGF or by IgE stimmulation [11]. These findings suggest that similar pathways may be involved in the secretion induced either by NGF or by IgE stimmulation. The right ionic composition of the extracellular fluid and the exact signaling pathway involved in NGF induced histamin secretion indicate the importance of NGF in various inflammatory and allergic deseases.

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