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REVIEW

# From airway inflammation to inflammatory bowel disease: Eotaxin-1, a key regulator of intestinal inflammation

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**Abstract** Eotaxin-1 (CCL-11) is a potent eosinophil chemoattractant that is considered a major contributor to tissue eosinophilia. Elevated eotaxin-1 levels have been described in various pathologic conditions, ranging from airway inflammation, to Hodgkin lymphoma, obesity and coronary artery disease. The main receptor for eotaxin-1 is CCR3; however, recent evidence indicates that eotaxin-1 may also bind to other receptors expressed by various cell types, suggesting a more widespread regulatory role for eotaxin-1 beyond the recruitment of eosinophils.

Eotaxin-1 is also strongly associated with various gastrointestinal (GI) disorders. Although the etiology of inflammatory bowel disease (IBD) is still unknown, eotaxin-1 may play a key role in the development of mucosal inflammation.

In this review, we summarize the biological context and effects of eotaxin-1, as well as its potential role as a therapeutic target, with a special focus on gastrointestinal inflammation.


**Contents**



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## 1. Introduction

Human eotaxin-1 is a CC chemokine with preferential activity on eosinophils. Two additional human eosinophil selective CC chemokines were later identified and named eotaxin-2 [1] and eotaxin-3 [2,3]. These three eotaxins are also known as CCL11 (eotaxin-1), CCL24 (eotaxin-2) and CCL26 (eotaxin-3) [4].

Eotaxins belong to the family of chemokines (chemotactic cytokines). These small secreted peptides typically regulate the chemoattraction of leukocytes and are important immune modulators [5]. The chemokines are classified according to the position of the first two out of four conserved cysteine residues and are sub-divided into four families: CXC, CC, C and CX3C. The CC chemokines have their cysteine residues located adjacent to each other and, in general, serve as potent chemoattractants for eosinophils, basophils, monocytes and lymphocytes [5].

Eotaxin-1 (the initially recognized eotaxin) was first described in allergic airway inflammation in guinea pigs [6] and was further established as a key player in mediating tissue eosinophilia [7]. Since then, numerous studies have demonstrated the role of eotaxin-1 in various target cells via multiple signaling pathways [1,8–18]. Much of our knowledge about eotaxin-1 is indeed derived from airway inflammation and allergic studies, but elevated eotaxin-1 levels have also been reported in other pathologic conditions, ranging from coronary heart disease to Hodgkin lymphoma [19,20].

The expression of the various eotaxins is cell-type specific. Many cell types can produce eotaxin-1 (Fig. 1). Eotaxin-1 is secreted by eosinophils, macrophages, lymphocytes, fibroblasts, smooth muscle endothelial cells, epithelial cells and chondrocytes. Eotaxin-2 and eotaxin-3 are functional homologues that are mainly released by epithelial and endothelial cells [4]. Specifically within the gastrointestinal tract, a

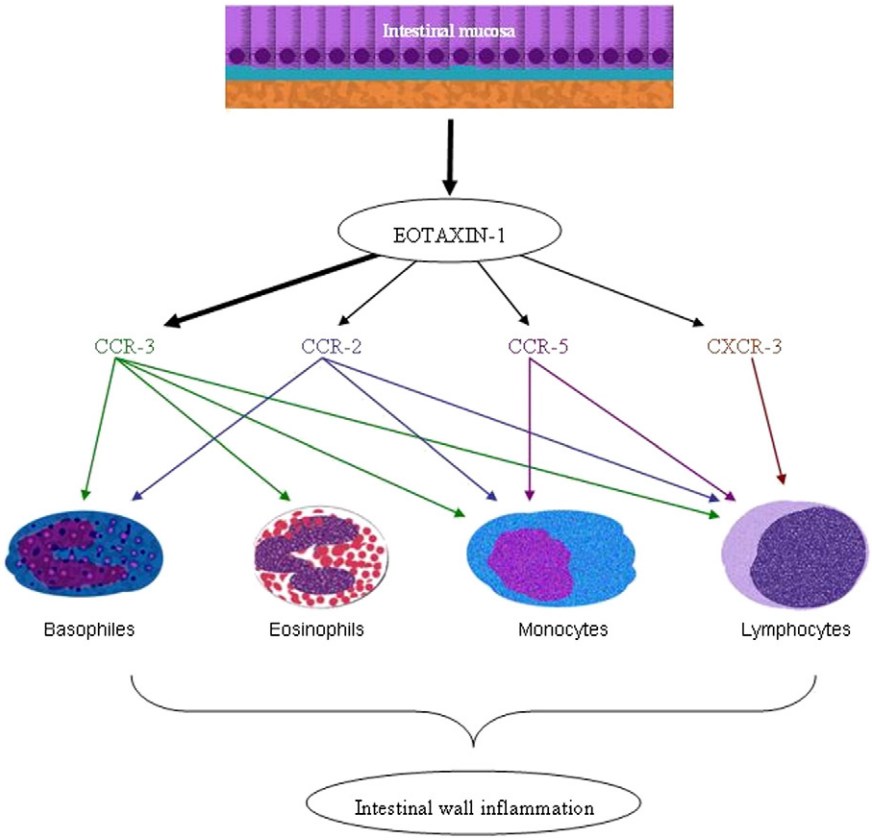


**Figure 1**