IL-26 Is Overexpressed in Rheumatoid Arthritis and Induces Proinflammatory Cytokine Production and Th17 Cell Generation

Submitted by Emmanuel Lemoine on Thu, 10/16/2014 - 14:02

Titre
IL-26 Is Overexpressed in Rheumatoid Arthritis and Induces Proinflammatory Cytokine Production and Th17 Cell Generation

Type de publication
Article de revue

Auteur
Corvaisier, Murielle [1], Delneste, Yves [2], Jeanvoine, Henry [3], Preisser, Laurence [4], Blanchard, Simon [5], Garo, Erwan [6], Hoppé, Emmanuel [7], Barré, Benjamin [8], Audran, Maurice [9], Bouvard, Béatrice [10], Saint-André, Jean-Paul [11], Jeannin, Pascale [12]

Pays
Etats-Unis

Editeur
Public Library of Science

Ville
San Francisco

Type
Article scientifique dans une revue à comité de lecture

Année
2012

Langue
Anglais

Date
25/09/2012

Numéro
9

Pagination
e1001395

Volume
10

Titre de la revue
PLoS Biology

ISSN
1544-9173

Mots-clés
Bone Marrow Cells [13], Cytokines [14], Inflammatory bowel disease [15], Memory T cells [16], Monocytes [17], Rheumatoid arthritis [18], Secretion [19], T cells [20]
Interleukin-26 (IL-26), a member of the IL-10 cytokine family, induces the production of proinflammatory cytokines by epithelial cells. IL-26 has been also reported overexpressed in Crohn’s disease, suggesting that it may be involved in the physiopathology of chronic inflammatory disorders. Here, we have analyzed the expression and role of IL-26 in rheumatoid arthritis (RA), a chronic inflammatory disorder characterized by joint synovial inflammation. We report that the concentrations of IL-26 are higher in the sera of RA patients than of healthy subjects and dramatically elevated in RA synovial fluids compared to RA sera. Immunohistochemistry reveals that synoviolin+ fibroblast-like synoviocytes and CD68+ macrophage-like synoviocytes are the main IL-26-producing cells in RA joints. Fibroblast-like synoviocytes from RA patients constitutively produce IL-26 and this production is upregulated by IL-1-beta and IL-17A. We have therefore investigated the role of IL-26 in the inflammatory process. Results show that IL-26 induces the production of the proinflammatory cytokines IL-1-beta, IL-6, and tumor necrosis factor (TNF)-alpha by human monocytes and also upregulates the expression of numerous chemokines (mainly CCL20). Interestingly, IL-26-stimulated monocytes selectively promote the generation of RORgamma t+ Th17 cells, through IL-1-beta secretion by monocytes. More precisely, IL-26-stimulated monocytes switch non-Th17 committed (IL-23R− or CCR6− CD161−) CD4+ memory T cells into Th17 cells. Finally, synovial fluids from RA patients also induce Th17 cell generation and this effect is reduced after IL-26 depletion. These findings show that IL-26 is constitutively produced by RA synoviocytes, induces proinflammatory cytokine secretion by myeloid cells, and favors Th17 cell generation. IL-26 thereby appears as a novel proinflammatory cytokine, located upstream of the proinflammatory cascade, that may constitute a promising target to treat RA and chronic inflammatory disorders.

Résumé en anglais

Interleukin-26 (IL-26), a member of the IL-10 cytokine family, induces the production of proinflammatory cytokines by epithelial cells. IL-26 has been also reported overexpressed in Crohn’s disease, suggesting that it may be involved in the physiopathology of chronic inflammatory disorders. Here, we have analyzed the expression and role of IL-26 in rheumatoid arthritis (RA), a chronic inflammatory disorder characterized by joint synovial inflammation. We report that the concentrations of IL-26 are higher in the sera of RA patients than of healthy subjects and dramatically elevated in RA synovial fluids compared to RA sera. Immunohistochemistry reveals that synoviolin+ fibroblast-like synoviocytes and CD68+ macrophage-like synoviocytes are the main IL-26-producing cells in RA joints. Fibroblast-like synoviocytes from RA patients constitutively produce IL-26 and this production is upregulated by IL-1-beta and IL-17A. We have therefore investigated the role of IL-26 in the inflammatory process. Results show that IL-26 induces the production of the proinflammatory cytokines IL-1-beta, IL-6, and tumor necrosis factor (TNF)-alpha by human monocytes and also upregulates the expression of numerous chemokines (mainly CCL20). Interestingly, IL-26-stimulated monocytes selectively promote the generation of RORgamma t+ Th17 cells, through IL-1-beta secretion by monocytes. More precisely, IL-26-stimulated monocytes switch non-Th17 committed (IL-23R− or CCR6− CD161−) CD4+ memory T cells into Th17 cells. Finally, synovial fluids from RA patients also induce Th17 cell generation and this effect is reduced after IL-26 depletion. These findings show that IL-26 is constitutively produced by RA synoviocytes, induces proinflammatory cytokine secretion by myeloid cells, and favors Th17 cell generation. IL-26 thereby appears as a novel proinflammatory cytokine, located upstream of the proinflammatory cascade, that may constitute a promising target to treat RA and chronic inflammatory disorders.

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DOI
10.1371/journal.pbio.1001395 [22]

Lien vers le document
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PLoS Biol

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