

Documents

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High-content multimodal analysis supports the IL-7/IL-7 receptor axis as a relevant therapeutic target in primary Sjögren's syndrome

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Abstract

Objective: While the involvement of IL-7/IL-7R axis in pSS has been described in relation to T cells, little is known about the contribution of this pathway in relationship with other immune cells, and its implication in autoimmunity. Using high-content multiomics data, we aimed at characterizing IL-7R expressing cells and the involvement of IL-7/IL-7R pathway in pSS pathophysiology. **Methods:** An IL-7 signature established using RNA-sequencing of human PBMCs incubated with IL-7 was applied to 304 pSS patients, and on RNA-Seq datasets from tissue biopsies. High-content immunophenotyping using flow and imaging mass cytometry was developed to characterize peripheral and in situ IL-7R expression. **Results:** We identified a blood 4-gene IL-7 module (IKZF4, KIAA0040, PGAP1 and SOS1) associated with anti-SSA/Ro positiveness in patients as well as disease activity, and a tissue 5-gene IL-7 module (IL7R, PCED1B, TNFSF8, ADAM19, MYBL1) associated with infiltration severity. We confirmed expression of IL-7R on T cells subsets, and further observed upregulation of IL-7R on double-negative (DN) B cells, and especially DN2 B cells. IL-7R expression was increased in pSS compared to sicca patients with variations seen according to the degree of infiltration. When expressed, IL-7R was mainly found on epithelial cells, CD4+ and CD8+ T cells, switched memory B cells, DN B cells and M1 macrophages. **Conclusion:** This exhaustive characterization of the IL-7/IL-7R pathway in pSS pathophysiology established that two IL-7 gene modules discriminate pSS patients with a high IL-7 axis involvement. Their use could guide the implementation of an anti-IL-7R targeted therapy in a precision medicine approach. © 2023 Elsevier Ltd

Author Keywords

Anti-IL-7R therapy; IL-7 pathway; Imaging mass cytometry; Multiomics; Primary Sjögren's syndrome

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