

Medical or Research Professionals/Clinicians

Topic area: *Basic and translational research*

Specific topic: *8. SLE, Sjögren's and APS - etiology, pathogenesis and animal models*

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ABERRANT EXPRESSION OF IL-22RA1 ON HEMATOPOIETIC CELLS AS IMMUNOLOGICALLY SIGNATURE OF PRIMARY SJOGREN'S SYNDROME AND SJOGREN-ASSOCIATED NON-HODGKIN LYMPHOMAS

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My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2013:

No

Is the first author applying for a travel bursary?: No

Is the first author of this abstract an undergraduate medical student?: No

Background: Interleukin (IL)-22 is a potent mediator of cellular inflammatory responses that has been recently reported to play a role in the pathogenesis of primary Sjogren's Syndrome (p-SS) (1, 2) and of T and B lymphomas. IL-22 biological activity is initiated by binding to a cell-surface complex composed of two subunits, IL-22R1 and IL-10R2 receptor chains, and further regulated by interactions with a soluble binding protein, IL-22BP. Unlike the IL-10R2, which is constitutively expressed in many human tissues, IL-22R1 is not detectable in immune cells.

Objectives: Aim of this study was to better characterize the role of IL-22 axis in the pathogenesis of p-SS and p-SS-associated lymphomas.

Methods: Minor salivary gland biopsies were obtained from 30 patients with p-SS and 20 with non-specific chronic sialoadenitis (n-SS) and evaluated by RT-PCR for IL-22, IL-22R1 and IL-22BP expression. The protein expression of IL-22, IL-22R1 and p-STAT3 was evaluated by immunohistochemistry and IL-22R1-expressing cells were characterized by confocal microscopy. Flow cytometry analysis of IL-22R1 expression was also conducted on peripheral blood mononuclear cells (PBMCs) from p-SS (n=30), n-SS (n=20), SLE (n=20) and rheumatoid arthritis (n=20) patients and normal controls (n=30). PBMCs isolated from 10 p-SS and 10 controls were also cultured with (or without) recombinant IL-22 and the modulation of the transcripts for pro-inflammatory cytokines was assessed by RT-PCR. Paraffin embedded sections of non-Hodgkin lymphomas from 5 p-SS patients were finally evaluated for the expression of IL-22R1.

Results: IL-22, STAT3 and IL-22BP but not IL-22R1 transcript levels were significantly up-regulated in the inflamed salivary glands of p-SS but not in n-SS. Immunohistochemistry confirmed the increased salivary expression of IL-22 and p-STAT3 also demonstrating a significant increased protein levels of IL-22R1 in p-SS. Confocal microscopy analysis showed that IL-22R1 was aberrantly and strongly expressed in monocytes/macrophages infiltrating the p-SS salivary glands and these cells also co-expressed p-STAT3, suggesting the occurrence of autocrine activation of p-STAT3. CD68+ cells obtained from the peripheral blood also aberrantly expressed IL-22R1 in p-SS patients. IL-22R1 expression on cells of hematopoietic origin was never observed in control disease patients, n-SS and healthy controls. The stimulation with recombinant IL-22 of PBMCs from p-SS but not controls significantly up-regulated the expression of IL-17 and IL-22. Non-Hodgkin lymphoma tissues from p-SS patients were also characterized by the aberrant expression of IL-22R1 on macrophages and neoplastic B cells.

Conclusions: The aberrant expression of IL-22RA1 on cells of hematopoietic origin seems to be a specific immunological signature of patients with p-SS and p-SS associated lymphomas and suggests a fundamental role of IL-22 signaling in the pathogenesis of p-SS and its neoplastic evolution. Targeting of IL-22 pathway may represent a successful therapeutic strategy in p-SS patients.

References: 1. Ciccia F, et al. Ann RheumDis 2012. 2. Ciccia F, et al. Ann Rheum Dis 2012.

Disclosure of Interest: None Declared