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ORAL PRESENTATION

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Skewed X-chromosomal inactivation impacts T regulatory cell function in systemic sclerosis

JCA Broen^{1,4*}, ILM Wolvers-Tettero², L Geurts-van Bon^{1,4}, M C Vonk¹, MJH Coenen³, R Lafyatis⁴, TRDJ Radstake^{1,4†}, A W Langerak^{2†}

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Aim

To investigate the role of X chromosomal inactivation (XCI) in systemic sclerosis (SSc) and its effects on fork-head box P3 (Foxp3) expression in T regulatory cells (Tregs).

Patients and methods

217 women with SSc and 107 healthy women (controls) were included in the study. From these subjects, DNA was isolated from total peripheral blood mononuclear cells, plasmacytoid dendritic cells, T cells, B cells, myeloid dendritic cells and monocytes after magnetic bead separation. All samples were assessed for skewed XCI patterns with the Human Androgen Receptor Assay. The outcome was assessed by linear regression. CD4+CD25+ cells were then isolated and intracellular Foxp3 expression was assessed by flow cytometry.

Results

Skewing was not associated with increased age in patients with SSc, in contrast to the control population ($r=0.45$, $p<0.0001$). Taking this into account, a significantly higher frequency of skewed XCI was found in patients with SSc compared with controls ($p=0.001$). No difference in skewing was observed between the immune cell subsets. In addition, a higher concentration of Foxp3+ cells exhibiting a lower Foxp3 mean fluorescence intensity was found in the patients with SSc, with profound XCI skewing (both $p<0.001$) associated with less efficient suppressive activity ($p=0.012$).

Conclusions

Skewed XCI plays a role in susceptibility to SSc, is not restricted and influences Foxp3 expression and the suppressive capacity of Tregs.

Author details

¹Dept. of Rheumatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. ²Dept. of Immunology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands. ³Dept. of Human Genetics, Radboud University Nijmegen Medical Centre Nijmegen, The Netherlands. ⁴Dept. of Rheumatology, Boston University School of Medicine, Boston, MA, USA.

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† Contributed equally

¹Dept. of Rheumatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Full list of author information is available at the end of the article