A75 **SKewed X-CHROMOSOMAL INACTIVATION PATTERNS
ARE PRESENT IN SYSTEMIC SCLEROSIS AND
ASSOCIATED WITH FOXP3 EXPRESSION**

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Objective To investigate the possible role of X-chromosomal inactivation (XCI) in systemic sclerosis (SSc) and clinical subtypes. The authors also examined the presence of skewing in

immune cell subsets and the effects of XCI on Foxp3 expression in CD4CD25 cells.

Methods A total of 217 women with SSc and 107 healthy female controls were included in the study. From these subjects the authors isolated DNA from peripheral blood mononuclear cells, plasmacytoid dendritic cells (BDCA4+), T cells (CD3), B cells (CD19), myeloid dendritic cells (CD1C) and monocytes (CD14) after magnetic bead separation. All samples were assessed for skewed XCI patterns by use of the HUMARA assay. Outcome was classified into four groups corresponding to the skewing ratio. Next, CD4CD25 cells were isolated and intracellular Foxp3 expression was assessed by flow cytometry.

Results The authors found a significantly higher frequency of skewed XCI in SSc patients compared with healthy controls ($p=0.009$). After comparing the subjects with the highest level of XCI skewing with the overall group, the difference became even more clear (SSc: $p=0.002$, OR 2.24 (95% CI 1.29 to 3.92)). In addition, the authors found an association with clinical phenotypes. (lcSSc: $p=0.024$, OR 1.901 (95% CI 1.004 to 3.680) and dcSSc: $p=0.001$, OR 2.65 (95% CI 1.39 to 5.05)). No difference in skewing was observed among the immune cell subsets. In addition, the authors found a higher concentration of Foxp3 positive cells, exhibiting a lower Foxp3 MFI in the SSc patients with profound XCI skewing (both $p<0.001$). The latter was associated with less efficient suppressive activity ($p=0.012$).

Conclusion Skewed XCI plays a role in susceptibility to SSc, is not caused by a single cell subset and influences Foxp3 expression and suppressive capacity.