Premature senescence of naïve T-cells in Sjögren's syndrome and systemic lupus erythematosus

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Purpose:

To study the possible occurrence of early thymic involution and premature senescence of naïve CD4+ T-cells in patients with Sjögren's syndrome (SjS) and systemic lupus erythematosus (SLE).

Methods:

Table 1: Patients' characteristics

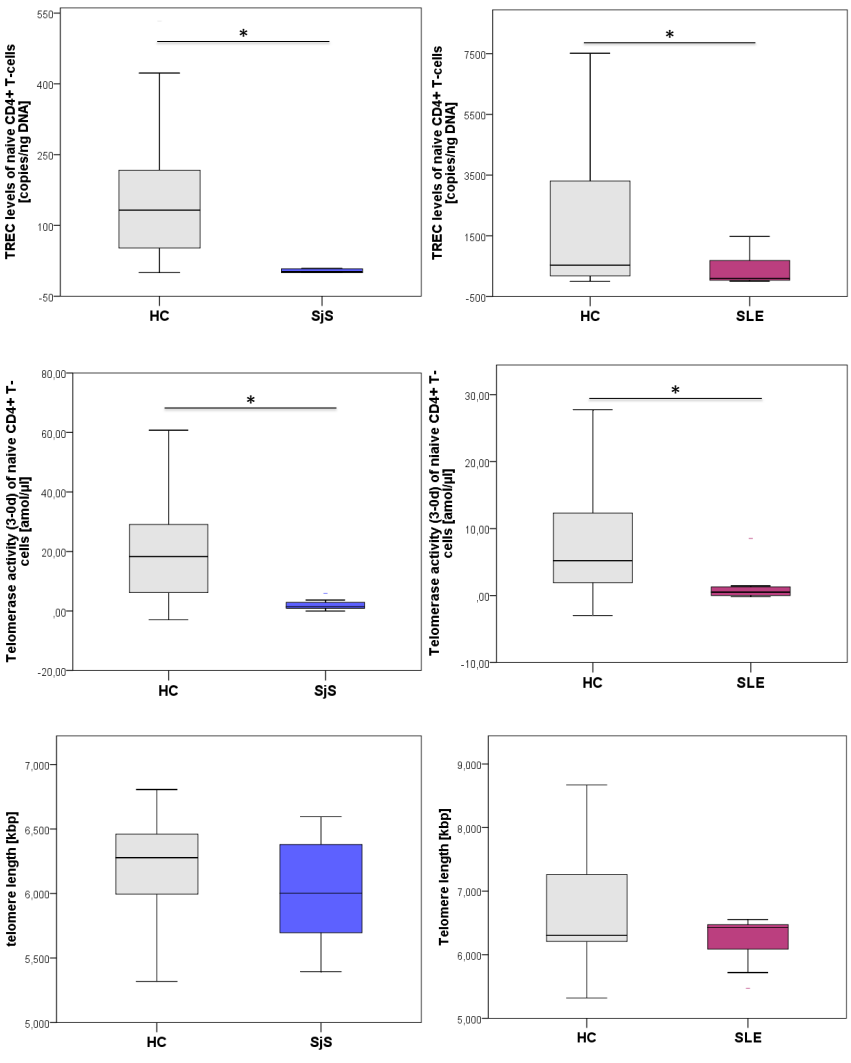
	SjS	HC_{SjS}	SLE	HC_{SLE}
Age [years]*	62.7 [31.9-75.9]	54.5 [36.3-71.4]	40.0 [34.1-54.3]	38.3 [23.3-54.8]
Female, n [%]	15 [93.8]	17 [65.4]	7 [77.8]	27 [69.2]
Disease Duration [years]*	3.5 [0.3-12.1]	-	8.6 [0.0-24.2]	-
Disease activity scores				
SLEDAI*	-	-	6.0 [0.0-36.0]	-
ECLAM*	-	-	2.5 [0.0-9.5]	-
ESSDAI*	1.5 [0.0-13-0]	-	-	-
ESSPRI*	4.0 [1.0-8.3]	-	-	-

*values are displayed as median and range

Prospective, cross-sectional study on 16 SjS patients (median age 62.7 [31.9-75.9], 93.8% female), 9 SLE patients (40.0 [34.1-54.3], 77.8%) and 50 healthy controls (HCs). HCs were split into two age-matched control groups (15 HC assigned to both control groups): 26 HC_{SjS} (54.5 [36.3-71.4], 65.4%; p=0.170) and 39 HC_{SLE} (38.3 [23.3-54.8], 69.2%; p=0.296). Prevalence of memory (CD45RO+) and activated (intracellular Ki67+) CD4+ T-cells was assessed by flow cytometry according to standard surface and intracellular staining protocols. Naïve (CD45RA+) CD4+ T-cells were isolated by MACS technology. Telomere length and T-cell receptor excision circles (TREC) were measured by real-time PCR. Telomere length was chosen as parameter for cellular senescence and TRECs for the evaluation of thymic function. Telomerase activity was analyzed according to the Telomeric Repeat Amplification Protocols (TRAP).

Results:

A decline in thymic output as indicated by the number of TRECs in naïve CD4+ T-cells was observed in SjS patients compared to HC_{SjS} (2 [0-45] vs. 132 [0-15544], p=0.000). Similar results were observed for the comparison of SLE and HC_{SLE} (93 [7-1477] vs. 132 (0-15544), p=0.031). The prevalence of memory CD4+ T-cells was increased in SjS patients compared to HC_{SjS} (8.57% of total lymphocytes [2.77-12.78] vs. 5.81% [0.14-14.75], p=0.013) while no difference was found between SLE patients and HC_{SLE} (4.68% [0.85-13.36] vs. 4.07% [0.02-11.91], p=0.321). The number of activated Ki67+ CD4+ T-cells was low in all groups. To test if the reduction in thymic output leads to a higher need for peripheral proliferation we performed telomere length as well as telomerase activity analysis. We observed significantly impaired telomerase activity in both, SjS (1.37 [-0.02-92.05]) and SLE patients (0.50 [-12.13-8.54]) compared to their respective control groups (HC_{SjS} 18.33 [-2.98-60.76], p=0.001; HC_{SLE} 5.21 [-2.98-60.76], p=0.003). Telomere length was not different in either of the disease-groups compared to HCs (SLE 6.43 [5.47-6.56] vs. HC_{SLE} 6.30 [5.32-8.67], p=0.361), apart from a slight trend toward shorter telomeres in the SjS cohort (6.00 [5.40-6.60] vs. HC_{SjS} 6.28 [5.32-8.67], p=0.104).



Conclusion:

These data indicate a premature decline in thymic output as well as impaired enzymatic function of telomerase in naïve CD4+ T cells of SjS and SLE patients.