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Investigating the role of circulating Follicular T helper lymphocytes in Lupus Nephritis

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INTRODUCTION

TFH cells and autoimmunity

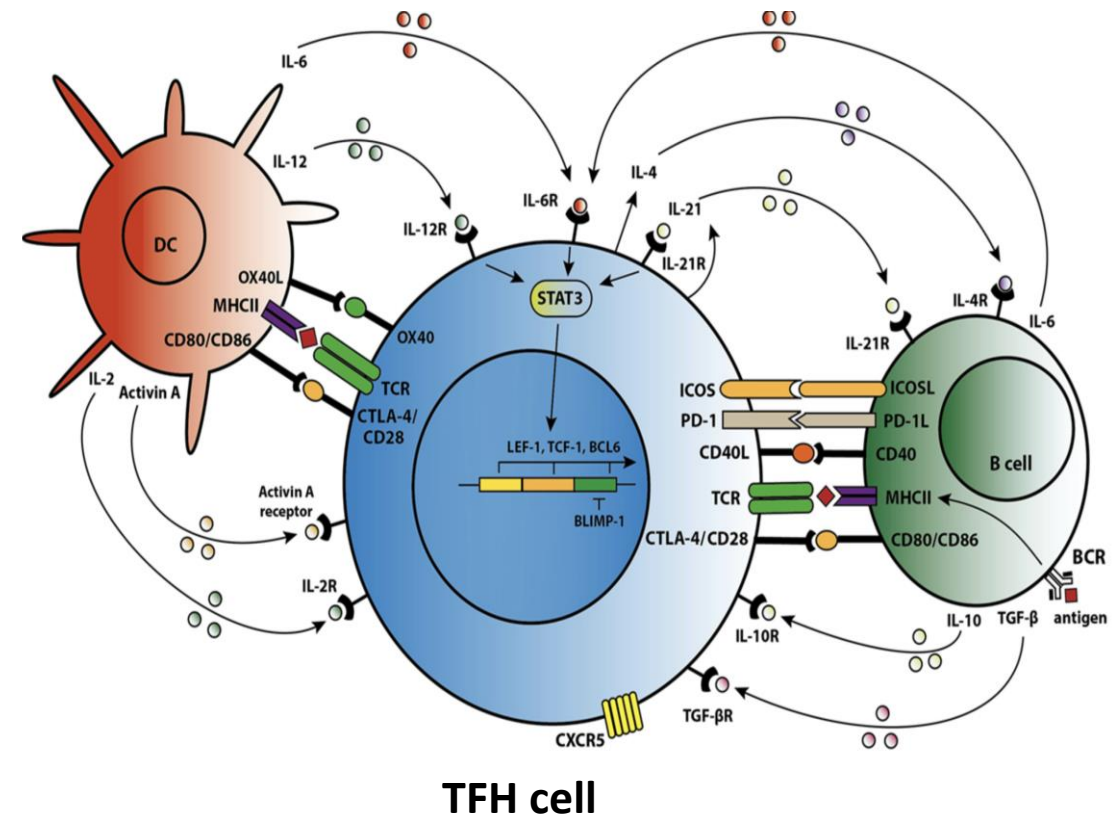
Autoimmune diseases are caused by a breakdown of immune tolerance.

Proliferation of self-reactive B cells with generation of high-affinity autoantibodies participate to the pathophysiology of these disorders



Tfh cells as possible actors in their pathogenesis

!!!Studies regarding contribution of Tfh cells in autoimmune disorders have been initially limited to animal models, essentially because of difficulties in investigating Tfh cells from human SLO !!!



INTRODUCTION

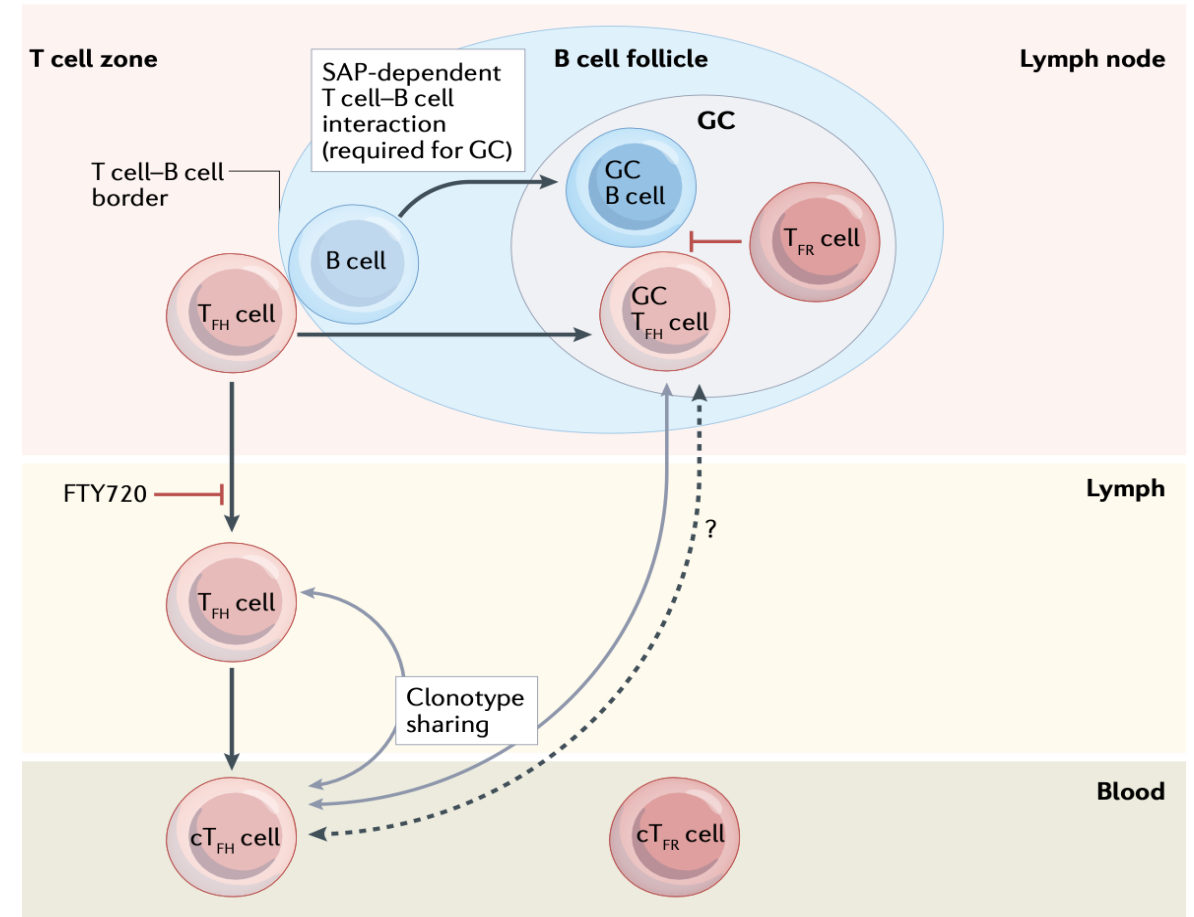
Circulating TFH (cTFH) cells and autoimmunity

- Increased numbers of cTfh cells
- Correlation with the frequency of circulating plasmablasts or plasma cells
- Lack of knowledge regarding the exact biology of cTfh
- cTFH1, cTFH2, cTFH17 – origin?function?

SLE and cTFH

- Significant increase in the frequency of the circulating Tfh-like cells in patients with SLE
- Positive association with disease activity in SLE

Gensous N et al, *Front Immunol.* 2018 Jul 17;9:1637
 Ueno H et al. *Nat Immunol.* 2015 Feb;16(2):142-52
 H. Xu et al *Cell. Immunol.* 295 (1) (2015) 46–51
 J.Y.Choi et al, *Arthritis Rheum.* 67 (4) (2015) 988–999
 X.Zhang et al *Lupus* 24 (9) (2015) 909–917



Walker LSK. *Nat Rev Immunol.* 2022 Sep;22(9):567-575.

AIM

- Describe the population of circulating-TFH cells in patients with Lupus Nephritis (LN) and associate them with disease activity.

MATERIAL AND METHODS (1)

- Cross-sectional study
- Inclusion criteria
 - Adults 18-60 years old
 - SLE diagnosis based on the EULAR/ACR 2019 criteria
 - Lupus nephritis diagnosis by renal biopsy based on the ISN/RPS 2016
 - Estimated GFR >30ml/min/m²
- Exclusion criteria
 - Diabetes mellitus, malignancy, hematological disorder
 - Presence of chronic, active or recent (<6 months) infection
 - Therapy with monoclonal antibodies in the past or cyclophosphamide during the last 6 months

MATERIAL AND METHODS (2)

Flow cytometry

- cTFH (CD4+CD45RA-CXCR5+) cells, and their subsets, defined as
- cTFH1 (CD4+CD45RA-CXCR5+CXCR3+CCR6-),
- cTFH2 (CD4+CD45RA-CXCR5+CXCR3-CCR6-),
- cTFH17 (CD4+CD45RA-CXCR5+CXCR3-CCR6+)
- activated-cTFH or cTFH-ICOS+ (CD4+CD45RA-CXCR5+ICOS+).



RESULTS

	SLE	HC	<i>p</i>
n	14	8	
Age (years)	38(20-60)	31.5(28-41)	NS
Female n (%)	13 (92.8)	8 (100)	NS
WBC (cell/ μ L)	8100 (4800-12500)	5750 (4400-8700)	0.004
Neutrophils (cell/ μ L)	5900 (3400-11400)	3250 (2700-5900)	0.002
Lymphocytes (cell/ μ L)	1231 (500-3962)	1190 (602-2057)	NS
Serum urea (mg/dl)	31 (16-56)	28 (15-60)	NS
Serum creatinine (mg/dl)	0.69 (0.61-1.4)	0.59 (0.55-0.9)	NS
Time since SLE diagnosis (months)	79.5 (1-348)	-	-
Time since LN diagnosis (months))	12 (1-140)	-	-
C3 (mg/dl)	63.7 (24.9-141)	-	-
C4 (mg/dl)	12 (3.9-30.4)	-	-
SLEDAI score (on evaluation)	6 (4-21)	-	-
Uprot (mg/24h)	1067.5 (44-12000)	-	-

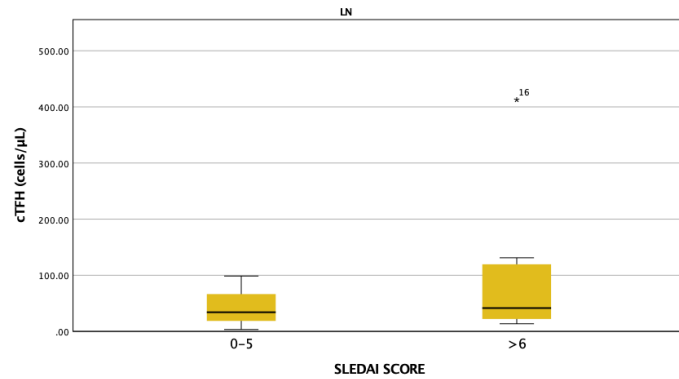
RESULTS

HC vs LN

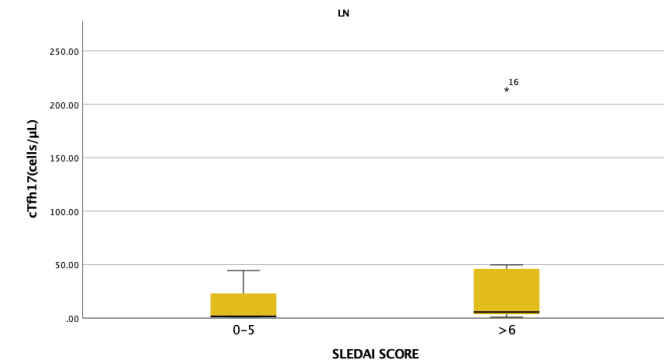
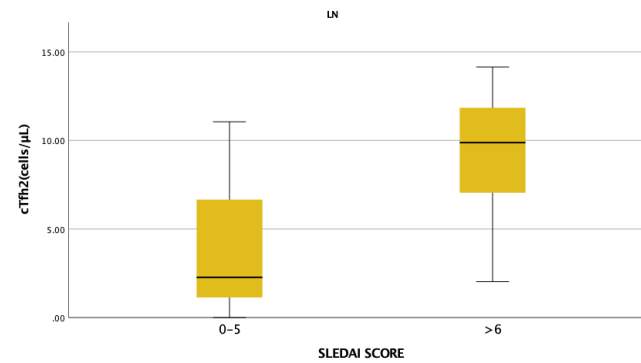
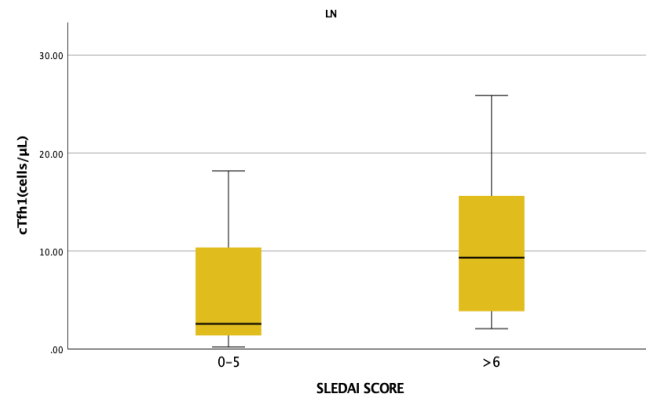
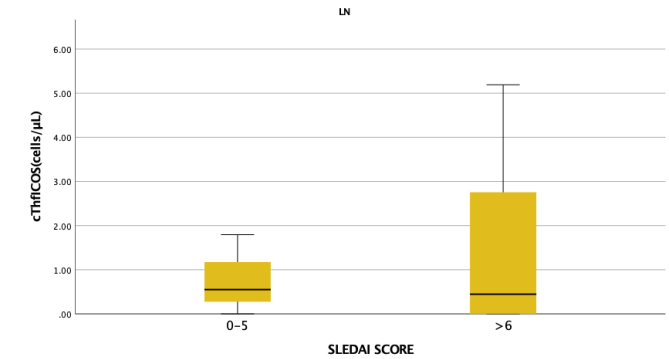
	HC	LN	<i>p</i>
n	8	14	
Lymphocytes (cells/μL)	1388 (601-2057)	1231 (500-3960)	0.721
CD4 (%)	42.75 (35.6-45.2)	46.5 (35-59.4)	0.061
CD4(cells/μL)	601.5 (232-732)	564 (222-1842)	0.708
cTfh(%)	8.8 (1.9-12.1)	11 (0.6-22.4)	0.708
cTfh(cells/μL)	43.5 (13.3-69.6)	41.6 (3.4-412.7)	0.708
cTfh1(%)	4 (1.6-29.1)	7.1 (2.6-62.2)	0.206
cTfh1(cells/μL)	1.9 (0.4-13.3)	6.7 (0.2-25.9)	0.16
cTfh2(%)	3.9 (1.5-70)	8.8 (0-42.3)	0.673
cTfh2(cells/μL)	1.82 (0.46-32)	9.88 (0-14.15)	0.261
cTfh17(%)	43.5 (1.3-52.7)	39.5 (1.9-53.5)	0.64
cTfh17(cells/μL)	16.9 (0.6-29.2)	6.58 (0.79-213.8)	0.708
cThfICOS(%)	0.05 (0-0.3)	0.2 (0-0.7)	0.397
cThfICOS(cells/μL)	0.256 (0-1)	0.9 (0-5.2)	0.247

RESULTS

SLEDAI-2K SCORE

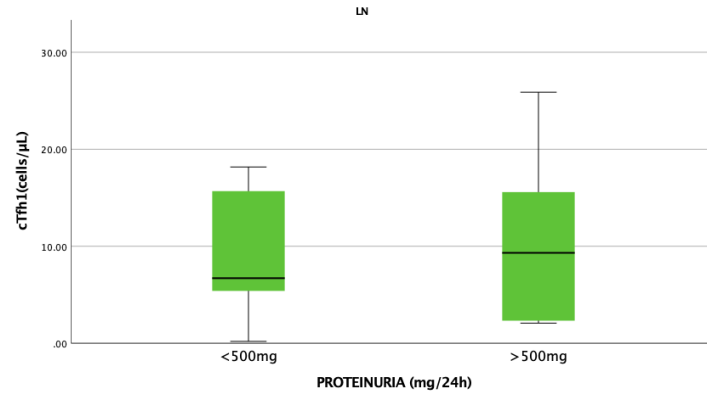


	0-5	>6	<i>p</i>
N	4	7	
Female	4	6	NS
Age (ys)	37.5 (24-50)	39 (20-60)	NS

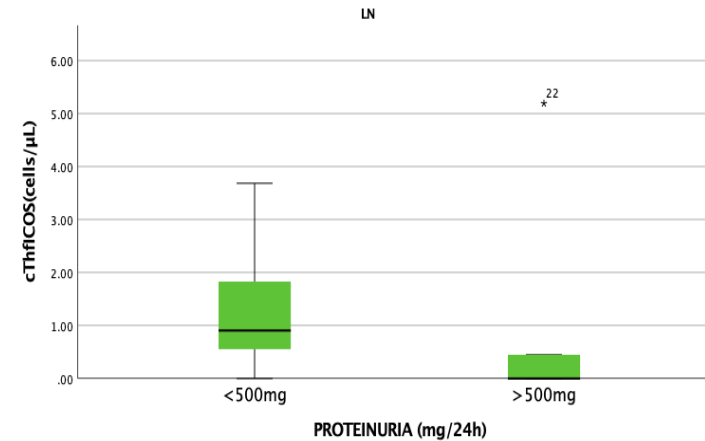
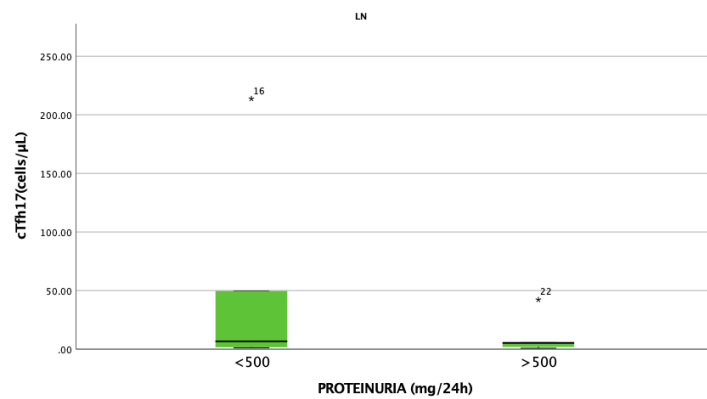


RESULTS

PROTEINURIA



	<500mg/24h	>500mg/24h	<i>p</i>
N	5	4	
Female	4	3	NS
Age (ys)	46 (24-70)	33 (20-43)	NS



CONCLUSIONS

- cTFH cells were similar in LN compared to HC
- An obvious shift towards cTFH1 and cTFH2, against cTFH17 was noticed in LN patients compared to HC
- Increased SLEDAI score was followed by an increase in all cTFH compartments (cTFH1, cTFH2, cTFH17, cTFH-ICOS+)
- Proteinuria levels were associated with increased cTFH1 but reduced cTFH17 and cTFH-ICOS+
 - Involvement of different pathogenic mechanisms?
 - possibility of an appealing therapeutic target for LN?

THANK YOU!
