higher expression of adhesion molecules suggesting a link between this pathway and changes in SGEs immune phenotype.

Disclosure of Interests: : Serena Colafrancesco: None declared, cristiana barbati: None declared, Valentina Iannizzotto: None declared, Linda Mastromanno: None declared, Saba Nayar: None declared, Elena Pipi: None declared, angelica gattamelata: None declared, francesco ciccia Grant/research support from: pfizer, novartis, roche, Consultant of: pfizer, novartis, lilly, abbvie, Speakers bureau: pfizer, novartis, lilly, abbvie, cristiano alessandri Grant/research support from: Pfizer, Francesca Barone: None declared, fabrizio conti Speakers bureau: BMS, Lilly, Abbvie, Pfizer, Sanofi, Roberta Priori: None declared
DOI: 10.1136/annrheumdis-2020-eular.5212

THU0221

EVIDENCE FOR A PATHOGENIC ROLE OF EXTRA-FOLLICULAR, IL-10 PRODUCING CCR6+B-HELPER T-CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS

M. Gerosa^{1,2}, F. Facciotti³, P. Larghi³, R. Bosotti³, C. Vasco³, N. Gagliani^{4,5}, C. Cordiglieri³, E. Rottoli⁶, A. E. Penatti⁷, L. M. Argolini², B. Karnani³, Y. Kobayashi⁴, M. Bombaci³, J. P. Van Hamburg⁸, R. Gualtierotti⁹, S. Gatti¹⁰, S. Torretta¹⁰, L. Pignataro^{7,11}, S. W. Tas⁸, R. Caporali^{2,12}, S. Abrignani^{3,12}, M. Pagni^{3,9}, F. Grassi^{3,9}, P. L. Meroni¹³, R. Flavell⁴, J. Geginat³. ¹University of Milan, Department of Clinical Science and Community Health, Milan, Italy; ²ASST PINI-CTO, Clinical Rheumatology Unit, Lupus Clinic, Milan, Italy; ³INGM-National Institute of Molecular Genetics "Romeo ed Enrica Invernizzi", Milan, Italy; ⁴Department of Immunobiology, School of Medicine, Yale University, New Haven, United States of America; ⁵Department of Medicine & Department of General, Visceral and Thoracic Surgery, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; ⁶Institute for Research in Biomedicine, Bellinzona, Switzerland; ⁷University of Milan, Milan, Italy; ⁸Amsterdam UMC, University of Amsterdam, Academic Medical Center, Amsterdam, Netherlands; ⁹Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; ¹⁰Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico, Milan, Italy; ¹¹Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico Milano, Milan, Italy; ¹²Department of Clinical Science and Community Health, University of Milan, Milan, Italy; ¹³IRCCS Istituto Auxologico Italiano, Milan, Italy

Background: IL-10 plays a key role in systemic lupus erythematosus (SLE) pathogenesis, promoting B-cell response. IL10 is mainly secreted by regulatory T-cells, but follicular helper T-cells (T_{FH}), also produce it. We previously identified a subset of CCR6⁺IL7R⁺T-cells in human tonsils providing IL-10-dependent B-cell help. These CCR6⁺T-cells were able to produce IL-10, inducing IgG production.

Objectives: to investigate a possible role of CD4⁺CCR6⁺IL7R⁺T-cells in SLE pathogenesis.

Methods: 37 patients fulfilling the ACR criteria for SLE have been included. Disease activity was assessed by 2k-SLEDAI. PBMC were analyzed by flow cytometry, using specific lineage markers. CCR6⁺IL7R⁺T-cells purified from total PBMC of SLE patients or healthy donors (HD) were co-cultured with autologous CD20⁺B-cells. IL-10, IL-17, total IgG and anti-dsDNA antibodies titers in patients serum and culture supernatants were assessed by ELISA. Embedded sections of lymph nodes from 8 SLE patients were analyzed by immunofluorescence (IF).

Results: IL10 levels were significantly higher in SLE patients (Fig 1A). CD4⁺CCR6⁺IL7R⁺T-cells were significantly increased in SLE, in particular in those with higher disease activity and higher IL10 levels. CD4⁺CCR6⁺IL7R⁺T-cells levels associated with anti-dsDNA positivity. CCR6⁺IL7R⁺T-cells of SLE patients induced production of IgG and anti-dsDNA IgG (in anti-dsDNA + patients) from autologous B-cells, providing spontaneous help for autoantibody production *ex vivo* (Fig 1B-C). The IF study of lymph nodes of SLE patients showed that IL-10-producing CCR6⁺T-cells were highly abundant and co-localized with B-cells at follicle margins.

Fig 1

Conclusion: our study revealed a novel population of extra-follicular B-helper T-cells, which produce IL-10 and could play a prominent pathogenic role in SLE. Further studies will clarify if this potentially pathogenic cell population might represent a possible future therapeutic target.

References:

- [1] Facciotti F. J Allergy Clin Immunol. 2016; Geginat J. Semin Immunol. 2019; Tsokos GC. Nat Rev Rheumatol. 2019

Tab 1: SLE patients characteristics

		(n=37)
Demographics		
Female/Male, n		37/5
Age, years, median (IQR)		44 (38-49)
Disease duration, years, median (IQR)		19 (11-26)
Lab tests		
ANA		86%
*anti-dsDNA (%)		46%
medium/high titre		41%
Disease activity and clinical manifestations		
SLEDAI-2K, median (min-max)		3.5 (0-24)
Moderate/high activity		19%
Ongoing therapy		
Prednisone dose mg/day, median (IQR)		7,5mg (2,5 – 20)
hydroxychloroquine		78%
Immunosuppressants		87%

Fig 2

Disclosure of Interests: : Maria Gerosa: None declared, Federica Facciotti: None declared, Paola Larghi: None declared, Roberto Bosotti: None declared, Chiara Vasco: None declared, Nicola Gagliani: None declared, Chiara Cordiglieri: None declared, Elsa Rottoli: None declared, Alessandra Emiliana Penatti: None declared, Lorenza Maria Argolini: None declared, Bhavna Karnani: None declared, Yasushi Kobayashi: None declared, Mauro Bombaci: None declared, Jan Piet Van Hamburg: None declared, Roberta Gualtierotti: None declared, Stefano Gatti: None declared, Sara Torretta: None declared, Lorenzo Pignataro: None declared, Sander W. Tas: None declared, Roberto Caporali Consultant of: AbbVie; Gilead Sciences, Inc.; Lilly; Merck Sharp & Dohme; Celgene; Bristol-Myers Squibb; Pfizer; UCB, Speakers bureau: Abbvie; Bristol-Myers Squibb; Celgene; Lilly; Gilead Sciences, Inc.; MSD; Pfizer; Roche; UCB, Sergio Abrignani: None declared, Massimiliano Pagni: None declared, Fabio Grassi: None declared, Pier Luigi Meroni: None declared, Richard Flavell: None declared, Jens Geginat: None declared

DOI: 10.1136/annrheumdis-2020-eular.1532