Abstract 1803 Table 2 Serologies

	BC4d and/or EC4d Pos	BC4d and EC4d Neg	Overall	
	n=85	n=100	n=185	p-value
MAP Positive (n=184)	77 (92%)	52 (52%)	129 (70%)	<0.0001
ANA (ELISA) positive	80 (94%)	71 (71%)	151 (82%)	<0.0001
Anti-dsDNA (Crithidia luciliae) positive	46 (54%)	20 (20%)	66 (36%)	<0.0001
Low C3 or C4	32 (38%)	11 (11%)	43 (23%)	<0.0001
Anti-Sm positive (n=159)	13 (19%)	4 (4%)	17 (11%)	0.008
Anti-U1RNP positive (n=181)	36 (44%)	22 (22%)	58 (32%)	0.002
Anti-RNP70 positive	24 (29%)	14 (14%)	38 (21%)	0.02
Anti-Cq1 positive	26 (31%)	14 (14%)	40 (22%)	0.007
APLA positive				
ACL IgM+, ACL IgG+, B2GP IgM+ or B2GP IgG+ (n=172)	16 (21%)	8 (9%)	24 (14%)	0.03
Anti-Ro60 positive	45 (53%)	40 (40%)	85 (46%)	0.1
Anti-Ro52 positive	26 (31%)	18 (18%)	44 (24%)	0.06
Anti-La/SSB positive	9 (11%)	6 (6%)	15 (8%)	0.3

scores. Numerically more CB-CAPs positive patients had SLEDAI rash and met SLEDAI renal criteria. There was no difference in medication use or features of polysymptomatic distress such as widespread pain, fatigue, or depression (table 1).

Serologic activity emerged as a hallmark of CB-CAPs positivity. CB-CAPs positive patients were more likely to have positive ANA, anti-Sm, anti-U1RNP, anti-RNP70, anti-C1q and anti-phospholipid antibodies than those who were CB-CAPs negative (table 2). Serologic markers of disease activity including elevated levels of anti-dsDNA and decreased C3 or C4 also tracked with CB-CAPs positivity (table 2).

Conclusion Narrowing the heterogenous clinical and immunologic features of SLE into endotypical subgroups is a crucial step toward precision medicine and personalized care in SLE. CB-CAPs positive patients represent an important subset of patients who are characterized by greater serologic activity and internal organ pathology. Moreover, the cumulative burden of SLE activity is greater in those with CB-CAPS positivity, as measured by the ACR/EULAR criteria score. CB-CAPs positivity could provide both diagnostic and prognostic information with implications for improved disease monitoring. Further studies are needed to assess the effects of targeted therapeutics and the long-term outcomes of the CB- CAPs positive endotype.

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1901 THE TOLEROGENIC EFFECTS OF IL-2 ON T REGULATORY CELLS (TREGS) ARE TGF-β DEPENDENT

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Background We and others have previously shown that IL-2 is essential for TGF-β to allow conversion of naïve $CD4^+CD25^-$ T cells into $CD4^+CD25^+Foxp3^+$ Tregs. To further those studies, we recently used IL-2- loaded nanoparticles (NPs) coated with anti-CD2 antibody (Ab) to target both T cells and NK cells in lupus mice, identifying a key role of a population of TGF-β-producing NK cells in the induction of the $CD4^+$ and $CD8^+$ $Foxp3^+$ Tregs that prevented disease.

Methods Anti-CD2 Ab-coated NPs made of polylactic-co-glycolic acid (PLGA) and encapsulating IL-2 or IL-2/TGF-β were used to inhibit a lupus-like disease characterized by a human anti-mouse graft versus host disease (GVHD) that develops after transfer of human PBMCs into immunodeficient NOD SCID mice.

Research NPs containing only IL-2 protected mice from autoimmune disease similarly to NPs containing both IL-2 and TGF-β. Remarkably, the blockade of TGF-β signaling with an ALK-V inhibitor not only abolished the protective effects of the NPs but also reduced the survival of the diseased mice.

Conclusions In the absence of TGF-β, IL-2 induces pathogenic T effector cells instead of promoting the induction of protective Tregs. This key role of TGF-β in the induction of Tregs has relevance for the ongoing clinical trials that employ low-dose IL-2 or IL-2 muteins in SLE and other autoimmune diseases to expand functional Tregs. Since lymphocyte production of TGF-β is decreased in SLE, our study suggests that in the immunotherapeutic management of SLE, one needs to correct the deficits of both IL-2 and TGF-β to optimally induce and expand functional Tregs.

2001 α-KETOGLUTARATE-DEPENDENT KDM6 HISTONE DEMETHYLASES EPIGENETICALLY REGULATE INTERFERON STIMULATED GENE EXPRESSION IN LUPUS

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The authors have declared that no conflict of interest exists.

Objective To investigate the hypothesis that interferon (IFN) stimulated gene (ISG) expression in systemic lupus erythematosus (SLE) monocytes is linked to changes in metabolic reprogramming and epigenetic regulation of ISG expression.

Methods Monocytes from healthy volunteers and SLE patients at baseline or following IFNα treatment were analyzed by extracellular flux analysis, proteomics, metabolomics, chromatin immunoprecipitation and gene expression.

Treatment of SLE monocytes or pristane-treated C57BL/6 mice with GSKJ4 assessed the effects of histone demethylases KDM6A/B on ISG expression.