Remission-Relapses in Systemic Lupus Erythematosus

clinical and immunological insights

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31-05-2025

Περίγραμμα

- Flares: prognostic significance
- Presumed mechanisms and clinical applications
- Remission and ”treating-to-target”
- Immunological basis of remission in SLE
- Therapeutic implications

Τι ορίζουμε ως «έξαρση» στο ΣΕΛ

” ***A flare is a measurable increase in disease activity in one or more organ systems involving new or worse clinical signs and symptoms and/or laboratory measurements.***

It must be considered clinically significant by the assessor and usually, there would be at least consideration of a change or an increase in treatment "

LUPUS™ Foundation of America, Inc.

Ruperto N, et al. *Lupus*. 2011; 20: 453–62

Ποσοτικοποίηση των εξάρσεων σε ασθενείς με ΣΕΛ

Mild/Moderate flare
• **Increase in SLEDAI by ≥3 points** (but not to >12 points)
• **New or worse**: discoid, photosensitive, profundus, cutaneous vasculitis, bullous lupus, nasopharyngeal ulcers, serositis, arthritis, fever
• **Increase or added prednisone, but to <30 mg/day (equivalent)**
• **Added NSAID or HCQ** (for SLE activity)
• Increase in PhGA by ≥1 (but not to >2.5)

Petri M et al. N Engl J Med 2005;353

Ποσοτικοποίηση των εξάρσεων σε ασθενείς με ΣΕΛ

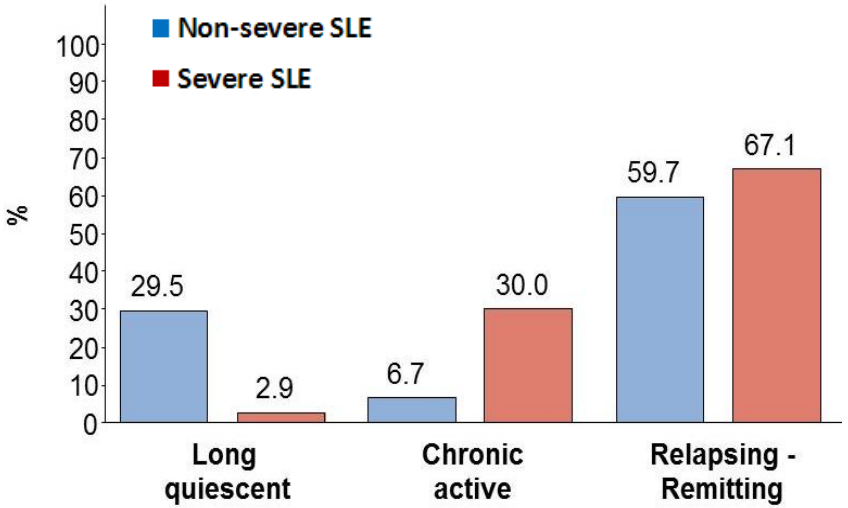
Mild/Moderate flare	Severe flare
• Increase in SLEDAI by ≥3 points (but not to >12 points)	• **Increase in SLEDAI to >12 points**
• New or worse: discoid, photosensitive, profundus, cutaneous vasculitis, bullous lupus, nasopharyngeal ulcers, serositis, arthritis, fever	• **New/worse:** CNS-SLE, vasculitis, nephritis, myositis, platelet <60.000/μL, hemolytic anemia (Hb <7 g/L or ↓ Hb > 3 g/L) (* requiring doubling of prednisone dose or ≥30 mg/day or hospitalization)
• Increase or added prednisone, but to <30 mg/day (equivalent)	• Increase or added **prednisone to ≥30mg/day** equivalent • Pulses of **IV methylprednisolone**
• Added NSAID or HCQ (for SLE activity)	• **Added CY, AZA, MTX or MMF** • **New biological drugs** • **Hospitalization <u>due to SLE activity</u>**
• Increase in PhGA by ≥1 (but not to >2.5)	• Increase in PhGA to >2.5

Petri M et al. N Engl J Med 2005;353

Η πλειοψηφία των ασθενών με ΣΕΛ ακολουθεί το πρότυπο με εναλλαγές «εξάρσεων» και «υφέσεων»

LyCOS

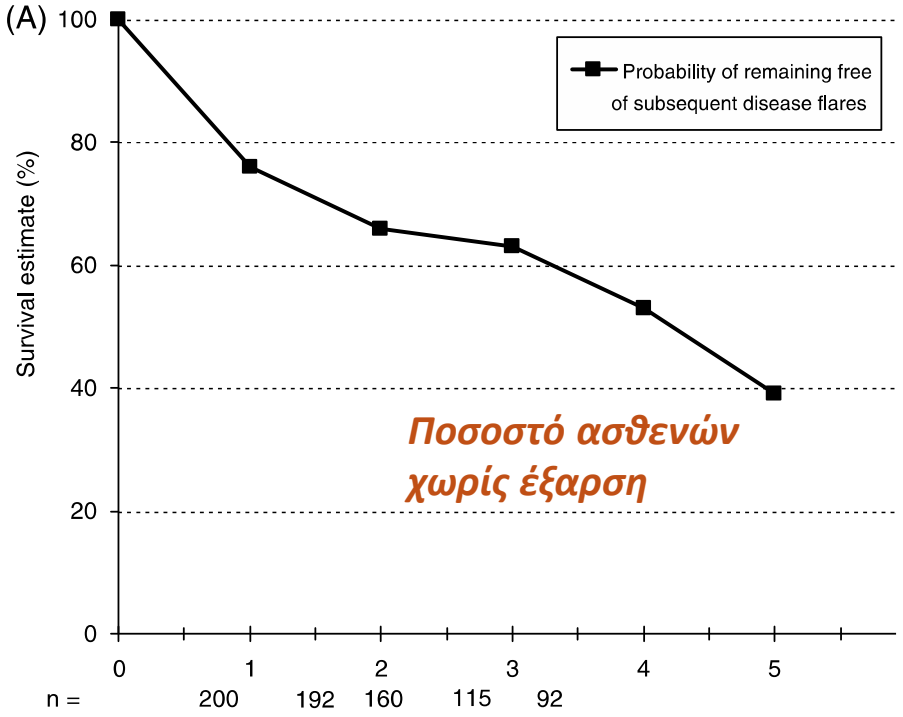
Ασθενείς ΣΕΛ	381
Φύλλο (♀)	91%
Ηλικία (έτη) (mean ± SD)	47.3 ± 15.2
Περιγραφή νόσου	
Μη-μείζονα	81.0%
Μείζονα [#]	**19.0%**
Νεφρίτιδα	19.7%
ενεργός νεφρίτιδα	7.1%
Πρότυπο ενεργότητας ΣΕΛ	
Μακροχρόνια ύφεση	24.7%
Υποτροπιάζουσα	**60.6%**
Χρόνια ενεργός	**11.6%**



[#] *Συμμετοχή του νεφρικού, νευρολογικού, καρδιαγγειακού ή αναπνευστικού συστήματος τους τελευταίους 6 μήνες, με ανάγκη θεραπείας με πρεδνιζόνη >7.5 mg/day ή/και ανοσοκατασταλτικά*

Bertsias G, et al. *Lupus*. 2016; 25(12):1385-94

Οι εξάρσεις στο ΣΕΛ είναι συχνές παρά τη λήψη θεραπείας



Συχνότητα

- ≈ 20–25% στα πρώτα 1–2 έτη
- ≈ 40–66% στα 5–10 έτη

Σοβαρότητα

- Ήπιες/μέτριες εξάρσεις (70-80%)
- Σοβαρές (20-30%)

Κλινικές εκδηλώσεις, κυρίως:

- Βλεννογονο-δερματικές
- Αρθρίτιδα
- Αιμοποιητικό
- Νεφροί (30–40%)
- Ανοσολογικό σύστημα

Conti F, *et al*. *PLoS One*, 2012; 7:e45934, Gilboe IM, *et al*. *J Rheumatol*, 2001; 28:266-74, Nikpour M, *et al*. *Arthritis Rheum*, 2009; 61:1152–1158, Vlachoyiannopoulos PG, *et al*. *Lupus*, 1993; 2:303-12, Nossent J, *et al*. *Lupus*. 2010; 19:949-56, Zen M, *et al*. *Clin Exp Rheumatol*, 2012; 30:856–863, Petri M, *et al*. *J Rheumatol*, 2009; 36:2476–2480, Ines L, *et al*. *Rheumatology*, 2014; 53:85–89, Alonso MD, *et al*. *Medicine*, 2011; 90:350-8, Bujan S, et al. *Ann Rheum Dis*, 2003; 62:859-65

Flares in the Cretan SLE registry (I)

N=354 with moderate/severe SLE and follow-up ≥6 months → median follow-up time: 66 months

No. patients with no flares, 1 flare or ≥2 flares:

	Any flare*	**Mild-moderate***	**Severe***
No flares	29	61	90
One flare	56	94	80
≥2 flares	269	199	184

No. flares per patient

Median	3	2	1
P25	2	1	0
P75	6	3	2

** excluding baseline visit since all patients had flare at baseline*

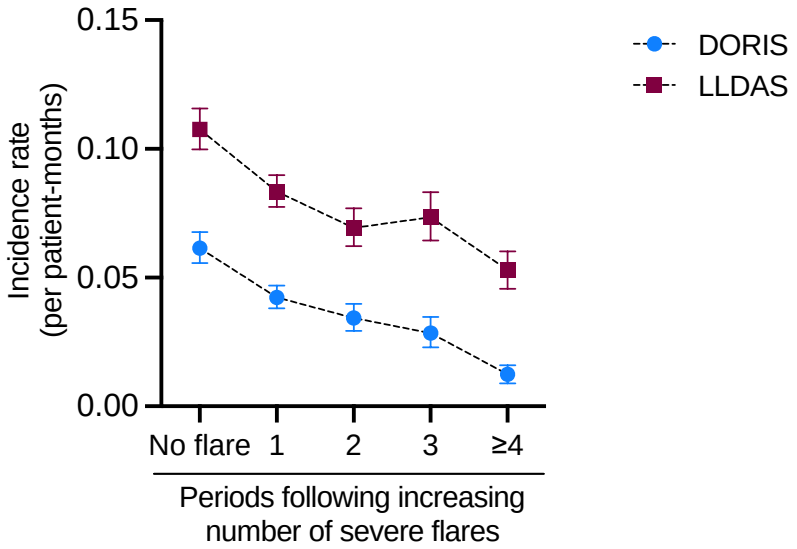
Unpublished data

Flares in the Cretan SLE registry (II)

Flares as a driver of organ damage in SLE patients

	Mild/moderate flares				Severe flares			
	IRR	95% LB	95% UB	P value	IRR	95% LB	95% UB	P value
SDI increase at next visit	1.46	1.02	2.08	0.0396	1.68	1.18	2.39	0.0043
SDI increase within 6 months	1.33	1.02	1.73	0.0357	1.86	1.37	2.51	0.0001
SDI increase within 12 months	1.23	1.00	1.50	0.0495	1.63	1.29	2.05	0.0000
SDI increase within 24 months	1.28	1.06	1.54	0.0091	1.65	1.33	2.04	0.0000

Each flare reduces the likelihood of future attainment of low disease activity (LLDAS) or remission (DORIS)



Unpublished data

Ασθενείς σε αυξημένο κίνδυνο για έξαρση ΣΕΛ

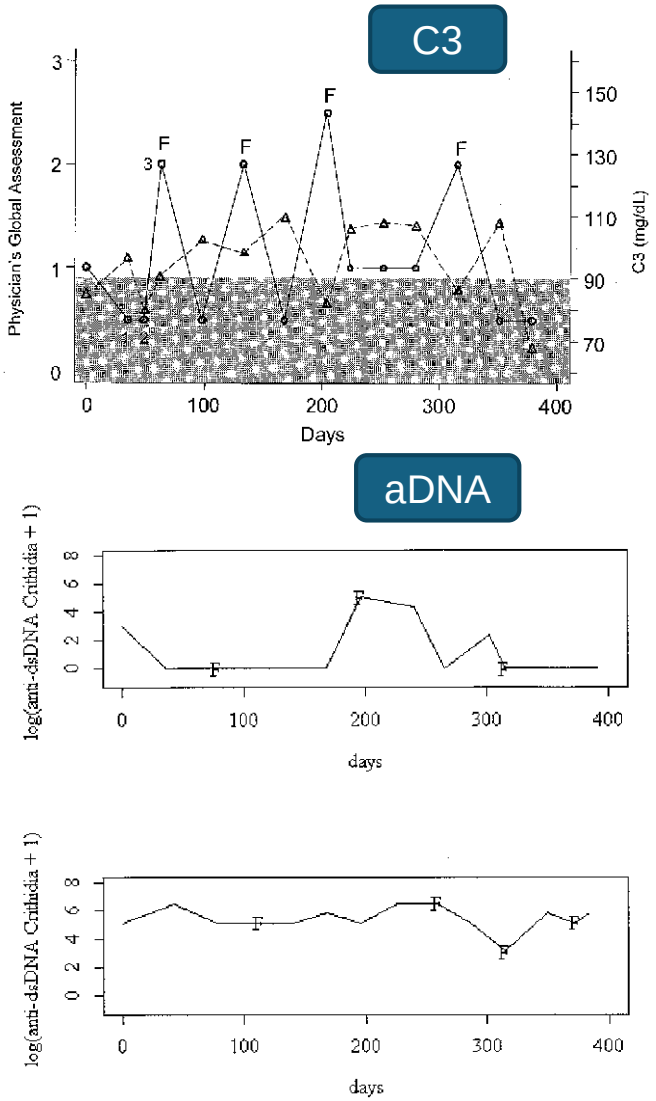
Risk factors

- **Ethnicity** (African-American, OR 1.8)
- **Younger patients** (≤25 years) (HR 2.1)
- **Early disease** (≤3 years)
- **Previous disease activity** (OR 1.42 per 1-unit SLEDAI; neurological [OR 10.9, HR 2.5–3.1]; renal [HR 2.0–4.8]; vasculitis [HR 1.7–1.8]; thrombocytopenia)
- Need for **glucocorticoids** (OR 2.4) or **immunosuppressive agents** (HR 3.2) during the previous year
- **Withdrawal or no use of HCQ** (OR 2.5)
- **Immunologic activity** (↓ C3/C4 and/or ↑ anti-dsDNA, OR 2.2–2.8)

Kostopoulou M, et al. *Lupus*. 2022; 31(3): 307-318; Conti F, *et al. PLoS One*, 2012; 7:e45934, Nikpour M, *et al. Arthritis Rheum*, 2009; 61:1152–1158, Petri M, *et al. J Rheumatol*, 2009; 36:2476–2480, Ines L, *et al. Rheumatology*, 2014; 53:85–89, Petri M, *et al. Arthritis Rheum*, 2013; 65:2143–2153, Ziakas PD, *et al. Ann Rheum Dis*, 2007; 66: 130–131, Swaak AJ, et al. *Ann Rheum Dis*, 1989; 48: 455–460, Mirzayan MJ, *et al. Rheumatology*, 2000; 39:1316–1319

Ποια η κλινική σημασία της «ανοσολογικής έξαρσης»;

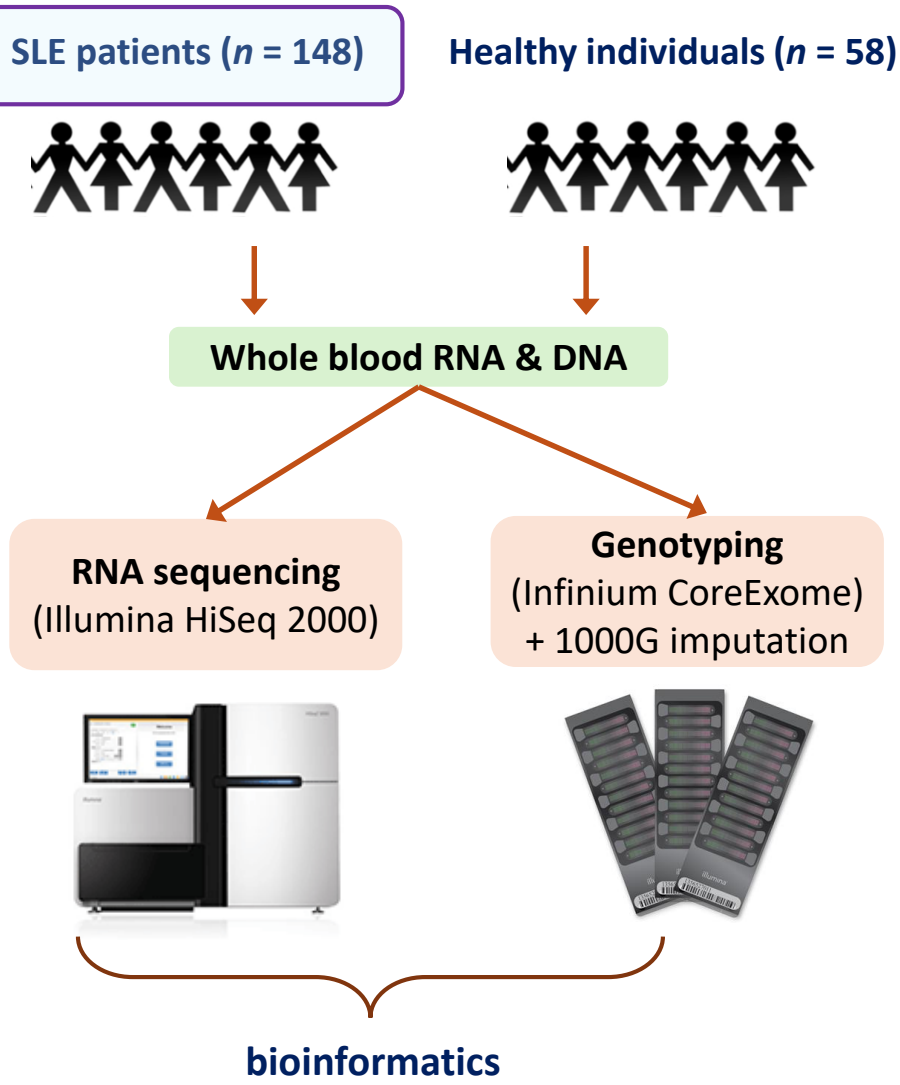
- Συνυπάρχει συχνά με κλινική επιδείνωση της νόσου
- Μέτρια προγνωστική αξία (50–70%) για μελλοντική κλινική υποτροπή
- Η **σύγχρονη προοδευτική μείωση του C3 και αύξηση των anti-dsDNA αντισωμάτων** έχει υψηλή (>90%) ειδικότητα για μελλοντική κλινική υποτροπή του ΣΕΛ
- <u>Η μεμονωμένη ορολογική ενεργότητα ΔΕΝ πρέπει να θεραπεύεται</u>



Ho A, et al. *Arthritis Rheum*. 2001; 44: 2350–7 and 2342–9
Miyawaki A, et al. *Lupus*. 2018; 27: 2093–2100

Molecular characterization of SLE by RNA-seq

SLE characteristics	
Females	**84%**
Ethnicity (Caucasian)	**99%**
Age (years)	**40 ± 14**
No. ACR criteria	**5.3 ± 1.5**
Physician Global Assessment	
Inactive	**32%**
Mild activity	**12%**
Moderate/high activity	**56%**
Major organ involvement	
Renal	**24%**
Hematology	**18%**
CNS	**11%**
Cardiorespiratory	**6%**



Panousis N, *et al*. ARD. 2018

UNIVERSITY OF CRETE

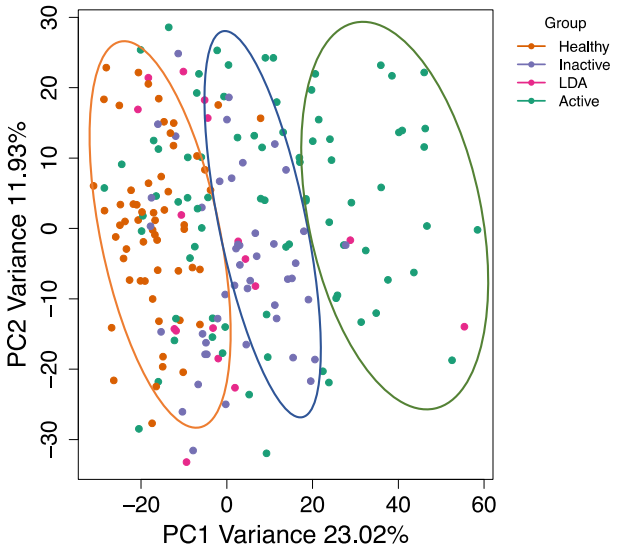
UNIVERSITÉ DE GENÈVE

Changes in transcriptome correlate with SLE activity/severity

PCA analysis of DEGs:

- ✓ **PC1 can differentiate active / inactive SLE / healthy individuals**
  - ✓ ***Low disease activity state* is close to the *inactive state***

A



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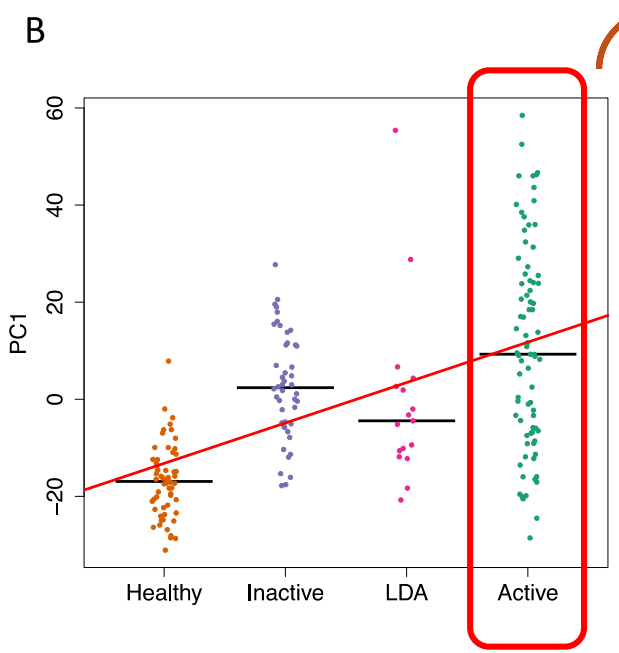


Enrichment in KEGG:

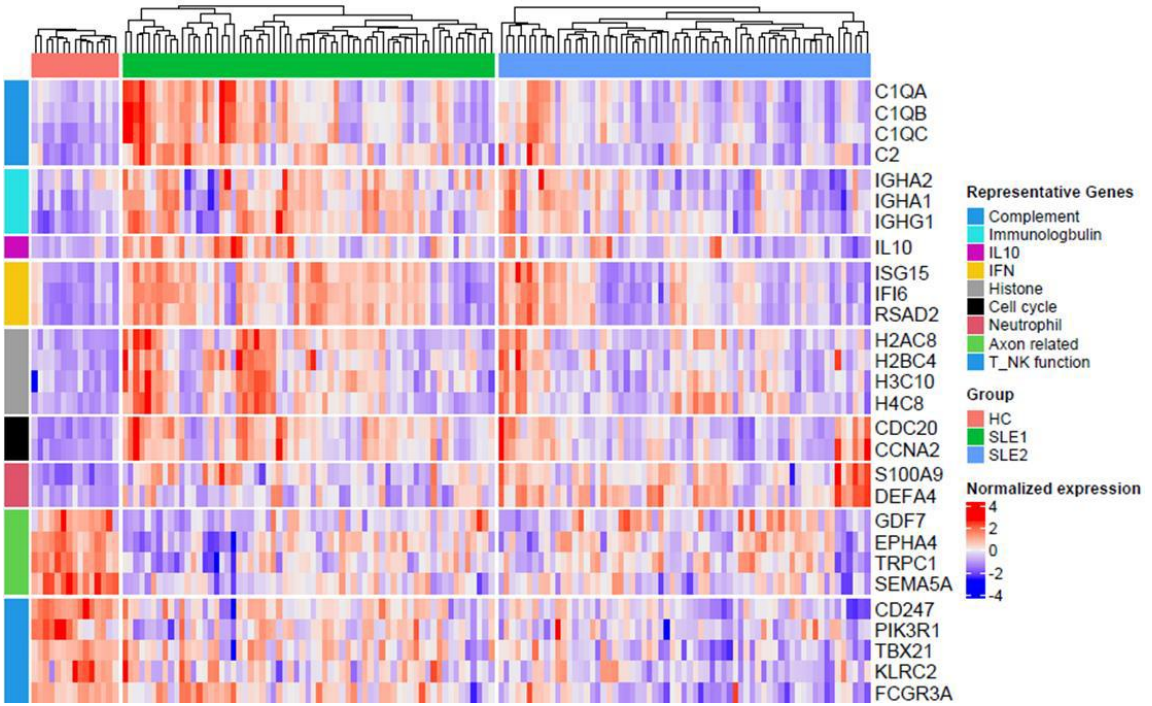
- ✓ **Oxidative phosphorylation**
- ✓ **Cell cycle**

GO terms:

- ✓ **Protein ubiquitination**
- ✓ **Electron transport chain**
- ✓ **Protein phosphorylation**
- ✓ **Response to stress**

Panousis N, *et al*. ARD. 2018

Blood transcriptome analysis during SLE flare (n=65 hospitalized patients)

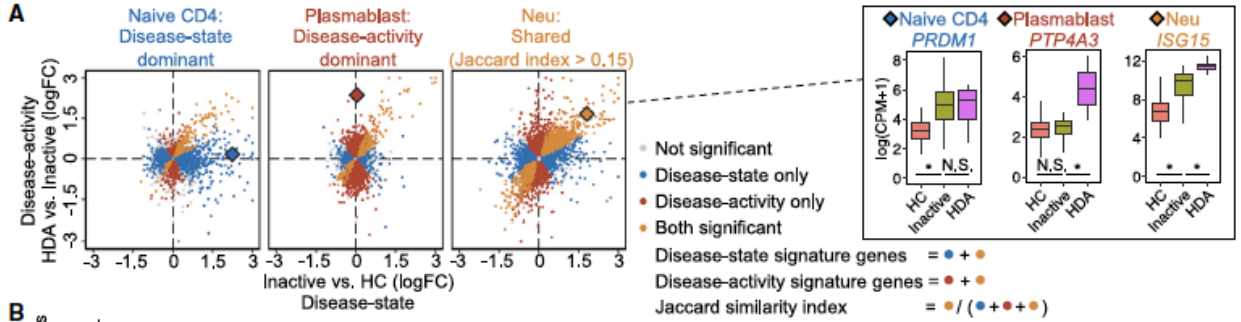


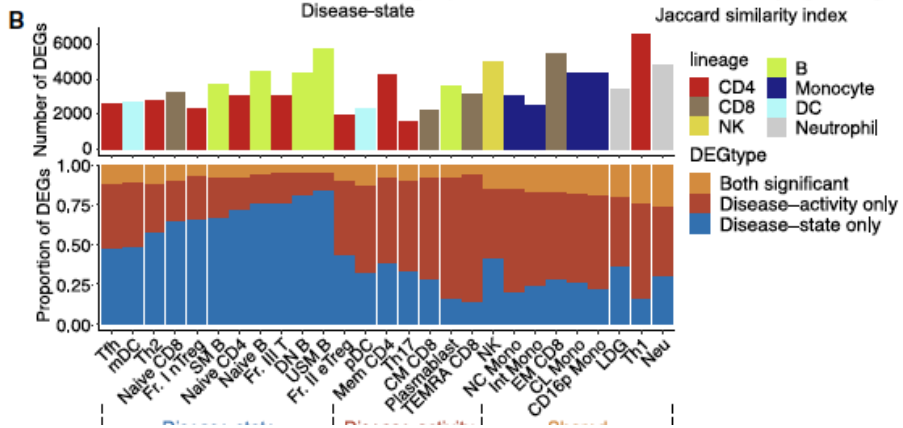
Key genes:

- complement components (C1QA/C1QB/C1QC/C2),
- Immunoglobulins (IGHA2/IGHA1/IGHG1, etc),
- cytokines (IL10),
- interferon-induced molecules (ISG15/IFI6/RSAD2, etc),
- histones (H2AC8/H2BC4/H3C10/H4C8, etc),
- cell checkpoint proteins (CDC20/CCNA2, etc) and
- neutrophil function molecules (S100A9/DEFA4/MPO, etc)

Rheumatology. 2024; 63, 2810–2818

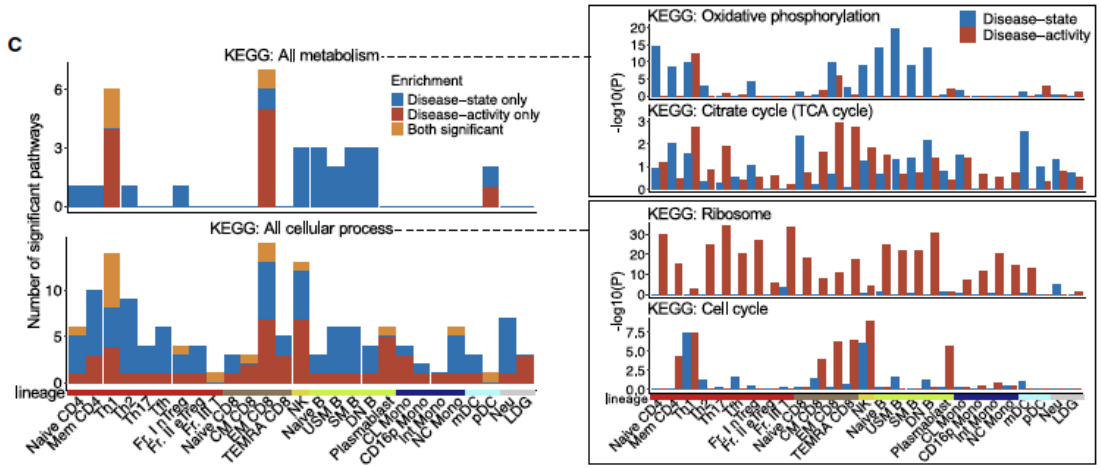
Cell-type-specific contributions to SLE activity/flare





Examples of activity signatures

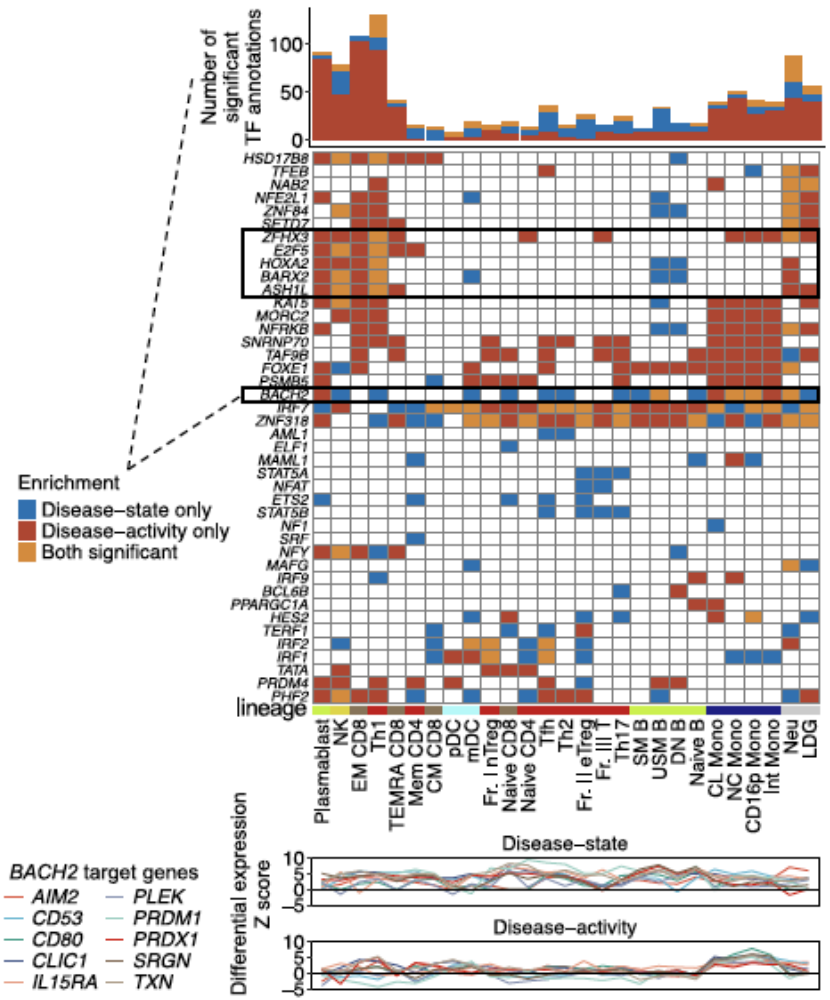
- IL12A/B (switched memory B cells [SM B])
- IL1B/CCL2/CCL8 (monocyte lineage)
- IL18/TNFSF15 (neutrophil lineage)
- IL21 and CXCL13 (B-cell antibody production)



- **Oxidative phosphorylation**: enriched mostly in disease-state signatures (e.g., B-lineage cells)
- **Citrate cycle**: enrichment in activity signatures (e.g., memory CD8-lineage cells).
- **Ribosome and cell cycle** (e.g., Th1, NK, and memory CD8-lineage cells): enriched predominantly in disease-activity

Nakano et al., 2022, Cell 185, 3375–3389

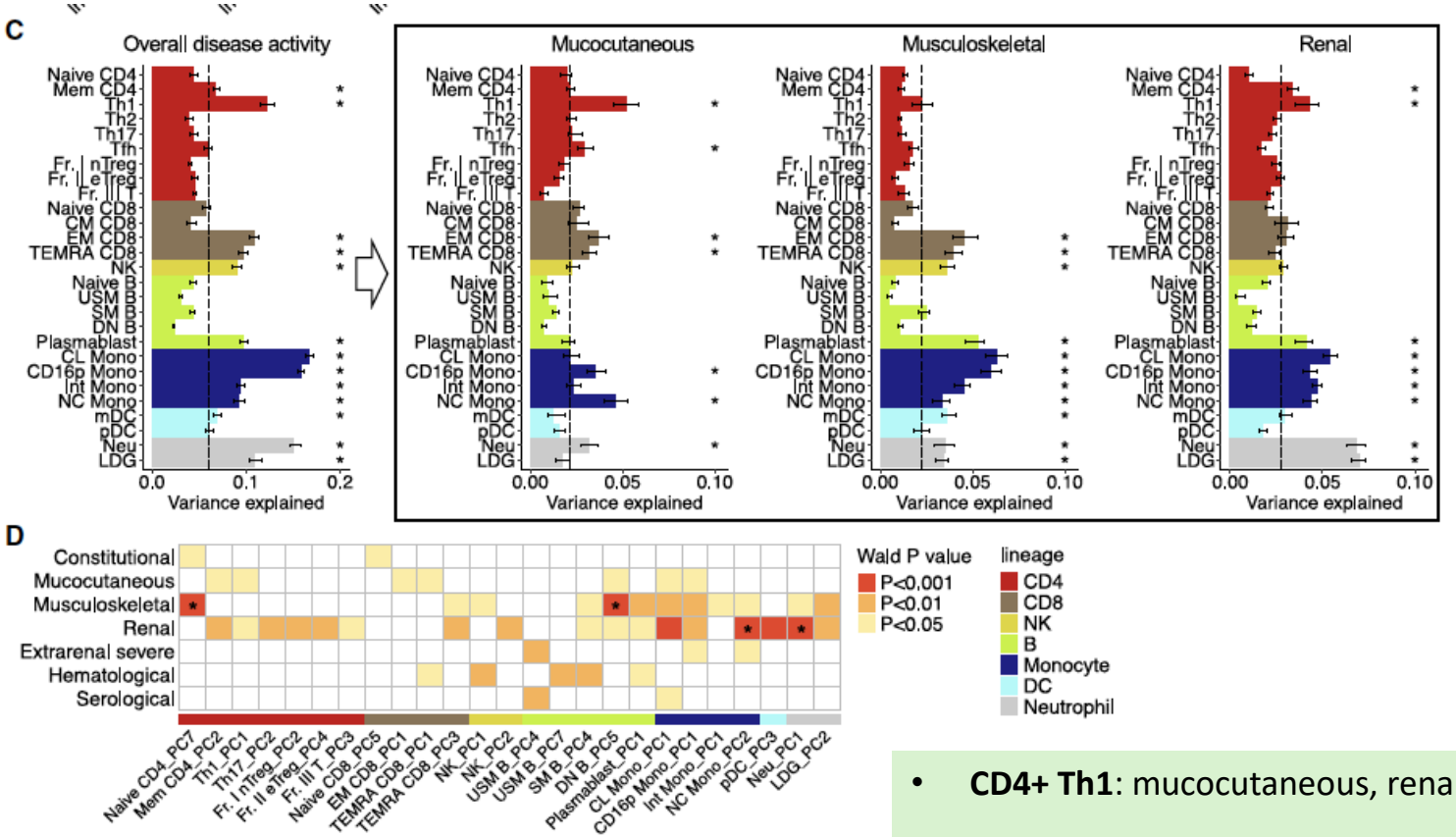
Transcription factors underly activation of SLE



- **Cell cycle regulators** (E2F families): strong enrichment in activity signatures (Th1, NK, memory CD8-lineage cells, and plasmablasts)
- **BACH2**: significant enrichment in disease-activity signatures (monocyte- and neutrophil-lineage cells)

Nakano et al., 2022, Cell 185, 3375–3389

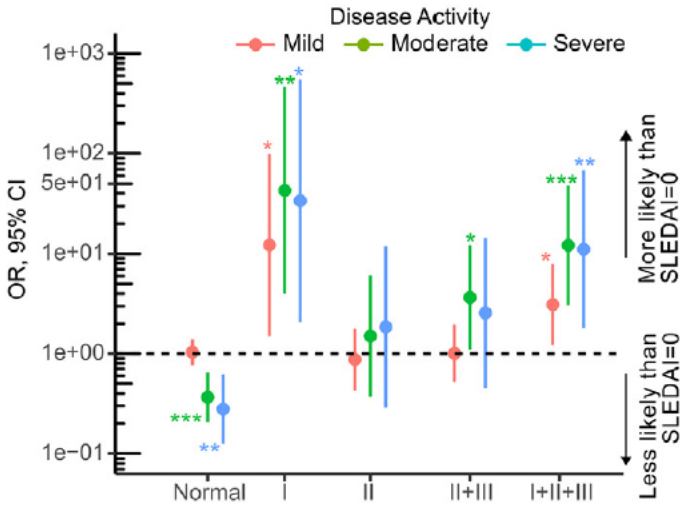
Distinct immune cell types may contribute to organ-specific SLE activity



- **CD4+ Th1**: mucocutaneous, renal
- **Monocyte-lineage** cells: musculoskeletal, renal
- **Neutrophil-lineage cells**: renal
- **Plasmablasts**: renal

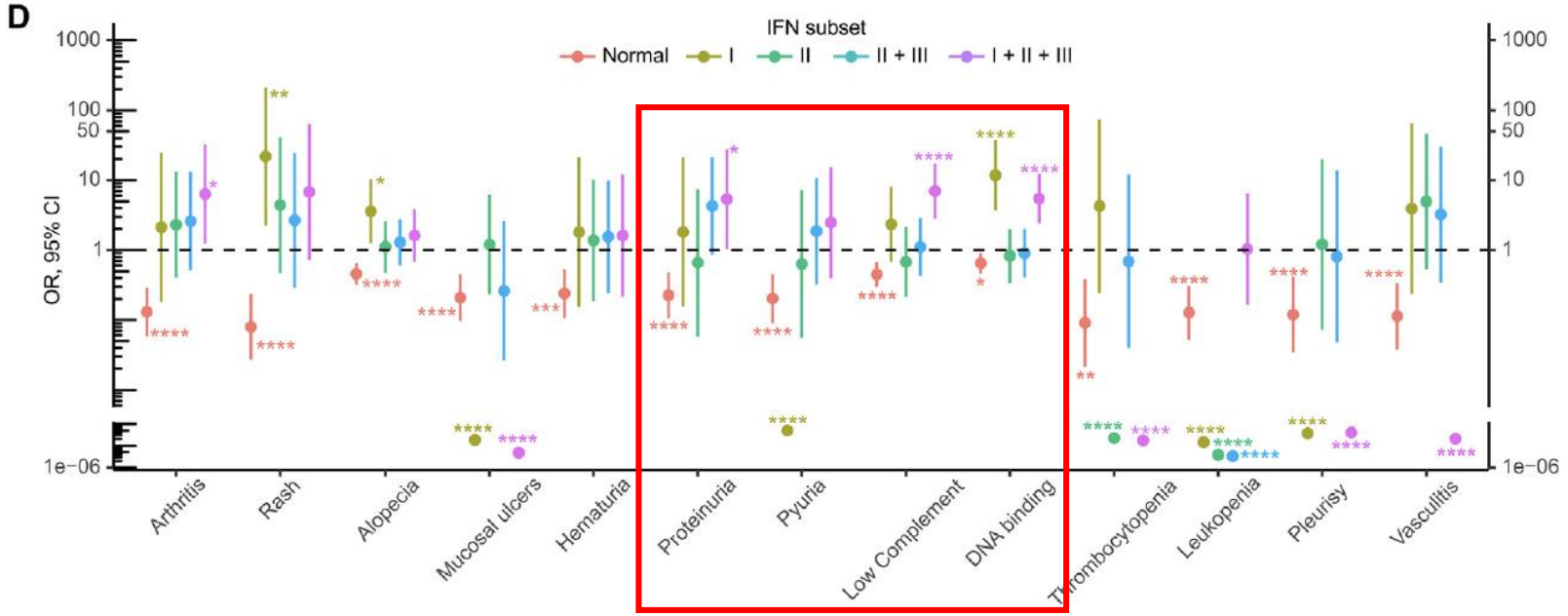
Nakano et al., 2022, Cell 185, 3375–3389

Differential bioactivity from interferons (type I, II, III) in active/flaring SLE



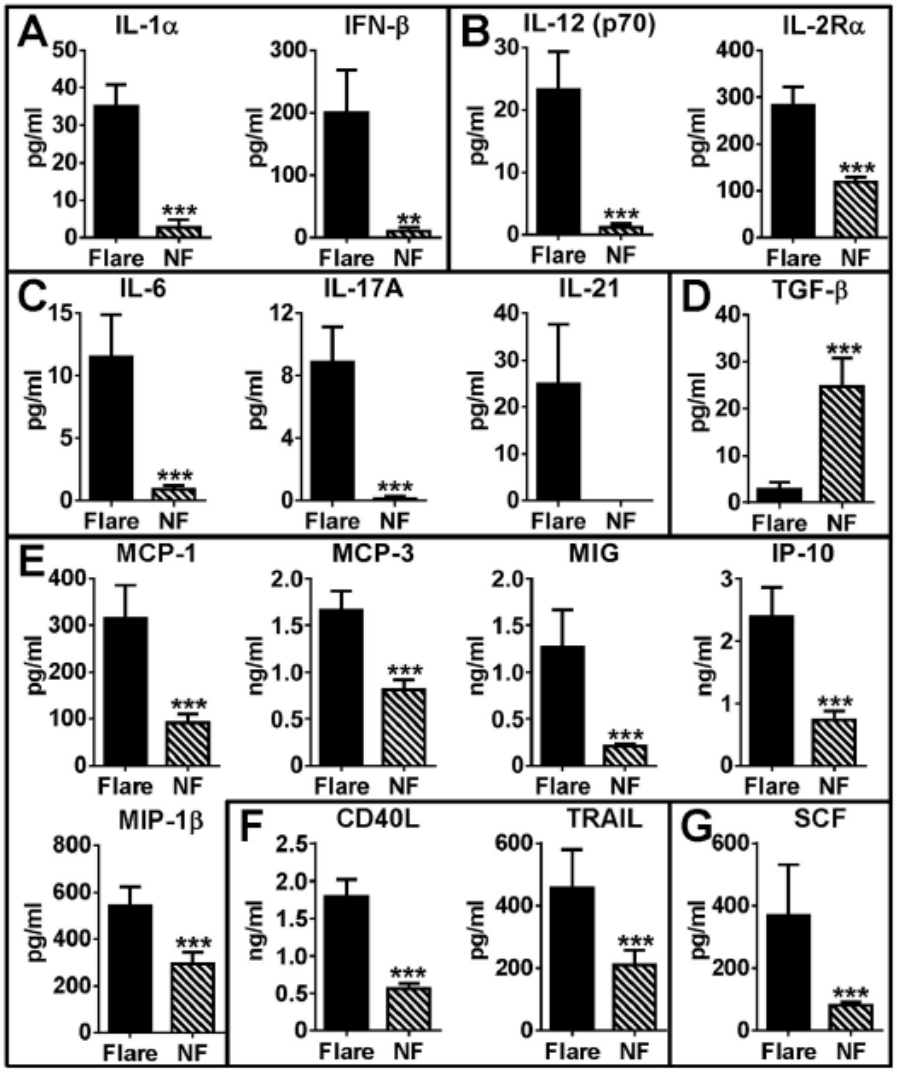
IFN bioassay

Type I IFN corresponds to 'basal' SLE disease; types II and III underly active/severe SLE



Gomez-Banuelos et al., 2024, Cell Reports Medicine 5, 101569

Immunological deregulations precede the clinical appearance of flare

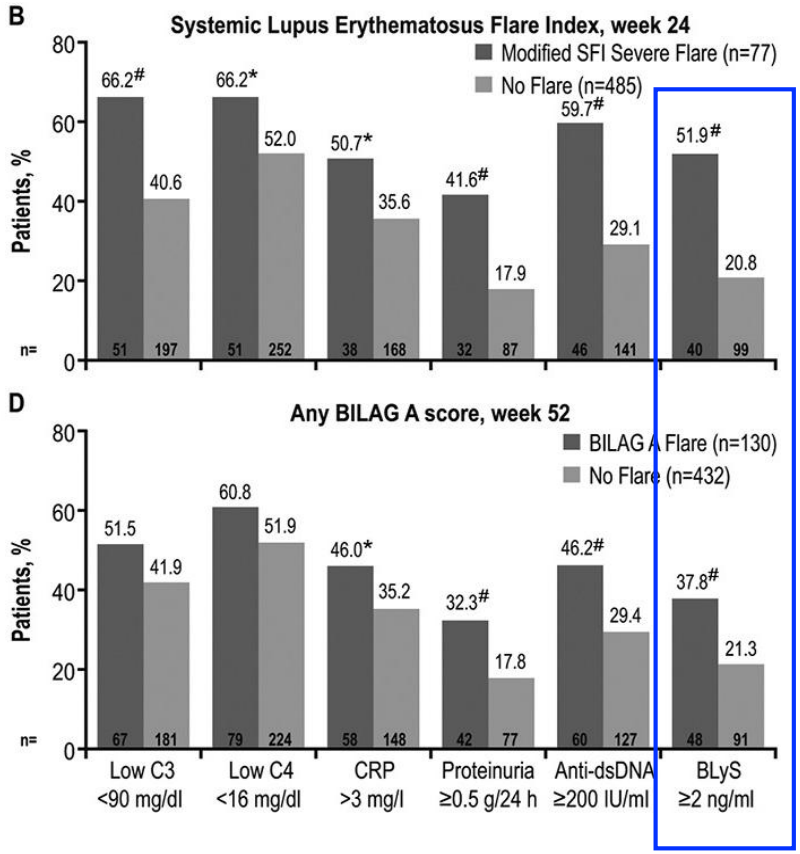


- 6 or 12 weeks prior to flare (SELENA_SLEDAI)
- **Stable SLE patients** exhibited increased levels of the regulatory mediators IL-10 and TGF-b
- **Transcriptome analysis:** the early flare group had differential gene expression in monocyte, T- cell, interferon, and inflammation modules, as well as significantly higher frequencies of activated (aCD11b+) neutrophils and monocytes, and activated (CD86hi) naïve B cells

M.E. Munroe et al. / Journal of Autoimmunity 78 (2017) 70-78; Scientific Reports | (2019) 9:8590

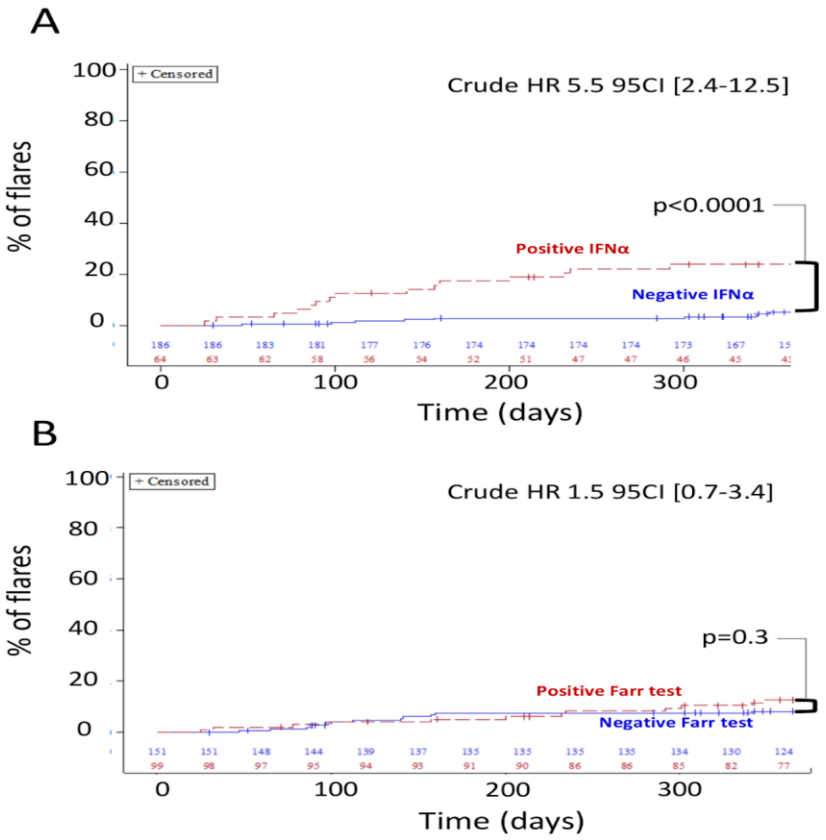
Ασθενείς σε αυξημένο κίνδυνο για έξαρση ΣΕΛ

Αυξημένα επίπεδα BLyS



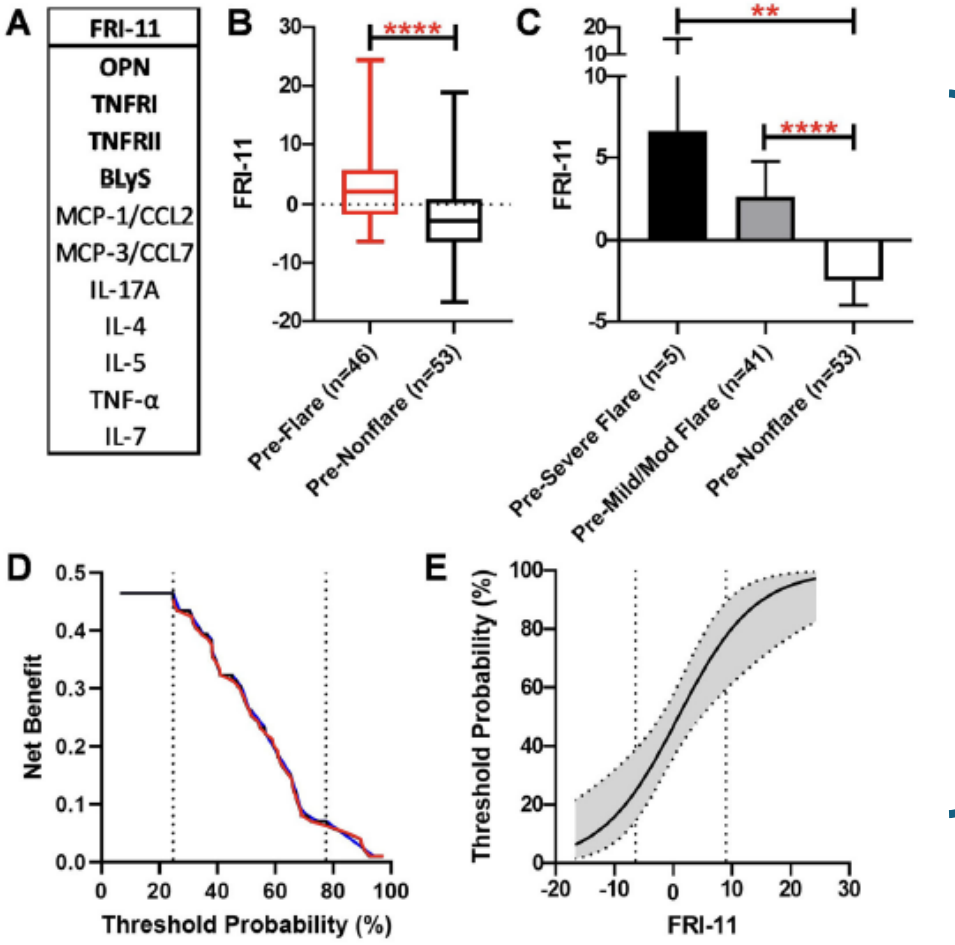
Petri M, et al. *Arthritis Rheum*. 2013; 65(8):2143-53

Αυξημένα επίπεδα IFNα



Ann Rheum Dis. 2019; 78(12): 1669-76

Forecasting impeding SLE flares through measurement of soluble mediators



	AUC			Correlation with hSLEDAI @ FU		
Effect Size	AUC	95% CI	p-value	Spearman r	95% CI	p-value
0.907	0.755	0.660-0.849	<0.0001	0.434	0.253 to 0.585	*<0.0001*

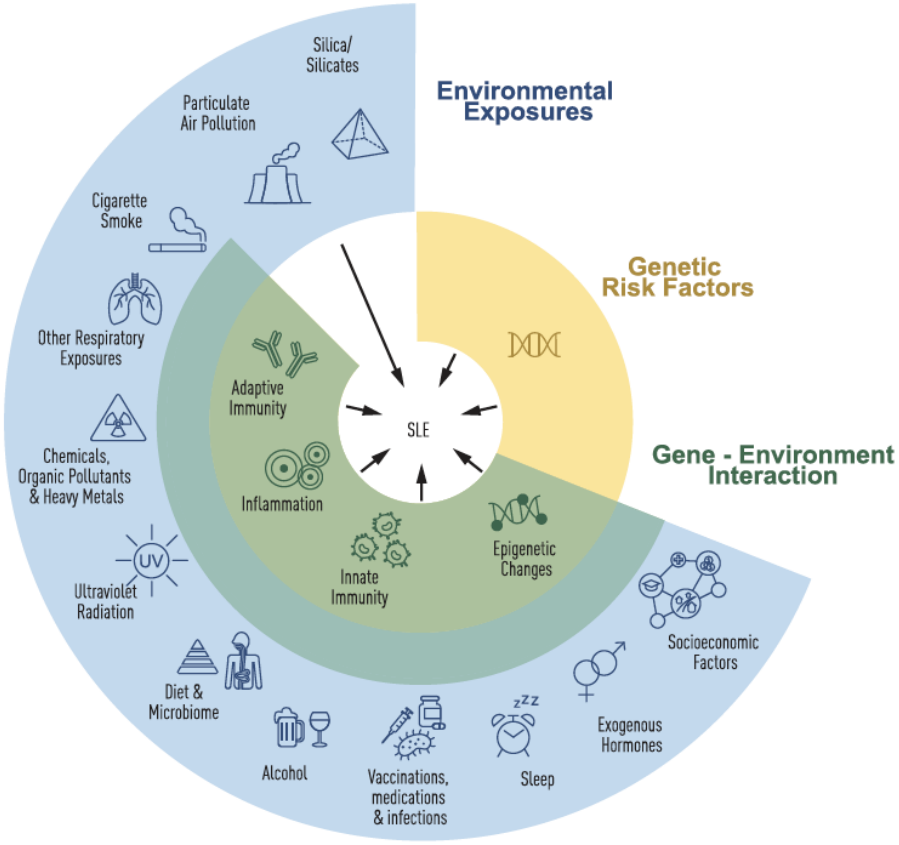
Positive/Negative Cutoff = 0					
Odds Ratio (95% CI)	Sensitivity	Specificity	PPV	NPV	p-value
5.2 (2.1-12)	0.67	0.72	0.67	0.72	*0.0001*

Low Range Cutoff = -6.4 (24% Threshold Probability)					
Odds Ratio (95% CI)	Sensitivity	Specificity	PPV	NPV	p-value
18 (2.6-191)	0.97	0.28	0.54	0.94	*0.0003*

High Range Cutoff = 9.0 (76% Threshold Probability)					
Odds Ratio (95% CI)	Sensitivity	Specificity	PPV	NPV	p-value
9.3 (1.5-107)	0.15	0.98	0.88	0.57	*0.0233*

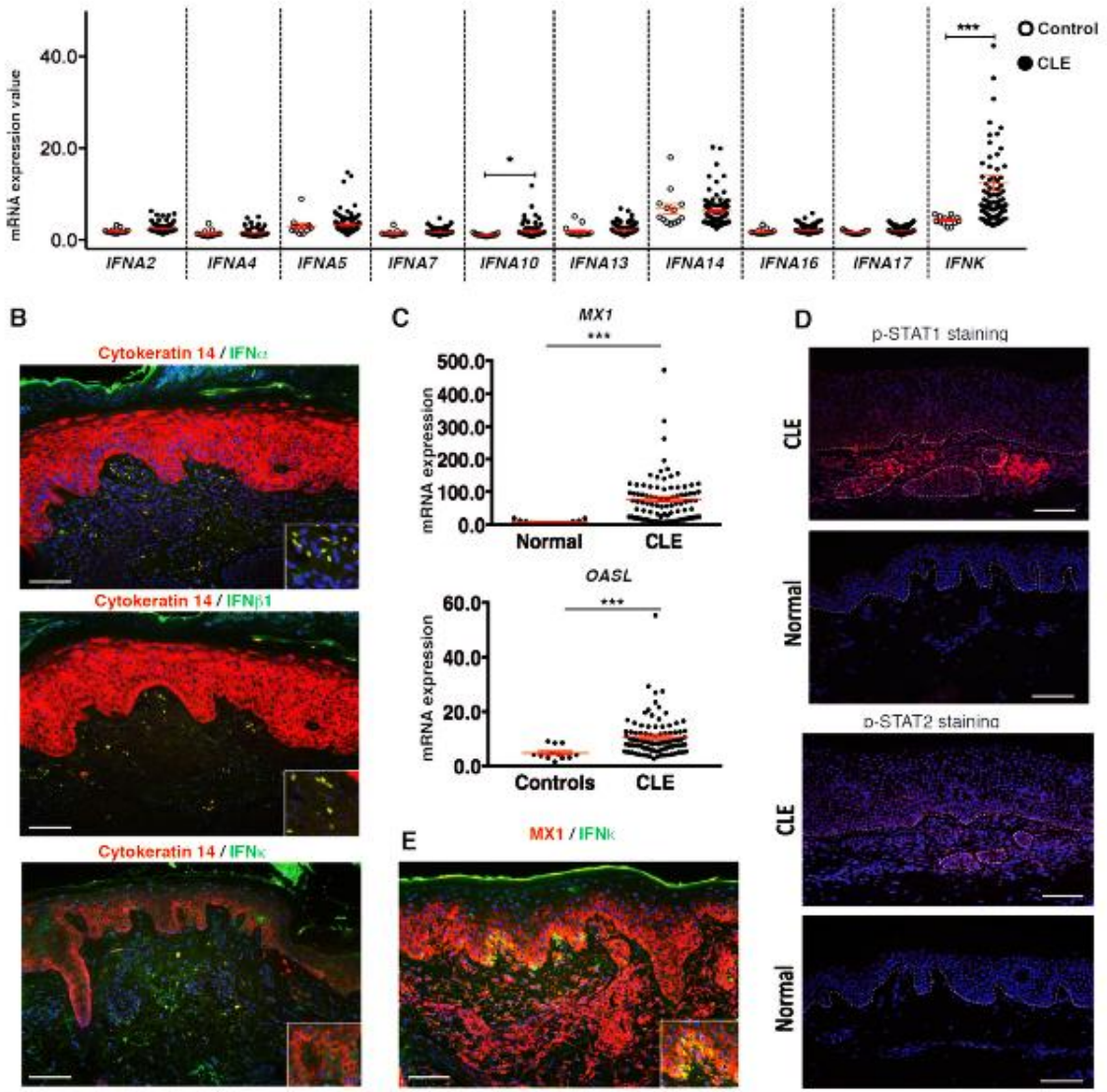
Arthritis & Rheumatology. Vol. 75, No. 5, May 2023, pp 723–735

What might be triggering flares in SLE?



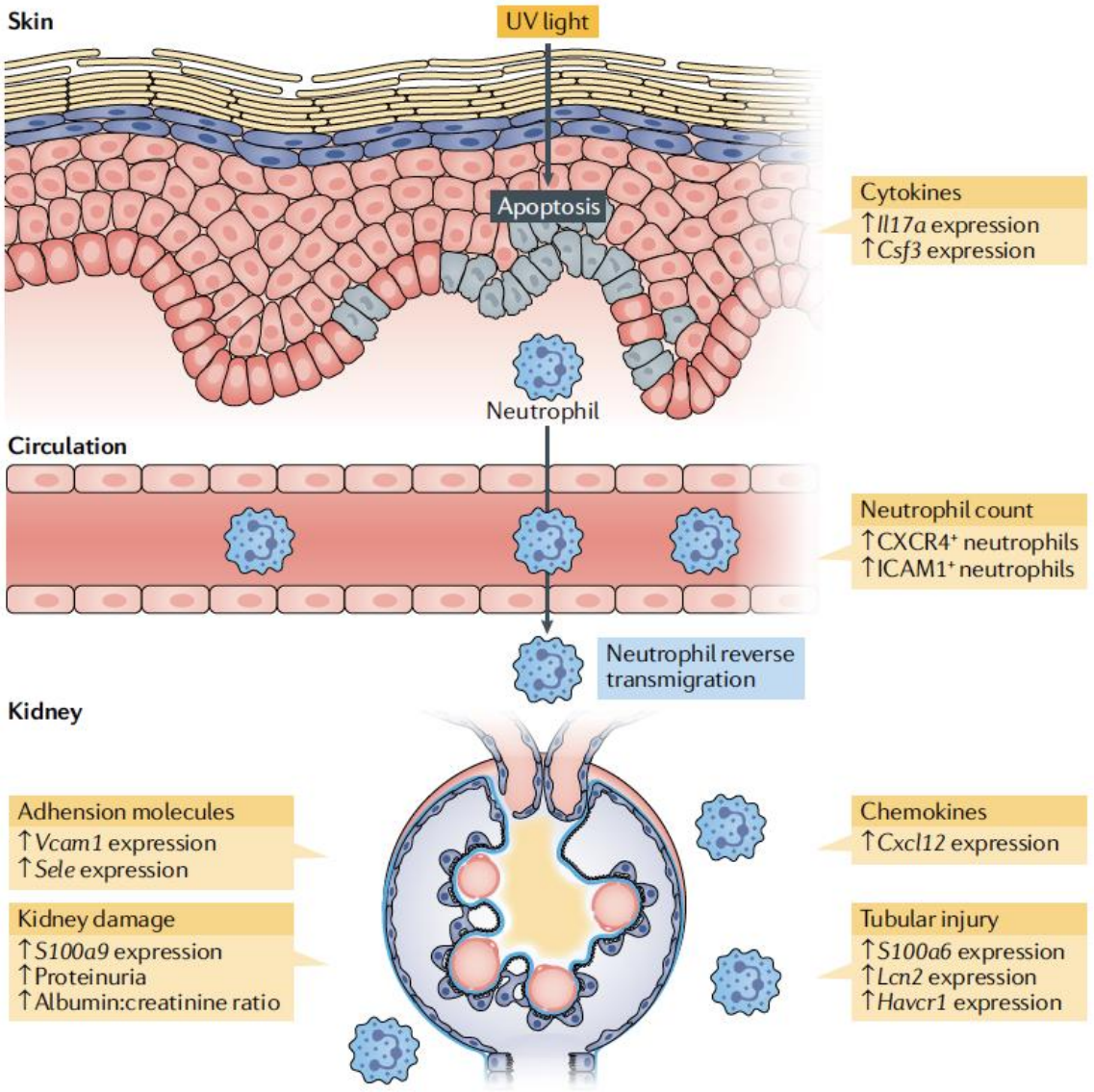
Journal of Internal Medicine, 2022, 291; 755–778

Photosensitivity induces the production of type I IFN (IFN-κ) by keratinocytes possibly through RNA damage and TLR-3 signaling



Nat Med. 2012 Aug;18(8):1286-90

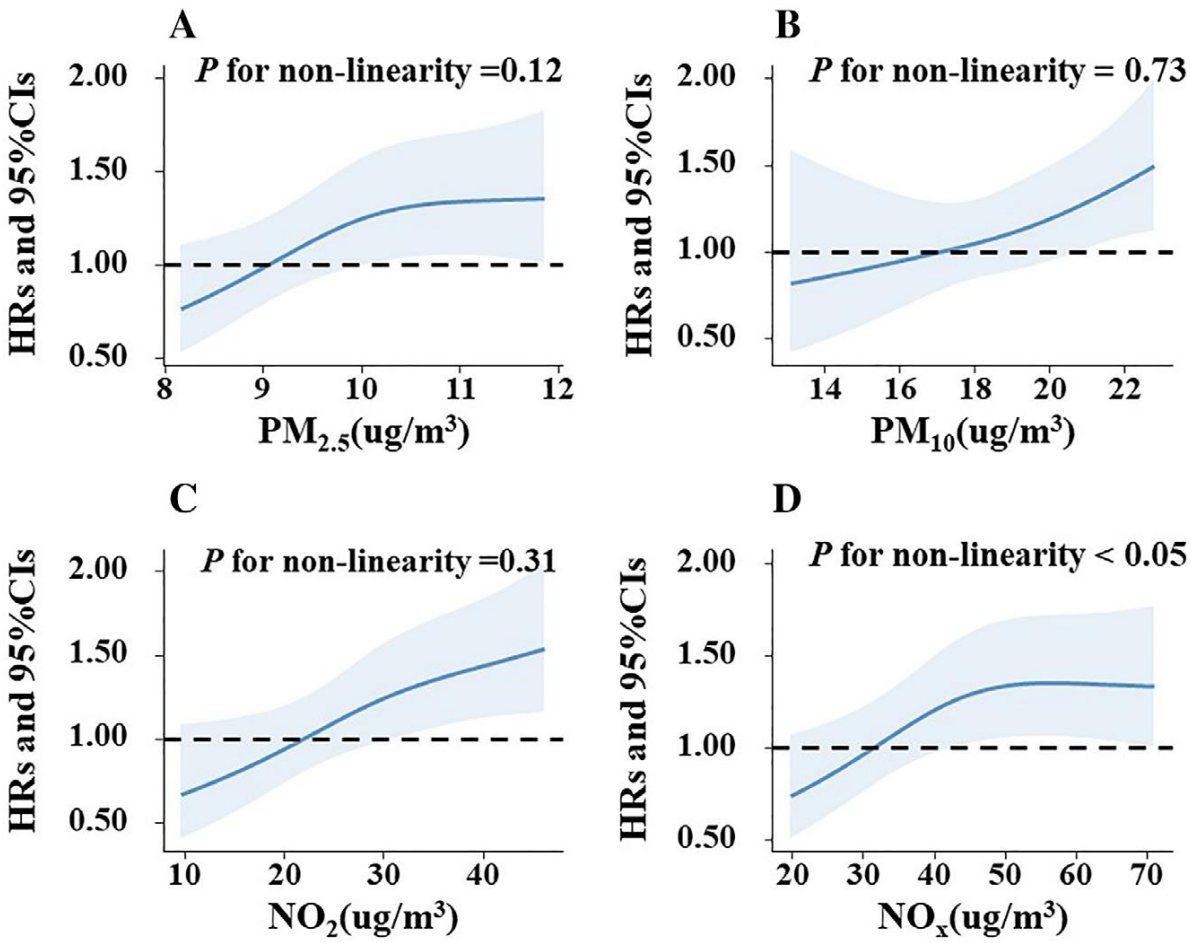
How can photosensitivity trigger a systemic SLE flare?



Proc Natl Acad Sci U S A. 2021 Jan 19;118(3):e2019097118

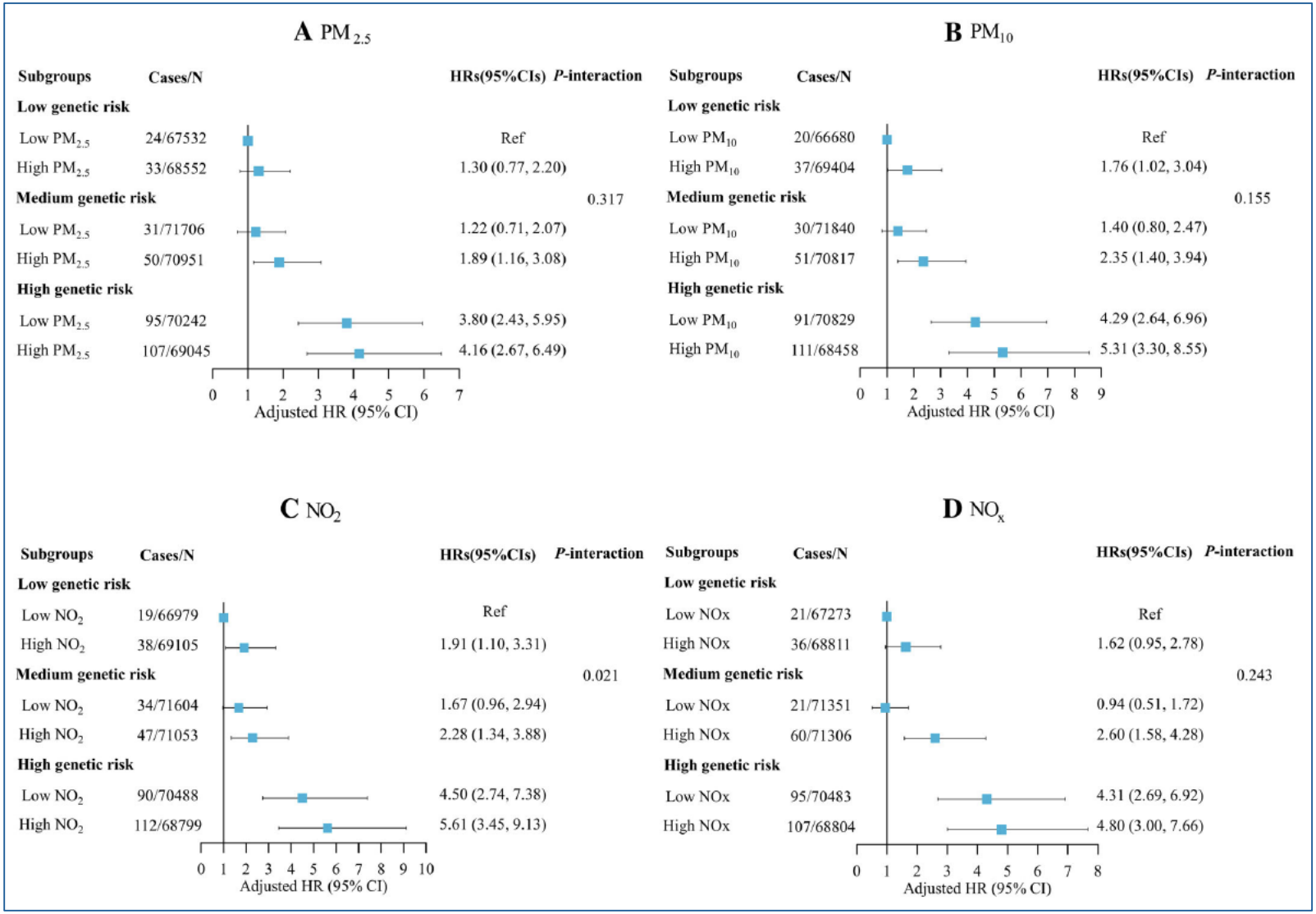
Air pollution and SLE disease

- 459,815 participants from the UK Biobank.
- Concentrations of air pollutants were estimated by land-use regression model
- Polygenic risk scores



Arthritis & Rheumatology. Vol. 76, No. 10, October 2024, pp 1530–1537

Air pollution and SLE disease



Arthritis & Rheumatology. Vol. 76, No. 10, October 2024, pp 1530–1537

Περίγραμμα

- Flares: clinical aspects and prognostic significance
- Possible triggering factors and presumed mechanisms
- Remission and ”treating-to-target”
- Immunological basis of remission in SLE
- Therapeutic implications

Remission and low disease activity in SLE: consensus-based definitions with extensive validation (RCTs, RWE)

Features	DORIS-remission	LLDAS
Main purpose	Defines a state of remission in SLE	Represents a state of low disease activity in SLE
1 Disease Activity Score — Objective assessment	Clinical SLEDAI=0	SLEDAI-2K ≤4 with no activity in major organ systems (renal, CNS, cardiopulmonary, vasculitis, fever), and no haemolytic anaemia or gastrointestinal activity
Physician assessment		No new lupus disease activity compared with the previous assessment
2 Physician Global Assessment	<0.5 (0–3)	≤1 (0–3)
3 Glucocorticoids	Prednisolone ≤5 mg/day or equivalent	Prednisolone ≤7.5 mg/day or equivalent
Other treatments	Stable antimalarials, immunosuppressives and biologics	Well-tolerated standard maintenance doses of immunosuppressive drugs and approved biological agents

CNS, central nervous system; DORIS, Definitions Of Remission In SLE; LLDAS, Lupus Low Disease Activity State; RCT, randomised controlled trial; RWE, real-world evidence; SLE, systemic lupus erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000

Arnaud L, et al. Lupus Sci Med 2024;11:e001114

Attainment of the treatment targets is linked to improved outcomes in patients with SLE

Low disease activity and remission

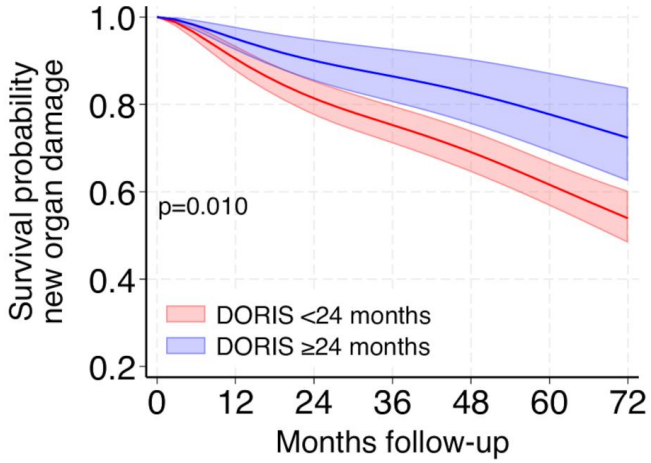
1. Reduced organ damage accrual[1,2]
2. Reduced flares[2,3]
3. Reduced hospitalisations[4]
4. Reduced direct healthcare costs[5]
5. Improved HRQOL[3]
6. Reduced mortality[3]

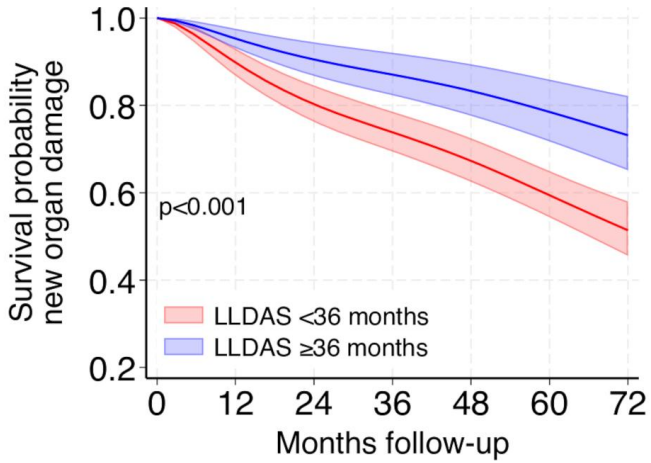
DORIS, Definitions Of Remission In SLE; HRQOL, health-related quality of life; LLDAS, Lupus Low Disease Activity State; SLE, systemic lupus erythematosus

1. Zen M, et al. Ann Rheum Dis 2015;74:2117–2122; 2. Golder V, et al. Lancet Rheumatol 2019;1:e103–e110;
3. Ugarte-Gil MF, et al. Lupus Sci Med 2021;8:e000542; 4. Reátegui-Sokolov C, et al. Lupus 2019:28;1344–1349; 5. Barber M, et al. Ann Rheum Dis 2024;83:1295–1303

Sustained (at least 2 years) achievement of the treatment targets ensures the highest protection against organ damage

	At least one visit	Sustained attainment
DORIS (remission)	62% of patients	**≥2 continuous years**: 20% of patients
		RR (new damage): 0.53 (95% CI 0.37, 0.75) **86% specificity**
LLDAS (low disease activity)	93% of patients	**≥3 continuous years**: 28% of patients
		RR (new damage): 0.58 (95% CI 0.44, 0.76) **81% specificity**





CI, confidence interval; DORIS, Definitions Of Remission In SLE; LLDAS, Lupus Low Disease Activity State; RR, relative risk; SLE, systemic lupus erythematosus

Pitsigavdaki S, et al. Ann Rheum Dis 2024;83:464-474

Achievement of the treatment targets correlates with reversal of inflammatory/genomic perturbations in PBMCs

- RNA-sequencing in the peripheral blood of 321 SLE patients
- 17.4% in remission (DORIS)
- 28.3% in LLDAS (but not DORIS)

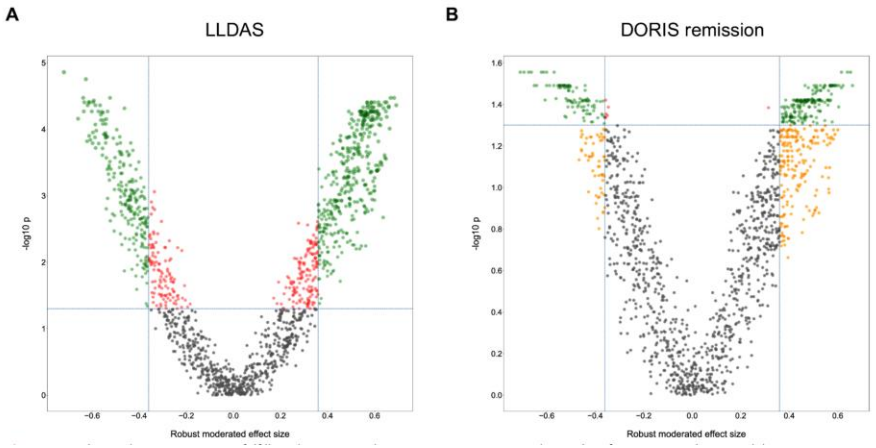
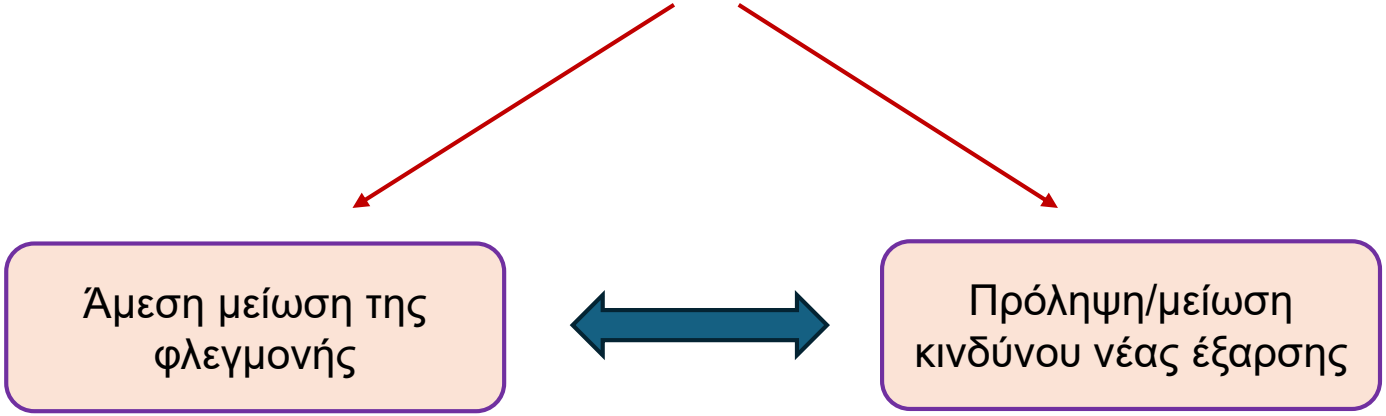


Table 3 Summary of relevant mechanisms and supporting evidence

Mechanism	Finding
DNA repair	Increased in LLDAS/DORIS remission; downregulated in active SLE.
	Reduced GG-NER and TC-NER in active renal SLE.
	Reduced POLB-dependent long patch base excision repair pathway in active renal SLE.
RNA metabolism	tRNA processing and post-transcriptional modification of mRNA metabolism of non-coding mRNA associated with LLDAS/DORIS remission.
Gene expression	Reduced caspase-related apoptosis in active renal SLE.
	Increased in LLDAS/DORIS remission.
Immune system *Type I IFN*	Reduced type I IFN responses in LLDAS/DORIS remission.
	No association with active neurological, respiratory, musculoskeletal, mucocutaneous, or renal SLE.
	Associations with haematological activity.
Immune system *TLR pathways*	TLRs downregulated in LLDAS/DORIS remission.
	Association between SLE activity and TLR1:TLR2 and TLR6:TLR2 heterodimers.
	TLR2 associated with active renal SLE.
	Activation of TLR3, TLR4, and TLR5 cascades in patients with active disease.
Immune system *Interleukins*	IL-1, IL-4, IL-13, IL-6, IL-7, IL-10, IL-17, and IL-20 family associated with active SLE.
	IL-2, IL-3, IL-5, and GM-CSF signalling associated with LLDAS/DORIS remission.
Immune system *Inflammasome*	Inflammasome and related pathways associated with active SLE.
	NLRP3 showed a trend toward an association with active renal SLE.
Immune system *CTLA-4*	CTLA-4 pathway upregulated in LLDAS/DORIS remission.
Immune system *DAP-12*	DAP-12-related pathways upregulated in LLDAS/DORIS remission.
Immune system *PD-1*	PD-1 pathway function increased in LLDAS/DORIS remission.
Metabolism	Acetylation increased in LLDAS/DORIS remission.
	Eicosanoid reduction linked to the absence of renal involvement.
	Reduction of eicosanoids and leukotrienes linked to LLDAS/DORIS remission.

Parodis I, et al. *Ann Rheum Dis*. 2024

Αντιμετώπιση των εξάρσεων & διατήρηση της ύφεσης

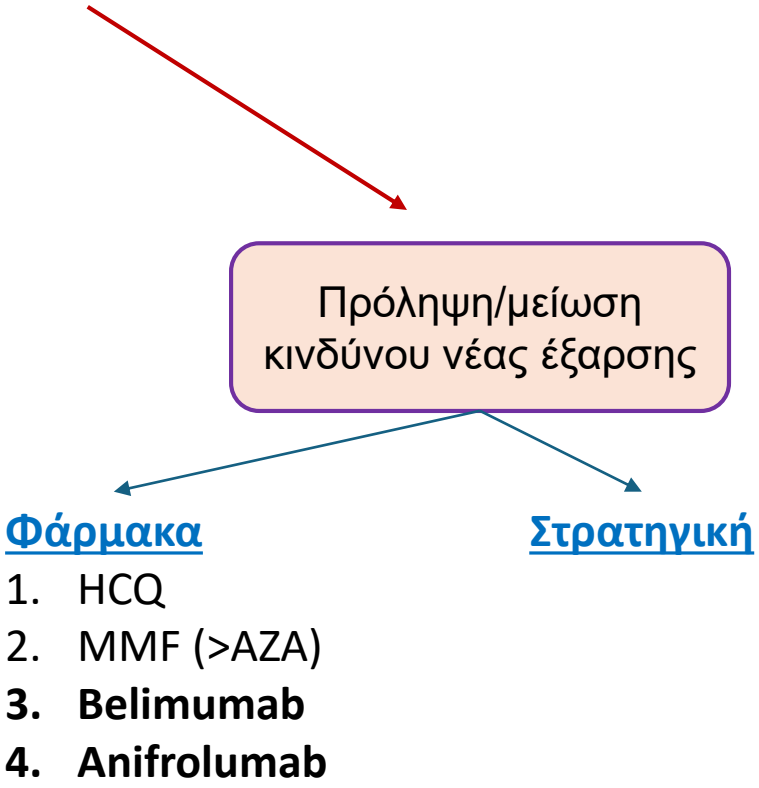


- **Γλυκοκορτικοειδή**
- Ανοσοκατασταλτική/-τροποποιητική/βιολογική θεραπεία

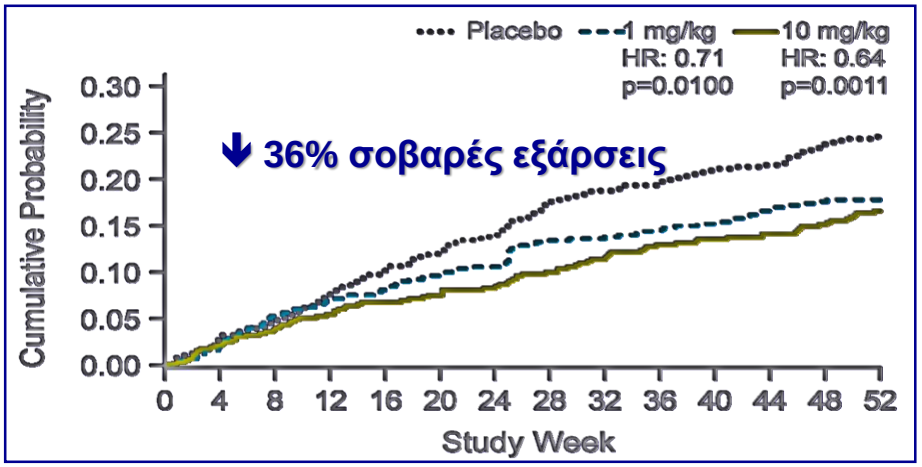
- **Φάρμακα**
- **Στρατηγική!**

+ συμπτωματική θεραπεία, έλεγχος συννοσηροτήτων

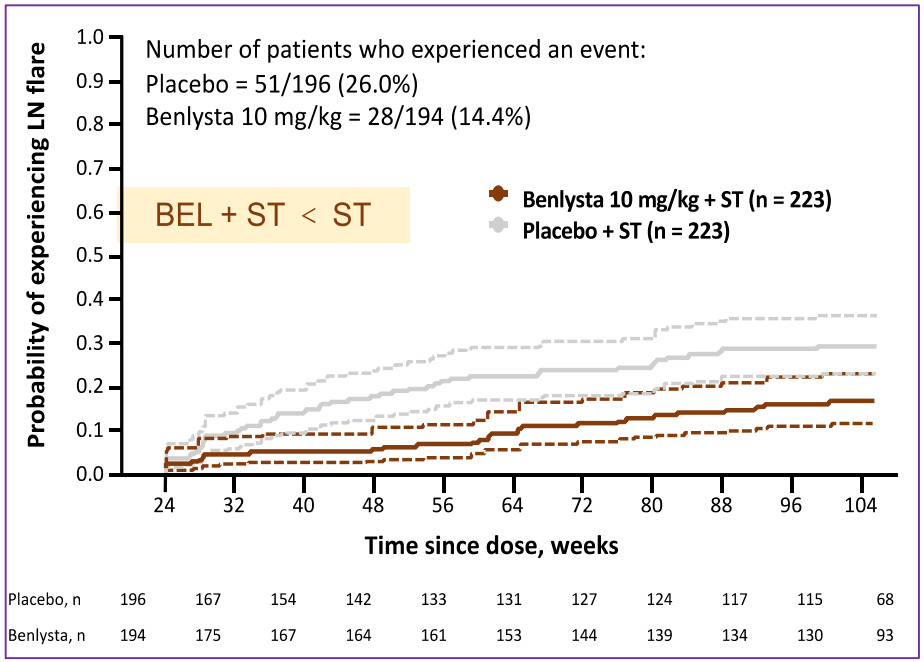
Αντιμετώπιση των εξάρσεων



Belimumab και μείωση υποτροπών στο ΣΕΛ



ΣΕΛ

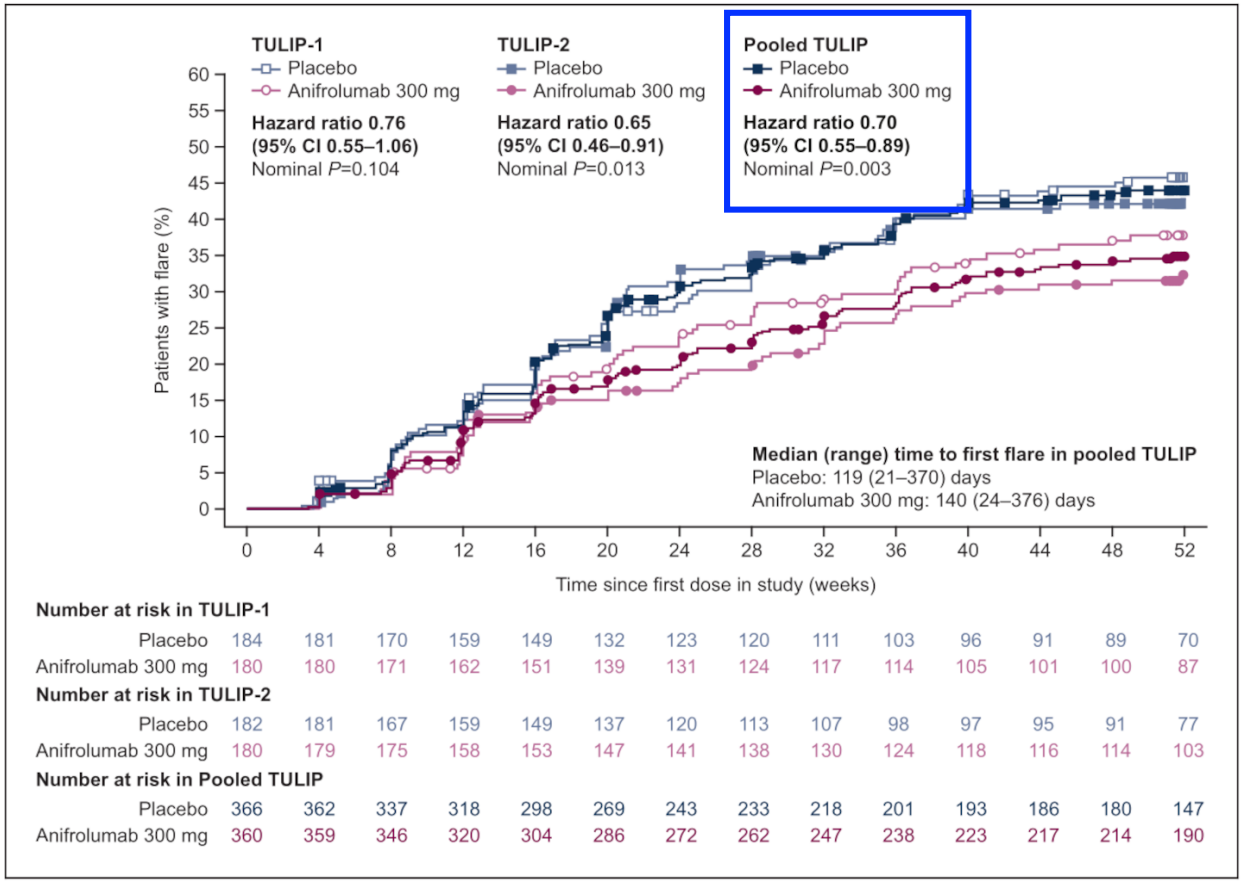


Νεφρίτιδα ΣΕΛ

Ενισχυμένο κλινικό όφελος με παρατεταμένη χρήση του φαρμάκου

Navarra SV, *et al. Lancet* 2011; 377:721–731;
Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930;
van Vollenhoven RF, *et al. Ann Rheum Dis* 2012; 71:1343–1349; Rovin BH, et al. Kidney Int 2022;101:403–413

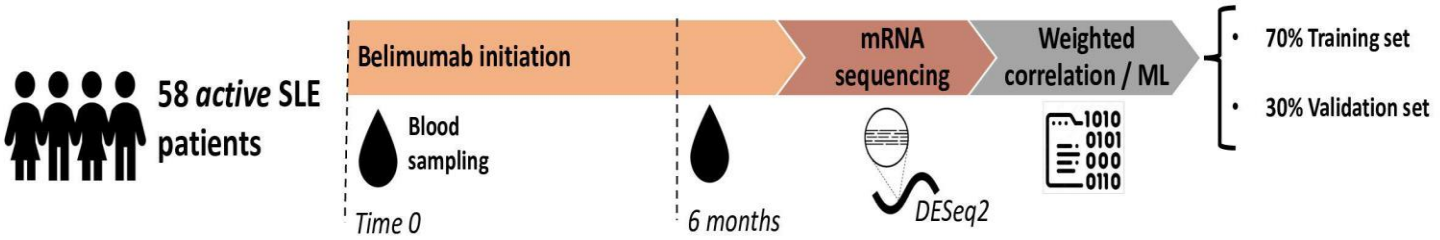
Anifrolumab και μείωση υποτροπών στο ΣΕΛ



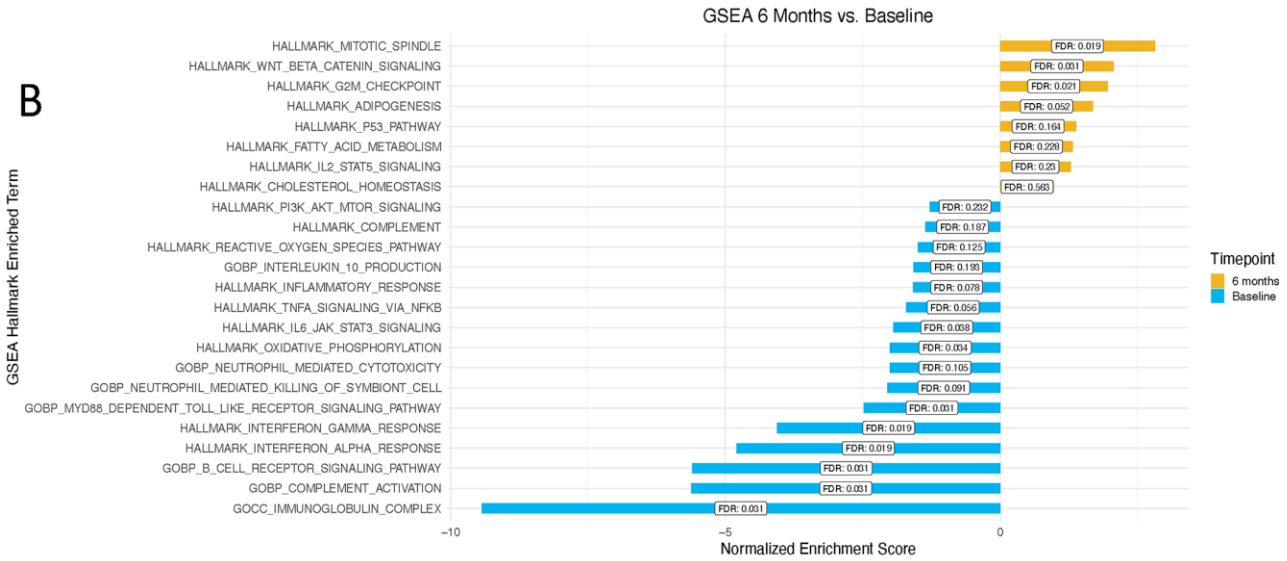
Of patients who achieved sustained glucocorticoid reductions from ≥10 mg/day at baseline, more remained flare-free with anifrolumab (40.0% vs. 17.3% with placebo)

Furie R, et al. Lupus. 2021

Molecular basis for the putative disease-modifying effect of biological agents in SLE (1/2)



- **Belimumab induced widespread transcriptome changes**
- Suppression of pathways related to B cells, type I/II interferon, IL-6/STAT3 and neutrophil activation
- Effects more pronounced among patients with LLDAS
- **Amelioration of the SLE 'susceptibility' signature** in the LLDAS group

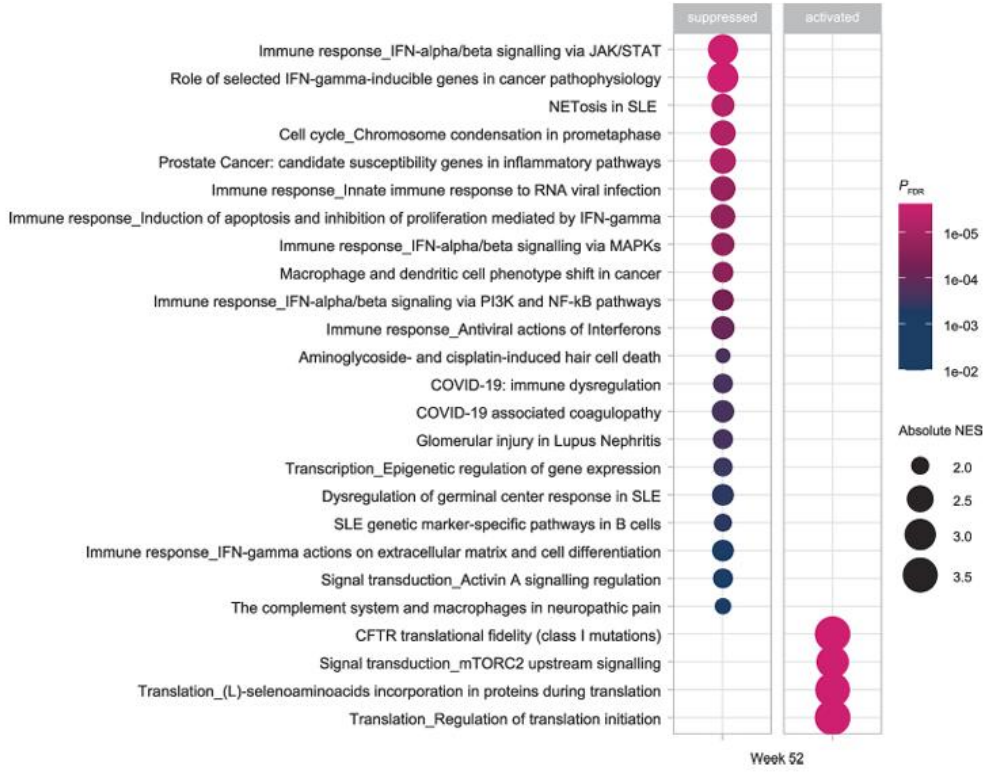


DESeq, differential gene expression, sequencing; FDR, false discovery rate; GSEA, gene set enrichment analysis; IL, interleukin; LLDAS, Lupus Low Disease Activity State; ML, machine learning; mRNA, messenger RNA; SLE, systemic lupus erythematosus; STAT, signal transducer and activator of transcription

Moysidou GS, et al. Ann Rheum Dis 2025;84:262-273

Molecular basis for the putative disease-modifying effect of biological agents in SLE (2/2)

Pathway analysis for genes that were downregulated or upregulated by anifrolumab*

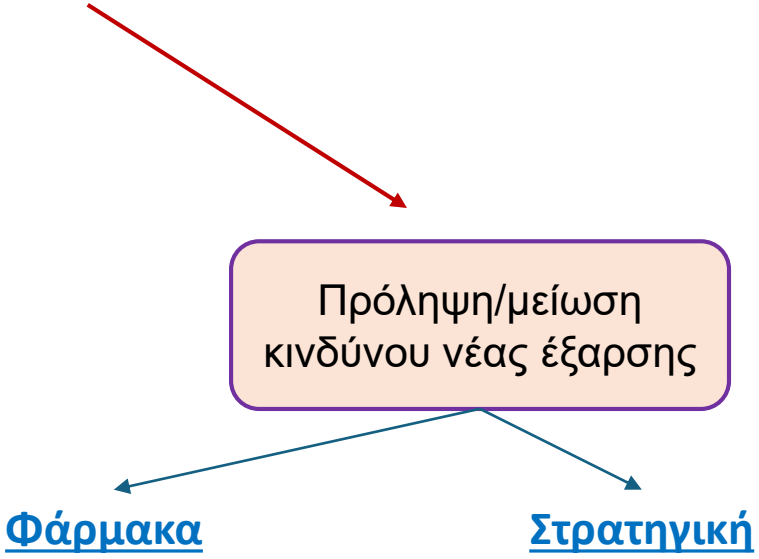


Type I IFN blockade with anifrolumab modulated multiple inflammatory pathways downstream of type I IFN signalling, including **apoptotic, innate and adaptive mechanisms** that play key roles in SLE immunopathogenesis

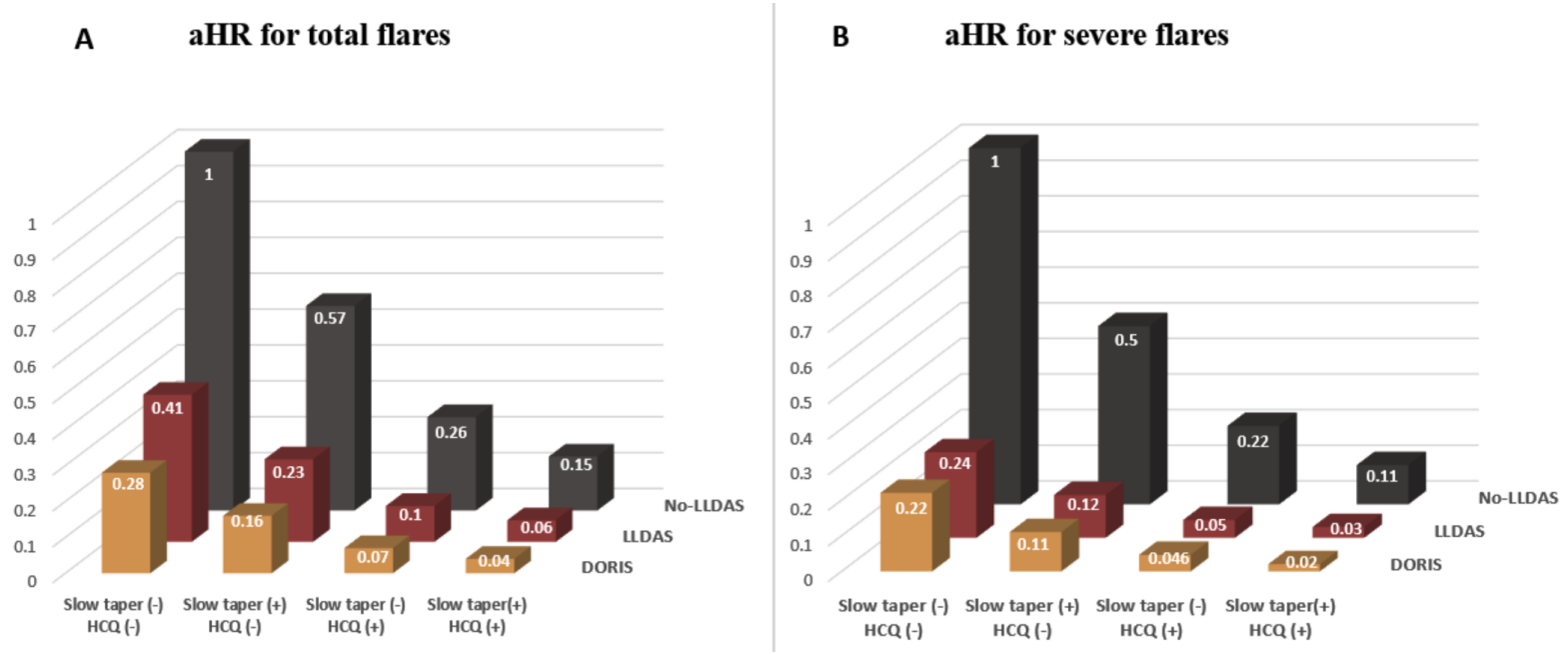
*The top 25 most significantly dysregulated pathways in patients receiving anifrolumab (n=241) vs (n=250) at week 52 in pooled TULIP-1 and TULIP-2 data ($P_{FDR} \leq 0.001$)
COVID-19, coronavirus disease 2019; CFTR, cystic fibrosis transmembrane conductance regulator; IFN, type I interferon; IFNAR1, type I interferon receptor 1; JAK, Janus kinases; MAPK, mitogen-activated protein kinase; mTORC2, mammalian target of rapamycin complex 2; NES, normalized enrichment score; NET, neutrophil extracellular traps; NF-kB, nuclear factor kappa B; PFDR, false discovery rate-adjusted p value; PI3K, phosphatidylinositol 3-kinase; RNA, ribonucleic acid; SLE, systemic lupus erythematosus; STAT, signal transducer and activator of transcription

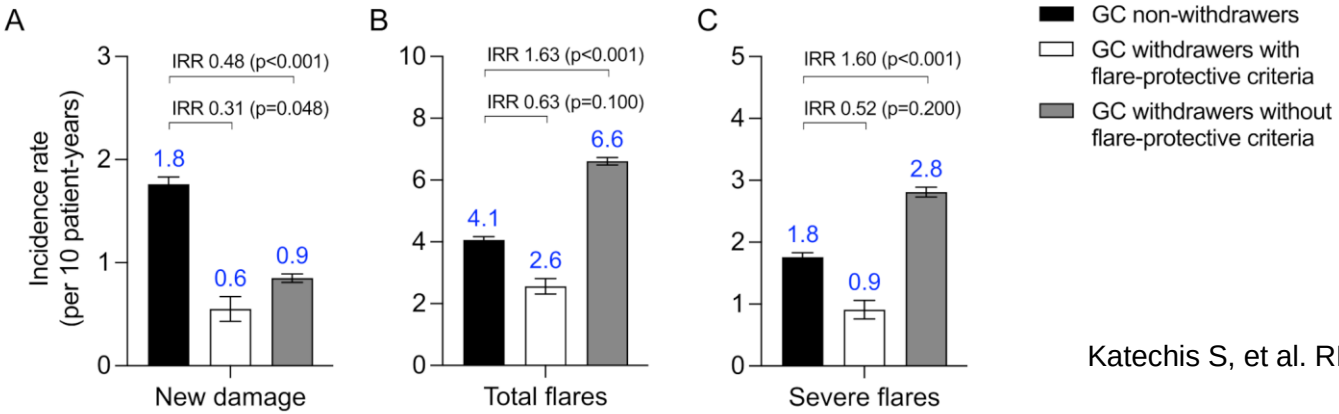
Baker T, et al. Ann Rheum Dis 2024;83:1018–1027

Αντιμετώπιση των εξάρσεων



A strategy to reduce flares after GC withdrawal: slow GC tapering, use of HCQ, achievement of remission or low disease activity





Katechis S, et al. RMD Open. 2025; 11(1): e005118.

Βασικά σημεία

- Οι **εξάρσεις** απαντούν συχνά σε ασθενείς με ΣΕΛ και **συνεισφέρουν σημαντικά στο φορτίο της νόσου**. Η πρόληψή τους αποτελεί **μείζονα θεραπευτικό στόχο** στη νόσο

- Η ανοσολογική και μοριακή βάση των υποτροπών είναι πολύπλοκη και περιλαμβάνει πολλαπλούς κυτταρικούς τύπους και μονοπάτια.

- Νεότερες τεχνολογίες (high-throughput) και εφαρμογή σε καλά χαρακτηρισμένες κοορτές ασθενών μπορούν να βοηθήσουν στην αποσαφήνιση των μηχανισμών εξάρσων

- Περιορισμένες γνώσεις για την κατάσταση της ύφεσης, ιδίως της «βαθιάς ύφεσης»

- Οι νεότερες βιολογικές θεραπείες όπως το belimumab και το anifrolumab, επιτυγχάνουν **σταθεροποίηση της νόσου** και σημαντική μείωση του κινδύνου εξάρσεων