Unique monocyte transcriptomic profiles are associated with sub-clinical atherosclerosis in women with systemic lupus erythematosus (SLE)

Laurel Woodridge[1,2,3]

Elvira Chocano[1,2,3], Dr. Paul Ashford[2], Dr. George Robinson[3], Dr. Kirsty Waddington[3], Prof. Anisur Rahman[3], Prof. Christine Orengo[2], Prof. Liz Jury[3], Prof. Inés Pineda-Torra[1]

[1]Centre for Cardiometabolic and Vascular Science and [2]Centre for Rheumatology, Division of Medicine, University College of London, 5 University Street, London, WC1 E6JF. [3] Institute of Structural and Molecular Biology, University College London, Gower Street, London, WC1E 6BT, UK.

1.0 Background

Cardiovascular disease (CVD) is a leading cause of mortality in women with Systemic Lupus Erythematosus (SLE) through accelerated atherosclerosis. Both diseases are characterised by chronic inflammation and dysregulated immune cell function.

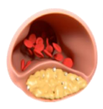
***Aim**:* To identify differences in molecular profiles of SLE patients with (SLE-P) and without (SLE-NP) sub-clinical atherosclerosis to explore biological mechanisms and potential diagnostic biomarkers.

2.0 Cohort

CVD-free women
UCLH

1. SLE-NP N=7
Lesion free

2. SLE-P N=11
Sub-clinical atherosclerotic plaques

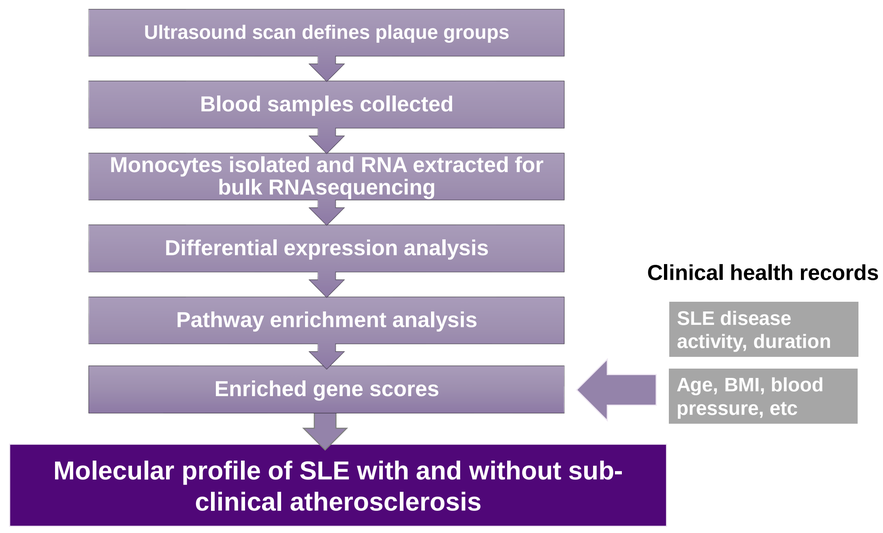


Non-invasive ultrasound scan

Carotid and femoral arteries

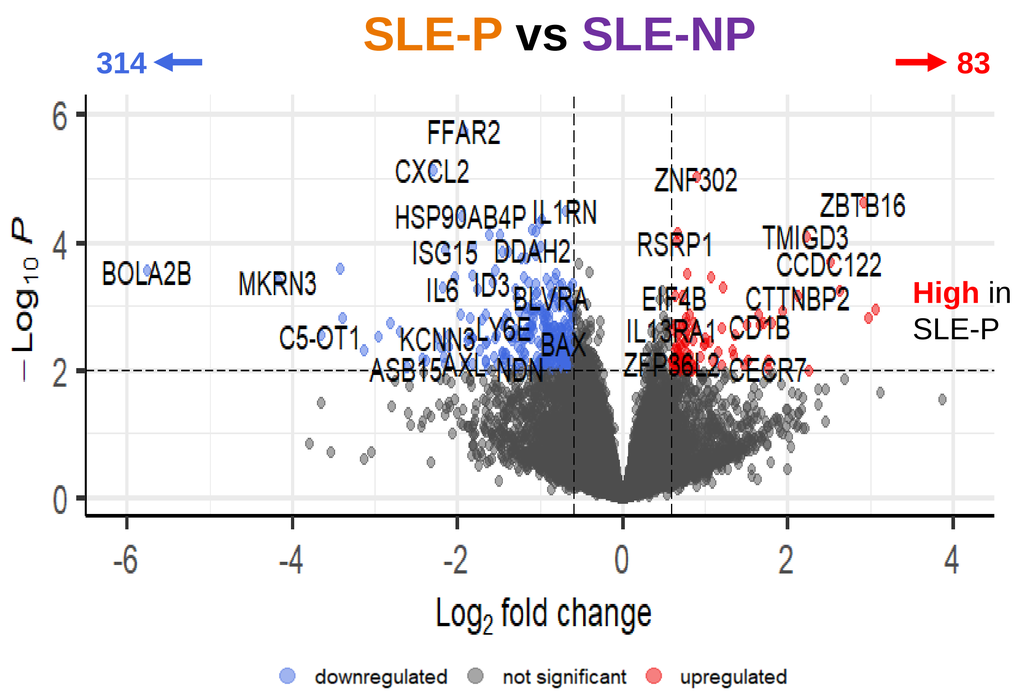
Plaque measures:
Intima media thickness, grey scale medium, plaque area, plaque thickness and plaque length

3.0 Methods

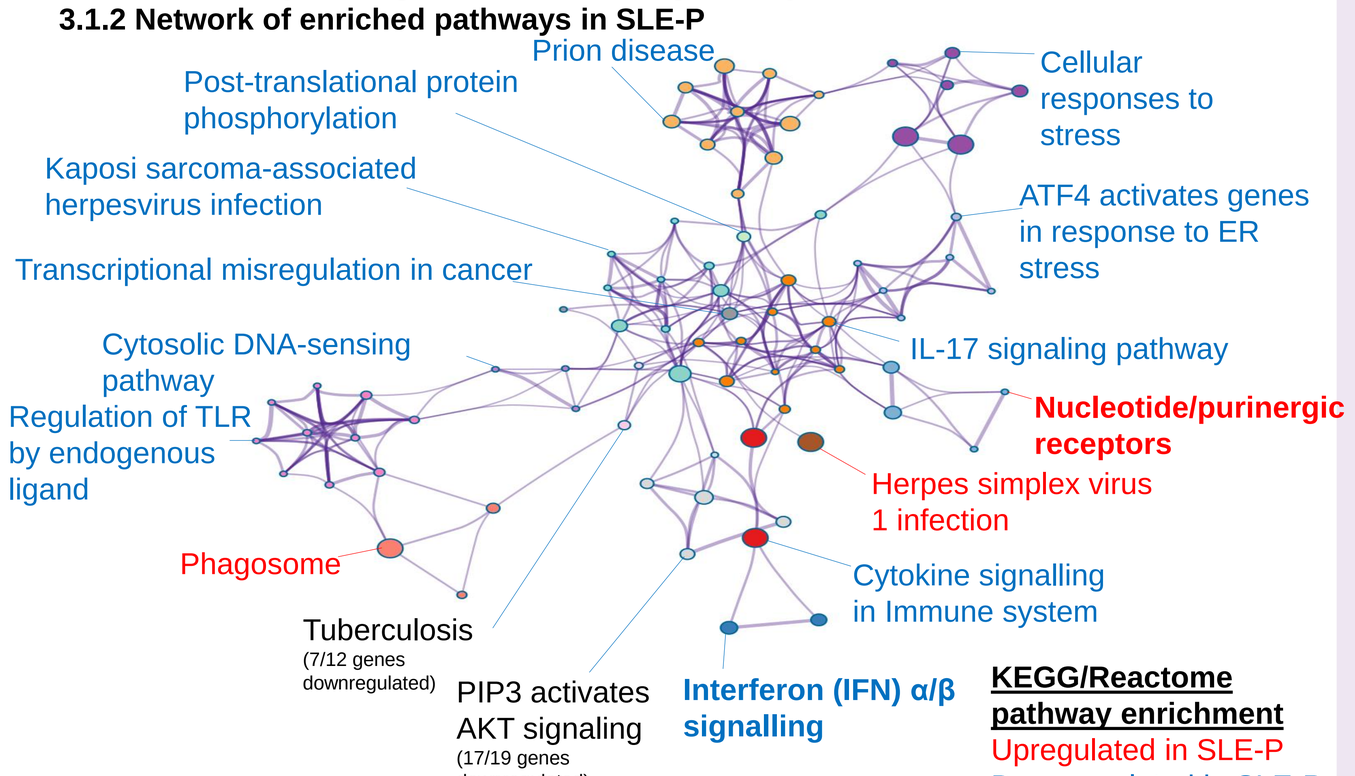


4.1. Monocyte gene expression profiles in SLE with atherosclerosis are defined by changes in immunoregulatory mechanisms

4.1.1 Monocyte differential gene expression

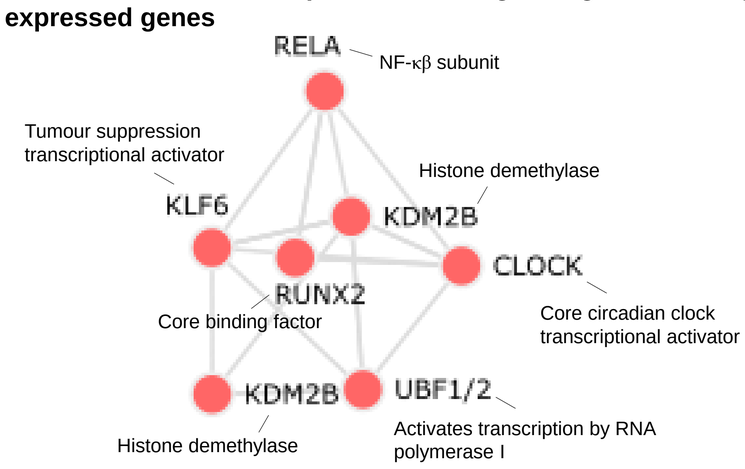


3.1.2 Network of enriched pathways in SLE-P



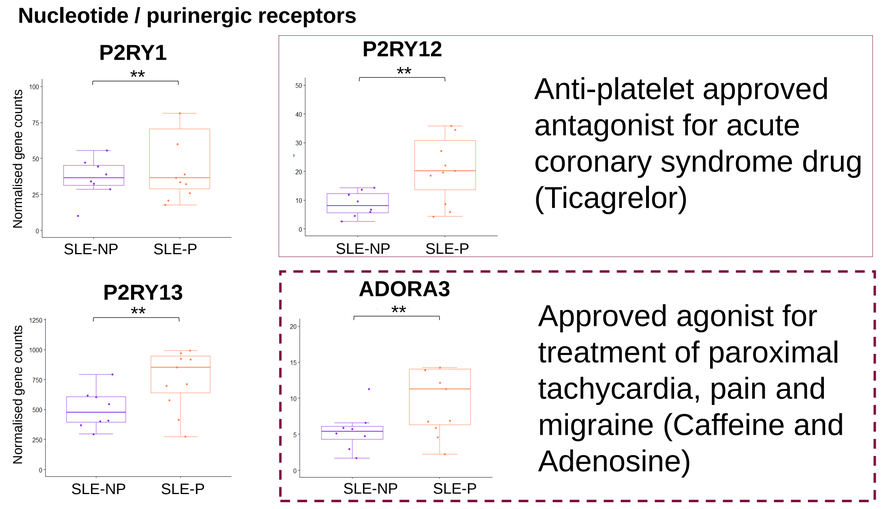
4.2. Transcriptomes of SLE patients with sub-clinical plaque show complex dysregulation of cell signalling mechanisms

4.2.2 Network of transcription factors regulating differentially expressed genes



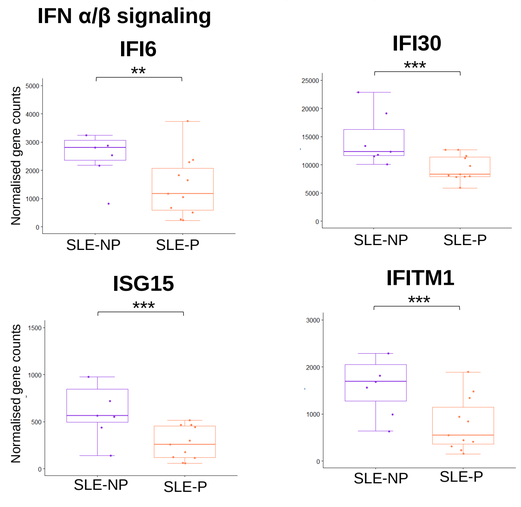
4.2.3 Upregulated pathways

Nucleotide / purinergic receptors



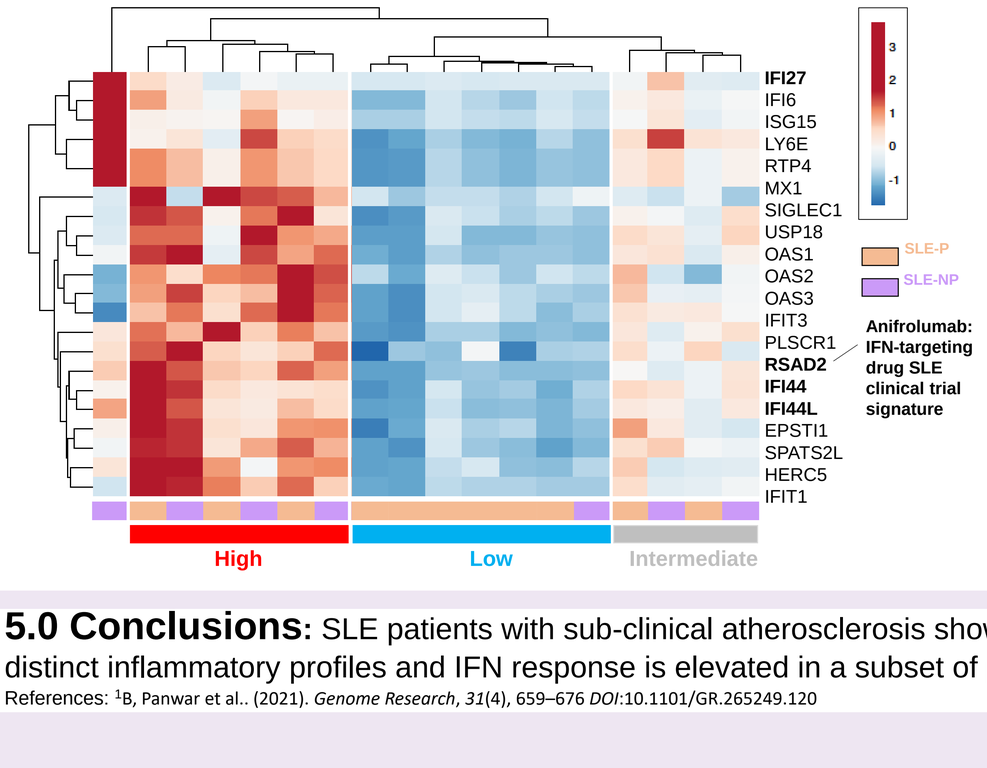
3.2.4 Downregulated pathways:

IFN α/β signaling



4.3. Inflammation downregulated in SLE-P but IFN response does not predict plaque status

4.3.1 Unsupervised hierarchical identifies distinct IFN signature[1] sub-groups

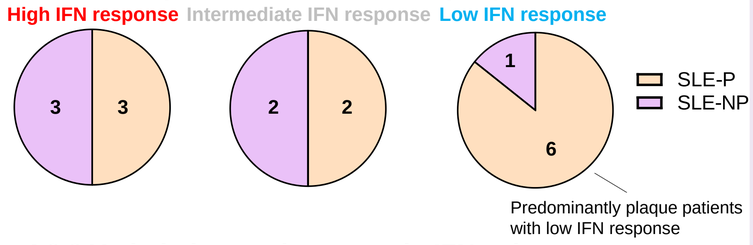


4.3.2 IFN sub-groups clinically indistinct by disease activity and CVD risk factors

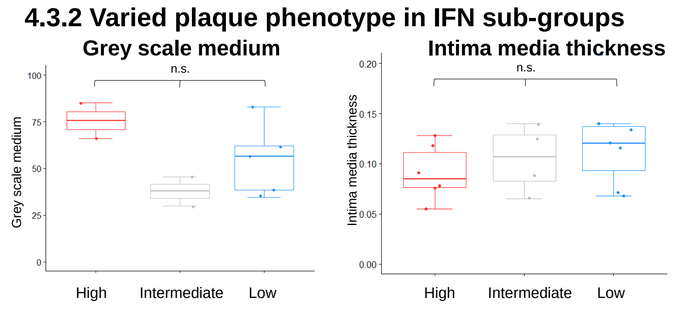
	High	Intermediate	Low
N	6	4	7
Age	48	52	57
MAP	101	101	81.7
BMI	25.6	28.3	24.8
Disease duration	28.3	20	25.7
Disease activity (BILAG)	3.67	0.75	1.86

MAP – mean arterial pressure. BMI – body mass index. Mean values in table. No difference in clinical measures (above), and disease markers (anti-dsDNA titres, C3, ESR and CRP).

4.3.2 IFN response does not define plaque status



4.3.2 Varied plaque phenotype in IFN sub-groups



5.0 Conclusions: SLE patients with sub-clinical atherosclerosis show gene expression differences from patients that remain plaque free. Sub-groups can be defined by distinct inflammatory profiles and IFN response is elevated in a subset of patients but a higher IFN response does not predict atherosclerosis .

References: [1]B, Panwar et al.. (2021). *Genome Research*, *31*(4), 659–676 *DOI*:10.1101/GR.265249.120

*** p<0.05 ** p<0.01 *** p<0.001 **** p<0.0001**

laurel.woodridge.19@ucl.ac.uk

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