IDENTIFICATION OF TISSUE-ASSOCIATED REMODELLING ENDOTYPES IN RHEUMATIC DISEASE COHORTS

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Background

Ankylosing spondylitis (AS), psoriatic arthritis (PsA), and systemic lupus erythematosus (SLE) are distinct rheumatological diseases, however they may share some common molecular features.

Diagnosis and treatment strategies are challenging due to the considerable heterogeneity within each disease.

Central to these conditions is an imbalance between *fibrolysis* and *fibrosis* within affected tissues.

Methods

Samples:

Baseline serum samples from clinical studies:

- AS (NCT02437162/8787)[1], N=66
- PsA (NCT03158285)[2], N=267
- SLE (NCT02349061)[3], N=97
- Healthy donors (Discovery LS, BioIVT), N=77

Biomarkers:

Skin/bone formation (PRO-C1) and degradation (C1M). Cartilage formation (PRO-C2) and degradation (C2M). Fibrosis (PRO-C3, PRO-C6) and fibrolysis (C3M, C6M). Basement membrane turnover (PRO-C4) and degradation (C4M). Hypertrophic chondrocytes (C10C). Citrullinated and degraded vimentin (VICM).

Statistics:

- K-means clustering (k = 3) assessed biomarker profile similarities across disease groups and were compared to healthy donors.
- Clinical parameters for each disease in the clusters were assessed by Kruskal-Wallis tests or χ^2 tests with Holm adjusted p values

Hypothesis

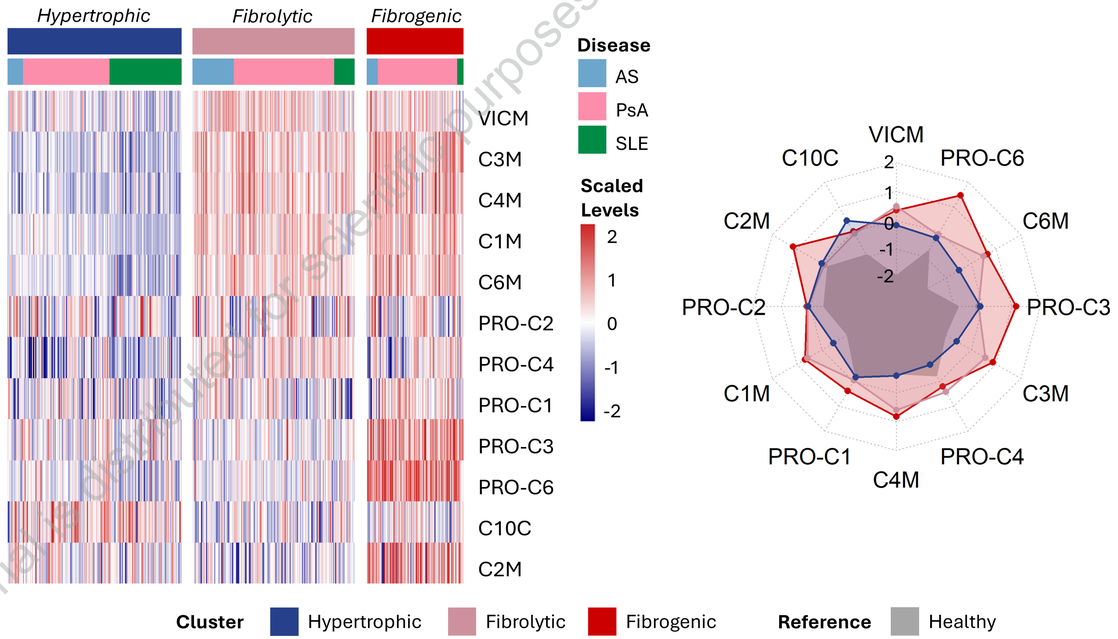
Endotyping patients across rheumatological diseases *using tissue-associated remodelling biomarkers will* ***identify shared disease pathways*** *that can be targeted for* ***more effective and personalised treatment****.*

Conclusion

- Biomarker clustering revealed **three cross-disease subgroups** with varying disease activity and remodelling profiles.
- These profiles highlight disease heterogeneity, **revealing clinically relevant endotypes**.
- Identifying biomarker endotypes **may guide targeted treatments and inform drug repurposing across rheumatological diseases**.

Results

Three tissue-associated remodelling endotypes were identified across AS, PsA and SLE patients.



Significant differences in various clinical parameters were observed across the three biomarker endotypes.

		Hypertrophic (n = 171)	Fibrolytic (n = 156)	Fibrogenic (n = 93)	*P value*
AS	**N (%)**	15 (22.7%)	40 (60.6%)	11 (16.7%)	
	CRP, mg/dL	0.6	1.8	1.5	<0.001
	ASDAS	3.7	4.7	4.3	0.001
PsA	**N (%)**	86 (33.3%)	96 (37.2%)	76 (29.5%)	
	Females, n (%)	52 (60.5%)	38 (39.6%)	27 (35.5%)	0.002
	CRP, mg/dL	0.7	2.2	2.5	<0.001
	PASI	4.0	8.0	5.4	0.001
	DAS28	4.9	5.4	5.6	<0.001
	BSA (PsO)	6.0	11.5	12.5	0.003
	vdH-S	10.2	22.5	21.2	0.004
SLE	**N (%)**	72.9%	20.8%	6.3%	

AS; ankylosing spondylitis, ASDAS; ankylosing spondylitis disease activity score, BSA; body surface area, CRP; c-reactive protein, DAS28; disease activity score in 28 joints, PASI; psoriasis area severity index, PsA; psoriatic arthritis, PsO; psoriasis, SLE; systemic lupus erythematosus, vdH-S; van der Heijde-Sharp.

References:

1. Deodhar et al., Arthritis Rheumatol 2019; 71:258–270
2. Mease et al., Lancet 2020; 395: 1126–1136
3. van Vollenhoven et al., Lancet 2018; 392: 1330–1339

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