

Methods: We assessed the expression of cytotoxic effector molecules and transcription factors in CD4+ T cells in synovial fluid (n=21) and paired peripheral blood (n=16) from ACPA- and ACPA+ RA patients by multi-parameter flow cytometry. We performed single cell sequencing, in combination with 5' TCRab sequencing, on purified CD4+ T cells from the peripheral blood (PB) and synovial fluid (SF) of ACPA+ RA patients (n=7).

Results: Flow cytometry experiments show that Granzyme-B+ Perforin-1+ CD4+ CTL are significantly increased in the SF of ACPA+ RA patients as compared to ACPA- RA patients (p=0.0072). The presence of CD4+ CTL could be confirmed by single cell sequencing in SF of each ACPA+ RA patient tested (n=7). Moreover, we found that the adhesion G-protein coupled receptor GPR56 is selectively expressed on the recently described peripheral helper (T_{PH}) T-cell subset¹¹ and associates with the expression of tissue resident memory markers LAG-3, CXCR6 and CD69. In blood, we confirmed a previous report¹² showing that GPR56 delineates cytotoxic CD4+ T cells. Finally, expanded TCR clones expressing cytotoxic effector molecules were identified in synovial fluid of ACPA+ RA patients and, for some patients, in their corresponding peripheral blood.

Conclusion: We identified GPR56 as a marker of T_{PH} cells in SF of ACPA+ RA patients that associates with tissue residency receptors. The combination of single cell sequencing and multi-parameter flow cytometry highlights the importance of CD4+ CTL in ACPA+ RA and suggests a potential therapeutic target (Figure 1).

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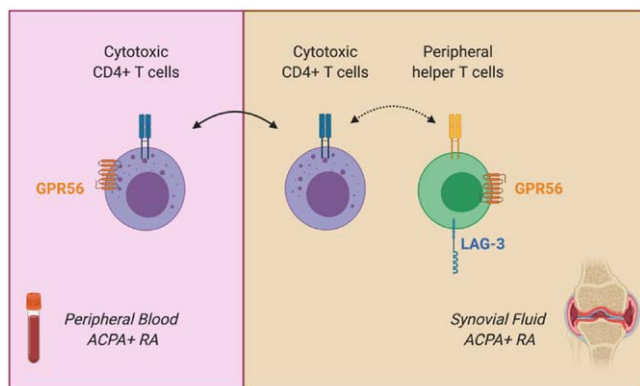


Figure 1. Cytotoxic CD4+ T cells and GPR56+ peripheral helper CD4+ T cells are two T-cell subsets identified in SF of ACPA+ RA patients.

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OP0073

SINGLE-CELL TRANSCRIPTOMICS UNCOVERS DEFECTIVE BONE MARROW EARLY B CELL DEVELOPMENT IN A SUBSET OF LUPUS PATIENTS ASSOCIATED WITH AGGRAVATED INFLAMMATION

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that occurs when the body's immune system attacks own tissues and organs. B cells play a central role in SLE pathogenesis by producing autoantibodies as well as antibody-independent functions. Peripheral B cell abnormality is well known in lupus patients such as expansions of plasmablasts and atypical memory B cells, which are associated with active diseases. However, little is known about the B cell development in the bone marrow of lupus patients.

Objectives: We conduct this survey to explore the disorder of the B cell development in the bone marrow of lupus patients.

Methods: In this study, we have performed the scRNASeq to profile the bone marrow B cell compartment in lupus patients and healthy donors.

Results: We identified that in a subset of lupus patients, the early B cells (proB and preB cells) were strongly decreased, which were confirmed by flow cytometry in an expanded cohort. Furthermore, bone marrow B cells from these patients showed a strong proinflammatory signature revealed by pathway analysis. Interestingly, BCR repertoire analysis showed that the IGHV-4-34 was highly enriched in these patients, indicating an enhanced B cell tolerance defect. Finally, a panel of proinflammatory cytokines (TNF- α , IL-1 α , IL-12p70, IFN- γ , et al.) were strongly increased in the bone marrow plasma of these patients compared with early B normal patients and healthy donors, confirming a localized proinflammatory microenvironment.

Conclusion: Altogether, the current study has revealed that a defective early B cell development in lupus patients is associated with a more severe B cell tolerance defect and aggravated inflammation, which may shed new light on developing novel therapies by targeting relevant pathways.

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Education

OP0074

A FRAMEWORK OF POTENTIAL INTERVENTIONS TO ACCELERATE GENDER-EQUITABLE CAREER ADVANCEMENT IN ACADEMIC RHEUMATOLOGY

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Background: A growing number of professional societies in clinical and medically related disciplines investigate evidence, make recommendations, and take action to advance gender equity. Evidence on women's advancement and leadership in the context of the European Alliance of Associations for Rheumatology, EULAR, is limited [1].

Objectives: The objective of the EULAR Task Force on Gender Equity in Academic Rheumatology was to establish the extent of the unmet need for support of female rheumatologists, health professionals and non-clinical scientists in academic rheumatology and develop a framework to address this through EULAR and Emerging EULAR Network (EMEUNET).

Methods: Potential interventions to accelerate gender-equitable career advancement in academic rheumatology were gathered from a narrative review of the relevant literature, expert opinion of a multi-disciplinary Task Force (comprised of 23 members from 11 countries), data from the surveys of EULAR scientific member society leaders, EULAR and EMEUNET members, and EULAR Executive Committee members. These interventions were rated by Task Force members, who ranked each according to perceived priority on a five-point numeric scale from 1 = very low to 5 = very high.

Results: A framework of 29 potential interventions was formulated, which covers six thematic areas, namely, EULAR policies, advocacy and communication, EULAR Congress and associated symposia, training courses, mentoring/peer support, and EULAR funding (Figure 1).

Theme	Intervention	Level of priority, Mean	SD
EULAR policies	Requirements for EULAR Centres of Excellence to demonstrate commitment to gender equity	4.5	0.8
	Gender-equitable EULAR committees, working groups, and task forces	4.4	0.8
	Gender-equitable grants committees	4.0	0.9
Advocacy and communication	Gender-equitable editorial boards and peer-review in rheumatology journals	3.9	1.0
	Campaigns to increase visibility of female role models and promote women's leadership	4.5	0.7
	Raising awareness of unconscious bias and gender equity issues in rheumatology	4.3	1.0
EULAR Congress and associated symposia	Promoting gender-sensitive clinical practice, research and training	4.1	1.0
	Engaging national rheumatology groups to develop country-specific support	3.6	1.2
	Monitoring gender equity of chairs and invited speakers (invitees and acceptances)	4.6	0.7
Training courses (open to men and women)	Increasing visibility of female role models	4.4	0.7
	Family- and child-friendly policies	4.1	1.2
	Code of Conduct expressing and enforcing the values of diversity and inclusion	4.1	0.9
Mentoring/peer support (open to men and women)	EULAR no male only panel pledge	4.0	1.1
	Collating a register of female experts in field	3.5	1.3
	Leadership skills training	4.2	0.7
EULAR funding	Training and support for writing grant applications	4.0	0.8
	High-impact scientific writing masterclasses	3.8	1.0
	Effective work-life balance management training	3.8	0.9
EULAR Congress and associated symposia	Speaking/presentation/communication skills training	3.7	0.9
	Unconscious bias training	3.7	1.0
	Promotion and salary negotiation training	3.6	1.0
Mentoring/peer support (open to men and women)	Peer to peer mentorship programmes	4.2	1.1
	Information on training/career pathways	4.0	1.0
	Senior sponsorship programmes	3.8	1.0
EULAR funding	Effective work-life balance training	3.6	1.1
	Monitoring gender equity in EULAR funding	4.3	0.7
	Career grants for mid/senior women academics	4.0	1.1
EULAR funding	Funding calls for research on gender-sensitive clinical practice, research, and training	4.0	1.1

Figure 1. A framework of potential interventions with the levels of priority, mean and standard deviation (SD)

Conclusion: The framework provides structured interventions for accelerating gender-equitable career advancement in academic rheumatology.

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OP0075

EVALUATION OF A VIRTUAL REALITY TEACHING CONCEPT FOR MEDICAL STUDENTS DURING THE SARS-COV-2 PANDEMIC

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Background: The ongoing COVID-19 pandemic has disrupted face-to-face teaching of medical students and forced efforts in finding alternative approaches. In order to help maintain high-quality education, a new virtual reality (VR)-based concept for training medical students in rheumatic and musculoskeletal diseases (RMD) has been developed. This VR training concept is based on the integration of real patient data with two- and three-dimensional visualized pathological joints from X-ray and computed tomography generated images.

Objectives: To evaluate the practicability and acceptance of the VR training application in the digital curricular education of medical students during the COVID-19 pandemic.

Methods: A short refresher lecture on rheumatic diseases (duration 60 minutes) was followed by presenting the VR training concept to the students. The VR training concept included the demonstration of three virtual patients with early rheumatoid arthritis, rheumatoid arthritis psoriatic arthritis regarding the symptoms, current medical problems, disease patterns at the imaging (conventional radiographs and high-resolution computed tomography) and therapy options. The practicability and acceptance of the VR was evaluated by medical students using a survey.

Results: The study encompassed 237 medical students (163 female, 73 male, one diverse, age range 20 to 40 years). 72 % of the participants rated the virtual teaching as good or very good. 87 % presented an expanded knowledge for rheumatoid arthritis and psoriatic arthritis through the VR. Moreover, 91 % reported that the lecture provided a deeper understanding of RMD. Furthermore, 60 % of the students asked for additional courses by VR.

Conclusion: The study highlighted the usefulness of innovative VR tools for teaching medical students digitally about RMD. VR applications can be a complementary educational modality for medical students, especially during the COVID-19 pandemic, to provide students with the best possible clinical experience while ensuring that patient, student, and staff safety is not compromised.



Figure 1. A Screen view of virtual reality included three virtual patients with early rheumatoid arthritis (RA), RA, and psoriatic arthritis (PsA) and B demonstration of structural damage in RA and PsA using hand X-ray and high-resolution quantitative computed tomography images.

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