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Supplementary information

Antigen-driven T cell responses in rheumatic diseases: insights from T cell receptor repertoire studies

In the format provided by the authors and unedited

Supplementary Table 1: TCR repertoire findings in spondyloarthropathies

Main findings of TCR repertoire studies in SpA conditions, reactive arthritis (ReA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and associated conditions, such as acute anterior uveitis (AAU). For the different groups and types of tissue studied, the (N) number of individuals or samples is indicated where applicable. HC, healthy controls; PB, peripheral blood; SF, synovial fluid; ST, synovial tissue; NR, not reported; N.S., not shared (for HLA carriage or clonotype detection). Particularly relevant studies highlighted in bold.

Method	Groups / # HLA typing	Tissue / Population	Diversity and clonality	Biased V-usage	Reported clonotypes-functional associations	Ref.
Ag reactivity	ReA (4) and AS (2) / #HLA-B*27+	SF / CD8+ T cell lines (354)	NR	NR	CTL clones reactive to uninfected and bacteria-infected B*27+ APCs	1
Ag reactivity + PCR + Sequencing	ReA (3) and HC (1, B*27 +/-) / #HLA-B*27+	PB + SF / T cell lines (27 B*27+ and 14 B*27-)	NR	Vβ13, Vβ14, Vβ17	Clones reactive to enterobacteria or self-antigens	2
Spectratyping + Sequencing	RA (6) / #HLA-DRB1* typing (4/6)	PB + SF / T cells	Clonotypic expansions in SF and PB	Biased V gene usage in SF compared to PB	Identical clones in different joints and PB (BV17-BJ2S1 and BV18-BJ2S3)	3
Ag reactivity	PsA (14), HC (12) and Atopic Dermatitis (6). / #NR	PB / T cells	NR	NR	Reactivity (IFNγ production) to group A beta-haemolytic streptococcal M6 peptide, homolog to human keratin	4
Spectratyping + Sequencing	**ReA (7) / #HLA-B*27+**	**PB + SF / T cells**	**NR**	**NR**	**CD8+ T cell expansions carrying Vβ1-J2S3 in SF**	**5**
PCR + sequencing	PsA (9) and HC (6) / #HLA-typing, N.S.	PB + SF + Skin / T cells	NR	PB expansions: BV5S1, BV6S7, BV8S3, BV12S2, BV13S1, and BV23S1 SF and Skin dominating expansions: BV1S1, 3S1 and 7S1 .	Common expansions between SF and skin, also homologous between patients (numerous sequences reported)	6

PCR + sequencing	Chronic RA (31), early RA (7), OA (5), PsA (4) and HC (10) / #NR	PB + SF/ST / T cells	Higher diversity in chronic vs early RA	Yes in SF (shared between joints). N.S. among patients	Many reported (BV2 and BV4). N.S. among patients	7
Spectratyping + Sequencing	**PsA (6) and HC (8) / #HLA-B 27052/5701, 0702/44031, 0801/3501, 0702/0801, 0801/5501, and 27052/1402.**	**Paired PB + SF / CD8+ and CD4+ T cells**	**Clonality of CD8 T cells in SF >> PB > CD4 T cell in SF. No CD4 clonality in PB**	**BV16 oligoclonality**	**32 major CD8+ T cell oligoclonal expansions (inc. BV16-CASSQS(P/M)GGTQY- BJ2S3) and some among CD4+ T cells. N.S. among patients.**	**8**
Spectratyping + Sequencing	ReA (16), AS (4), RA (6) and B*27+ HC (7) / #HLA-B*27+	PB + SF / T cells	NR	NR	Vβ1-CASSVG(V/I/L)(Y/F)STDTQYF-J2S3	9
PCR + Sequencing	PsA (14) / #N.D.	Paired PB + SF + Skin (3) or PB + SF (11) / T cells	NR	SF vs PB: increase of TRBV13.1, TRBV15 and others (heterogeneous). Skin vs PB: increased of TRBV2, TRBV3 and TRBV14	No strong evidence of clonal expansion. Reported shared SF and Skin clonotypes	10
Spectratyping	PsA: before (4), before and during methotrexate treatment (5), and in active disease (5) / #NR	PB + SF / CD8+ and CD4+ T cells	Diverse repertoire, with homologous expansions among CD8 T cells (persistent but responding to metotrexate treatment).	NR	CD8+ T cells clonotypes (many EBV-specific TCRs). Numerous sequences reported (including homologs of BV14-SQSPGGTQY)	11
Spectratyping	RA SF (6), RA PB (2) and PsA SF (3) / #	PB + SF / T cells	Oligoclonal repertoire of VLA1+ SF T cells, different from VLA1- SF T cells and VLA1+ PB T cells	NR	NR	12

NGS (Multiplex PCR)	**AS (191 - B*27+, 43 - B*27-) and Controls (227: 174 SLE, 19 HC, 24 mechanical back pain and unknown HLA type, and 10 B*27+ HC) / #HLA-B*27+/-**	**PB / T cells and CD8+/- T cells**	**NR**	**NR**	**Motif association with B*27+ AS, present among CD8+ T cells (6 published and 15 new)**	**13**
NGS	**PsA and HC (5) / #NR**	**PB + Skin / CD8+ T cells**	**Skin Trm cell contain oligoclonal CD103+CD49a+ CTLs (involved in vitiligo) and IL-17-producer CD8+CD49a- Trm (involved in psoriatic skin inflammation)**	**TRBV27 epidermal T cells**	**NR**	**14**
NGS (5'-RACE)	AS (25) and HC (13 new + 95 published) / #HLA-B*27+/-	PB + SF (5 AS) / T cells	NR	NR	8 homologous clones (TRBV9-CASSVGLYSTDTQYF-TRBJ2-3 motif) in PB CD8+ T cells of AS patients (frequency 0.006-0.00008%). Enriched in SF.	15
NGS + Algorithm-based identification of motif-Ag-reactivity	axSpA (21) / #HLA-B*27+	PB (21) + SIJ-Fluid (2) / T cell subsets: CD8+, CD4+CD45RA+, and CD4+CD45RO+	Clonality of Temra correlates with disease activity and of CD4+CD8+ T cells with disease progression	NR	Shared CDR3s among CD4+CD45RO+ and CD8+ T cells in active patients	16
NGS (Multiplex PCR)	**AS (47) and HC (38) / #HLA-B*27+/-**	**PB / CD4+ and CD8+ T cells**	**Increased diversity and reduced clonality in AS (B*27+/-). No differences with anti-TNF treatment**	**AS-CD4 repertoires enriched for TRBV11, TRBV13, TRBV21, TRBV5, and TRBV3 AS-CD8 repertoires enriched in TRBV5 Low disease status prediction value**	**AS-associated CD8 expansions (variable V-J, 5 using TRBV27, 1 frequently reported in SpA): CASSVGLFSTDTQYF, CASSLSGGNTEAFF, CASSLSGQGYEQYF, CASSLGRAYEQYF, CASSLGSTYEQYF, CASSLGRTGELFF, CASSLGTYGYTF, CASSQGTGELFF, CASSTGTGGYEQYF, CASSSGTGGNQPQHF AS-associated CD4 expansions (variable V-**	**17**

					J): CASRGTGNQPQHF, CASSRGGSYEQYF, CASSLTGGNQPQHF **Expanded EBV and CMV-specific clonotypes in AS patients.**	
NGS (Multiplex PCR)	PsA (3) / #NR	PB + SF / Bulk memory, IL-17A+IFNγ+/− (Tc17) or IL-17A−IFNγ+ (Tc1) memory CD8+ T cells	NR	NR	Synovial Tc17 cells are a polyclonal subset of proinflammatory Trm cells (expressing CXCR6)	18
scRNAseq (10X 5')	**PsA (9) / #HLA-typing, N.S.**	**Paired PB + SF (7) or ST (2) / CD4+ and CD8+ T cells (total 41k cells)**	**Clonal expansions of CD8 T cells (TRAV27+ ZNF683+ CD8 cluster) and CD4+ Tregs in joints compared to PB**	**TRBV27 and TRBV28**	**Clonal convergence in GLIPH groups (numerous CDR3 reported).**	**19**
NGS (5'RACE) for TCRA + TCRB	**PsA (17) and AS (35) / #HLA-B*27 or HLA-B*38 alleles (Clonal expansions shared between patients with shared HLA alleles)**	**SF (28) + PB (35) / T cells**	**Ag-driven CD8 expansions associated with SpA are enriched in SpA SF > SpA PB > HC PB. Presence maintained over time.**	**NR**	**HLA-B*27: TRBV9-CASSVGLYSTDTQYF-TRBJ2-3, TRBV5-5-CASSLGLAGGPNTGELFF-TRBJ2-2, TRBV2-CASRTGVPYEQYF-TRBJ2-7, TRBV7-9-CASSSRDYTYEQYF-TRBJ2-7** **HLA-B*38: TRBV10-2-CASSESPGNSNQPQHF-TRBJ1-5, TRBV19-CASSPGTDTQYF-TRBJ2-3, TRBV6-5-CASSYGQLSTDTQYF-TRBJ2-3, TRBV29-1-CSVEVWDSSYNEQFF-TRBJ2-1, TRBV5-1-CASSLKRNEQFF-TRBJ2-1**	**20**

scRNAseq and Ag-screening	**AS (7+4) and AAU (4) / #HLA-B*27+**	**PB + AS-SF + AAU-Ocular Fluid / T cells (all CD3+, CD8+ or TRBV9+CD8+)**	**NR**	**NR**	**TRBV9-J2-3/TRAV21 clone and their cognate peptides from human (GPER1, PRPF3, RNASEH2B,...) and bacterial (YEIH, gspD,...) proteins**	**21**
scRNAseq	AS (10 B*27+, 4 B*27-) and RA (3 B*27-) / #HLA-B*27+/-	PB + SF / Ag-experienced CD8+ T cells	NR	Biased V gene usage in B*27+ AS SF compared to PB, particularly of TRAV families	TRAV21 expansions in SF	22
scRNAseq (10X 5')	PsA (4) / #NR	SF / CD8+ T cells	NR	NR	Polyclonal CD161+CCR6+ Tc17 Trm cells with a pro-inflammatory profile (IL-17A+TNFα+IFNγ+) specifically enriched in PsA. Presence of CD4+ Treg-like Trm in both PsA and RA.	23
scRNAseq (10X 3' and 5') + Bulk TCR sequencing	Immune checkpoint inhibitor-arthritis (5), RA and PsA / #NR	PB + SF + ST / T cells and CD8+ T cells	NR	NR	Expansion of activated $CD38^{hi}$CD127- CD8+ T cells in ICI-arthritis vs RA and PsA (bound to anti-PD1 drug)	24
Therapeutic TRBV9 depletion	AS (1) / #HLA-B*27	TRBV9 cells	NR	NR	Sustained clonotype depletion and remission with anti-TRBV9 therapy	25
TCR (scRNAseq) and Ag-screening	**AS (2) and AAU (14) / # HLA-B27**	**PB + ocular fluid (29 CD8 T cells with disease associated TCRs)**	**NR**	**TRAV21. TRBV9 not strictly required**	**YeiH-specific CD8 T cells express a mucosal gene set indicative of intestinal differentiation (CD161, integrin a4b7, and CCR6)**	**26**

Supplementary Table 2: TCR repertoire findings in rheumatoid arthritis

Main findings of TCR repertoire studies in rheumatoid arthritis (RA). For the different groups and types of tissue studied, the (N) number of individuals or samples is indicated where applicable. HC, healthy controls; PB, peripheral blood; SF, synovial fluid; ST, synovial tissue; NR, not reported; N.S., not shared (for HLA carriage or clonotype detection). Particularly relevant studies highlighted in bold.

Method	**Groups / # HLA typing**	**Tissue / Population**	**Diversity and clonality**	**Biased V-usage**	**Reported clonotypes-functional associations**	**Ref.**
Southern blot	RA (11) and OA (3) / #NR	PB + ST / T cell clones	Clonality in ST vs PB	NR	NR	27
PCR + Sequencing	RA (9) vs arthritic (PsA and Reiter´s Sindrome) (3) and non-arthritic (11) controls. / #HLA-typing, N.S.	PB + SF / T cells	NR	Synovial Vβ14 (compared to PB and other conditions)	Yes. N.S. among patients	28
PCR + Sequencing	RA (5) / #HLA-typing, N.S.	SF / T cells	NR	Synovial Vβ3, Vβ14, and Vβ17	Superantigen binding sequences	29
PCR	RA (24), arthritic control (OA/JCA, 4) and HC (15) / #HLA-typing, N.S.	PB + SF (13) + ST (8) / T cells	NR	Increased Vβ6, Vβ14 and Vβ15 in synovial T cells. Decreased Vβ1, Vβ4, Vβ5.1, Vβ10, Vβ16, and Vβ19	NR	30
PCR + Southern blot + Sequencing	Juvenile RA (27) / #HLA-DR4+	PB (3) + SF (2) + ST (2) / T cells	NR	Vβ14 enrichment	(Vβ14) CAS-GSPDAGW-TDTQY (Jβ2.3) and other minor expansions	31
FC + Southern blot	RA (14, SF+PB) and HC (21, PB) / #NR	PB + SF / T cells	NR	Vα2 in SF vs PB	NR	32
PCR + Sequencing	Early RA (5) and HLA-matched HC / #HLA-DRB1*04	PB + SF / CD4+ T cell clones	NR	Expansions of Vβ3+, Vβ14+, and Vβ17+	NR	33
PCR	RA (13) / #HLA-typing, N.S.	PB + Synovial Membrane / T cells	NR	Increase in Vβ3, Vβ17, and Vβ22. Decrease in Vβ4	NR	34

Spectratyping + Sequencing	RA (6) / #HLA-DRB1* typing (4/6)	PB + SF / T cells	Clonotypic expansions in SF and PB	Biased V gene usage in SF compared to PB	Identical clones in different joints and PB (BV17-BJ2S1 and BV18-BJ2S3)	3
RT-PCR + SSCP + sequencing	RA (6) / #YES	Paired PB + SF + ST / T cells	Trend to clonal repertoire in early RA	Jβ2.1	Various CDR3 reported, converging among different tissue samples of the same patient	35
Sequencing	RA (2), at different time points / #HLA-DR4+	PB + ST (membrane) / T cells	Persistence of a fraction of clones over time, but overall spreading effects	TRBD usage	Yes. CDR3-Valine insertions and GXXG and TSG motifs	36
PCR + Sequencing	Seropositive RA (15), PsA (11), HC (20), and 7 families with siblings RA-affected (9) or unaffected (13) / #HLA-DRB1 typing	PB + SF / CD4+ T cells	Clonal expansion in PB CD4+ T cells, partially shared by unaffected siblings	NR	Some CDR3 reported	37
FC + PCR + Sequencing	RA (30) and HC (30) / #HLA-DRB1 typing	PB / CD28+ vs CD28- CD4+ T cells	Oligoclonality of CD4+ CD28- T cells in RA	NR	Some CDR3 reported	38
Multiplexed PCR	RA (32) and controls (25) / #HLA-DR4	PB / CD8+ T cells	NR	Vβ3 oligoclonal CD8+ T cells	9 dominant Vβ3 clonotypes, some shared CDR3 sequences	39
PCR	RA (8) / #HLA-DR typing	PB + SF / T cells	Reduced TRAV and TRBV diversity in early RA SF	Predominance of TRAV17 in early RA	NR	40

PCR + Spectratyping + Sequencing	RA / #NR	PB + SF / T cells	Clonal expansion in SF, persistent but fluctuating over time.	SF tissue bias compared to PB	SF clonotype BV8-BJ2S3 increase over time	41
PCR	**Healthy monozygotic twins (6 pairs), monozygotic twins discordant for RA (6 pairs), and siblings of a large family (9), including RA (3) / #HLA-typing, N.S.**	**PB / CD4+ T cells**	**RA-associated alterations among CD4+ T cells**	**NR**	**NR**	**42**
Spectratyping + Sequencing	Long-standing RA (11) / #NR	PB + SF / CD4+ and TRBV2+ CD4+ T cells	Clonal populations among CD4+ T cells	TCRBV2+ expansions	NR	43
FC + PCR + Sequencing	RA (3) / #HLA-DR4:04	Paired PB + SF / CD4+ T cells	NR	Biased Vβ sharing between joints but not PB within patients	Homologous TCRA and TCRB sequences among joint in RA patients, but not PB. Similar TCRα and TCRβ chains among RA patients, including: BV14-CASSLGTEGYGYTFG-BJ1.2 and AV1S2-CAVRXSGSARQLTFG-AJ22	44
Spectratyping	RA (14) and controls (12) / #HLA-DRB1 alleles	PB / CD8+ and CD8- T cells	Clonotype expansions	Yes	Reported dominant CDR3s	45
PCR + sequencing	Chronic RA (31), early RA (7), OA (5), PsA (4) and HC (10) / #NR	PB + SF/ST / T cells	Higher diversity in chronic vs early RA	Yes in SF (shared between joints). N.S. among patients	Many reported (BV2 and BV4). N.S. among patients	7
FC	RA (19), including early (8) and long-standing (7) RA, SpA (21) and controls (10) / #HLA-DRB1 typing	PB (4) + SF (8+7) + Subcutaneous Nodules (19) from RA / T cell lines	Reduced diversity in early diseased tissue (SF or nodules) vs control.	Vα2	Signs of clonotype associations and preferential binding to joint tissues	46
FC + Ag reactivity	RA (20), SLE (18), SSc (13), SS (17), Behçet's disease (20), and HC (13) / #CD1d	PB / NKT (TRAV24+TRBV11+ CD4-CD8- NKT)	NR	NR	Reduced BV11+ AV24AJ18+ regulatory NKT cells reactive to alpha-Gal-Cer-like natural ligands	47

FC + Ag reactivity (tetramer)	RA (5) and JIA (1) / #All HLA-A02+, 1 HLA-B8+	PB + SF / CD8+ T cells	NR	Yes	Clonal CD8+ T cells specific for EBV, CMV, and influenza are enriched in SF vs PB in inflammatory arthritis	48
FC + Spectratyping	JRA (9) at onset and treatment naive / #NR	PB + SF / CD4+ and CD8+ T cells	Oligoclonal SF repertoire, mostly among CD8+ T cells	NR	NR	49
Spectratyping of BV6 and BV14	RA (94) / #NR	PB / CD4+CD28- T cells	NR	Correlation of CD4+CD28- T cell abundance and BV14 (BV14-BJ1S2 and BV14-BJ2S3 rearrangements)	NR	50
FC + PCR + Spectratyping	RA (37) and OA controls (7) / #HLA-typing. 43% HLA-DRB1*0405.	PB + SF/ST / T cells	NR	BV14 and BV16 in synovium of RA, predominantly in CD8+ T cells. BV16 correlation with DRB1*0405	Reported BV14/BV16 clonotype sequences (shared motifs among patients): BV16-CASSQADGTHYEQFFGPG-J2S7, BV14-CASSSGGSLFYEQYFGPG-J2S7	51
FC + Ag reactivity	RA (23) and HC (22) / #CD1d	Paired PB + SF or ST / NKT	NR	NR	Reduction in BV11+AV24+ iNKT in PB, SF and ST, with reduction of IL4/IFNγ ratio.	52
Spectratyping	RA SF (6), RA PB (2) and PsA SF (3) / #	PB + SF / T cells	Oligoclonal repertoire of VLA1+ SF T cells, different from VLA1- SF T cells and VLA1+ PB T cells	NR	NR	12
PCR + Spectratyping	RA (11 - ACPA+ , 7 - ACPA-) , and SpA controls (10) / #NR	PB + ST / T cells	Oligoclonal synovial T cell expansions in ACPA+ RA compared to ACPA- RA. No impact of RF status	Yes, in synovium of ACPA+RA	Some CDR3 reported	53
Ag reactivity	RA (28) and HC (18) / #NR	PB / T cells	NR	NR	>60% reactivity to citrullinated aggrecan peptide Agg(84-103) in RA, inducing CD4+IL17+ cells	54

FC + Ag reactivity	RA (46, 23 untreated, newly diagnosed patients), HC (22) and recent-onset joint pain (27) / #CD1d	PB / iNKT	Inverse correlation of iNKT frequency and inflammatory levels (CRP). Therapy increase iNKT frequency. Normal iNKT frequency predicts non-RA joint pain.	NR	NR	55
Ag reactivity (proliferation, activation and multiplex immunoassay)	RA (60), OA (32) and HC (32) / #HLA-B and HLA-DRB1 and DRB3–5 typing	PB / T cells	NR	NR	T cell reactivity to proteoglycan aggrecan epitopes (p263–282) in RA and OA, homologous and cross-reactive to YscL translocation protein L (pY68–82)	56
NGS	**Early RA (6) and established RA (6) / #NR**	**PB + SF / T cells**	**Diversity increases with disease progression**	**TRBV6.5, TRBV5.6 and TRBV29.1, among others**	**Highly expanded clones are patient-specific. Overlap among ST > SF > PB**	**57**
FC	SLE (3 active and 3 in remission) and HC (10) / #NR	PB / Foxp3+ Helios+ Treg	Skewed repertoire and reduced diversity in Foxp3+ Helios+ Treg in active SLE.	Vβ13.1	NR	58
RT-qPCR	Acute RA (4), chronic RA (8) and HC (12) / #NR	PB + SF / T cells	Unclear	Yes, also between blood and SF	NR	59
FC + Spectratyping	RA (17), before and after 12-month Abatacept treatment / #NR	PB / T cells	Treatment-induced increase diversity related to reduced CD4+CD28- T cell clonotype expansions	YES	NR	60
NGS + scRNAseq	RA (5) / #HLA-DRB1	PB (5) + SF (1) / Expanded CD4+ T cells	NR	NR	Expanded clones show signature of continuous stimulation.	61

FC + Functional Evaluation	Early RA (27) and HC (21) / #CD1d	PB / iNKT cell clones (296)	Reduction of high-affinity iNKT clones in early RA. No change with treatment.	Low-affinity iNKT-TCRs	NR	62
FC + NGS	JIA (6) and RA / #NR	Paired PB + SF / Circulating pathogenic CD4+ T cells (CPT, HLA-DR+ CD25 low/−)	Diversity of PB T cells > CPT (PB) > SF T cells. Abundance of CPT correlate with treatment resistance and disease activity in JIA and RA	NR	CPT are enriched in SF clonotypes	63
Ag reactivity + Spectratyping	Early-RA (90), of which 55 at two time points / #HLA-DRB1*04	PB / Coll261-273-specific T cells secreting IL-13 and IL-17	Association of disease activity with Collagen-p261-273-specific T cells carrying TRBV25 in HLA-DR4+ RA.	TRBV25 in Coll261-273-specific T cells	NR	64
Ag reactivity + NGS	RA (15) and HC (5), both HLA–DRB1*10:01 / #HLA–DRB1*10:01	PB / cit-CII-reactive CD4+ T cells	NR	Cit-CII–specific clones showed higher usage of Vβ6.1, Vβ6.3, and Vβ18, and Jβ1.1 and Jβ2.2	Presence of CD4+ T cell reactivity to cit-CII, binding (with low affinity) to HLA–DRB1*10:01 but not to HLA–DRB1*04:01	65
NGS	JIA (11: 8 PB + 3 SF), children with Lyme arthritis (2 SF) and HC children (3 PB) / #HLA-class II typing	PB + SF / Tregs	Restricted repertoire in Tregs in PB and SF	Increased usage of TRBV7 and reduced TRBV3	Clonotype sharing among JIA but not Lyme arthritis	66
Ag reactivity (tetramers)	10 HLA-DRB1*14:02+ Indian North American patients with RA, 10 HLA-DRB1*14:02+ ACPA− FDRs and 6 HLA-DRB1*14:02+ non-INA HC subjects	PB	NR	TRBV20–1, TRBV30, TRAV13–2 and TRAV26–1	Oligoclonal autoreactive CD4+ effector T cells against citrulline and arginine forms of vimentin59-71, with different phenotypic characteristics.	67

NGS (Adaptive Biotechnologies)	JIA (11) / #NR	Paired PB + SF / iaTregs (inflammation-associated (HLA-DR+) Tregs)	NR	NR	PB-inflammation-associated Tregs (HLA-DR+) are enriched in clonotypes of SF-Tregs, and share TCRs with pathogenic effectors. Patient-specific repertoire, N.S.	68
NGS	RA (22) and HC (18) / #HLA-DRB1	PB / Naive vs Memory CD4+ T cells	Reduced diversity in memory CD4+ T cells with risk-HLA carriage, Dis. Act. and serum IL-2 in RA	Yes	NR	69
NGS	**RA (13) / #HLA-DPB1, HLA-DQB1 and HLA-DRB1 typing**	**Paired PB+SF+ST (7), PB+SF (3) and PB+ST (3) / T cells**	**Within an RA patient, clonality and overlap of ST-ST > ST-SF > ST-PB**	**NR**	**NR**	**70**
NGS	824 individuals (including RA) / #HLA-typing, N.S.	PB / CD8+ and CD4+ T cells	NR	Stronger bias in men	Expansions of CD8 T cells in RA, especially in men, are less dependent on high HLA-binding than in CD4 T cells	71
NGS (5' RACE)	JIA (7, TCR analysis in 4), control children (17) or adults (33) / #NR	PB + SF / PD1+ vs PD1- CD8+ T cells	NR	NR	Clonal expansion of PD1+ CD8 SF T cells compared to PD1-, with active and Trm phenotype	72
NGS + statistical approach	**SLE (877), RA (206) and HC (439) / #NR**	**PB / T cells**	**Diversity of HC > RA > SLE. Public clonotypes and disease-associated clones correlate with disease activity/treatment resistance**	**Differences in V, J and V-J pairing**	**198 SLE-associated and 53 RA-associated TCRs. 12 shared clones: TRBV7-J1-1 CASSLYENTEAFF, TRBV2-J2-5 CASSEGAGGGETQYF, TRBV/-J1-1 CASSLEAVNTEAFF, TRBV15-J2-5 CATSRVAGETQYF, TRBV2-J2-5 CASSGTGGAETQYF, TRBV15-J2-7 CATSRGTVSYEQYF, TRBV7-J1-1 CASSLETVNTEAFF, TRBV6-J2-7 CASSYSGADEQYF, TRBV5-J1-2 CASSLDGKGYTF, TRBV12-J2-5 CASSFEETQYF, TRBV4-J1-2**	**73**

					CASSQDLGTGGASGYTF, TRBV27-J2-3 CASSSRLAGGTDTQYF	
NGS (Multiplex-PCR)	RA (8): adalimumab only (2), adalimumab+rituximab (3), and adalimumab+tocilizumab (3) / #NR	PB / T cells	Trend to increased TCR repertoire diversity with treatment response. No differences among treatments	NR	NR	74
NGS	**RA (12) and HC (8) / #NR**	**PB / CD4+ T cell subsets: naïve, effector, Tcm, Tem, Th1, Th17, and Tregs**	**Higher clonality of Tem and Th17 and lower clonality for Tregs. Th17 diversity and abundance correlated with disease activity.**	**TRBV3-1 increase across different subpopulations and in SF**	**Clonotype expansions shared among Tem and Th17**	**75**
NGS	RA (4) / #NR	SF / Memory CD8 T cells (CD45RA-) subsets: CD69+CD103+, CD69+CD103- and CD69-CD103-	Oligoclonal repertoire in Trm (CD69+CD103+-) SF CD8 T cells	NR	NR	76
NGS	RA (20) and First-Degree Relatives (20), at 3 pre-clinical stages / #NR	PB / T cells	Clonality of RA > symptomatic RA-FDR > asymptomatic RA-FDR. No clonal expansion correlations with disease progression	NR	Diverse CDR3s. Most frequent ones CASSLGQAYEQYF, CASSPNTDTQYF, CASSPGQGGETQYF, CASSPGSYGYTF, CASSRDRGNYGYTF.	77
FC + NGS (Nested-PCR)	RA (FC, 9; NGS, 3) / #NR	SF + PB / PD-1^{hi} and PD-$1^{low/-}$ CXCR5-CD4+ T cells in SF and	NR	Bias of TRBV usage among $PD1^{high}$ Tph cells (Vβ9, Vβ18)	Expansion of Tph cells in SF (different repertoire than synovial $PD1^{low}$ or circulating memory T helpers). Tph autoreactivity in vitro, regulated by PD1.	78

		CD45RA-CD4+ T cells in PB				
Ag reactivity (tetramer, APC-stimulation and FluoroSpot)	RA (9) and HC (7) / #HLA-DRB1*04:01	PB + SF (7) / CD4+ T cells	NR	NR	Reactivity against cit-TNC among CD4+ T cells in PB (with Th2/Th17 phenotype) and SF	79
scRNAseq + Ag reactivity (tetramer)	RA (8) / #HLA-DRB1*04:01	PB + SF / T cells	NR	NR	cit-TNC-reactive clones (TRBV20-1)	80
Ag reactivity + Sequencing	RA (2) and HC (2) / #HLA-DRB1:04:01	PB / T cells	NR	Mouse TRBV4+ /TRAV6+ pairing. Human TRBV3-1 usage (the ortholog of mouse TRBV4)	Mouse CDR3b motif “(L)DW(G)”	81
scRNAseq (10X)	**RA (4 ACPA+, 4 ACPA–) / #NR**	**Paired PB + SF / CD4+ T cells**	**NR**	**NR**	**Expanded clonotypes in SF are within CXCL13high Tph CD4+ T cells, with a subset expressing GPR56, LAG-3 and the tissue-resident memory receptors CXCR6 and CD69**	**82**
scTCR seq	RA (11 - ACPA+ , 5 - ACPA-) / #NR	ST / T cells	NR	Biased usage of TRBV20-1 in CD4+ cells from ACPA+ patients	Presence of virus-specific TCRs. High frequency of double TRA chain.	83
Bulk RNAseq + MiXCR recovery of T/BCR	ImmuNexUT database (407 donors with 10 IMIDs and HC) / #HLA associations with IRR	PB / Different lymphocyte populations	NR	Risk HLA associations with TRBV usage of naive and effector CD4+ T cells.	Public clones accumulating among Th17	84
Ag reactivity	RA (29) and HC (12) / #HLA-DRB1 typing	PB / T cells	NR	NR	Identified 6 new Ags recognised by RA-CD4+ T cells: Gelsolin, Histone H2B, cit-Histone H2B, cit-	85

					Proteoglycan 4, Histone H4, MPO, cit-Agrecan	
NGS (Multiplex PCR)	RA (176, before and after 3 and 6 months treatment) and HC (439) / #NR	PB / T cells	Reduced diversity and increase in hyperexpanded clones correlating with Dis. Act. Therapeutic efficacy associates with recovered richness. No differences between ANA+ and ANA- RA.	Global skew of V/J gene usage, not defined changes	Shorter CDR3 sequences. Match with 6 reporter RA-clones: CASSLDGKGYTF/ CASSLTDVAYEQYF/ CASSSRLAGGTDTQYF/ CASSYSGNDEQYF/ CATSRGTVSYEQYF/ CATSRVAGETQYF.	86
Bioinformatic TCR extraction	RA (196) and healthy or rheumatic controls / #NR	SF + PB / T cells	NR	NR	Database of high-frequency synovial TCR sequences in RA	87
scRNAseq (10X)	**RA seropositive (12) / #NR**	**Paired PB (10) + ST (12) / T cells**	**NR**	**Vδ1 gdT cells**	**Synovial enriched populations: oligoclonal CD8+ GzmK+ and likely-viral reactive, oligoclonal CD4+ Tph, Tfh and Tregs, and activated MAIT and Vδ1 γδT cells. Presence but no activation/expansion of viral-reactive clones.**	**88**
scRNAseq (10X 3' and 5') + Bulk TCR sequencing	Immune checkpoint inhibitor-arthritis (5), RA and PsA / #NR	PB + SF + ST / T cells and CD8+ T cells	NR	NR	Expansion of activated CD38^{hi}CD127- CD8+ T cells in ICI-arthritis vs RA and PsA (bound to anti-PD1 drug)	24
Ag reactivity (tetramers)	**ACPA+ RA / #HLA-DR4**	**PB and cell lines**	**NR**	**Preferential TRAV26-1 usage**	**T cells reactive to citrullinated epitopes presented by HLA-DR4**	**89**

Supplementary Table 3: TCR repertoire findings in systemic lupus erythematosus

Main findings of TCR repertoire studies in systemic lupus erythematosus (SLE) and associated comorbidities, such as lupus nephritis (SLE-NE). For the different groups and types of tissue studied, the (N) number of individuals or samples is indicated where applicable. HC, healthy controls; CTD, connective tissue disease; PB, peripheral blood; SF, synovial fluid; ST, synovial tissue; NR, not reported; N.S., not shared (for HLA carriage or clonotype detection). Particularly relevant studies highlighted in bold.

Method	Groups / # HLA typing	Tissue / Population	Diversity and clonality	Biased V-usage	Reported clonotypes-functional associations	Ref.
Ag reactivity (proliferation)	SLE and CTD / #NR	PB / T cells	NR	NR	T cell proliferation against U1 snRNP A, with overlapping B and T cell epitopes	90
PCR + sequencing	SLE (8) and HC (5) / #NR	PB / γδT cells	NR	Predominance of Vδ1 and Vδ2 with restricted junctional diversity	Reported CDR3 sequences	91
Sequencing	**SLE-LN (5) / #HLA-typing, N.S.**	**Cell lines / Autoantibody inducer CD4+ T cell lines (42)**	**NR**	**Vα8**	**CDR3 sequences reported, with shared motifs. Reactivity to nonhistone chromosomal protein HMG and nucleosomal histone proteins**	**92**
Spectratyping	SLE (5) and HC (2). Females / #NR	PB / T cells	Oligoclonality correlating with active disease	Wide effects	NR	93
Spectratyping + SSCP	SLE (9: 5 active and 4 inactive disease) and HC (9) / #NR	PB / T cells	Reduced diversity. Clonality correlates with disease activity.	No bias observed	NR	94
PCR + SSCP	SLE (10: 5 inactive, 3 active and 2 active + serositis) and HC (10) / #HLA-typing, N.S.	PB + pleural and pericardial effusions / T cells	Clonotypic expansion in active disease, further expanded in pleural and pericardial effusions	No bias observed	Shared rearrangements	95
Ag reactivity	SLE or mixed CTD (6) / #NR	PB / T cells	NR	NR	T cell clone reactivity to U1 snRNP 70kd, B and D polypeptides	96

PCR + Southern blot + Sequencing	SLE (4) / #HLA-DR and -DQ typing	PB + Skin / T cells	Diverse skin repertoire	NR	LXG motif in the CDR3 of skin-accumulated T cells from two patients. Various CDR3 reported	97
PCR + Southern blot + Sequencing	SLE-LN (20, including 10 pediatric SLE) and HC (10) / #NR	PB + Kidney (4) / T cells	Oligoclonal repertoire in kidney of SLE-LN, not in PB	Biased usage in Kidney	Vb6 - Jb1.1 rearrangement in Kidney	98
PCR + Sequencing	SLE (5) at different time points / #NR	PB (5) + Kidney (1) / T cells	Change in clonotypes during active disease.	NR	Reported BV5S1, BV8 and BV14 clonotypes. Homologous motifs within CDR3s	99
Spectratyping + Sequencing	**SLE (10) and HC (4) / #NR**	**PB / CD4+ T cells**	**Restricted CD4+ TCR repertoire. Clonality correlates with disease activity.**	**Vβ15**	**Numerous reported sequences. Acidic amino acids in CDR3s**	**100**
Nested PCR + Southern Blot	SLE-LN (12) / #NR	PB + Kidney / T cells	NR	Preferential usage of Vβ8, Vβ9, Vβ14, Vβ20	Oligoclonal expansions in Vβ8 and Vβ20 clonotypes. High IL-4 and IL-10 expression on intrarenal T cells	101
Spectratyping + Sequencing	SLE (20) and HC (6) / #NR	PB / T cells	Reduced diversity	Prominent usage of AV8, AV14, AV23, AV30, AV31, BV2, BV8, BV11, BV14, BV16, BV19 and BV24. Biased V usage correlated with disease activity	Reported CDR3 sequences. Conserved GGX amino acid motif in both α- and β-chains	102
PCR + Sequencing	**SLE-LN (25) / #NR**	**PB + Kidney / CD4+ and CD8+ T cells**	**Reduced diversity. CD8 T cell tubulitis associated with progressive disease**	**Yes**	**Shared PB and renal CD8+ T cell BV3-CASSLFLANRRDRGSDTQYF and BV6-CASRLDNAPNNEGFF**	**103**
FC	SLE (3 active and 3 in remision) and HC (10) / #NR	PB / Foxp3+ Helios+ Treg	Skewed repertoire and reduced diversity in Foxp3+ Helios+ Treg in active SLE.	Vβ13.1	NR	58

FC + Spectratyping	SLE (15) before, during and after i.v. Ig treatment / #NR	PB / Tregs	TCR perturbations respond to treatment	NR	NR	104
FC	Children with newly diagnosed SLE (9), T1D (15) and HC (31) / #NR	PB / CD4+ T cells	Abnormalities in SLE repertoire	Increased TRBV16 in SLE CD4+ T cells	NR	105
NGS	SLE (11) at 3 time points (quiescence, preflare, and flare stages) and HC (12) / #NR	PB / T cells	Reduced diversity. No TCR repertoire changes with flares	No preferential Vβ or Jβ gene usage among the top 100 expanded clones	NR	106
NGS (Multiplex-PCR)	SLE (10) and HC (10) / #NR	PB / T cells	Reduced diversity	Increased TRBV10-2 and TRBV23-1 Reduced TRBV3-1, TRBV6-2, TRBV6-3, TRBV6-4, TRBV7-1, TRBV12-5, TRBV18 and TRBV21-1	SLE-public CDR3 (shared by all): CARVPRAV∼NTGELFF CANYGYTF CASSLGYEQYF CAS∼FF	107
NGS (Multiplex PCR)	SLE (2), with corticoid treatment at 3 time points: before, 1 and 3 months after treatment) / #NR	PB / T cells	Repertoire changes (diversity, V usage and CDR3 expansions) in response to treatment	TRBV2, TRBV19, TRBV20 and TRBV28	Reported CDR3s	108

FC	SLE patients (27), SLE family members (47), sporadic SLE (37), and unrelated HC (15) / #NR	PB / T cells	NR	Increased Vβ5.2, Vβ11 and Vβ16, and reduced Vβ3, Vβ4, Vβ7.1 and Vβ17. Vβ17 is differentially expressed among sporadic and familial SLE. Vβ9 usage characterize familial SLE (cases and healthy relatives)	NR	109
NGS + statistical approach	**SLE (877), RA (206) and HC (439) / #NR**	**PB / T cells**	**Diversity of HC > RA > SLE. Public clonotypes and disease-associated clones correlate with disease activity/treatment resistance**	**Differences in V, J and V-J pairing**	**198 SLE-associated and 53 RA-associated TCRs. 12 shared clones: TRBV7-J1-1 CASSLYENTEAFF, TRBV2-J2-5 CASSEGAGGGETQYF, TRBV/-J1-1 CASSLEAVNTEAFF, TRBV15-J2-5 CATSRVAGETQYF, TRBV2-J2-5 CASSGTGGAETQYF, TRBV15-J2-7 CATSRGTVSYEQYF, TRBV7-J1-1 CASSLETVNTEAFF, TRBV6-J2-7 CASSYSGADEQYF, TRBV5-J1-2 CASSLDGKGYTF, TRBV12-J2-5 CASSFEETQYF, TRBV4-J1-2 CASSQDLGTGGASGYTF, TRBV27-J2-3 CASSSRLAGGTDTQYF**	**73**
NGS (Multiplex-PCR)	SLE-LN (10) and HC (10) / #NR	PB / T cells	Reduced diversity. No disease activity correlation	Yes	NR	110
scRNAseq (10X 3') + CDR3 cDNA amplification	**SLE (162) and Controls (99) / #NR**	**PB / T cells**	**Repertoire-restricted cytotoxic GZMH+ CD8+ T cells, but not CD4+ T cells.**	**NR**	**No differences in top expansions. Expansion of CD8+ T cells showing cytotoxic over ISG signature profile.**	**111**

Supplementary Table 4: TCR repertoire findings in Sjögren's syndrome

Main findings of TCR repertoire studies in Sjögren's syndrome (SS). For the different groups and types of tissue studied, the (N) number of individuals or samples is indicated where applicable. HC, healthy controls; PB, peripheral blood; SG, salivary gland; LSG, labial SG; NR, not reported; N.S., not shared (for HLA carriage or clonotype detection). Particularly relevant studies highlighted in bold.

Method	Groups / # HLA typing	Tissue / Population	Diversity and clonality	Biased V-usage	Reported clonotypes-functional associations	Ref.
FC	SS (12) and Controls [age-, sex- and HLA-matched (9) and HLA-unmatched (10)] / #Most of them HLA-A1-Cw7-B8-DR3.	PB / T cells	NR	Reduced Vβ6.7a, influenced by HLA carriage	NR	112
FC + Immunofluorescence	SS: HLA-DR3+ (5) and DR3- (7) / #HLA-DR3	Paired PB + SG (8) and PB (4) / T cells	NR	Increase in Vβ2 in PB and increase in Vβ2 and Vβ8 in SG. No differences in DR3+ vs DR3-	NR	113
PCR	SS (2) / #NR	Lips / T cell clones	NR	Vα17.1, Vα11.1 and Vα2	NR	114
PCR + Sequencing	SS (5) and HC (5) / #HLA-typing, N.S.	PB + SG + Lacrimal Gland / T cells	Diverse tissue repertoire similar to PB. No change with disease duration	No	No shared clones between tissues. Reported CDR3 sequences	115
PCR (Vα and Vβ)	SS (primary (11) and secondary (9)) / #NR	PB + LSG / T cells	NR	Restricted TRBV usage in SG vs Blood	NR	116
PCR	SS / #NR	PB + LSG + Kidney / T cells	Higher clonality in kidney vs LSG and PB	Predominance of Vβ2 in kidney with indications of clonal expansion	Conserved arginine at position 96 in the CDR3	117
PCR	**SS (6) / #NR**	**SG / T cells (6) and T cell lines (16)**	**NR**	**NR**	**Ro(SSA) 52 kDa Reactive CD4+ T Cells (Vb2 and Vb13 with conserved CDR3)**	**118**

PCR–SSCP + Sequencing	SS (4) / #HLA-typing, N.S.	PB + LSG + Lacrimal Glands / T cells	NR	Vβ2 and Vβ13 in LSG	Conserved motifs in CDR3s. Common CDR3 in SG and LG: Vb4-1 CSVEDGT*STDTQ Jb2.3 Vb13-2 CASSYSADINGEL Jb2.2 Vb14-1 CASRSPSAGLNTEA Jb1.1 Vb14-2 CASSLSFNGGTGEQ Jb2.7	119
Ag reactivity	SS (1) / #HLADRB1*0803, 1501	LSG / T cell lines	NR	NR	DEREQLRILG (203-212 peptide from Ro/SS-A 52 kDa protein) is recognised by autoreactive T cells	120
PCR–SSCP + Sequencing	SS (12) and Controls (5) / #NR	LSG / T cells	NR	NR	Fas-sensitive T cells carry similar aa motifs in CDR3 region (reported).	121
PCR	SS (12) and chronic sialagenitis (3) / #NR	PB + LSG / T cells	TRAV repertoire restriction in LSG	Predominance of TRAV1 and TRAV3 in LSG	NR	122
FC + single-cell-PCR	SS (3) / #NR	LSG / BV2+ T cells (18 cells)	NR	NR	Conserved TRB motifs (RDxG, GNT, QGxxQETQ) and TRA motifs (EDxTG, or ExxTG) in BV2+ T cells from LSG. All are CD4+ T cells, overexpressing FasL, IL-2 and some IL-4	123
PCR–SSCP + Sequencing	SS (11): seropositive (6) vs seronegative human T lymphotropic virus type I (5) / #HLA-typing, N.S.	LSG / T cells	NR	Vβ5.2, Vβ6, and Vβ7 accumulate in the LSG from the HTLV-I+ and idiopathic SS patients	Vb7 with junctional motif QD*G	124
Multiplexed single-cell PCR	**SS (10) / #HLA DR3/DQ2 risk haplotype**	**PB + SG / Memory CD45RA-CD4+ T cells**	**Reduced diversity in SG. Clonality correlates with glandular dysfunction**	**Increased TRAV8-4, TRAV24, and TRAJ22 in SG vs PBMCs Reduced TRAV38-1, TRAJ27, TRAJ44, and TRBV29-1 in SG vs PBMCs**	**Shared similar clonal expansions within and among subjects (reported CDR3 sequences) . Increase frequency of double TCRα chains.**	**125**

Microengraving + sc-TCR-seq (nested RT-PCR)	**pSS (9) vs non-pSS/sicca controls (20) / #NR**	**LSG / IFNg/IL17A producing T cells**	**NR**	**TRBV restriction in SG Th1/Th17 cells from pSS**	**Common TRBV3-1/J1-2 (CLFLSMSACVW) in SG of pSS and controls. TRBV20-1/J1-1 (SVGSTAIPP*T) only in controls. pSS-unique motifs: 'VVSDTVLETAGE' from TRAV8–2/J5 and 'LSTD*E' from varying CDR3α chains**	**126**
scRNAseq (10X 3')	pSS (5) and HC (5) / #NR	PB / T cells	NR	NR	Expansion of CD4+ CTLs and CD4+ TRAV13-2+ T cell	127
Ag reactivity (ELISpot)	**SS (10) and HC (10) / #HLA-DR-restricted**	**PB / M3R-specific Th17 cells**	**NR**	**NR**	**M3- Receptor-Reactive Th17**	**128**
NGS (Multiplex-PCR)	**SS (260), at 3-time points, and database-sourced HC (439) / #NR**	**PB / T cells**	**Reduced diversity. Repertoire correlations with sensibility to treatment and comorbidities**	**More frequent: TRBV6-1, TRBV6-2, TRBV6-5, TRBV27, and TRBV10-3; TRBJ1-2, TRBJ1-6, and TRBJ1-4. Less frequent: TRBV20-1, TRBV28, TRBV11-2, TRBV18, TRBV3-1, TRBV4-1, and TRBV7-2; All TRBJ2 genes.**	**18 SS-associated TCRs (used for random-forest classification) 85 treatment-sensitivity associated TCRs**	**129**
scRNAseq (10X 5')	pSS (6) and HC (6) / #NR	PB / T cells	Reduced diversity	NR	Higher dual TCRα-chain expression in pSS patients. NKT cells seemed to have the highest degree of clonal expansion	130

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