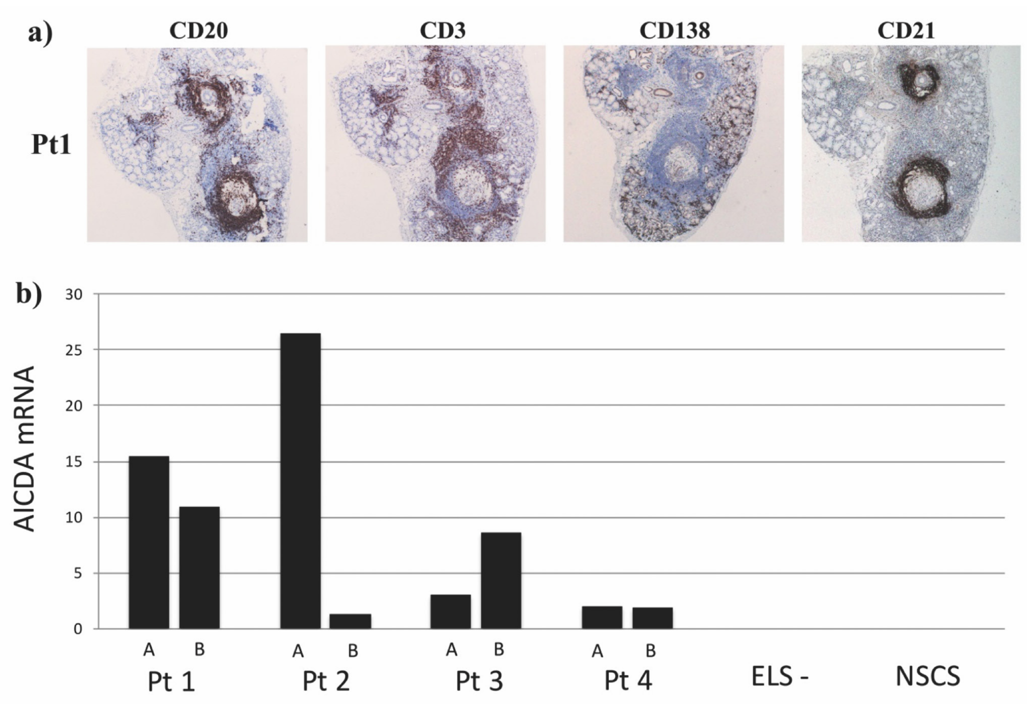
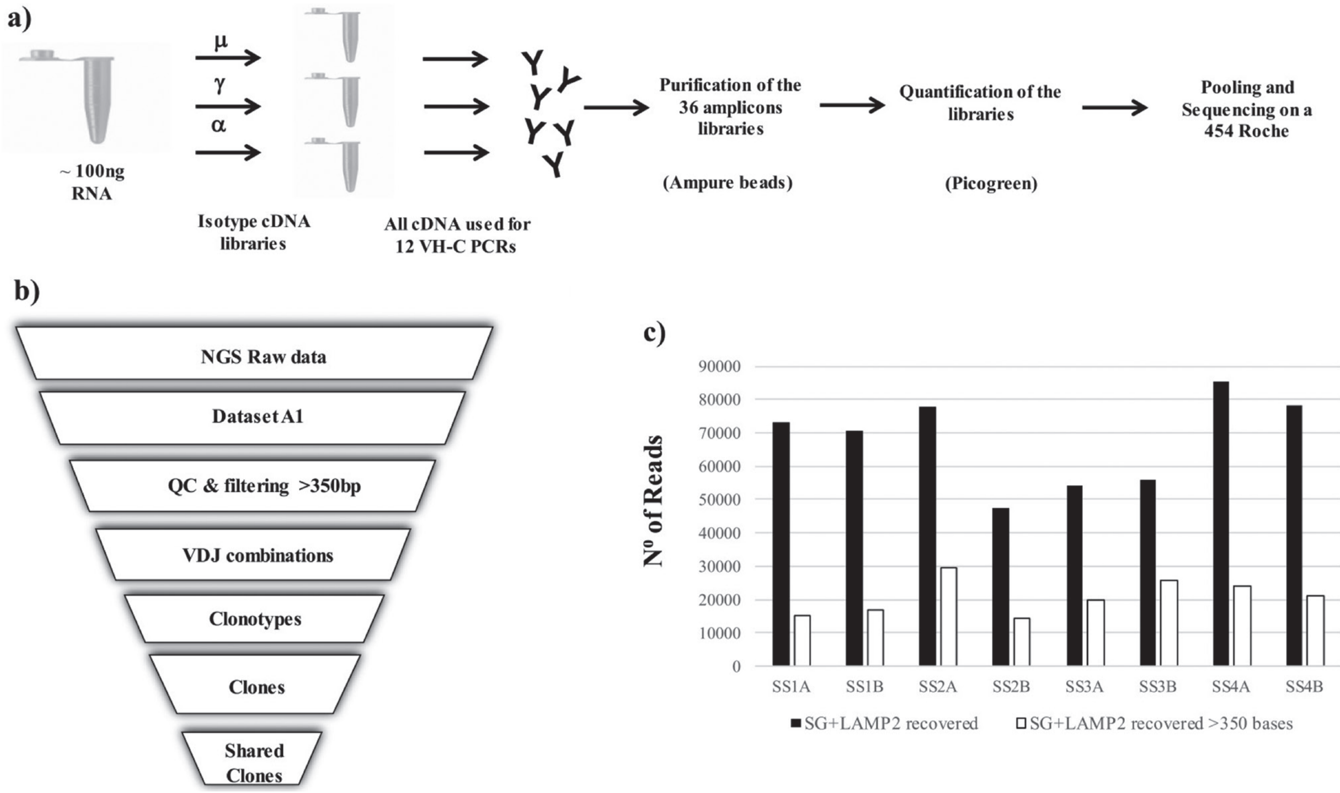
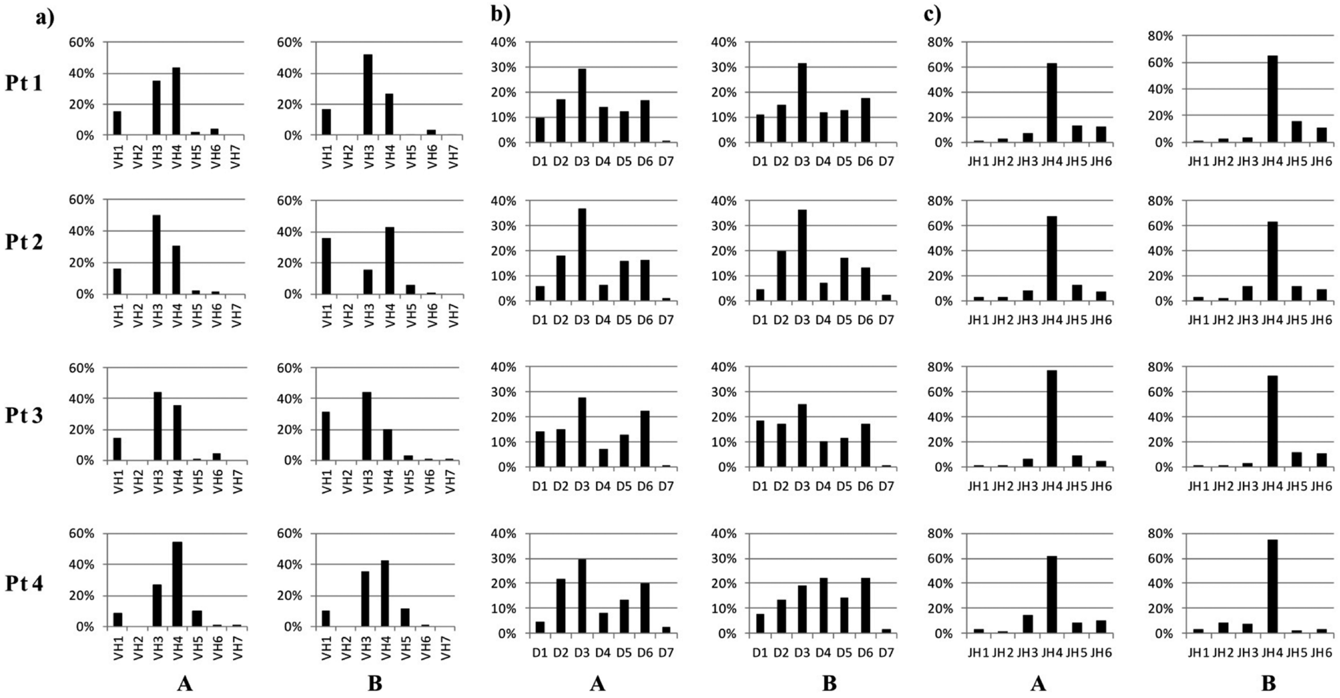
Supplementary Fig. S1. Immunohistochemistry staining and grading of mSGs for pt1.
a) IHC staining. Three mSGs, collected simultaneously; 2 were used for the NGS analysis while the third one was sectioned (3um), single stained with antibodies against CD20, CD3, CD138 and CD21 and graded following a previously published protocol (9).
b) Relative quantification of AICDA expression by Real Time PCR. RNA from two matched mSG from four patients selected for the NGS study was retro-transcribed to cDNA and the expression of AID enzyme (*AICDA*) measured. ELS - = RNA from a SS sample that did not show the presence of ELS; NSCS = Non-specific chronic sialadenitis.

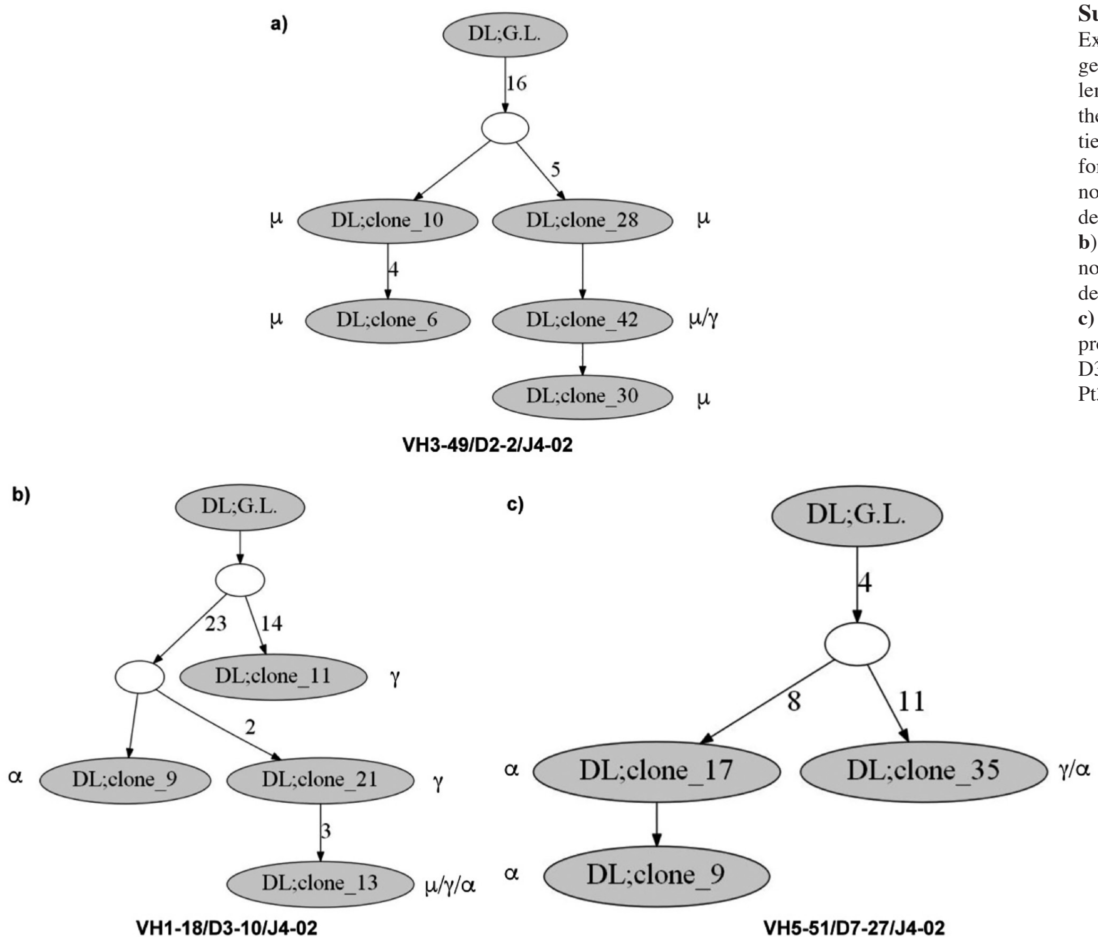




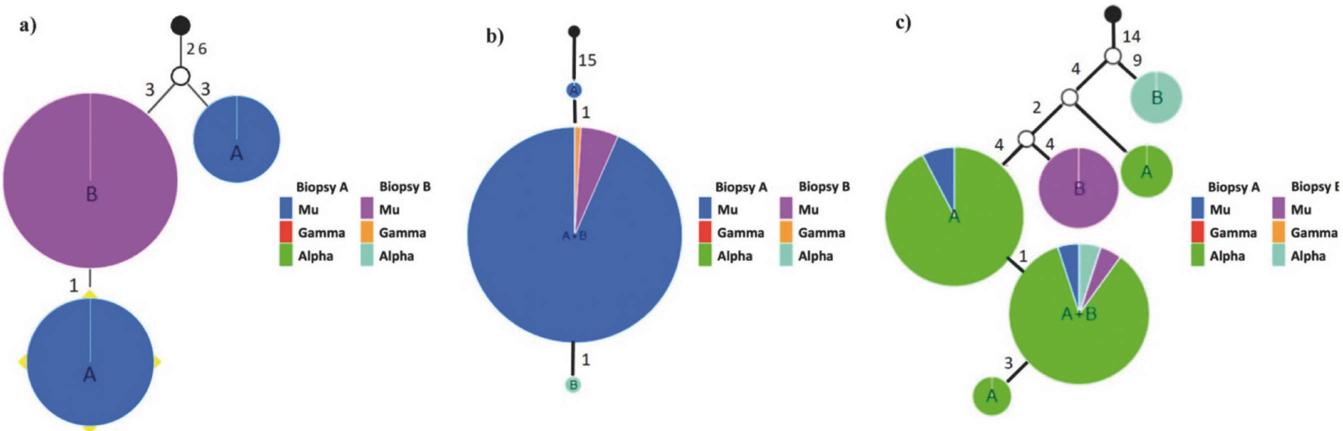
Supplementary Fig. S2. Steps for the preparation of the libraries and generation of the DatasetA1 used for our final analysis. **a)** Schematic representation of the different steps involved in the preparation of the libraries, from cDNA preparation using isotype specific primers to the pooling and sequencing on the 454 Roche sequencer. **b)** Pipeline showing the steps involved in identifying the reads belonging to the shared clones, used for generating the lineage trees. **c)** Histogram showing the total number of reads generated combining the shotgun (SG) and the Long Amplicon 2 (LAMP2) strategy before (black) and after selecting only those reads ≥ 350 bases long (white).



Supplementary Fig. S3. VH (left), DH (centre) and JH (right) usage and distribution across the 8 mSGs NGS libraries obtained after IgAT analysis. VH (**a**), D (**b**) and JH (**c**) gene usage is shown for the paired mSGs (A and B).



Supplementary Fig. S4. Examples of lineage trees generated for the most prevalent clonotypes detected in the mSGs biopsies from patients 2 and 3. **a)** Lineage tree for the most prevalent clonotype VH3-49/D2-2/J4-02, detected in the Pt2A library; **b**) Lineage tree for the clonotype VH5-51/D7-27/J4-02, detected in the Pt2B library; **c)** Lineage tree for the most prevalent clonotype VH1-69/D3-22/J5-01, detected in the Pt3B library.



Supplementary Fig. S5. Lineage Trees of representative clonotypes shared between paired mSGs. a) Pt1, clonotype VH4-59/D2-21/JH3-01. Only SHM. In this example a B cell clone with μ isotype migrates from mSG B to mSG A where it acquires one additional SHM. b) Pt3, clonotype VH4-39/D6-19/JH4-01. Only switch recombination. In this lineage tree a B cell clone μ isotype migrates from the mSG A (I) to mSG B (II) where it switches to γ (I). c) Pt2, VH4-39/D5-12/JH5-02. Both SHM and switch recombination. B cell clones, with same SHM but with μ and α isotypes, migrated from the mSG A (I) to mSG B (II) and (III) where they continue the SHM process (III) but also starts to switch into γ in (II).

Supplementary Table S1. Clinical information of the 4 patients included in the study.

SS patient ID	1	2	3	4
Sex	F	M	F	F
Age	76	61	56	64
	SS	SS	SS	SS
Diagnosis (at biopsy)				
Overlap autoimmune disease (at follow-up)	lcSSc	none	RA	none
Follow-up (years)	11	11	12 12	
anti-Ro/SSA	Neg	Pos	Neg	Neg
anti-La/SSB	Neg	Pos	Neg	Neg
ANA	Pos	Pos	Pos	Pos
IgM RF (pos >15UI/mL)	Neg	Pos	Pos	Neg
IgA (0.8-4) g/L	2.25	5.18	3.04	2.03
IgG (5.5-16.5) g/L	9.4	20	12.3	9.8
IgM (0.4-2) g/L	1.29	1.18	1.37	1.11
C3 (0.75-1.65) g/L	0.73	1.04	1.47	1.22
C4 (0.14-0.54) g/L	0.28	0.37	0.34	0.34
Cryoglobulins	No	No	No	No
ESSDAI at the biopsy	6	4	6	4
ESSDAI domains	A, H	H,B	A	A
Lymphoma	no	no	no	no
ELS Grading	G3	G3	G3	G3
ELS	Pos	Pos	Pos	Pos

F: female; M: male; SS: Sjögren's syndrome; lcSSc: limited cutaneous systemic sclerosis; RA: rheumatoid arthritis; Neg: negative; Pos: positive; RF: rheumatoid factor; ANA: anti-nuclear antibodies; ESSDAI: EULAR SS disease activity index; ELS: ectopic lymphoid structure; na: not available. ESSDAI domains: H: haematological; B: biological; A: articular.

Supplementary Table S2. Complete List of primers used for the preparation of cDNA and of the amplicon libraries.

Usage	Primer Name	Type of primer	Sequences
cDNA	Cμ	Reverse	GGAAGGAAGTCCGTGCGAGGC
	Cγ	Reverse	GGAAGGTGTGCACGCCGCTGGTC
	Cα	Reverse	TGGGAAGTTTCTGGCGGTCACG

Usage	Primer Name	Type of primer	Sequences
Library preparation	VH1	Forward	**AGAT**GTACATTCCCAGGTGCAGCTGGTGCAG
	VH1/5	Forward	**AGAT**GTACATTCCGAGGTGCAGCTGGTGCAG
	VH1-18	Forward	**AGAT**GTACATTCCCAGGTTCAGCTGGTGCAG
	VH1-24	Forward	**AGAT**GTACATTCCCAGGTCCAGCTGGTACAG
	VH3	Forward	**AGAT**GTACATTCTGAGGTGCAGCTGGTGGAG
	VH3-23	Forward	**AGAT**GTACATTCTGAGGTGCAGCTGTTGGAG
	VH3-33	Forward	**AGAT**GTACATTCTCAGGTGCAGCTGGTGGAG
	VH3-9	Forward	**AGAT**GTACATTCTGAAGTGCAGCTGGTGGAG
	VH4	Forward	**AGAT**GTACATTCCCAGGTGCAGCTGCAGGAG
	VH4-34	Forward	**AGAT**GTACATTCCCAGGTGCAGCTACAGCAGTG
	VH4-39	Forward	**AGAT**GTACATTCCCAGCTGCAGCTGCAGGAG
	VH6-1	Forward	**AGAT**GTACATTCCCAGGTACAGCTGCAGCAG

Usage	Primer Name	Type of primer*	Sequences
Library preparation	Cμ	Fusion Reverse	**AGAT**GGAAGGAAGTCCTGTGCGAGGC
	Cγ	Fusion Reverse	**AGAT**GGAAGGTGTGCACGCCGCTGGTC
	Cα	Fusion Reverse Nested	**AGAT**TGGGAAGTTTCTGGCGGTCACG
	Cα	Fusion Reverse Semi-Nested	**AGAT**GTCCGCTTTCGCTCCAGGTCACACT

Sequencing was performed using a multiplexing strategy; SS samples were modified with the AGAT MID tag, highlighted in bold. The VH2 family genes, that represent about 3% of productive rearrangements in SS (Foreman, *Autoimm Rev* 2007) were not investigated in this study.
*A semi-nested PCR strategy was used for the amplicons Iγ-μ and -γ and α combination of nested and seminested for PCR Iγ-α.

Supplementary Table S3. Examples of CDR3 regions for different VDJ rearrangements, clonotypes and clones.

a. VDJ COMBINATIONS

VDJ	VH	N1	DH	P	N2	JH	CDR3 - AA	CDR3 LENGTH
IGHV4-39-01/IGHD4-17-01/IGHJ4-02	tgtgcgagac	ggcgg	gactacggtgactac		cgact	ctcctgg	CARRRDYGDYRLSW	14
IGHV4-39-01/IGHD5-12-01/IGHJ3-02	tgtgcgagac	ccag	ggctggactggc		gcgg	gatgcctttggtatctgg	CARPRAGLARDAFGIW	16
IGHV4-39-01/IGHD6-6-01/IGHJ4-02	tgtgcg	tcctccag	taacagccagtcc	g	agagggtcggtctgcttttgagag	ctgg	CASSSNSQSERVGLLFEW	18

b. SAME VDJ BUT DIFFERENT CLONOTYPES

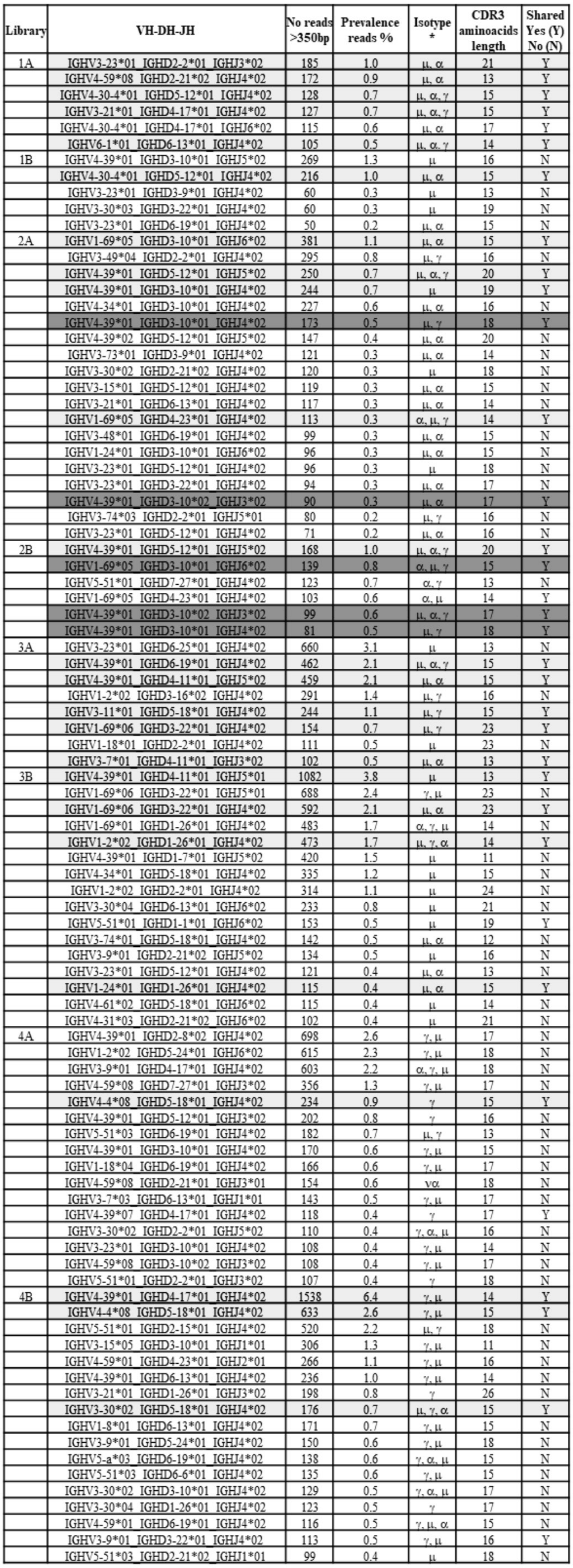
VDJ	CLONOTYPE	VH	P	N1	DH	P	N2	JH	CDR3 - AA	CDR3 LENGTH
IGHV4-39-01/IGHD4-17-01/IGHJ4-02	2	tgtgcgagac		ggcgg	gactacggtgactac		cgact	ctcctgg	CARRRDYGDYRLSW	14
IGHV4-39-01/IGHD4-17-01/IGHJ4-02	4	tgtgcgag			tgactccggtgatta		tgaatcttttgcga	ttgatttctgg	CASDSGDYESFAIDFW	16
IGHV4-39-01/IGHD4-17-01/IGHJ4-02	5	tgtgcgagaca	t	ctca	acggtgactac	gt	gggt	tttgactactgg	CARHLNGDYVGFDYW	15

c. DIFFERENT CLONES FROM THE SAME CLONOTYPE

VDJ	CLONOTYPE	CLONE	VH	P	N1	DH	P	N2	JH	CDR3 - AA	CDR3 LENGTH
IGHV4-39-01/IGHD4-17-01/IGHJ4-02	2	18	tgtgcgagac		ggcgg	gactacggtgactac		cgact	ctcctgg	CARRRDYGDYRLSW	14
IGHV4-39-01/IGHD4-17-01/IGHJ4-02	2	48	tgtgcgagac		ggcgg	gactacggtgactac		cggct	ctcctgg	CARRRDYGDYRLSW	14
IGHV4-39-01/IGHD4-17-01/IGHJ4-02	2	38	tgtgcgagac		ggcgg	gactacggtgactac		cggct	ctactgg	CARRRDYGDYRLYW	14

Mutated bases (bold) are shown only for the different clones from the same clonotypes. Only clones with variants observed in the CDR3 region are shown in this examples. The variant observed in the CDR3 region of clone 48 is a synonymous whilst the one observed in the CDR3 region of clone 38 is a non synonymous.

Supplementary Table S4. Most prevalent clonotypes.
Only clonotypes with at least 50 reads were included in this analysis
In light grey are highlighted the clonotypes included in table 1,with a prevalence ≥1%, shared between the paired mSGs; In dark grey are shown those clonotypes shared with the paired mSGs and a prevalence <1%
*The order of the isotype corresponds to the prevalence of the isotype detected: going from more prevalent to less prevalent



Library	VH-DH-JH	No reads >350bp	Prevalence reads %	Isotype *	CDR3 aminoacids length	Shared Yes (Y) No (N)
1A	IGHV3-23*01_IGHD2-2*01_IGHJ3*02	185	1.0	μ, α	21	Y
	IGHV4-59*08_IGHD2-21*02_IGHJ4*02	172	0.9	μ, α	13	Y
	IGHV4-30-4*01_IGHD5-12*01_IGHJ4*02	128	0.7	μ, α, γ	15	Y
	IGHV3-21*01_IGHD4-17*01_IGHJ4*02	127	0.7	μ, α, γ	15	Y
	IGHV4-30-4*01_IGHD4-17*01_IGHJ6*02	115	0.6	μ, α	17	Y
	IGHV6-1*01_IGHD6-13*01_IGHJ4*02	105	0.5	μ, α, γ	14	Y
1B	IGHV4-39*01_IGHD3-10*01_IGHJ5*02	269	1.3	μ	16	N
	IGHV4-30-4*01_IGHD5-12*01_IGHJ4*02	216	1.0	μ, α	15	Y
	IGHV3-23*01_IGHD3-9*01_IGHJ4*02	60	0.3	μ	13	N
	IGHV3-30*03_IGHD3-22*01_IGHJ4*02	60	0.3	μ	19	N
	IGHV3-23*01_IGHD6-19*01_IGHJ4*02	50	0.2	μ, α	15	N
2A	IGHV1-69*05_IGHD3-10*01_IGHJ6*02	381	1.1	μ, α	15	Y
	IGHV3-49*04_IGHD2-2*01_IGHJ4*02	295	0.8	μ, γ	16	N
	IGHV4-39*01_IGHD5-12*01_IGHJ5*02	250	0.7	μ, α, γ	20	Y
	IGHV4-39*01_IGHD3-10*01_IGHJ4*02	244	0.7	μ	19	Y
	IGHV4-34*01_IGHD3-10*01_IGHJ4*02	227	0.6	μ, α	16	N
	IGHV4-39*01_IGHD3-10*01_IGHJ4*02	173	0.5	μ, γ	18	Y
	IGHV4-39*02_IGHD5-12*01_IGHJ5*02	147	0.4	μ, α	20	N
	IGHV3-73*01_IGHD3-9*01_IGHJ4*02	121	0.3	μ, α	14	N
	IGHV3-30*02_IGHD2-21*02_IGHJ4*02	120	0.3	μ	18	N
	IGHV3-15*01_IGHD5-12*01_IGHJ4*02	119	0.3	μ, α	15	N
	IGHV3-21*01_IGHD6-13*01_IGHJ4*02	117	0.3	μ, α	14	N
	IGHV1-69*05_IGHD4-23*01_IGHJ4*02	113	0.3	α, μ, γ	14	Y
	IGHV3-48*01_IGHD6-19*01_IGHJ4*02	99	0.3	μ, α	15	N
	IGHV1-24*01_IGHD3-10*01_IGHJ6*02	96	0.3	μ, α	15	N
	IGHV3-23*01_IGHD5-12*01_IGHJ4*02	96	0.3	μ	18	N
	IGHV3-23*01_IGHD3-22*01_IGHJ4*02	94	0.3	μ, α	17	N
	IGHV4-39*01_IGHD3-10*02_IGHJ3*02	90	0.3	μ, α	17	Y
	IGHV3-74*03_IGHD2-2*01_IGHJ5*01	80	0.2	μ, γ	16	N
	IGHV3-23*01_IGHD5-12*01_IGHJ4*02	71	0.2	μ, α	16	N
2B	IGHV4-39*01_IGHD5-12*01_IGHJ5*02	168	1.0	μ, α, γ	20	Y
	IGHV1-69*05_IGHD3-10*01_IGHJ6*02	139	0.8	α, μ, γ	15	Y
	IGHV5-51*01_IGHD7-27*01_IGHJ4*02	123	0.7	α, γ	13	N
	IGHV1-69*05_IGHD4-23*01_IGHJ4*02	103	0.6	α, μ	14	Y
	IGHV4-39*01_IGHD3-10*02_IGHJ3*02	99	0.6	μ, α, γ	17	Y
	IGHV4-39*01_IGHD3-10*01_IGHJ4*02	81	0.5	μ, γ	18	Y
3A	IGHV3-23*01_IGHD6-25*01_IGHJ4*02	660	3.1	μ	13	N
	IGHV4-39*01_IGHD6-19*01_IGHJ4*02	462	2.1	μ, α, γ	15	Y
	IGHV4-39*01_IGHD4-11*01_IGHJ5*02	459	2.1	μ, α	15	Y
	IGHV1-2*02_IGHD3-16*02_IGHJ4*02	291	1.4	μ, γ	16	N
	IGHV3-11*01_IGHD5-18*01_IGHJ4*02	244	1.1	μ, γ	15	Y
	IGHV1-69*06_IGHD3-22*01_IGHJ4*02	154	0.7	μ, γ	23	Y
	IGHV1-18*01_IGHD2-2*01_IGHJ4*02	111	0.5	μ	23	N
	IGHV3-7*01_IGHD4-11*01_IGHJ3*02	102	0.5	μ, α	13	Y
3B	IGHV4-39*01_IGHD4-11*01_IGHJ5*01	1082	3.8	μ	13	Y
	IGHV1-69*06_IGHD3-22*01_IGHJ5*01	688	2.4	γ, μ	23	N
	IGHV1-69*06_IGHD3-22*01_IGHJ4*02	592	2.1	μ, α	23	Y
	IGHV1-69*01_IGHD1-26*01_IGHJ4*02	483	1.7	α, γ, μ	14	N
	IGHV1-2*02_IGHD1-26*01_IGHJ4*02	473	1.7	μ, γ, α	14	Y
	IGHV4-39*01_IGHD1-7*01_IGHJ5*02	420	1.5	μ	11	N
	IGHV4-34*01_IGHD5-18*01_IGHJ4*02	335	1.2	μ	15	N
	IGHV1-2*02_IGHD2-2*01_IGHJ4*02	314	1.1	μ	24	N
	IGHV3-30*04_IGHD6-13*01_IGHJ6*02	233	0.8	μ	21	N
	IGHV5-51*01_IGHD1-1*01_IGHJ6*02	153	0.5	μ	19	Y
	IGHV3-74*01_IGHD5-18*01_IGHJ4*02	142	0.5	μ, α	12	N
	IGHV3-9*01_IGHD2-21*02_IGHJ5*02	134	0.5	μ	16	N
	IGHV3-23*01_IGHD5-12*01_IGHJ4*02	121	0.4	μ, α	13	N
	IGHV1-24*01_IGHD1-26*01_IGHJ4*02	115	0.4	μ, α	15	Y
	IGHV4-61*02_IGHD5-18*01_IGHJ6*02	115	0.4	μ	14	N
	IGHV4-31*03_IGHD2-21*02_IGHJ6*02	102	0.4	μ	21	N
4A	IGHV4-39*01_IGHD2-8*02_IGHJ4*02	698	2.6	γ, μ	17	N
	IGHV1-2*02_IGHD5-24*01_IGHJ6*02	615	2.3	γ, μ	18	N
	IGHV3-9*01_IGHD4-17*01_IGHJ4*02	603	2.2	α, γ, μ	18	N
	IGHV4-59*08_IGHD7-27*01_IGHJ3*02	356	1.3	γ, μ	17	N
	IGHV4-4*08_IGHD5-18*01_IGHJ4*02	234	0.9	γ	15	Y
	IGHV4-39*01_IGHD5-12*01_IGHJ3*02	202	0.8	γ	16	N
	IGHV5-51*03_IGHD6-19*01_IGHJ4*02	182	0.7	μ, γ	13	N
	IGHV4-39*01_IGHD3-10*01_IGHJ4*02	170	0.6	γ, μ	15	N
	IGHV1-18*04_IGHD6-19*01_IGHJ4*02	166	0.6	γ, μ	17	N
	IGHV4-59*08_IGHD2-21*01_IGHJ3*01	154	0.6	να	18	N
	IGHV3-7*03_IGHD6-13*01_IGHJ1*01	143	0.5	γ, μ	17	N
	IGHV4-39*07_IGHD4-17*01_IGHJ4*02	118	0.4	γ	17	Y
	IGHV3-30*02_IGHD2-2*01_IGHJ5*02	110	0.4	γ, α, μ	16	N
	IGHV3-23*01_IGHD3-10*01_IGHJ4*02	108	0.4	γ, μ	14	N
	IGHV4-59*08_IGHD3-10*02_IGHJ3*02	108	0.4	γ. μ	17	N
	IGHV5-51*01_IGHD2-2*01_IGHJ3*02	107	0.4	γ	18	N
4B	IGHV4-39*01_IGHD4-17*01_IGHJ4*02	1538	6.4	γ, μ	14	Y
	IGHV4-4*08_IGHD5-18*01_IGHJ4*02	633	2.6	γ, μ	15	Y
	IGHV5-51*01_IGHD2-15*01_IGHJ4*02	520	2.2	μ, γ	18	N
	IGHV3-15*05_IGHD3-10*01_IGHJ1*01	306	1.3	γ, μ	11	N
	IGHV4-59*01_IGHD4-23*01_IGHJ2*01	266	1.1	γ, μ	16	N
	IGHV4-39*01_IGHD6-13*01_IGHJ4*02	236	1.0	γ, μ	14	N
	IGHV3-21*01_IGHD1-26*01_IGHJ3*02	198	0.8	γ	26	N
	IGHV3-30*02_IGHD5-18*01_IGHJ4*02	176	0.7	μ, γ, α	15	Y
	IGHV1-8*01_IGHD6-13*01_IGHJ4*02	171	0.7	γ, μ	15	N
	IGHV3-9*01_IGHD5-24*01_IGHJ4*02	150	0.6	γ, μ	18	N
	IGHV5-a*03_IGHD6-19*01_IGHJ4*02	138	0.6	γ, α, μ	15	N
	IGHV5-51*03_IGHD6-6*01_IGHJ4*02	135	0.6	γ, μ	15	N
	IGHV3-30*02_IGHD3-10*01_IGHJ4*02	129	0.5	γ, α, μ	17	N
	IGHV3-30*04_IGHD1-26*01_IGHJ4*02	123	0.5	γ	17	N
	IGHV4-59*01_IGHD6-19*01_IGHJ4*02	116	0.5	γ, μ, α	15	N
	IGHV3-9*01_IGHD3-22*01_IGHJ4*02	113	0.5	γ, μ	16	Y
	IGHV5-51*03_IGHD2-21*02_IGHJ1*01	99	0.4	μ	18	N