Supplemental Information for:

Clonal analysis of SepSecS-specific B and T cells in autoimmune hepatitis

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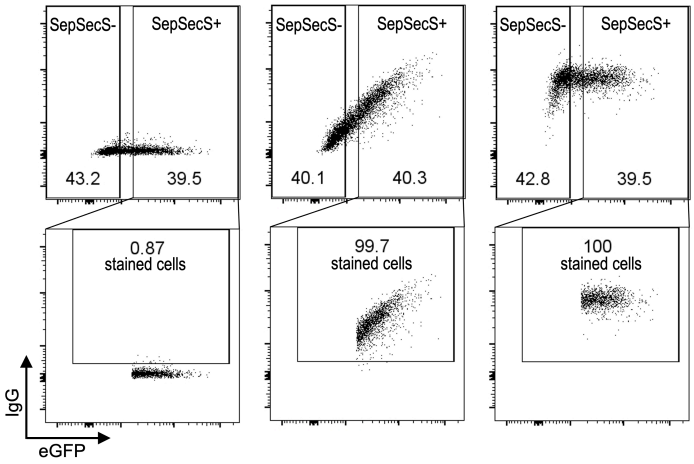
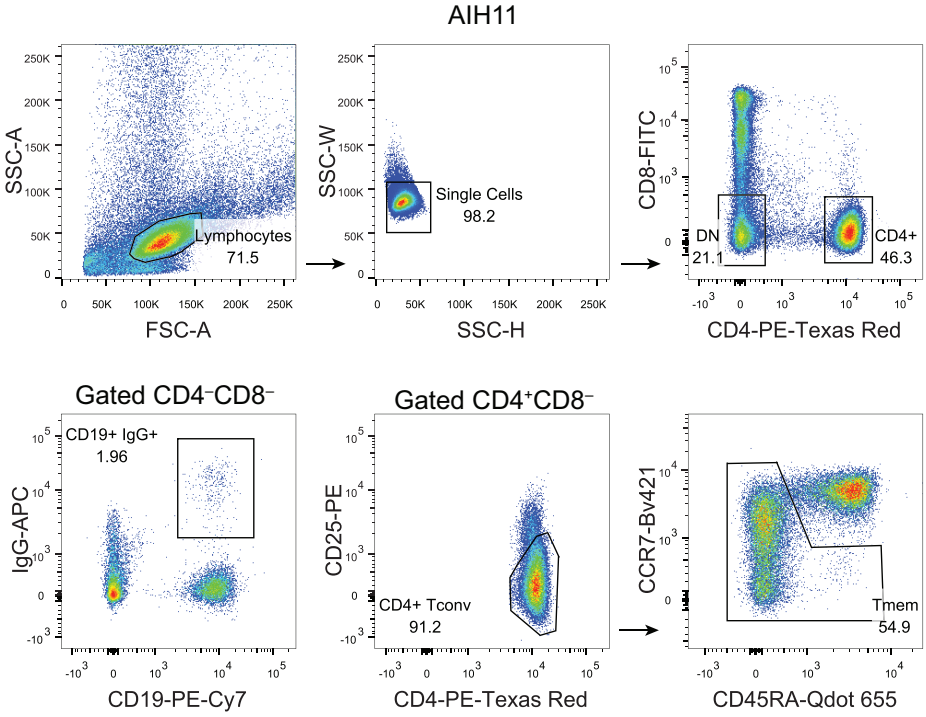
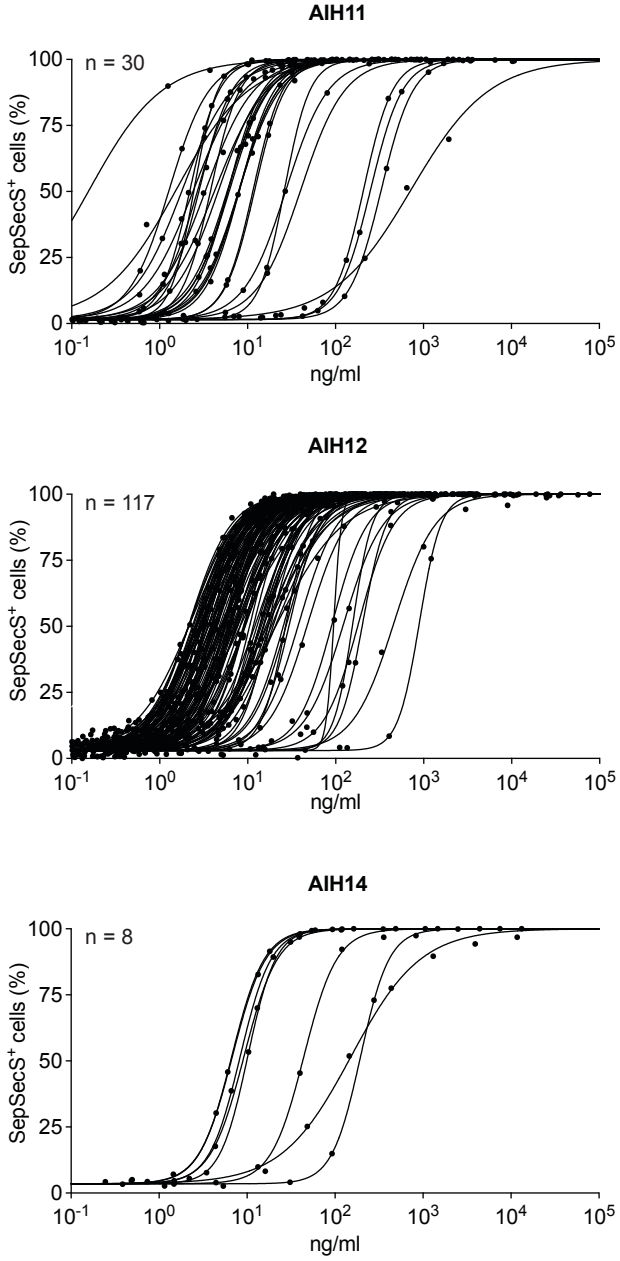


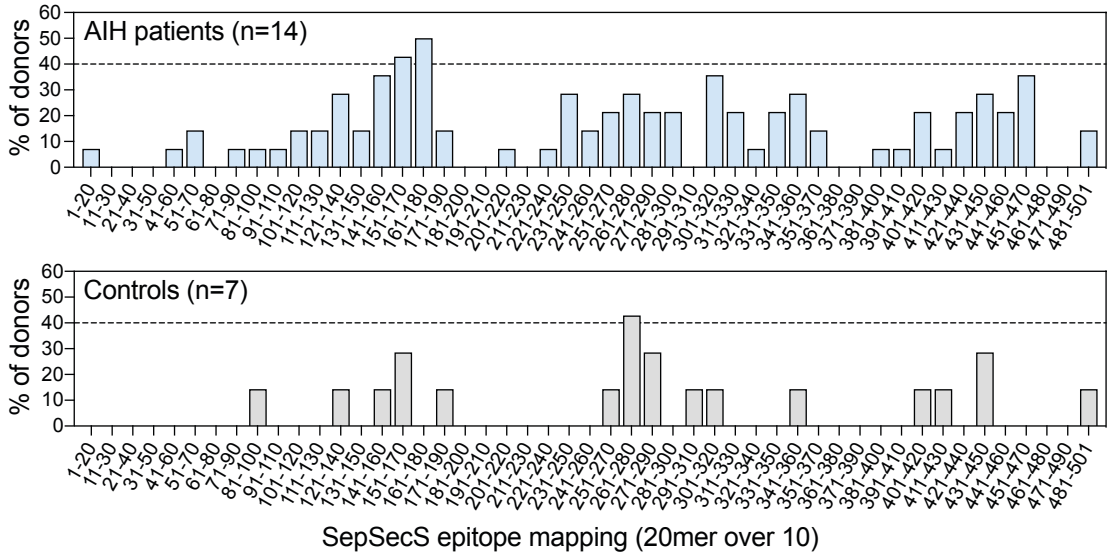
Supplemental Figure 1. Detection of SepSecS-reactive IgG in human sera using eGFP- and SepSecS-transfected EXPI-293 cells. Bound IgG was detected using Alexa Fluor 647-labeled anti-IgG antibodies. The 3 FACS plots are representative of sera with no SepSecS-binding antibodies (left), with SepSecS-specific binding antibodies (center, higher binding to transfected than non-transfected cells), and with unspecific-binding antibodies (right, equal binding to transfected and non-transfected cells).



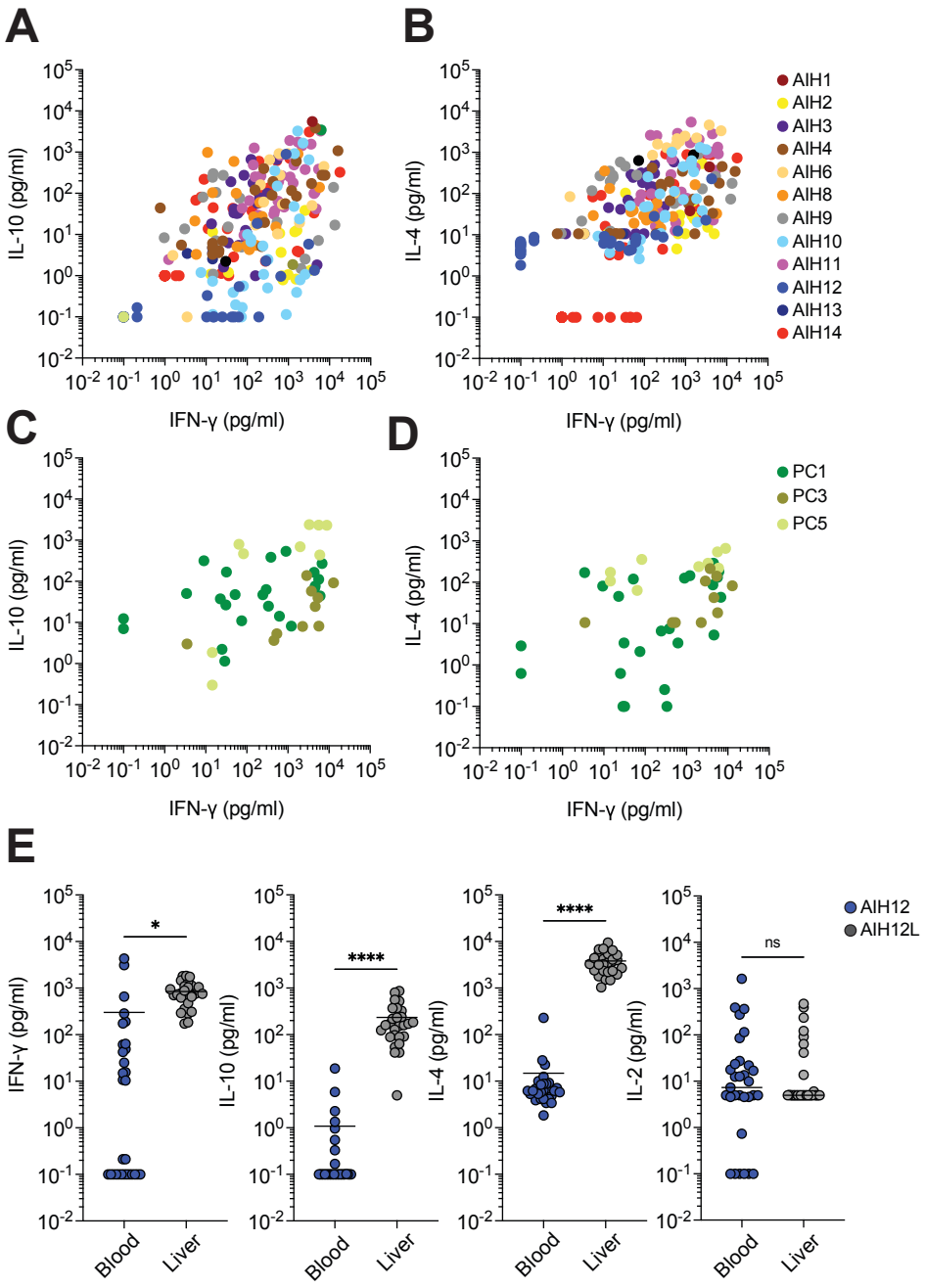
Supplemental Figure 2. Sorting of B cells and T cells from PBMCs. Sorting strategy to isolate IgG$^+$ B cells and total memory CD4$^+$ T cells from PBMCs. Representative dot plots from the sorting of PBMC sample from patient AIH11. Numbers represent percentages of gated populations.



Supplemental Figure 3. Binding of SepSecS-reactive monoclonal antibodies (mAbs) from AIH patients. Binding of antibodies in supernatants of EBV-transformed B cell clones from patients AIH11, AIH12 and AIH14 to SepSecS-transfectants as measured with flow-cytometry. The number of mAbs tested is also indicated.



Supplemental Figure 4. Percentage of individuals carrying T cell clones specific for different 20-mer segments of the SepSecS protein. The upper barplot represents AIH patients (n=14), while the lower barplot shows the control group (n=7).



Supplemental Figure 5. (**A-D**) Cytokine production of SepSecS-specific CD4$^+$ T cell clones from AIH patients (A, B) and pathological controls (C, D). (**E**) Cytokine production of SepSecS-specific CD4$^+$ T cell clones isolated from blood (already displayed in panels A, B) or liver biopsy (L) from patient AIH12. Cytokine concentration in the 48 h culture supernatants (obtained from epitope mapping experiments) was measured by Luminex assay. *p-value=0.01, **** p-value<0.0001, n.s. not significant, determined by unpaired t test.

Supplemental Table 1. Clinical features of the study population and of pathological controls

ID	Gender	Age (y)	Disease	Anti-SLA[A]	IAIHG score	Disease duration (y)	At time of blood donation:		HLA DRB1	
							Normal transa-minases	IS treatment		
AIH1	M	13	AIH-2	–	7	8	Yes	Aza	04:01	07:01
AIH2	F	69	AIH-1	–	6	1	Yes	PDN + MMF	03:01	13:01
AIH3	M	73	AIH-1	–	7	12	Yes	PDN + Aza	07:01	14:01
AIH4	F	73	AIH-1	+	8	10	Yes	PDN + Aza	04:04	13:01
AIH5	F	23	AIH-2	–	8	9	Yes	PDN + Aza	12:01	15:01
AIH6	F	72	AIH-1	–	7	6	Yes	PDN	04:01	08:01
AIH7	F	50	AIH-1	–	8	5	No	PDN + MMF	03:01	13:02
AIH8	F	27	AIH-1	–	7	4	No	PDN + MMF	11:01	15:01
AIH9	F	68	AIH-1	–	8	3	Yes	Aza	11:01	16:01
AIH10	F	67	AIH-1	–	6	8	Yes	PDN + MMF	08:01	15:02
AIH11	F	54	AIH-1	+	8	10	Yes	PDN + MMF	03:01	03:01
AIH12	F	48	AIH-1	+	8	28	No	PDN, MMF, Tac	03:01	03:01
AIH13	F	72	AIH-1	–	6	5	Yes	PDN + MMF	04:01	15:01
AIH14	F	25	AIH-1	+	6	3	Yes	PDN	13:01	15:01
AIH15	F	59	AIH-1	–	6	2	No	PDN + Aza	04:01	16:01
AIH16	F	53	AIH-1	–	4	0	No	None	03:01	08:01
AIH17	F	31	AIH-2	+	8	26	No	PDN + Aza	07:10	07:10
AIH18	F	27	AIH-1	–	8	11	Yes	PDN + Aza	03:01	03:01
AIH19	F	32	AIH-1	+	8	0	No	None	04:05	13:01
AIH20	M	18	AIH-1	+	7	0	No	None	01:02	13:01
Total	**F:M 17:3**	**Median 51.5**	**AIH-1: AIH-2 17:3**	**7 (35%)**	**Median 7**	**Median 5.5**	**No=8 Yes=12**	**IS=17 None=3**		
PC1	F	65	DILI	No	n.d.	7	Yes	None	04:05	13:02
PC2	F	47	PBC	No	n.d.	2	Yes	None	07:01	07:01
PC3	F	39	PBC	No	n.d.	10	Yes	None	07:01	13:01
PC4	F	26	PBC	No	n.d.	2	Yes	None	10:01	13:01
PC5	M	75	PSC	No	n.d.	10	Yes	None	03:01	16:02
PC6	F	77	PBC	No	n.d.	3	Yes	None	n.d.	n.d.
PC7	F	66	PBC	No	n.d.	5	Yes	None	08:01	11:01
PC8	F	54	PBC	No	n.d.	12	No	None	04:01	04:07
PC9	M	71	PBC	No	n.d.	0	No	None	03:01	08:01
Total	**F:M 7:2**	**Median 65**	**PBC=7**			**Median 5**	**No=2 Yes=7**	**None=9**		

[A]Tested at local hospitals. ID, patient identification code. AIH, autoimmune hepatitis patient. PC, pathological control. F, female. M, male. DILI, Drug-induced autoimmune liver injury. PBC, primary biliary cholangitis. PSC, primary sclerosing cholangitis. Aza, azathioprine. PDN, prednisone. Tac, Tacrolimus. MMF, mycophenolate mofetil. Anti-SLA, anti-soluble liver antigen antibody. IAIHG, international AIH group. IS, immunosuppression. HLA, human leukocyte antigens. n.d., not determined. AIH12 had undergone liver transplantation for severe autoimmune hepatitis, and experienced post-transplant recurrence at the time of blood collection.

Supplemental Table 2. Anti-SLA antibodies measured in AIH patients and controls

Donor	Anti-SLA	Commercial ELISA		In house assay ELISA		In house assay FACS		Frequency SepSecS-IgG$^+$ B cells In 10^6 PBMC
		OD450 1:800	Units	OD405 1:800	EDF_{50}	MFI 1:800	EDF_{50}	
AIH1	–	0.06	5	0.14	<50	620	<50	0.2
AIH2	–	0.05	<2	0.12	<50	1001	<50	1.1
AIH4	+	0.50	155	4.19	8973	22145	29114	23.8
AIH5	–	0.05	<2	0.12	<50	760	<50	0.2
AIH6	–	0.05	<2	0.15	<50	1100	<50	0.2
AIH7	–	0.05	<2	0.11	<50	931	<50	0.2
AIH9	–	0.06	<2	0.20	<50	1055	<50	0.5
AIH11	+	0.72	293	4.22	46199	63367	67358	16.5
AIH12	+	1.03	496	4.28	50005	67959	88038	129.0
AIH13	–	0.05	<2	0.27	53	951	<50	0.0
AIH14	+	0.08	9	4.18	9748	26087	16327	42.3
AIH18	–	0.05	<2	4.15	6748	14623	16944	43.5
HC3	n.d.	0.05	<2	0.11	<50	724	<50	0.3
HC12	n.d.	0.05	<2	0.15	<50	998	<50	0
HC13	n.d.	0.05	<2	0.12	<50	527	<50	0
HC14	n.d.	0.07	<2	0.11	<50	342	<50	0
HC15	n.d.	0.07	<2	0.13	<50	828	<50	3.1

Supplemental Table 3. V(D)J gene usage and EC_{50} values of SepSecS-binding mAbs

ID	B cell clone	Isotype		Heavy chain VDJ genes (% identity to germline)					Light chain VJ genes (% identity to germline)				EC_{50} (ng/ml)
AIH11	**9**	IgG1	κ	VH3-20	89.2	D3-22	JH4	85.4	VK1-39	93.9	JK1	91.7	4.0
	1	IgG1	κ	VH1-69	94.4	D3-22	JH6	88.7	VK1-5	95.3	JK1	89.5	4.3
	2	IgG1	κ	VH1-3	92.7	D2-2	JH6	82.3	VK1-39	95.0	JK4	100	2.4
	4	IgG3	λ	VH3-49	95.2	D3-10	JH6	87.1	VL1-51	97.5	JL3	97.1	7.1
	5	IgG2	λ	VH4-4	95.5	D2-8	JH4	91.7	VL2-11	94.8	JL3	91.9	2.2
	6	IgG1	κ	VH4-31	91.1	D6-13	JH4	83.3	VK3-20	94.3	JK5	94.3	28.0
	7	IgG2	λ	VH5-10-1	96.2	D6-6	JH3	94.0	VL2-23	94.8	JL3	100	2.2
	8-1	IgG1	κ	VH3-33	86.8	D6-19	JH4	95.8	VK1-5	93.6	JK1	100	3.5
	8-2	IgG1	κ	VH3-33	87.5	D6-19	JH4	95.8	VK1-5	93.9	JK1	100	2.6
	9	IgG1	κ	VH3-30	88.9	D6-19	JH4	93.8	VK1-5	94.6	JK1	94.7	6.1
	10	IgG1	κ	VH4-59	96.8	D3-22	JH2	92.5	VK3-15	97.5	JK2	94.9	4.0
	12	IgG1	κ	VH4-34	95.4	D4-23	JH4	91.7	VK4-1	97.3	JK1	97.4	5.2
	13	IgG1	λ	VH3-30	95.5	D3-3	JH6	77.4	VL1-44	96.1	JL2	89.2	3.2
	14	IgG1	κ	VH1-46	86.5	D3-22	JH3	98.0	VK1-39	90.0	JK2	91.4	5.1
	15	IgG1	κ	VH1-46	86.5	D6-19	JH3	98.0	VK1-39	90.0	JK4	80.6	3.7
	16	IgG1	κ	VH3-23	89.9	D3-22	JH4	97.9	VK3-15	97.1	JK3	97.1	3.1
	18	IgG1	λ	VH3-20	89.6	D1-26	JH4	87.5	VL3-21	95.7	JL3	94.7	8.0
	19	IgG1	κ	VH3-20	92.0	D3-22	JH4	97.9	VK1-5	93.9	JK2	87.2	3.4
	20	IgG1	κ	VH3-7	90.6	D2-2	JH6	80.7	VK4-1	95.0	JK1	100	4.4
	21	IgG1	κ	VH3-23	89.6	D1-14	JH6	85.5	VK2-30	96.3	JK2	100	4.3
	22	IgG1	κ	VH3-20	94.8	D3-10	JH5	90.2	VK3D-20	96.5	JK4	100	13.9
	23	IgG2	κ	VH3-15	93.5	D5-18	JH4	83.3	VK1-5	95.3	JK1	97.4	2.2
	24	IgG1	λ	VH3-20	92.0	D3-10	JH5	98.0	VL1-40	94.1	JL3	83.3	15.4
	25	IgG1	λ	VH3-23	89.9	D3-9	JH4	87.5	VL3-10	96.1	JL3	94.7	460.9
	26	IgG1	κ	VH3-23	95.5	D6-13	JH4	85.4	VK1-5	97.5	JK1	94.7	9.4
	27	IgG1	κ	VH3-23	86.7	D3-16	JH4	87.5	VK1-39	93.2	JK4	100	4.0
	28	IgG2	κ	VH3-20	92.4	D5-18	JH4	91.7	VK2-30	95.2	JK2	92.3	15.7
	29	IgG1	λ	VH4-34	90.9	D2-2	JH6	83.9	VL3-1	93.2	JL2	94.7	17.4
	30	IgG1	κ	VH3-23	83.3	D6-19	JH1	76.9	VK1-6	94.3	JK1	97.2	13.1
AIH12	**31**	IgG1	κ	VH3-7	89.6	D2-15	JH4	87.5	VK3-15	96.1	JK1	97.4	12.4
	32-1	IgG2	λ	VH3-23	86.3	D3-10	JH3	62.0	VL1-51	91.6	JL3	81.6	5.4
	32-2	IgG2	λ	VH3-23	86.7	D3-10	JH3	62.0	VL1-51	88.1	JL3	83.8	6.4
	32-3	IgG2	λ	VH3-23	85.6	D3-10	JH3	62.0	VL1-51	90.9	JL3	76.3	0.4
	33-1	IgG1	κ	VH3-23	89.9	D3-3	JH3	86.0	VK3-15	95.0	JK1	85.7	6.0
	33-2	IgG1	κ	VH3-23	92.0	D3-3	JH3	86.0	VK3-15	95.3	JK1	94.3	3.1
	33-3	IgG1	κ	VH3-23	91.7	D3-3	JH3	84.0	VK3-15	94.6	JK1	91.4	2.8
	34	IgG1	κ	VH4-34	89.1	D5-18	JH4	91.7	VK3-11	96.4	JK4	100	2.1
	35	IgG1	n.d.	VH4-59	93.7	D3-16	JH5	84.3	n.d.	n.d.	n.d.	n.d.	3.2
	36	IgG1	κ	VH3-66	88.4	D3-10	JH4	87.5	VK1-39	94.3	JK4	100	5.3
	37-1	IgG1	κ	VH1-69	87.2	D5-18	JH4	89.6	VK1-33	93.6	JK5	97.4	2.7
	37-2	IgG1	κ	VH1-69	87.9	D5-18	JH4	89.6	VK1-33	92.8	JK5	97.4	4.0
	38	IgG1	κ	VH1-69	93.1	D5-18	JH4	83.3	VK1-33	96.1	JK5	100	2.2
	39	IgG1	n.d.	VH1-3	92.6	D6-13	JH3	94.0	n.d.	n.d.	n.d.	n.d.	182.9
	41	IgG1	κ	VH4-39	91.1	D1-26	JH4	91.7	VK1-5	93.9	JK1	100	9.3
	42	IgG1	λ	VH2-26	97.6	D3-9	JH6	95.2	VL3-1	95.7	JL1	94.7	12.4
	43	IgG1	κ	VH4-31	91.4	D3-10	JH4	70.5	VK1-5	95.3	JK1	89.5	15.7
	44	IgG1	λ	VH4-59	89.1	D3-10	JH5	86.3	VL2-18	96.5	JL3	86.8	2.7
	45	IgG2	κ	VH3-11	92.0	D3-10	JH6	77.4	VK1-9	97.1	JK3	94.7	7.7
	46	IgG1	λ	VH1-24	91.0	D5-12	JH5	84.3	VL2-18	91.3	JL3	86.8	5.9
	47	IgG1	κ	VH3-23	93.4	D6-19	JH4	95.8	VK3-15	98.2	JK1	100	3.1
	49	IgG1	κ	VH3-20	92.4	D2-2	JH6	90.3	VK1-16	96.8	JK4	100	17.7
	50	IgG1	λ	VH4-31	92.1	D3-10	JH4	85.4	VL7-46	95.5	JL2	100	3.1
	51	IgG1	κ	VH3-20	89.1	D6-19	JH6	87.1	VK1-5	93.9	JK1	88.9	0.5
	53	IgG1	κ	VH4-61	97.3	D3-9	JH4	85.4	VK1-16	97.5	JK4	94.7	3.5
	54	IgG1	λ	VH4-34	91.6	D5-24	JH6	83.9	VL2-14	94.4	JL1	85.3	5.7
	55	IgG1	κ	VH4-34	90.9	D3-10	JH6	79.0	VK1-9	96.1	JK1	97.3	2.9
	56	IgG1	κ	VH4-4	97.6	D3-9	JH5	86.3	VK1-33	98.9	JK4	100	16.4
	nb	IgG1	n.d.	VH1-3	97.9	D3-22	JH3	96.0	n.d.	n.d.	n.d.	n.d.	n.d.
	7	IgG1	λ	VH5-10-1	90.3	D3-16	JH3	86.0	VL3-21	89.6	JL1	86.8	8.1
	8	IgG1	λ	VH1-3	86.8	D5-24	JH1	90.2	VL3-21	93.2	JL3	100	4.4
	9	IgG1	κ	VH3-23	78.1	D6-19	JH4	83.3	VK1-5	95.0	JK1	89.5	10.2
AIH14	**13**	IgG1	λ	VH4-39	92.1	D3-10	JH5	98.0	VL3-21	97.1	JL1	92.1	195.1
	14	IgG1	λ	VH2-70	93.1	D5-24	JH4	97.9	VL3-21	94.3	JL1	94.6	152.4
	19	IgG1	κ	VH3-23	85.4	D5-12	JH4	81.3	VK3-11	90.6	JK3	94.3	3.2
	20	IgG1	λ	VH4-59	82.8	D2-8	JH5	78.4	VL1-36	86.4	JL1	84.2	8.6
	21	IgG1	κ	VH3-33	93.8	D5-24	JH4	91.7	VK1-5	91.4	JK2	86.8	17.0

EC_{50} values based on SepSecS-transfected EXPI293 cells; n.d., not determined.

Supplemental Table 4. Summary of $CD4^+$ T cell clones obtained from AIH patients and controls

ID	Ex vivo T cell proliferation	Isolated T cell clones	SepSecS-specific T cell clones	
	$CFSE^{low}ICOS^+CD25^+$ (%)	n	n	%
AIH1	0.32	10	1	10
AIH2	0.27	53	15	28
AIH3	11.16	120	117	97
AIH4	1.15	200	147	73
AIH5	7.40	120	86	72
AIH6	0.42	60	26	43
AIH7	2.10	203	86	42
AIH8	1.33	96	13	13
AIH9	1.81	136	55	40
AIH10	0.06	30	27	90
AIH11	0.90	31	31	100
AIH12	22.30	180	168	93
AIH13	1.68	32	6	19
AIH14	0.54	93	52	56
AIH15	0.1	n.d.	–	–
AIH16	0.1	n.d.	–	–
AIH17	0.1	n.d.	–	–
AIH18	0.1	n.d.	–	–
AIH19	0.1	n.d.	–	–
AIH20	0.1	n.d.	–	–
AIH12 LB	11.7*	130	87	66.9
AIH16 LB	11.9*	41	0	0
PC1	0.47	96	13	13
PC2	0.77	96	24	25
PC3	0.09	39	10	26
PC4	0.36	120	32	27
PC5	0.78	96	64	67
PC6	0.05	n.d.	–	–
PC7	0.02	n.d.	–	–
PC8	0.06	n.d.	–	–
PC9	0.1	n.d.	–	–
HC1	0.20	96	15	16
HC2	0.03	192	73	38
HC3	0.52	10	1	10
HC4	0.1	n.d.	–	–
HC5	2.57	14	2	14
HC6	0.02	n.d.	–	–
HC7	0.15	n.d.	–	–
HC8	0.06	n.d.	–	–
HC9	0.1	n.d.	–	–
HC10	3.29	n.d.	–	–
HC11	0.1	n.d.	–	–
HC16	0.12	n.d.	–	–

AIH, autoimmune hepatitis patient. PC, pathological control. HC, healthy control. n.d., not done.
*Proliferation of liver biopsy-derived T cell lines

Supplemental Table 5. Cytokines produced by SepSecS-specific $CD4^+$ T cell clones from AIH patients and controls

ID	Clone n.	IFN-γ (pg/ml)	IL-10 (pg/ml)	IL-4 (pg/ml)
AIH1	1	3809.8	5512.5	446.4
	2	1287.1	1.9	38.1
AIH2	1	12.9	1.1	10.6
	2	663.2	3.7	10.6
	3	1521.9	0.8	65.2
	4	3441.2	1.4	15.3
	5	1614.2	12.5	24.4
	6	2540.4	38.4	533.7
	7	14.4	11.6	11.6
	8	700.4	1.0	20.2
	9	984.4	1.1	10.6
	10	35.1	1.2	102.4
	11	618.4	10.7	4.6
	12	1433.4	11.7	29.6
	13	738.5	0.8	29.9
	14	4977.7	1.8	10.6
AIH3	1	176.7	57.0	307.7
	2	176.6	25.7	502.5
	3	13.5	18.2	45.7
	4	47.8	41.6	290.8
	5	53.7	32.8	247.6
	6	26.7	1.6	41.7
	7	96.3	7.6	202.5
	8	40.2	192.1	69.3
	9	62.1	5.4	10.6
	10	90.8	12.6	185.0
	11	523.1	661.8	585.9
	12	138.8	179.4	148.7
	13	83.7	274.9	317.3
	14	98.6	10.7	10.6
	15	59.2	32.6	7.9
	16	307.5	100.0	48.3
	17	124.3	663.5	334.1
	18	95.7	11.2	192.6
	19	35.1	6.3	10.6
	20	159.2	1.0	146.1
	21	47.5	33.4	57.4
	22	199.4	77.6	106.6
	23	1.2	2.5	10.6
AIH4	1	1194.8	116.8	56.3
	2	14.4	3.3	10.6
	3	253.6	397.6	167.7
	4	424.7	193.2	67.5
	5	223.4	5.1	10.6
	6	264.3	19.6	140.5
	7	14.4	6.1	10.6
	8	4565.3	3861.2	33.3
	9	841.4	56.1	347.5
	10	0.8	44.0	10.6
	11	15990.1	1077.3	344.0
	12	20.2	3.6	10.6
	13	401.6	90.6	195.2
	14	1562.2	606.5	73.5
	15	6606.3	276.5	178.8
	16	2.5	5.5	10.6
	17	14.4	4.9	10.6
	18	20.6	4.0	10.6
	19	3652.3	173.2	67.3
	20	7751.3	273.1	452.3
	21	154.4	120.8	417.8

	22	25.6	7.0	10.6
	23	192.7	18.9	10.6
	24	1679.4	3254.3	10.6
AlH6	1	715.4	54.0	1854.3
	2	210.6	160.9	1588.4
	3	976.6	920.4	2482.3
	4	1.6	3.1	84.2
	5	158.5	16.9	848.4
	6	629.0	276.9	2134.9
	7	595.6	919.6	1554.5
	8	350.8	655.0	1298.8
	9	3.5	0.1	10.6
	10	3753.5	50.5	4600.8
	11	547.7	10.3	102.8
	12	7343.6	447.5	3332.3
	13	1874.2	19.3	2234.3
	14	1579.0	84.8	872.1
AlH8	1	47.7	596.2	36.1
	2	231.3	27.4	23.4
	3	162.7	5.4	34.7
	4	204.0	59.7	58.2
	5	112.8	4.3	22.8
	6	56.3	5.1	19.1
	7	10.9	984.0	353.9
	8	14.4	103.7	134.2
	9	144.5	27.0	26.1
	10	498.7	15.3	27.8
	11	96.9	5.4	29.2
	12	5.8	3.3	29.2
	13	1717.2	904.4	164.1
	14	54.3	100.4	39.4
	15	5715.2	139.2	32.7
	16	251.9	61.5	14.4
AlH9	1	73.1	5.0	634.0
	2	534.7	19.9	57.5
	3	13475.8	17.0	176.7
	4	14.9	299.7	195.6
	5	17.2	7.0	277.2
	6	3.0	13.7	21.5
	7	17.6	105.7	249.1
	8	26.1	273.6	579.2
	9	5359.2	7.2	260.8
	10	14.4	245.5	349.4
	11	34.3	15.3	462.8
	12	2571.9	2.5	130.1
	13	66.1	77.0	281.5
	14	2027.8	1.5	911.0
	15	12508.3	139.2	73.4
	16	1.0	8.4	10.8
	17	14.9	1.1	12.2
	18	8.4	80.7	268.3
	19	5.4	21.4	117.9
AlH10	1	75.7	0.2	2.6
	2	7.5	1.2	9.2
	3	320.2	2.5	29.8
	4	241.3	5.2	98.8
	5	1933.5	0.8	20.3
	6	2282.4	1659.9	1319.9
	7	1588.0	0.4	339.5
	8	890.1	0.1	72.0
	9	466.9	354.7	1014.3
	10	314.4	0.5	26.4
	11	52.1	0.2	5.7
	12	101.5	10.0	47.3
	13	1374.6	48.1	491.3
	14	1868.2	23.9	74.7

	15	14.6	0.1	3.7
	16	80.6	0.6	7.7
	17	3172.0	654.1	1164.9
	18	72.6	0.1	4.5
	19	14.4	0.7	6.1
	20	539.6	151.3	113.4
	21	2558.9	1.1	38.6
	22	45.6	0.4	50.5
	23	122.8	7.7	49.0
	24	251.3	1.1	10.8
	25	1413.4	922.3	626.7
	26	123.1	6.7	255.4
	27	883.5	886.1	454.3
AIH11	1	1079.1	1921.3	76.9
	2	147.7	1262.8	99.3
	3	788.6	46.3	109.4
	4	83.5	9.7	94.0
	5	4218.0	98.9	1022.2
	6	694.8	266.9	67.7
	7	446.5	31.3	288.4
	8	1105.1	248.4	69.8
	9	559.1	64.1	12.7
	10	579.1	192.2	19.6
	11	112.6	66.7	46.7
	12	156.3	251.1	40.3
	13	75.4	43.7	64.7
	14	3558.4	1564.8	945.0
	15	1329.6	789.7	548.1
	16	6079.3	3256.0	1337.7
	17	2140.7	1438.3	2042.8
	18	1309.0	178.8	1700.1
	19	4486.5	109.1	2814.5
	20	1368.9	490.2	5442.9
	21	5408.7	385.9	365.6
	22	140.9	489.0	2602.7
	23	464.9	37.5	685.9
	24	187.0	29.2	16.3
	25	2565.9	379.3	1181.9
	26	1709.0	1759.6	426.3
	27	215.6	264.9	36.1
	28	640.2	836.2	2876.7
	29	200.6	239.4	2538.4
	30	4719.3	42.0	22.9
	31	6296.9	3459.8	919.2
AIH12	1	0.1	0.1	3.4
	2	61.4	0.1	6.6
	3	0.1	0.1	4.8
	4	0.2	0.1	7.1
	5	15.6	0.1	7.1
	6	0.1	0.1	6.9
	7	0.1	0.1	4.1
	8	3118.1	5.9	22.7
	9	49.0	0.1	4.4
	10	0.1	0.1	3.9
	11	24.9	0.1	5.3
	12	10.7	0.3	9.2
	13	0.1	0.1	4.1
	14	14.9	0.1	6.2
	15	0.1	0.1	6.4
	16	42.4	0.1	4.1
	17	0.1	0.1	5.8
	18	190.8	0.1	10.0
	19	656.3	1.0	12.4
	20	174.5	18.7	28.0
	21	0.1	0.1	5.3
	22	0.1	0.1	6.2
	23	10.4	0.1	6.2

	24	0.1	0.1	1.8
	25	4316.5	1.3	228.4
	26	286.2	2.3	8.8
	27	0.2	0.2	8.8
	28	63.6	0.5	8.4
	29	0.1	0.1	5.8
	30	0.1	0.1	3.4
AIH13	1	14.4	4.7	10.6
	2	14.4	2.5	10.6
	3	3.5	3.5	10.6
	4	14.4	3.6	10.6
	5	29.9	2.2	10.6
AIH14	1	15.0	44.7	0.1
	2	1.0	1.0	0.1
	3	1.8	1.0	0.1
	4	1.0	1.0	0.1
	5	1.0	1.0	0.1
	6	46.9	2.8	0.1
	7	1.0	1.0	0.1
	8	1.0	1.0	0.1
	9	1.0	1.0	0.1
	10	1.0	1.0	0.1
	11	1.0	1.0	0.1
	12	1.0	1.0	0.1
	13	1.0	1.0	0.1
	14	1.0	1.0	0.1
	15	35.6	1.0	0.1
	16	2.2	1.0	0.1
	17	1.0	1.0	0.1
	18	1.0	1.0	0.1
	19	44.8	43.3	0.1
	20	1.0	1.0	0.1
	21	7.6	80.9	0.1
	22	1.0	1.0	0.1
	23	65.2	37.0	0.1
	24	1.0	1.0	0.1
	25	14.4	1.0	3.3
	26	5.6	68.2	82.6
	27	277.9	2.2	4.5
	28	33.0	13.8	4.9
	29	11.3	13.8	16.1
	30	525.9	619.9	166.6
	31	17967.0	325.3	729.0
	32	4191.0	33.3	883.4
	33	331.6	134.9	923.7
	34	1085.3	703.2	883.1
	35	8.9	219.5	90.6
	36	181.5	108.4	84.8
	37	193.2	599.4	77.7
	38	3211.0	3092.9	898.5
	39	23.7	1.1	3.3
	40	1808.4	3.8	25.6
	41	1648.2	3.9	47.8
	42	130.0	37.0	94.5

ID	Clone n.	IFN-γ (pg/ml)	IL-10 (pg/ml)	IL-4 (pg/ml)
PC1	1	51.8	47.6	119.6
	2	29.2	1.1	0.1
	3	31.8	169.0	0.1
	4	0.1	7.0	2.9
	5	74.6	11.0	2.1
	6	385.3	384.9	7.5
	7	335.5	24.8	0.1
	8	296.7	63.3	0.3

	9	3.4	50.4	170.8
	10	245.0	47.1	6.6
	11	4513.3	69.4	287.4
	12	4629.5	76.8	5.3
	13	1209.0	8.1	143.9
	14	9.0	316.8	81.2
	15	5608.7	112.0	131.1
	16	0.1	12.3	0.6
	17	4354.4	165.5	86.2
	18	30.9	26.8	3.4
	19	22.7	37.6	45.7
	20	6793.2	271.7	43.4
	21	621.7	14.2	3.4
	22	895.0	535.4	125.5
	23	25.0	2.2	0.6
	24	6054.4	44.1	180.6
PC3	1	3.5	3.0	10.6
	2	5656.1	8.2	18.4
	3	2276.9	8.0	10.6
	4	2862.3	138.1	107.0
	5	5376.1	39.8	141.1
	6	12894.5	92.2	82.2
	7	3742.4	57.9	214.5
	8	4605.0	24.4	42.7
	9	536.4	5.3	10.6
	10	458.3	3.6	10.6
PC5	1	14.4	1.9	174.1
	2	3320.7	2386.7	287.7
	3	14.4	0.3	107.1
	4	5637.4	2323.5	542.5
	5	8840.9	2308.9	658.0
	6	1974.7	696.6	238.9
	7	83.2	470.4	358.2
	8	5981.9	438.1	219.4
	9	64.5	792.4	63.5

ID	Clone n.	Clonotype	IFN-γ (pg/ml)	IL-10 (pg/ml)	IL-4 (pg/ml)
AIH12 LB	1	2	1802.8	866.4	1784.9
	2	2	1133.2	154.4	3746.2
	3	2	750.6	41.2	3994.6
	4	2	1459.0	799.9	3881.0
	5	2	701.4	323.8	2703.0
	6	2	770.1	524.6	1508.5
	7	2	944.2	558.4	1956.1
	8	2	638.6	171.3	2408.6
	9	2	729.8	160.2	1035.9
	10	2	1367.5	371.6	9487.0
	11	2	1054.0	171.3	4187.4
	12	2	624.9	123.8	3539.1
	13	2	1835.6	185.2	6799.7
	14	2	357.0	54.0	3267.7
	15	2	1742.5	96.9	5405.2
	16	2	701.0	41.2	4095.7
	17	2	474.1	5.0	6994.5
	18	2	1093.3	160.2	2343.0
	19	2	291.5	88.6	2216.5
	20	2	650.6	219.2	5114.5
	21	2	755.9	239.2	4419.6
	22	2	1035.2	232.7	6498.6
	23	2	886.4	369.9	3190.5
	24	3	172.5	91.4	1480.1
	25	3	282.2	127.6	5502.1
	26	3	309.5	88.6	3286.9
	27	3	183.5	63.8	2332.8

Supplemental Table 6. Primers for BCR and TRVB sequencing

BCR	
RT-PCR (constant region primers)	HuIgG-const-anti: 5'-TCTTGTCCACCTTGGTGTTGCT-3' Hu-CK-for: 5'- ACACTCTCCCCTGTTGAAGCTCTT-3' Clambda-as296: 5'-ACTGTCTTCTCCACGGTGCT-3'
VH primer mix: Reverse (constant region primer) Forward (variable region primers)	 IGHG1-4 Rev: 5'-ACGGTCACCACGCTGCTGAG-3' VHL1: 5'- TCACCATGGACTGSACCTGGA-3' VHL1_58: 5'-ATGGACTGGATTTGGAGG-3' VHL2: 5'-ATGGACACACTTTGCTMCAC-3' VHL2b: 5'-ATGGACATACTTTGTTCCAC-3' VHL3bis: 5'-TCACCATGGAGTTKGGGCTGAGC-3' VHL3-21: 5'-TCACCATGGAACTGGGGCTCCGC-3' VHL3-64-01: 5'-ATGACGGAGTTTGGGCTGAGC-3' VHL4: 5'-AGAACATGAAACAYCTGTGGTTCTT-3' VHL5: 5'-ATGGGGTCAACCGCCATCCT-3' VHL6: 5'-CAATGTCTGTCTCCTTCCTCATC-3' VHL7: 5'-ATGGACTGGACCTGGAGGATCC -3'
VK primer mix: Reverse (constant region primer) Forward (variable region primers)	 Ckappa_as266 (KasD): 5'-GACTTCGCAGGCGTAGACTT-3' VKL1bis: 5'-GCTCAGCTCCTGGGGCTYCTG-3' VKL2: 5'-CTGGGGCTGCTAATGCTCTGG-3' VKL3: 5'-TTCCTCCTGCTACTCTGGCTC-3' VKL4: 5'-CAGACCCAGGTCTTCATTTCT-3' VKL5: 5'-TCCCAGGTTCACCTCCTCAGC-3' VKL6: 5'-TTCTGCTSCTCTGGGTTCCA-3'
VL primer mix: Reverse (constant region primer) Forward (variable region primers):	 3'CL: 5'-CACYAGTGTGGCCTTGTTGGCTTG-3' VLL1bis: 5'-CCTCTCCTCCTCACYCTCCT-3' VLL2bis: 5'-ATGGCCTGGGCTCTGCTGCTC-3' VLL3a: 5'-ATGGCCTGGACCCCTCTC-3' VLL3b: 5'-ATGGCCTGGATCCCTCTM-3' VLL3-9/21: 5'-ATGGCCTGGACCGYTCTC-3' VLL3-22: 5'-ATGGCATGGGCCACACTCC-3' VLL4: 5'-TGGGTCTCCTTCTACCTAC-3' VLL4a: 5'-TCCTCCTCCACTGCACAGG-3' VLL5-7-9: 5'-ATGGCCTGGRCTCCTCTS-3' VLL8: 5'-ATGGCCTGGATGATGCTTC-3' VLL10: 5'-TCACTCACTCTGCAGTGTC-3'

TRBV	
Reverse (TRBC-rev84) Forward (Maxipool FRW mix)	5'-TGTGGCCTTTTGGGTGTGG-3' 5'-TCAGGTGTGATYCAATTTC-3' 5'-AGGTGTGATCCAATTTCG-3' 5'-TGTGTCCTGGTACCAACAG-3' 5'-GTATCGACAAGACCCAGG-3' 5'-GTATCGACAAGACCYGGG-3' 5'-CTCACCTGAATGCCCCAA-3' 5'-ATGTTYTGGTAYCGTCAG-3' 5'-CCTTTACTGGTACCDGCAGA-3' 5'-ACAGAGATGGGACAAGAAG-3' 5'-GCCATGTACTGGTAYMGA-3' 5'-CCCCATCTCTAATCACTTATAC-3' 5'-ACATCAAACCCCAACCTATAC-3' 5'-ACCAGCAGAAGTCAAGTCA-3' 5'-TGTSTACTGGTACCARCAG-3' 5'-GGGAAGGACAGAAAGCAAAA-3' 5'-TTACTCAGTTCCCCAGCC-3' 5'-AGATGCAGCCCAATGAAA-3' ACAGATGGGAAACGACAA-3' GTATCRACAAGAYCCAGGA-3'