Sustained High expression of multiple APOBEC3 cytidine deaminases in Systemic Lupus Erythematosus

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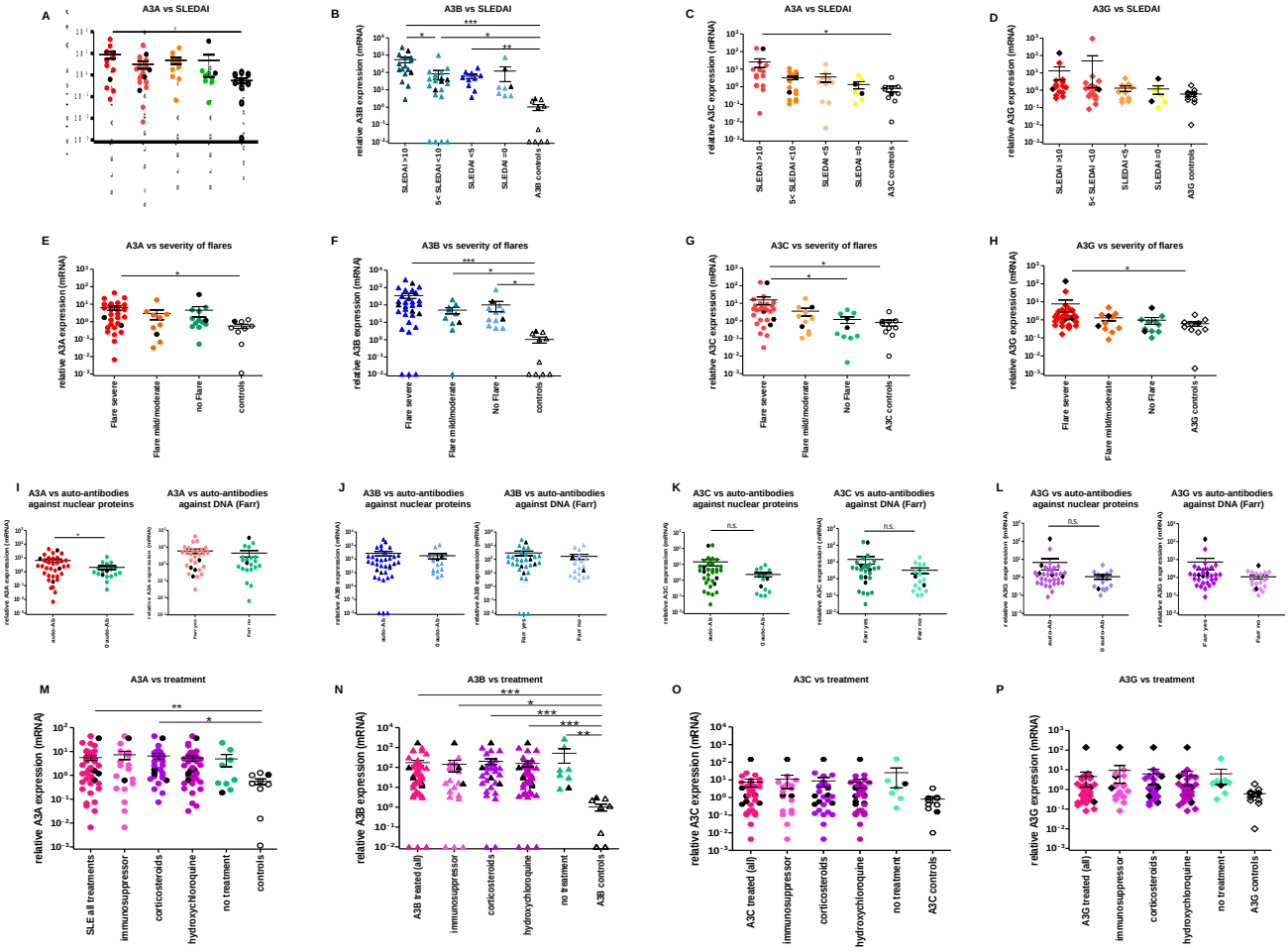
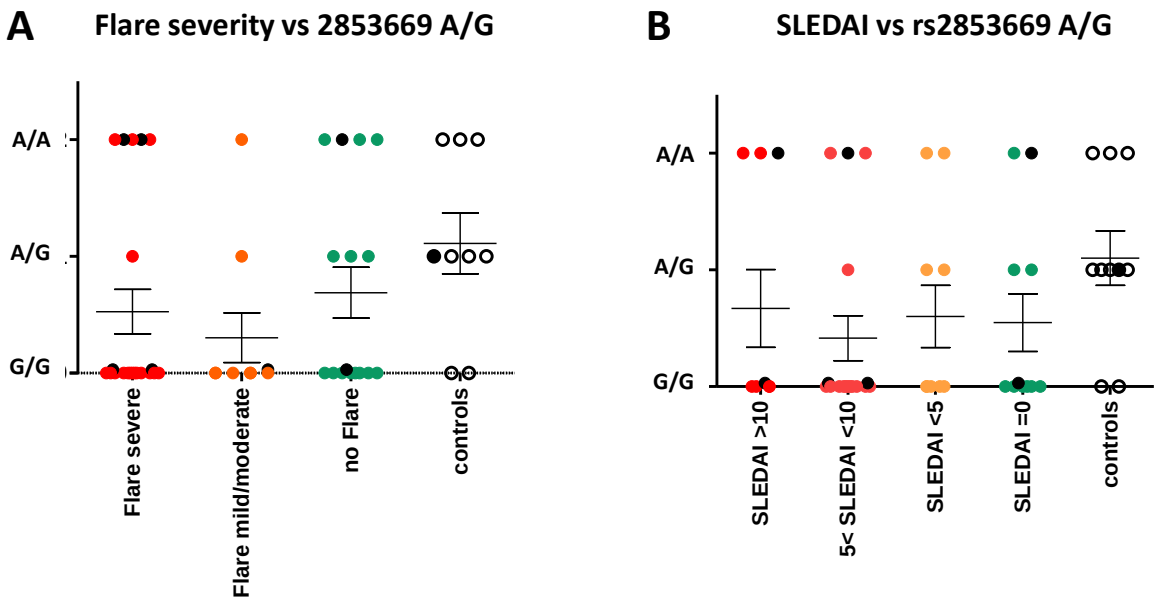
Supplementary Figures and Table



Supplementary Figure 1. *A3A*, *A3B*, *A3C* and *A3G* relative expression in SLE patients stratified by clinical status. A-D. *A3A* (**A**), *A3B* (**B**) *A3C* (**C**) and *A3G* (**D**) expression in relation to SLEDAI. **E-F.** *A3A* (**E**), *A3B* (**F**) *A3C* (**G**) and *A3G* (**H**) expression in relation to severity of flares. Patients were stratifed according to the presence and severity of flares or to the SELENA-SLEDAI Flare composite score as follows: SLEDAI = 0: non-active Lupus; 0<SLEDAI≤ 5: mild condition; 5< SLEDAI ≤10: medium activity; SLEDAI > 10: severe. **I-L.** *A3A* (**I**), *A3B* (J) *A3C* (**K**) and *A3G* (**L**) levels in patients with and without auto-antibodies against nuclear antigens and cellular DNA. **M-P.** *A3A* (**M**), *A3B* (N) *A3C* (**O**) and *A3G* (**P**)levels in relation to treatment. Relative A3A and *A3B* expression was normalized to the geometric mean of housekeeping genes *RPL13A* and *GAPDH* according to the Pfaffl method. Control C1 was used as calibrator for comparison and is therefore set to 1. Full black symbols represent patients heterozygous for the *A3AΔ3B* deletion. n.s.: not significant; n*: p<0.05; **: p<0.01; ***: p<0.001.



Supplementary Figure S2. **Prevalence of *TERT* promoter rs2853669 A/G alleles in SLE patients stratified according to flare severity (A) and SLEDAI (B).** Full black symbols represent patients heterozygous for the *A3A∆3B* deletion. *: p<0.05; **: p<0.01; ***: p<0.001.

A TERT promoter sequence amplified

gtcgggg**cca ggccgggctc ccagtggatt** cgcgggcaca gacgcccagg accgcgc**tcc c**cacgtggcg
gagggactgg ggacccgggc acccgtcctg ccccttcacc ttccagctcc gcctcctccg cgcggacccc
gccccgtccc gacccc**tccc** gggtccccgg cccagcccc**c tcc**gggccct cccagcccct ccccttcctt
tccgcggccc cgccctctcc tcgcggcgcg agtttcaggc agcgctgc**gt cctgctgcgc acgtgggaag cc**

B

file_name	Position	Type	Reference	Allele	Count	Coverage	Frequency	Average quality	rs2853669 polymorphism	rs2853669
controls										
./HN3YNAFXX_C1_S61_cut (Reads) va	59.0	SNV	C	T	35565.0	35896.0	0.990778917	35 435 709 264 726 500	wt biallelic	rs2853669 A/A
./HN3YNAFXX_C2_S62_cut (Reads) va	59.0	SNV	C	T	3486.0	7508.0	0.464304742	35 421 399 885 255 300	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_C3_S63_cut (Reads) va	59.0	SNV	C	T	4886.0	7586.0	0.644081202	3 539 787 146 950 470	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_C4_S64_cut (Reads) va	59.0	SNV	C	T	48033.0	48228.0	0.995956706	35 454 729 040 451 300	wt biallelic	rs2853669 A/A
./HN3YNAFXX_C5_S65_cut (Reads) va	59.0	SNV	C	T	3111.0	3192.0	0.97462406	35 423 657 987 785 200	wt biallelic	rs2853669 A/A
./HN3YNAFXX_C7_S67_cut (Reads) va	59.0	SNV	C	T	25867.0	54657.0	0.473260516	354 282 290 176 673	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_C8_S68_cut (Reads) va	59.0	SNV	C	T	813.0	1501.0	0.541638907	3 533 825 338 253 380	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_C9_S69_cut (Reads) va	59.0	SNV	C	T	1832.0	2796.0	0.655221745	35 400 109 170 305 600	polymorphism monoallelic	rs2853669 A/G
SLE patients										
./HN3YNAFXX_S3_S3_cut (Reads) vari	59.0	SNV	C	T	1879.0	3912.0	0.480316973	3 529 856 306 546 030	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_S4_S4_cut (Reads) vari	59.0	SNV	C	T	9294.0	9343.0	0.994755432	35 401 226 597 805 000	wt biallelic	rs2853669 A/A
./HN3YNAFXX_S5_S5_cut (Reads) vari	59.0	SNV	C	T	8165.0	8200.0	0.995731707	35 385 303 123 086 300	wt biallelic	rs2853669 A/A
./HN3YNAFXX_S6_S6_cut (Reads) vari	59.0	SNV	C	T	33250.0	33423.0	0.994823924	353 532 030 075 188	wt biallelic	rs2853669 A/A
./HN3YNAFXX_S12_S12_cut (Reads) v	59.0	SNV	C	T	2484.0	2785.0	0.891921005	35 420 692 431 561 900	wt biallelic	rs2853669 A/A
./HN3YNAFXX_S13_S13_cut (Reads) v	59.0	SNV	C	T	28404.0	28546.0	0.995025573	3 536 899 732 432 050	wt biallelic	rs2853669 A/A
./HN3YNAFXX_S17_S17_cut (Reads) v	59.0	SNV	C	T	51889.0	52128.0	0.995415132	3 534 882 152 286 610	wt biallelic	rs2853669 A/A
./HN3YNAFXX_S20_S20_cut (Reads) v	59.0	SNV	C	T	23773.0	43794.0	0.542836918	3 537 349 093 509 440	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_S24_S24_cut (Reads) v	59.0	SNV	C	T	8856.0	18181.0	0.48710192	35 385 840 108 401 000	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_S25_S25_cut (Reads) v	59.0	SNV	C	T	31014.0	67159.0	0.46179961	3 541 694 073 644 160	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_S26_S26_cut (Reads) v	59.0	SNV	C	T	62577.0	62839.0	0.995830615	35 415 663 902 072 600	wt biallelic	rs2853669 A/A
./HN3YNAFXX_S28_S28_cut (Reads) v	59.0	SNV	C	T	21171.0	38966.0	0.543319817	35 439 232 912 946 900	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_S34_S34_cut (Reads) v	59.0	SNV	C	T	11090.0	23349.0	0.474966808	35 122 001 803 426 500	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_S35_S35_cut (Reads) v	59.0	SNV	C	T	7439.0	13477.0	0.551977443	3 526 737 464 712 990	polymorphism monoallelic	rs2853669 A/G
./HN3YNAFXX_S36_S36_cut (Reads) v	59.0	SNV	C	T	49246.0	50237.0	0.980273504	3 541 461 235 430 280	wt biallelic	rs2853669 A/A
./HN3YNAFXX_S38_S38_cut (Reads) v	59.0	SNV	C	T	17222.0	17296.0	0.995721554	3 536 081 755 893 620	wt biallelic	rs2853669 A/A
./HN3YNAFXX_S50_S50_cut (Reads) v	129.0	SNV	C	T	565.0	51116.0	0.011053291	3 436 106 194 690 260		
./HN3YNAFXX_S52_S52_cut (Reads) v	59.0	SNV	C	T	2072.0	2123.0	0.97597739	3 533 735 521 235 520	wt biallelic	rs2853669 A/A

Supplementary Table S1. Mutations and polymorphisms in a fragment of the *TERT* core promoter from SLE patients and healthy controls. A fragment of the *TERT* promoter was amplified by PCR and sequenced using Illumina 2000. **A.** The sequence is shown at the bottom of the list of mutations. Primers are underlined and bolded. The rs2853669 polymorphism as well as *TERT* promoter mutations -146C>T and -126C>T are highlighted in yellow. The putative Ets/TCF binding sites are underlined. Note that the reference sequence has the rs2853669 A>G polymorphism and has lost the Ets/TCF binding site. **B**. Position, mutation, Sequence Coverage, strand bias, variant frequency and the rs2853669 A/G status are reported.
SNV: single nucleotide variant; wt: wild type