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Decreased *SMG7* expression associates with lupus-risk variants and elevated antinuclear antibody production

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Key Words

Systemic lupus erythematosus

Nonsense mediated mRNA decay

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Genetic association study

ABSTRACT

Objectives Following up the SLE GWAS identification of *NMNAT2* at rs2022013, we fine-mapped its 150kb flanking regions containing *NMNAT2* and *SMG7* in a 15,292 case-control multi-ancestry cohort and tested functions of identified variants.

Methods We performed genotyping using a custom array, imputation by IMPUTE 2.1.2, and allele specific functions using qRT-PCR and luciferase reporter transfections. SLE PBMCs were cultured with siRNAs to measure antinuclear antibody (ANA) and cyto/chemokine production in supernatants using ELISA.

Results We confirmed association at *NMNAT2*, and identified an independent signal at *SMG7* tagged by rs2702178 in European Americans (EA) only (P=2.4×10^{-8}, OR=1.23 [95%CI=1.14-1.32]). In complete linkage disequilibrium with rs2702178, rs2275675 in the promoter region robustly associated with *SMG7* mRNA levels in multiple expression quantitative trait loci datasets. The risk allele of rs2275675 was dose-dependently associated with decreased *SMG7* mRNA levels in PBMCs of 86 SLE patients and 119 controls (P=1.1×10^{-3} and 6.8×10^{-8}, respectively) and conferred reduced transcription activity in transfected HEK-293 and Raji cells (P=0.0035 and 0.0037, respectively). As a critical component in the nonsense-mediated mRNA decay pathway, SMG7 could regulate autoantigens including RNP and Sm. We showed *SMG7* mRNA levels in PBMCs correlated inversely with ANA titers of SLE patients (r=-0.31, P=0.01), and *SMG7* knockdown increased production of ANA and CCL19 in SLE PBMC cultures (P=2.0×10^{-5} and 2.0×10^{-4}, respectively).

Conclusions We confirmed *NMNAT2* and identified independent *SMG7* association with SLE. The inverse relationship between levels of the risk-allele associated *SMG7* mRNAs and ANAs suggested the novel contribution of mRNA surveillance pathway to SLE pathogenesis.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a prototype autoimmune disease characterized by autoantibody production resulting in tissue injury of multiple organs. A combination of genetic, epigenetic and environmental factors contributes to the pathogenesis of SLE. Recent genome-wide association studies (GWAS) have identified more than 50 susceptibility loci for SLE [1]. There is an ongoing effort to fine map these risk loci and to gain insights how they work to influence lupus manifestations.

Within the 1q25 region, rs2022013 located in the first intron of *NMNAT2* (encoding nicotinamide mononucleotide adenylyltransferase 2) was associated with SLE in the GWAS conducted by the International Consortium for Systemic Lupus Erythematosus Genetics (SLEGEN) (P=1.1×10^{-7}, OR=0.85) and in a large-scale replication study (P=1.5×10^{-3}, OR=0.92) using subjects of European ancestry [2, 3], suggesting *NMNAT2* as a SLE risk locus. NMNAT2 is a central enzyme of the nicotinamide adenine dinucleotide (NAD) biosynthetic pathway and mainly expressed in brain with a known function of delaying axon degeneration [4, 5]. Given no apparent clues for its involvement in immune dysregulation, we fine mapped this novel *NMNAT2* locus and neighboring genes for association with SLE in subjects from four ancestries.

In this study, we confirmed *NMNAT2* association with SLE susceptibility and identified independent association signals at the *SMG7* region in European American (EA). *SMG7*, located approximately 50 kb 5' of *NMNAT2*, encodes a component essential for nonsense-mediated mRNA decay (NMD) that controls mRNA quality, regulates gene expression and maintains genome stability [6]. We detected the SLE-risk alleles associated with decreased *SMG7* mRNA levels in peripheral blood mononuclear cells (PBMCs) of both SLE and healthy control subjects, and an inverse correlation between antinuclear autoantibody (ANA) titers and *SMG7* mRNA levels in SLE patients. *SMG7* reduction increased production of ANA and chemokine (C-C motif) ligand 19 (CCL19) in SLE PBMC cultures, suggesting that decreased

SMG7 expression impacts the NMD pathway mediated mRNA surveillance, contributing to autoantibody production in SLE.

METHODS

Subjects

DNA from individuals participating in Large Lupus Association Study 2 (LLAS2) recruited from multiple sites was processed at the Oklahoma Medical Research Foundation (OMRF). Each institution had Institutional Review Board (IRB) approval to recruit subjects and the overall study was approved by the IRB of OMRF. All SLE patients met American College of Rheumatology revised criteria for the classification of SLE [7].

Genotyping and quality control

Genotyping was performed using an Illumina custom bead array on the iSCAN instrument for 35 tag SNPs covering over 200kb of the *NMNAT2-SMG7* region and 347 admixture informative markers (AIMs). SNPs meeting the criteria as described [8] were included for subsequent genetic association tests.

Subjects with missing genotype rate >10%, shared identity by descent >0.4, or gender mismatch were removed. Global ancestry was estimated based on the genotype of AIMs, using principal components analysis [9] and ADMIXMAP [10] as described [11] and genetic outliers removed. Final clean data were from 15,292 unrelated subjects including EA, African Americans (AA), Asians (AS) and Hispanics enriched for Amerindian-European admixture (HS).

Imputation

Imputation was performed using IMPUTE 2.1.2 [12], with SNP and INDEL genotypes from the 1000 Genomes Project (version 3, Phase 1 integrated data, March 2012 release) as references. Imputed genotypes with information scores >0.9 and MAF >0.01 were further analyzed.

Quantitative real-time PCR

Total RNAs were purified using the AllPrep DNA/RNA mini kit (Qiagen) from PBMCs of EA subjects and reverse-transcribed into cDNA with the SuperScript II Reverse Transcriptase kit (Life Technologies). Transcript levels of *SMG7*, *SMG7-AS1* and a housekeeping gene *RPLP0* were measured in triplicates by quantitative real-time PCR using TaqMan assays (*SMG7*: Hs00539224_m1, *RPLP0*: Hs99999902_m1; Life Technologies), and their relative levels were calculated by the $2^{-\Delta\Delta Ct}$ method and Log_{10} transformed.

Autoantibody profiles of 68 SLE patients (including ANA, anti-dsDNA or antibodies to extractable nuclear antigens) were measured in the UCLA clinical laboratory at the time of blood draw, and these data were used to correlate with *SMG7* mRNA levels in PBMCs.

Plasmid construction and luciferase reporter assay

DNA sequences (0.3kb) surrounding rs2275675 or rs10911339 were PCR amplified using genomic DNA from homozygous subjects for the C allele (rs2275675) and the T allele (rs10911339) using following primers:

rs2275675, 5'-GGGGTACCGTAGAAAGAAAAGCAGAAC-3' (forward) and 5'-GAAGATCTGAGACCTGCACCAATAAG-3' (reverse); rs10911339, 5'-GGGGTACCGGTATGGGTGCCTAGC-3' (forward) and 5'-GAAGATCTCCAGGTGTGCAGACTTC-3' (reverse). The PCR products were digested using restriction enzymes KpnI and BglII and inserted into the pGL3-promoter luciferase reporter vector (Promega). The vectors for the other allele were made using the QuikChange Lightning Site-Directed Mutagenesis Kit (Stratagene). All constructs were sequenced to assure proper orientation and authenticity in the vector.

HEK-293 (human embryonic kidney cell line) and Raji B cells were obtained from the American Type Culture Collection. HEK-293 cells were maintained in Dulbecco's modified Eagle's medium supplemented with 10% FBS, seeded on a 24-well plate at a concentration of 2×10^5 cells/well and transiently transfected using Lipofectamine 2000 (Life Technologies) with 1 μg of rs2275675 vector (C or T), rs10911339 vector (C or T) or empty vector (pGL3-promoter) and 100 ng of pRL-SV40 vector (Renilla luciferase) as an internal control. Raji cells were grown in RPMI 1640 medium with 10% FBS, seeded on 24-well plates at a concentration of 2×10^6 cells/well and electroporated with 5μg of luciferase report constructs and 100 ng of Renilla control vector on a nucleofector device (Amaxa). The luciferase activity in total cell lysates was measured after 24 hours using a dual luciferase reporter assay system (Promega).

RNA Interference

Gene silencing by small interfering RNAs (siRNAs) was performed using the Accell® siRNA technology which achieves effective gene silencing in human primary cells without transfection reagents or viruses [13]. Pool of four siRNA sequences targeting *SMG7* was designed and synthesized by Dharmacon (SMG7 siRNA SMARTpool E-021305). Pool of siRNAs targeting glyceraldehyde-3-phosphate dehydrogenase (*GAPDH;* SMARTpool D-001930) was used as a positive control, and the non-targeting control pool (D-001910) designed to have minimal targeting of known genes in human cells was used as a negative control.

PBMCs from 13 SLE patients were isolated by Ficoll-Hypaque discontinuous gradient, resuspended in Accell delivery media plus 3μM siRNA, distributed to 96-well plate at 2×10^5 cells/well, and divided into *SMG7* silence group, *GAPDH* silence group (positive control), non-targeting group (negative control) and mock group (medium only) (n=6 per group for each sample). Cells were incubated at 37°C with 5% CO_2 for 5 days, then supernatants were collected and cells were harvested. Specific inhibition efficacy of *SMG7* and *GAPDH* was confirmed by quantitative PCR.

Enzyme-linked immunosorbent assay (ELISA)

ANA, CCL19, chemokine (C-X-C motif) ligand 10 (CXCL10), interleukin 6 (IL-6), IL-17, B-cell activating factor (BAFF) and interferon α (IFN-α) levels in supernatants were measured by ELISA kits (R&D Systems).

Statistical analysis

Allelic association test and conditional haplotype-based association test in each ancestral group were performed under a logistic regression model adjusted for gender and the first three principal components estimated using AIMs. The Bonferroni corrected *P*-value threshold was adjusted to $P<1\times10^{-3}$ on the basis of the maximum number of tests across all populations (49 independent variants with $r^2<0.8$). For trans-ancestral meta-analysis, a fixed effect model was applied if Cochran's Q statistic showed no evidence of genetic heterogeneity among odds ratios ($P>0.05$); otherwise, a random effect model was used. Association analyses were performed using PLINK v1.07 [14]. Pairwise LD values between SNPs were calculated using Haploview 4.2 [15]. For comparing the results between two groups, Student's *t*-test was conducted if the variance was normally distributed, whereas the Mann-Whitney U test was used if the variance was not normally distributed. Correlation between groups was evaluated using the Pearson rank test. A *P* value<0.05 was considered to be statistically significant.

RESULTS

To fine map the *NMNAT2* region, we conducted genotyping and imputation for genetic variants (SNPs/INDELs) within a 308 kb region at 1q25 containing genes *LAMC2*, *NMNAT2*, *SMG7-AS1* and *SMG7*. After applying quality control measures, 35 genotyped and 85 to 278 imputed SNPs (varying among different ancestries) were assessed for association with SLE in 15,292 unrelated case-control subjects from four ancestral groups: EA (3,438 SLEs vs. 3,417 controls), AA (1,679 vs. 1,934), AS (1,265 vs. 1,260) and HS (1,492 vs. 807) under a logistic regression model adjusting for gender and global ancestry (Figure 1).

The association of *NMNAT2* with SLE was confirmed in EA and HS ancestries

In the largest EA dataset, 135 SNPs spanning the entire *NMNAT2* were significantly associated with SLE after Bonferroni correction ($P<1.0\times10^{-3}$) for multiple comparisons (Figure 1B and Table S1). The SLE association at rs2022013 previously identified in the SLEGEN GWAS was confirmed in our EA subjects (minor allele frequency [MAF] 38.1% in cases vs. 42.4% in controls, $P=3.9\times10^{-7}$, OR=0.83 [95%CI=0.77-0.89]). Rs12146097 in the *NMNAT2* (NM_015039) intron 1 exhibited the strongest signal exceeding the GWAS significance level (16.7% vs. 12.9%, $P=1.5\times10^{-10}$, OR=1.38 [95%CI=1.25-1.53]).

In the HS dataset, significant associations with SLE were localized within the *NMNAT2* intron 1 after Bonferroni correction, with rs536586 showing the best signal (44.2% vs. 39.2%, $P=2.7\times10^{-4}$, OR=1.26 [95%CI=1.11-1.43]) (Figure 1B and Table S2). However, association of rs2022013 with SLE was not significant in HS ($P=0.11$).

In the AA and AS datasets, we observed only weak association at SNPs in the *NMNAT2* region ($P<0.05$) and none reached the Bonferroni-corrected significance level (Figure 1B and Table S3&S4).

Comparing across EA and HS, 8 SNPs ($P<1.0\times10^{-3}$) within a ~51 kb interval in the *NMNAT2* intron 1 showed consistent association with SLE in both EA and HS datasets, of which

6 SNPs (rs564146, rs681054, rs664422, rs502870, rs548292 and rs12146097, named as group 1) each showed a P_{meta}<5×10^{-8} in the trans-ancestral meta-analysis (Figure 1C and Table S5). Except rs12146097, the other 5 SNPs were in strong pairwise linkage disequilibrium (LD) with each other ($r^2\geq0.99$, D'=1.0) and with rs2022013 ($r^2\geq0.83$, D'≥0.96) in both EA and HS. In conditional haplotype-based association testing, conditioning on group 1 SNPs eliminated or reduced all other association signals in the *NMNAT2* region to baseline in HS, but revealed residual association in EA predominantly in the region 55 kb downstream within the *NMNAT2* intron 1 to intron 3 ($2.7\times10^{-4}\leq P_c\leq6.7\times10^{-4}$) (Table S1&S2). These results confirmed *NMNAT2* as a risk locus for SLE in EA and HS ancestries.

Independent association of *SMG7* with SLE in EA only

In EA, 21 SNPs located at ~32kb 5' of *NMNAT2* (named as group 2, Figure 1B) were strongly associated with SLE ($2.4\times10^{-8}\leq P\leq4.3\times10^{-7}$), of which rs2702178 in the *SMG7* intron 1 showing the best signal (40.8% vs. 36.2%, $P=2.4\times10^{-8}$, OR=1.23 [95%CI=1.14-1.32]) (Table S1). All 21 SNPs were in strong LD with each other ($r^2\geq0.98$, D'≥0.99), but in low LD with group 1 SNPs ($r^2\leq0.22$, D'≤0.73). Genetic effects of *NMNAT2* (group 1) and *SMG7* (group 2) appear to be independent in EA using the conditional testing, in which association signals detected at either group of SNPs retained significance when conditioning on another group (Figure S1). Unlike the findings in EA, SNPs in the *SMG7* region exhibited modest association with SLE ($7.5\times10^{-3}\leq P\leq0.02$) in HS and none passed the Bonferroni-corrected significance level (Table S2). The *SMG7* region was not well imputed in AA and AS datasets, which might explain their lack of significant associations (Table S3&S4). Taken together, we identified multiple SNPs in the *SMG7* region showing independent association with SLE in EA dataset only.

The SLE-associated SNPs identified in EA showed allelic differences in *SMG7* expression

Given group 1 (5.5kb at intron 1 of *NMNAT2*) and group 2 SNPs (97kb from promoter to intron 17 of *SMG7*) located in the non-coding regulatory regions, we assessed their potential functions using the UCSC Genome Browser (Figure S2). While group 1 SNPs showed low or modest overlap with regulatory elements, group 2 SNPs (especially rs2275675 at the promoter and rs10911339 in intron 1, r^2=1) were located in a region containing the H3K4Me3/H3K27Ac epigenetic marks for promoter/enhancer activity and overlapped with DNase hypersensitivity and transcription factor binding signals, suggesting that these identified SNPs might affect nearby genes expression.

We checked the expression quantitative trait locus (eQTL) datasets [16-20] to evaluate allelic differences in the expression of genes located in nearby +/- 250 kb region, including *LAMC1*, *LAMC2*, *NMNAT2*, *SMG7-AS1*, *SMG7*, *NCF2*, *ARPC5*, *APOBEC4* and *RGL1*. Both group 1 and group 2 SNPs were consistently associated with differential expression of *SMG7* in diverse cell types from European-derived donors, including fibroblasts, adipocytes, lymphoblastoid cell lines, peripheral blood cells, primary T, B cells and monocytes. Compared to group 1 SNPs, group 2 SNPs (tagged by rs10911353 or rs2275675) showed stronger eQTL effects that the SLE-risk alleles were associated with decreased *SMG7* levels (Table S6). The SLE-associated SNPs exhibited no eQTL evidence for the neighboring genes *LAMC1*, *LAMC2*, *NMNAT2*, *SMG7-AS1*, *APOBEC4* and *RGL1*, or only weak effects on genes *NCF2* and *ARPC5*, if at all, in blood cell types. Although expressed in the brain predominately, no eQTLs were reported at the *NMNAT2* locus in studies from human brain tissues, including cortex, caudal pons, cerebellum, thalamus and hippocampus [21-29]. Surprisingly, in addition to immune cell types, *cis* associations between SLE-risk SNPs and *SMG7* expression were also identified in brain tissues [24, 25], suggesting that modulation of expression levels is a likely functional mechanism of SLE-associated *SMG7* variants.

Dose-dependent association between the SLE-risk allele of rs2275675 and decreased *SMG7* levels

We sought further evidence supporting the eQTL findings by assessing the association of rs12146097 and rs2275675 with *SMG7* mRNA levels in PBMCs from 86 SLE patients and 119 controls of European ancestry. Consistently, the SLE-risk C allele of rs2275675 was dose-dependently associated with decreased *SMG7* mRNA levels in both SLE and controls subjects ($P=1.1\times10^{-3}$ and 6.8×10^{-8} in linear regression, respectively; Figure 2A). No significant differences in *SMG7* mRNA levels were observed between SLE patients and controls of the same genotype (genotype TT: $P=0.34$, CT: $P=0.12$, CC: $P=0.87$, SLE vs. controls in *t* test). The SNP rs12146097 was not significantly associated with *SMG7* expression in our samples, which might be due to fewer carriers of the minor allele (MAF: 14% of rs12146097 compared to 37% of rs2275675 in Europeans; 1000 Genomes data).

Long non-coding RNAs (lncRNAs, typically >200nt) are actively transcribed genes without protein-coding potential [30]. lncRNA expression often correlates with its *cis* protein-coding genes, which is subject to strong eQTL regulation [31]. Located 0.4kb upstream of *SMG7* is lncRNA *SMG7-AS1* (SMG7 antisense RNA 1) and rs2275675 is in its second intron. Of interest, transcript levels of *SMG7* and *SMG7-AS1* were positively correlated in control PBMCs ($r=0.60$, $P=3.5\times10^{-9}$; Figure S3A). The risk allele of rs2275675 was also associated with decreased *SMG7-AS1* levels ($P=0.008$, Figure S3B).

Given that rs2275675 and its linked SNP rs10911339 ($r^2=1$) are located in a region exhibiting epigenetic marks of active promoters/enhancers (Figure S2), we performed luciferase reporter assays to test their effects on transcription activity. Cell lysates transfected with the rs2275675 risk C-allele construct showed significantly lower luciferase activity than those transfected with the non-risk T-allele construct in both HEK-293 and Raji cells ($P=0.0035$ and 0.0037, respectively; Figure 2B). There were no significantly allelic differences observed using the rs10911339 constructs (Figure 2C). Taken together, consistent results from *ex vivo* and *in* *vitro* studies indicated that rs2275675 might best tag SLE-associated SNPs within the *SMG7* region to affect *SMG7* expression, with the risk allele conferring decreased *SMG7* mRNA levels.

Decreased SMG7 levels associated with increased ANA titers

The NMD pathway degrades mRNAs with premature termination codons (PTCs), preventing the production of truncated proteins that could function in dominant-negative or other deleterious mechanisms [32]. Given that SMG7, together with other SMGs, mediate the phosphrylation and dephosphorylation of UPF1 (a key effector of NMD) [33], we hypothesize that decreased SMG7 levels may affect the efficiency of NMD, thereby leading to accumulation of NMD-susceptible messenger ribonucleoprotein particles (mRNPs) and autoantibody production in SLE. To test this hypothesis, we first assessed the correlation of *SMG7* mRNA levels and ANAs in 68 European-derived SLE patients. We observed a significant inverse correlation that patients with higher ANA titers had lower *SMG7* mRNA levels in PBMCs (r=-0.31, *P*=0.01; Figure 3A).

Next, we performed siRNA-mediated knock down of *SMG7* levels in SLE PBMCs to assess whether autoantibody production might be affected by *SMG7* expression *in vitro*. To minimize confounding factors caused by disease activity or medications, the selected 13 patients were all in clinical remission defined by SLE Disease Activity Index SELENA Modification (SELENA-SLEDAI) score <4 [34], prednisone dosage less than 15 mg/d and had a positive ANA at the time of blood draw. PBMCs from patients were cultured for 5 days in the presence or absence of siRNA targeting *SMG7*, *GAPDH* (as positive control), or siRNA with a non-targeting sequence (as negative control), respectively. After confirming the specific inhibition efficacy of *SMG7* (Figure S4), we measured ANA levels in culture supernatants. Consistent with the *ex vivo* finding of inverse correlation between *SMG7* levels and ANA titers in SLE patients, PBMCs treated with *SMG7* siRNA showed a 7.6% increase in ANA production (P=2.0×10^{-5}, as compared to the negative control group; Figure 3B). Given that autoantibody production requires T, B cell help and some cyto/chemokines produced by T/B cells have been found to be overexpressed in SLE patients correlating with disease activity or autoantibody titers, we also tested if SMG7 was linked to the cyto/chemokine disturbance by measuring levels of CCL19, CXCL10, IL-6, IL-17, BAFF and IFN-α in culture supernatants. CCL19, an IFN-regulated chemokine that has been implicated as a biomarker for lupus activity [35], was significantly increased in the *SMG7* siRNA treated group compared to those in the negative control group ($P=2.0\times10^{-4}$; Figure 3C). There were no differences in other tested cyto/chemokines between groups treated with specific siRNAs (Figure S5). Taken together, decreased *SMG7* levels could affect the production of ANA and CCL19 in PBMCs of SLE patients, supporting a potential role for SMG7 in contributing to autoantibody production.

DISCUSSION

By trans-ancestral fine mapping of the *NMNAT2/SMG7* region, we confirmed previously GWAS reported association with SLE at the *NMNAT2* locus and identified multiple SNPs located within the *SMG7* locus showing strong and independent associations with SLE in EA ancestry. Of interest, the risk alleles of SLE-associated SNPs at both *NMNAT2* and *SMG7* loci showed association with decreased expression levels of *SMG7*, but not *NMNAT2* in publically available eQTL datasets conducted in immune cells from European donors. Consistently, rs2275675, located in the *SMG7* 5' regulatory region, was experimentally confirmed to best tag SLE-associated SNPs within the *SMG7* region affecting *SMG7* expression, as shown by the risk allele dose-dependently associated with low *SMG7* mRNA levels in PBMCs and reduced transcription activity in transfected cell lines. SLE patients with higher ANA titers had lower *SMG7* mRNA levels in their PBMCs and inhibition of *SMG7* expression increased ANA and CCL19 production in SLE PBMC cultures. Thus, our data demonstrated both *NMNAT2* and *SMG7* as SLE risk genes on 1q25 and implicated the NMD pathway affected by lowered SMG7 expression promotes the development of SLE manifestation.

The NMD, part of RNA surveillance pathways, post-transcriptionally regulates a considerable fraction of the transcriptomes [36]. PTC-containing mRNAs, arising from nonsense or frameshift mutations, errors in alternative splicing, or programmed DNA rearrangements occurred in T-cell receptor (TCR) and immunoglobulin (Ig) genes, comprise the major group of NMD substrates [33]. Truncated proteins encoded by such PTC-bearing mRNAs possess deleterious dominant-negative or gain-of-function activity in cells, so that an escape from NMD can result in clinical phenotypes [37]. In the case of SLE, rare mutations leading to production of PTC-containing mRNAs of *DNASE1*, *DNASE1L3 and TREX1* have been associated with disease risk [38-40]. In addition, NMD can modulate the expression of approximate 10% of physiological mRNAs involved in diverse cellular processes, including spliceosomal components snRNP and Sm which are autoantigens in SLE patients [33, 41]. As a key component of the

NMD pathway, SMG7 interacts with SMG5 regulating the phosphorylation and dephosphorylation of UPF1 (a functional core of the NMD machinery) [33, 42]. Depletion of SMG7 or other SMG members could inhibit NMD activity in mammalian cells, resulting in enhanced expression levels of PTC-containing transcripts [43]. Based on these findings, we created a working hypothesis that inefficiency of NMD pathway attributable to decreased *SMG7* expression may cause accumulation of truncated proteins and mRNPs, leading to autoantibody production in SLE. Support evidence for this hypothesis included that a) low *SMG7* mRNA levels were found to be correlated with high ANA titers in SLE patients, and b) inhibition of *SMG7* expression increased ANA production in SLE PBMC cultures. However, in terms of subtypes of ANAs, we did not observe significant associations between *SMG7* expression and anti-dsDNA, Ro/SSA, La/SSB, RNP or Sm antibodies, partially due to the limited sample size of seropositive patients (Figure S6). In addition to ANA, we also found elevated CCL19 production after silencing of *SMG7* in SLE PBMCs, suggesting a potential role of SMG7 in regulation of CCL19 levels in SLE. CCL19, specifically binding to the chemokine receptor CCR7, promotes migration/interaction of B-Th cells, formation of germinal center and production of high-affinity, class-switched antibodies [44, 45]. How SMG7 depletion affects autoantibody and CCL19 production are currently unclear.

Based on imputation, multiple SNPs within the *SMG7* locus were identified to be strongly associated with SLE in EA and their genetic effects were independent of those in the *NMNAT2* region. To our knowledge, our data provides the first evidence in support of *SMG7* as a novel SLE risk gene in EA. The genotyping platform used in the published SLE European GWAS [2, 46-48], which contained 10 *SMG7* SNPs, could only capture 74 of the 115 common SNPs (MAF>1%) within +/- 5kb of *SMG7* with r^2>0.9 in EA (according to the 1000 Genome Project data), resulting in the absence of *SMG7* association with SLE. In HS, the minor alleles of *SMG7* SNPs also showed higher frequencies in SLE patients than controls, similarly as in EA, but none reached the Bonferroni-corrected significance level (Table S2). Given the lack of evidence for genetic heterogeneity across EA and HS (*P*>0.48 for Q statistic), insufficient statistical power due to the relatively small sample size might help explain the lack of association in HS (98% power in EA; 40% in HS). We did not detect significant association signals at *NMNAT2/SMG7* region in AA and AS datasets. It is possible that a) this region in these two ancestries was not imputed as well as in EA; and b) other SLE-associated variant(s) specific for AA and AS failed to be captured by SNPs used in this study due to different LD patterns. The association of *NMNAT2/SMG7* with SLE in AA and AS awaits further investigation.

The underlying causal SNP(s) driving association signals in the *SMG7* region could not be identified using only genetic association study because of their strong LD strength. Based on the ENCODE functional annotation, these SLE-associated SNPs, especially rs2275675 and rs10911339, are located in a regulatory region with potential impact on gene regulation through alterations in transcriptional activity and epigenetic modifications. Consistent with results of eQTL datasets, the significant decreased levels of *SMG7* mRNA in PBMCs from individuals carrying the SLE-risk C allele of rs2275675, along with the notable lower level of C-allele containing luciferase reporter activity, supported that rs2275675 might best tag SLE-associated *SMG7* SNPs affecting *SMG7* expression. Further analysis by the HaploReg database predicted allelic differences of rs2275675 in binding to a transcription factor *THAP1* that encodes THAP domain-containing apoptosis associated protein 1 with functions involved in endothelial cell proliferation and proapoptotic processes [49, 50]. The exact molecular mechanism by which rs2275675 may regulate *SMG7* expression is therefore yet to be experimentally validated.

The association of *NMNAT2* with SLE at rs2022013, previously identified by the SLEGEN GWAS in EA, was confirmed in our independent EA subjects only. Under the assumption that the minor allele of rs2022013 confers genetic risk with an odds ratio of 0.83 (determined in EA), the power to detect a significant association ($P<1\times10^{-3}$) for EA samples reaches 97%, but only 36% in HS, 43% in AS and 51% in AA datasets. In addition to rs2022013, we identified 6 SNPs within a small interval in the *NMNAT2* intron 1 exhibiting consistent and strong association with SLE in EA and HS. In HS, all other *NMNAT2* associations with SLE were eliminated or reduced to baseline after conditioning test, suggesting that underlying causal variant(s) at *NMNAT2* could be captured by these 6 SNPs. However, similar conditioning test in EA revealed residual associations, requiring further refinement of genetic effects within *NMNAT2* to localize putative causal variant(s) in EA.

Proximity to the *NMNAT2*/*SMG7* region at 1q25 is *NCF2*, encoding a subunit of NADPH (nicotinamide adenine dinucleotide phosphate) oxidase complex involved in the reactive oxygen species (ROS) generation. Genetic associations of *NCF2* with SLE include three non-synonymous SNPs (H389Q that leads to reduced NADPH oxidase activity and ROS production, R395W and V297A) and three intronic variants (rs10911359, rs34423782 and rs34680162) [51, 52]. None of them showed strong LD with SNPs at the *NMNAT2*/*SMG7* locus according to the 1000 Genome Project data (Figure S7). Association signals within the *NMNAT2*/*SMG7* region in EA and HS identified by this study may not be driven by SLE-associated SNPs at *NCF2*.

In summary, we confirmed previous GWAS reported *NMNAT2* association with SLE and identified *SMG7* as a novel risk gene for SLE in EA. Our data showed a link between SLE-associated variants in the *NMNAT2*/*SMG7* locus and decreased *SMG7* mRNA levels, and provided evidence for functional relevance of SMG7 in production of ANA and chemokines in SLE. Given *SMG7* encoding a protein involved in the NMD pathway, our study implicates the novel contribution of this important regulatory pathway to the SLE pathogenesis. Further investigation of its effects may lead to new direction for development of therapeutic targets for SLE.

Figure legend:

Figure 1. Association of SNPs in the *NMNAT2/SMG7* region with SLE. (A) The genomic structure of the *NMNAT2/SMG7* region and positions of genetic variants are indicated. (B) The allelic *P* value ($-\log_{10}P$ value) of each genetic variant with SLE is plotted against its position as a circle (genotyped) or a triangle (imputed) for European American (EA), Amerindian/Hispanic (HS), African American (AA) and Asian (AS), respectively. Genetic variants are highlighted using different colors according to their strength of linkage disequilibrium (r^2) with rs2022013 (shown as a blue diamond). The dashed line represents a Bonferroni corrected $P<1\times10^{-3}$. Arrows identify rs2022013 and SNPs demonstrating the most significant association signals in each ancestry. Black rectangle identifies group 2 SNPs at *SMG7* locus strongly associated with SLE in EA and the best-associated SNP rs2702178 is indicated. (C) Trans-ancestral meta-analysis is conducted on 8 SNPs that remain significant associations after Bonferroni correction in both EA and HS. Black rectangle identifies group 1 SNPs at the *NMNAT2* intron 1 showing P_{meta} values exceeding the GWAS significance level. The dashed line represents the significance level of 5×10^{-8}.

Figure 2. The SLE-risk C allele of rs2275675 associated with decreased *SMG7* expression. (A) Association of rs2275675 genotypes with *SMG7* mRNA levels in PBMCs from European-derived SLE patients and healthy controls, respectively. Box plots show median, upper and lower quartiles, with whiskers denoting 10% and 90% percentiles. Outlying values are shown in black symbols. (B&C) Allelic differences of rs2275675 and rs10911339 in luciferase activity. Data show the mean ± SEM results of three independent experiments.

Figure 3. Decreased *SMG7* levels associated with increased ANA production. (A) Inverse correlation of ANA titers and *SMG7* mRNA levels in patients with SLE. (B&C) Increased ANA and CCL19 levels after *SMG7* silencing in SLE PBMCs. PBMCs from ANA positive SLE patients (n=13) were incubated for 5 days in the presence or absence of siRNA targeting *SMG7*,

GAPDH or siRNA with a non-targeting sequence (NC), respectively. ANA (B) and CCL19 (C) levels in the culture supernatants were measured by ELISA, and plotted as fold change with respect to mock (culture medium only). Results are presented as mean ± SEM.

Figure S1. Conditional association testing between SNPs in the *NMNAT2* and *SMG7* region in EA. Six SNPs in the *NMNAT2* region showing a combined $P_{meta}<5\times10^{-8}$ in the trans-ancestral meta-analysis of EA and HS ancestries and 21 SNPs within the *SMG7* region showing strong association with SLE in EA are named as group 1 and group 2, respectively. The dashed line represents the significance level of $P=0.05$.

Figure S2. Bioinformatic analyses of the SLE-associated SNPs identified in EA. The Encyclopedia of DNA Elements (ENCODE) Integrated Regulation super-track in the UCSC Genome browser is used to evaluate overlap between genomic regulatory elements and the SLE-associated group1 (A) and group 2 SNPs (B). The super-track contains information on gene transcription, DNase hypersensitivity clusters, ChIP-seq defined transcription factor binding regions and histone marks consistent with promoter/enhancer regions from multiple cell lines. For histone modifications, DNase hypersensitivity and transcription factor clusters, signal values are shown as grayscale-colored items, with the darkness of the box proportional to the signal strength observed in any cell line. Arrows identify group 2 SNPs rs2275675 and rs10911339 ($r^2=1$) showing strong overlap with regulatory elements.

Figure S3. *SMG7-AS1* expression associated with *SMG7* and rs2275675. (A) Transcript levels of *SMG7-AS1* and *SMG7* were positively correlated in PBMCs from healthy controls. (B) Association of rs2275675 genotypes with *SMG7-AS1* mRNA levels in PBMCs from healthy controls.

Figure S4. Decreased *SMG7* mRNA levels by *SMG7* siRNA in PBMCs. PBMCs from SLE patients (n=13) were incubated for 5 days in the presence or absence of siRNA targeting *SMG7*, *GAPDH*, or siRNA with a non-targeting sequence (NC), respectively. The percentages of viable cells were >90% before and after the culture, and no differences were observed in cell viability among groups. *SMG7* (A) and *GAPDH* (B) mRNA levels were measured by RT-PCR, and plotted as fold change with respect to mock (culture medium only). A 76.3% reduction of *SMG7* mRNA levels was observed only in culture cells treated with siRNA specific for *SMG7*, while a 77.6% reduction of *GAPDH* mRNA levels was detected only in the positive control group treated with *GAPDH* siRNA. Results are presented as mean ± SEM.

Figure S5. Production of cytokines and chemokines after *SMG7* silencing in SLE PBMCs. PBMCs from SLE patients (n=13) were incubated for 5 days in the presence or absence of siRNA targeting *SMG7*, *GAPDH* or siRNA with a non-targeting sequence (NC), respectively. CXCL10 (A), IL-6 (B), IL-17 (C), BAFF (D) and IFN-α (E) levels in the culture supernatants were measured by ELISA, and plotted as fold change with respect to mock (culture medium only). Results are presented as mean ± SEM.

Figure S6. No association between *SMG7* expression and anti-dsDNA, Ro/SSA, La/SSB, RNP or Sm antibodies. Each symbol represents an individual sample and horizontal lines show mean ± SEM values.

Figure S7. LD and frequencies of SLE-associated SNPs at the *NMNAT2*/*SMG7* and *NCF2* region. (A) Pairwise LD values (r^2) of SLE-associated SNPs at the *NMNAT2*/*SMG7* and *NCF2* region in each ancestry according to the 1000 Genome Project Data. (B) SNP frequency in each ancestry. EA: European American, HS: Amerindian/Hispanic, AA: African American, AS: Asian.

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Table S1. Allelic association of *NMNAT2/SMG7* SNPs with SLE in European American

Type	SNP	Position	Annotation	Tested Allele	Frequency		***P***	OR [95%CI]	P_c
					SLE (n=3438)	CTRL (n=3417)			
I	rs648809	183208842	*LAMC2* intron 20	G	8.9%	11.0%	***1.6E-05***	0.77[0.68-0.87]	0.03
I	rs3768593	183212548	*LAMC2* 3'UTR	G	14.8%	16.4%	2.6E-03	0.86[0.78-0.95]	0.10
I	rs10797863	183213410	*LAMC2* 3'UTR	T	9.0%	11.1%	***2.4E-05***	0.77[0.69-0.87]	0.03
I	rs10429829	183214883	Intergenic	C	9.8%	11.8%	***4.2E-05***	0.79[0.70-0.88]	0.05
I	rs10429830	183214927	Intergenic	A	9.8%	11.9%	***4.1E-05***	0.79[0.70-0.88]	0.05
I	rs563015	183215236	Intergenic	C	15.6%	17.2%	1.6E-03	0.86[0.78-0.94]	0.07
G	rs539443	183215457	Intergenic	C	15.9%	17.5%	1.3E-03	0.86[0.78-0.94]	0.05
I	rs504895	183215522	Intergenic	C	16.0%	17.6%	1.5E-03	0.86[0.78-0.94]	0.07
I	rs649954	183216448	Intergenic	A	16.0%	17.6%	1.5E-03	0.86[0.78-0.94]	0.07
I	rs2021320	183219348	*NMNAT2* 3'UTR	T	9.8%	11.9%	***4.1E-05***	0.79[0.70-0.88]	0.05
I	rs549191	183220937	*NMNAT2* 3'UTR	G	15.9%	17.6%	1.4E-03	0.86[0.78-0.94]	0.06
I	rs79353094	183222982	*NMNAT2* intron 10	A	9.8%	11.9%	***4.1E-05***	0.79[0.70-0.88]	0.05
I	rs4652787	183225089	*NMNAT2* intron 10	A	15.8%	17.6%	***8.0E-04***	0.85[0.77-0.94]	0.05
I	1-183225475	183225475	*NMNAT2* intron 10	T	9.7%	11.7%	***7.6E-05***	0.79[0.71-0.89]	0.07
I	rs599303	183227761	*NMNAT2* intron 10	G	15.5%	17.4%	***3.3E-04***	0.84[0.76-0.92]	0.03
I	rs12565393	183228306	*NMNAT2* intron 10	T	9.8%	11.9%	***5.1E-05***	0.79[0.70-0.88]	0.06
I	rs79157659	183228375	*NMNAT2* intron 10	A	9.8%	11.9%	***5.1E-05***	0.79[0.70-0.88]	0.06
I	rs473189	183229872	*NMNAT2* intron 10	T	15.5%	17.4%	***3.8E-04***	0.85[0.77-0.93]	0.03
I	rs659712	183232058	*NMNAT2* intron 8	G	15.3%	17.2%	***5.8E-04***	0.85[0.77-0.93]	0.04
I	rs12024028	183232982	*NMNAT2* intron 8	C	9.2%	11.0%	***4.8E-05***	0.78[0.69-0.88]	0.05
I	rs779153	183233018	*NMNAT2* intron 8	A	14.7%	16.7%	***2.2E-04***	0.83[0.75-0.92]	0.03
I	rs10911291	183233815	*NMNAT2* intron 8	A	9.7%	11.7%	***4.7E-05***	0.79[0.70-0.88]	0.05
I	rs609648	183234329	*NMNAT2* intron 8	C	14.5%	16.3%	1.3E-03	0.85[0.77-0.94]	0.10
I	rs656664	183237940	*NMNAT2* intron 8	G	14.5%	16.3%	1.1E-03	0.85[0.77-0.94]	0.09
I	rs10911294	183238100	*NMNAT2* intron 8	T	9.7%	11.7%	***4.4E-05***	0.79[0.70-0.88]	0.05
I	rs498993	183240470	*NMNAT2* intron 8	C	14.5%	16.3%	1.1E-03	0.85[0.77-0.94]	0.09
I	rs594488	183241262	*NMNAT2* intron 8	G	14.5%	16.3%	1.2E-03	0.85[0.77-0.94]	0.09
I	rs16860727	183241781	*NMNAT2* intron 8	A	9.6%	11.7%	***4.4E-05***	0.79[0.70-0.88]	0.06
G	rs10911295	183245285	*NMNAT2* intron 8	A	9.7%	11.7%	***4.2E-05***	0.79[0.70-0.88]	0.06
I	rs12404011	183247022	*NMNAT2* intron 8	C	9.6%	11.5%	***8.4E-05***	0.80[0.71-0.89]	0.08

				Tested	**Frequency**				
Type	**SNP**	**Position**	**Annotation**	**Allele**	**SLE (n=3438)**	**CTRL (n=3417)**	***P***	**OR [95%CI]**	**P_c**
G	rs10494561	183247090	*NMNAT2* intron 8	T	9.8%	11.7%	***1.4E-04***	0.80[0.72-0.90]	0.11
I	rs10911297	183250163	*NMNAT2* intron 7	A	8.3%	10.2%	***1.0E-04***	0.78[0.69-0.89]	0.03
G	rs607332	183253213	*NMNAT2* intron 6	A	36.2%	37.0%	0.33	0.96[0.90-1.04]	--
G	rs603850	183253959	*NMNAT2* intron 5	G	40.9%	41.2%	0.56	0.98[0.91-1.05]	--
I	rs500530	183254972	*NMNAT2* intron 5	T	36.3%	37.0%	0.40	0.97[0.90-1.04]	--
G	rs588492	183255067	*NMNAT2* intron 5	G	38.3%	37.1%	0.14	1.06[0.98-1.14]	--
I	rs685575	183255232	*NMNAT2* intron 5	G	43.0%	41.2%	0.05	1.08[1.00-1.16]	0.19
I	rs2480767	183257218	*NMNAT2* intron 4	T	36.0%	36.8%	0.34	0.96[0.89-1.04]	--
I	rs946173	183260659	*NMNAT2* intron 3	G	15.1%	12.3%	***2.7E-06***	1.28[1.16-1.42]	2.7E-04
I	rs944189	183261710	*NMNAT2* intron 3	A	35.6%	36.6%	0.11	0.94[0.87-1.01]	--
G	rs10797864	183262569	*NMNAT2* intron 2	T	36.2%	37.6%	0.05	0.93[0.86-1.00]	0.37
G	rs10752907	183263356	*NMNAT2* intron 1	T	47.1%	50.4%	***1.8E-05***	0.86[0.80-0.92]	0.36
G	rs10797865	183263629	*NMNAT2* intron 1	C	37.6%	37.2%	0.34	1.04[0.96-1.12]	--
I	rs115872210	183263797	*NMNAT2* intron 1	T	15.3%	12.4%	***1.9E-06***	1.28[1.16-1.42]	2.7E-04
G	rs10752908	183264093	*NMNAT2* intron 1	C	37.5%	37.2%	0.37	1.03[0.96-1.11]	--
I	rs61811578	183264343	*NMNAT2* intron 1	T	15.2%	12.4%	***2.6E-06***	1.28[1.15-1.42]	2.9E-04
I	rs10911298	183264510	*NMNAT2* intron 1	G	36.3%	37.5%	0.07	0.94[0.87-1.01]	--
I	rs12077208	183264654	*NMNAT2* intron 1	T	35.7%	37.2%	0.04	0.93[0.86-1.00]	0.44
I	rs10797866	183264742	*NMNAT2* intron 1	T	36.3%	37.5%	0.07	0.94[0.87-1.01]	--
I	rs10797867	183264849	*NMNAT2* intron 1	T	36.3%	37.5%	0.07	0.94[0.87-1.01]	--
I	rs10797868	183264906	*NMNAT2* intron 1	C	36.3%	37.5%	0.08	0.94[0.87-1.01]	--
I	rs11810250	183265024	*NMNAT2* intron 1	T	36.1%	35.9%	0.50	1.03[0.95-1.11]	--
I	rs10797869	183265044	*NMNAT2* intron 1	C	36.3%	37.5%	0.08	0.94[0.87-1.01]	--
I	rs11805583	183265160	*NMNAT2* intron 1	C	37.8%	37.5%	0.40	1.03[0.96-1.11]	--
I	rs12072223	183265263	*NMNAT2* intron 1	A	15.2%	12.3%	***2.8E-06***	1.28[1.15-1.42]	2.9E-04
I	rs12092487	183265280	*NMNAT2* intron 1	T	15.2%	12.4%	***4.0E-06***	1.27[1.15-1.41]	3.3E-04
I	rs7545564	183265381	*NMNAT2* intron 1	A	36.3%	37.5%	0.07	0.94[0.87-1.01]	--
I	rs7535453	183265670	*NMNAT2* intron 1	T	36.0%	37.1%	0.08	0.94[0.87-1.01]	--
I	rs7535467	183265710	*NMNAT2* intron 1	T	36.3%	37.6%	0.07	0.93[0.87-1.00]	--
I	rs7523495	183265736	*NMNAT2* intron 1	C	36.3%	37.5%	0.07	0.94[0.87-1.01]	--
I	rs12046529	183265801	*NMNAT2* intron 1	T	8.5%	10.5%	***6.1E-05***	0.78[0.69-0.88]	0.04
I	rs4652794	183266096	*NMNAT2* intron 1	C	36.3%	37.5%	0.07	0.93[0.87-1.01]	--
G	rs4652795	183266182	*NMNAT2* intron 1	C	36.3%	37.6%	0.07	0.93[0.87-1.01]	--

				Tested	Frequency				
Type	SNP	Position	Annotation	Allele	SLE (n=3438)	CTRL (n=3417)	*P*	OR [95%CI]	P_c
I	rs4652796	183266278	*NMNAT2* intron 1	G	36.3%	37.5%	0.07	0.94[0.87-1.01]	--
I	1-183266611	183266611	*NMNAT2* intron 1	A	8.5%	10.6%	***4.5E-05***	0.78[0.69-0.88]	0.03
I	rs6672141	183266643	*NMNAT2* intron 1	A	48.3%	49.9%	0.15	0.95[0.88-1.02]	--
I	rs6672163	183266814	*NMNAT2* intron 1	C	36.3%	37.5%	0.08	0.94[0.87-1.01]	--
I	rs6672269	183266884	*NMNAT2* intron 1	C	36.2%	37.4%	0.08	0.94[0.87-1.01]	--
G	rs10752910	183267183	*NMNAT2* intron 1	C	47.0%	50.2%	***4.8E-05***	0.86[0.81-0.93]	0.48
I	rs6669787	183267249	*NMNAT2* intron 1	C	37.8%	37.5%	0.42	1.03[0.96-1.11]	--
I	rs12134014	183267520	*NMNAT2* intron 1	C	37.8%	37.5%	0.45	1.03[0.96-1.11]	--
I	rs12096687	183267920	*NMNAT2* intron 1	A	14.7%	11.8%	***1.1E-06***	1.30[1.17-1.45]	2.8E-04
I	rs12081719	183268041	*NMNAT2* intron 1	A	14.6%	11.8%	***1.5E-06***	1.30[1.17-1.44]	3.7E-04
I	rs12076412	183268127	*NMNAT2* intron 1	A	14.6%	11.8%	***1.8E-06***	1.29[1.16-1.44]	4.2E-04
I	rs12076457	183268236	*NMNAT2* intron 1	A	14.6%	11.8%	***1.8E-06***	1.29[1.16-1.44]	4.2E-04
I	rs12076462	183268267	*NMNAT2* intron 1	A	14.4%	11.6%	***3.3E-06***	1.29[1.16-1.43]	6.7E-04
I	1-183268483	183268483	*NMNAT2* intron 1	T	7.9%	9.9%	***7.0E-05***	0.78[0.69-0.88]	0.02
I	rs61811580	183269660	*NMNAT2* intron 1	A	14.2%	11.5%	***4.7E-06***	1.29[1.16-1.43]	1.1E-03
I	rs16860763	183270797	*NMNAT2* intron 1	T	19.3%	18.3%	0.23	1.06[0.97-1.16]	--
I	rs16860767	183271536	*NMNAT2* intron 1	C	17.7%	16.7%	0.23	1.06[0.96-1.17]	--
G	rs6687056	183272295	*NMNAT2* intron 1	C	25.1%	26.8%	0.02	0.91[0.84-0.98]	0.18
I	rs12748895	183272486	*NMNAT2* intron 1	T	47.3%	44.5%	***7.3E-04***	1.13[1.05-1.21]	0.80
G	rs2276879	183273751	*NMNAT2* intron 1	T	19.2%	18.4%	0.29	1.05[0.96-1.15]	--
I	rs10911300	183274239	*NMNAT2* intron 1	G	7.1%	9.0%	***9.8E-05***	0.78[0.68-0.88]	0.01
I	rs529558	183275110	*NMNAT2* intron 1	A	27.6%	30.1%	3.3E-03	0.89[0.82-0.96]	0.30
I	rs60404994	183275147	*NMNAT2* intron 1	A	7.2%	9.1%	***1.1E-04***	0.78[0.68-0.88]	0.01
I	rs869740	183276903	*NMNAT2* intron 1	T	7.1%	9.0%	***1.2E-04***	0.78[0.68-0.88]	0.01
I	rs869741	183277081	*NMNAT2* intron 1	A	7.1%	9.0%	***9.2E-05***	0.77[0.68-0.88]	0.01
G	rs536586	183278553	*NMNAT2* intron 1	A	45.1%	41.7%	***7.2E-05***	1.15[1.08-1.24]	0.14
I	rs12566804	183278682	*NMNAT2* intron 1	T	18.9%	18.1%	0.33	1.05[0.96-1.15]	--
I	rs602182	183279029	*NMNAT2* intron 1	T	44.6%	41.4%	***1.4E-04***	1.15[1.07-1.23]	0.27
I	rs951420	183279912	*NMNAT2* intron 1	T	18.9%	18.1%	0.32	1.05[0.96-1.15]	--
I	rs2050701	183281919	*NMNAT2* intron 1	G	29.2%	31.7%	4.4E-03	0.89[0.83-0.97]	0.03
I	rs2050700	183282196	*NMNAT2* intron 1	T	29.3%	31.7%	4.2E-03	0.89[0.83-0.96]	0.03
I	rs551452	183283098	*NMNAT2* intron 1	T	29.3%	31.7%	4.0E-03	0.89[0.83-0.96]	0.04
I	rs636315	183283950	*NMNAT2* intron 1	A	29.3%	31.7%	4.2E-03	0.89[0.83-0.96]	0.03

				Tested	Frequency				
Type	**SNP**	**Position**	**Annotation**	**Allele**	**SLE (n=3438)**	**CTRL (n=3417)**	***P***	**OR [95%CI]**	**P_c**
I	rs10911303	183284987	*NMNAT2* intron 1	T	7.4%	9.4%	***5.8E-05***	0.77[0.68-0.88]	0.01
I	rs7530144	183285003	*NMNAT2* intron 1	T	10.8%	9.9%	0.15	1.09[0.97-1.22]	--
I	rs10911305	183286777	*NMNAT2* intron 1	A	51.0%	47.2%	***1.7E-05***	1.17[1.09-1.26]	0.30
I	rs10911307	183289710	*NMNAT2* intron 1	T	7.2%	9.2%	***3.2E-05***	0.76[0.67-0.87]	0.01
I	rs1411392	183290050	*NMNAT2* intron 1	C	29.2%	31.7%	2.6E-03	0.89[0.82-0.96]	0.03
I	rs1411393	183290145	*NMNAT2* intron 1	A	50.9%	46.8%	***4.0E-06***	1.18[1.10-1.27]	0.41
I	rs1411394	183290194	*NMNAT2* intron 1	T	29.2%	31.7%	2.5E-03	0.89[0.82-0.96]	0.03
I	rs2480768	183290647	*NMNAT2* intron 1	A	29.1%	31.8%	1.8E-03	0.88[0.82-0.96]	0.03
I	rs12046401	183292291	*NMNAT2* intron 1	G	18.4%	19.5%	0.12	0.93[0.85-1.02]	--
I	rs1338371	183293267	*NMNAT2* intron 1	T	29.4%	31.9%	2.7E-03	0.89[0.82-0.96]	0.03
I	rs10911309	183293707	*NMNAT2* intron 1	G	51.1%	47.2%	***9.6E-06***	1.17[1.09-1.26]	0.35
I	rs687392	183294416	*NMNAT2* intron 1	T	29.4%	31.9%	3.3E-03	0.89[0.83-0.96]	0.03
I	rs4651152	183294430	*NMNAT2* intron 1	G	51.1%	47.2%	***9.5E-06***	1.17[1.09-1.26]	0.35
I	rs77251524	183294890	*NMNAT2* intron 1	G	10.8%	10.0%	0.16	1.09[0.97-1.22]	--
I	rs12045638	183295069	*NMNAT2* intron 1	T	7.4%	9.4%	***5.5E-05***	0.77[0.68-0.87]	0.01
I	rs4549998	183295930	*NMNAT2* intron 1	G	51.1%	47.2%	***9.6E-06***	1.17[1.09-1.26]	0.34
I	rs4630090	183296270	*NMNAT2* intron 1	T	51.0%	47.1%	***7.7E-06***	1.17[1.10-1.26]	0.36
I	rs12033696	183297422	*NMNAT2* intron 1	T	50.9%	47.1%	***1.1E-05***	1.17[1.09-1.26]	0.32
I	rs12750586	183297476	*NMNAT2* intron 1	A	51.1%	47.2%	***9.6E-06***	1.17[1.09-1.26]	0.34
I	rs12122499	183297613	*NMNAT2* intron 1	C	51.1%	47.2%	***9.6E-06***	1.17[1.09-1.26]	0.34
I	rs12122568	183297826	*NMNAT2* intron 1	C	50.9%	47.0%	***8.5E-06***	1.17[1.09-1.26]	0.34
I	rs12130199	183298008	*NMNAT2* intron 1	T	51.0%	47.2%	***9.5E-06***	1.17[1.09-1.26]	0.33
I	rs12145095	183298049	*NMNAT2* intron 1	A	51.0%	47.2%	***9.5E-06***	1.17[1.09-1.26]	0.33
I	rs616545	183298150	*NMNAT2* intron 1	G	29.4%	31.9%	3.4E-03	0.89[0.83-0.96]	0.03
I	rs10911310	183298219	*NMNAT2* intron 1	C	50.9%	47.0%	***7.5E-06***	1.17[1.10-1.26]	0.36
I	rs10911311	183298342	*NMNAT2* intron 1	T	50.5%	46.4%	***3.2E-06***	1.18[1.10-1.27]	0.35
I	rs74954899	183298374	*NMNAT2* intron 1	G	10.8%	10.0%	0.19	1.08[0.96-1.21]	--
I	rs10797873	183298463	*NMNAT2* intron 1	C	51.0%	47.2%	***8.2E-06***	1.17[1.09-1.26]	0.40
I	rs10797874	183298495	*NMNAT2* intron 1	C	51.0%	47.2%	***8.2E-06***	1.17[1.09-1.26]	0.41
G	rs10797875	183298502	*NMNAT2* intron 1	C	50.8%	47.0%	***1.3E-05***	1.17[1.09-1.26]	0.31
I	rs4651153	183298610	*NMNAT2* intron 1	C	51.1%	47.2%	***9.8E-06***	1.17[1.09-1.26]	0.34
I	rs10911312	183299013	*NMNAT2* intron 1	G	51.1%	47.2%	***9.1E-06***	1.17[1.09-1.26]	0.36
I	rs10911313	183299153	*NMNAT2* intron 1	A	51.1%	47.2%	***9.1E-06***	1.17[1.09-1.26]	0.36

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]	P_c
					SLE (n=3438)	CTRL (n=3417)			
I	rs1330224	183299502	*NMNAT2* intron 1	A	51.1%	47.2%	***9.1E-06***	1.17[1.09-1.26]	0.36
I	rs953273	183299611	*NMNAT2* intron 1	G	51.1%	47.2%	***9.1E-06***	1.17[1.09-1.26]	0.36
I	rs485677	183299623	*NMNAT2* intron 1	T	29.4%	31.9%	3.2E-03	0.89[0.83-0.96]	0.03
G	rs953274	183299881	*NMNAT2* intron 1	C	51.1%	47.2%	***8.1E-06***	1.17[1.09-1.26]	0.43
I	rs16860810	183299974	*NMNAT2* intron 1	G	7.2%	9.2%	***4.4E-05***	0.77[0.68-0.87]	0.01
I	rs67820432	183300112	*NMNAT2* intron 1	C	51.1%	47.2%	***9.1E-06***	1.17[1.09-1.26]	0.36
I	rs952446	183300311	*NMNAT2* intron 1	G	51.1%	47.2%	***9.1E-06***	1.17[1.09-1.26]	0.36
I	rs2020986	183300515	*NMNAT2* intron 1	A	51.1%	47.2%	***9.1E-06***	1.17[1.09-1.26]	0.36
I	rs677002	183302490	*NMNAT2* intron 1	C	17.7%	18.9%	0.08	0.92[0.84-1.01]	--
I	rs548208	183303352	*NMNAT2* intron 1	A	29.2%	31.7%	2.9E-03	0.89[0.82-0.96]	0.03
I	rs12034392	183303443	*NMNAT2* intron 1	A	7.2%	9.3%	***2.5E-05***	0.76[0.67-0.86]	0.01
I	rs12048443	183303467	*NMNAT2* intron 1	T	7.2%	9.3%	***2.5E-05***	0.76[0.67-0.86]	0.01
I	rs546435	183303537	*NMNAT2* intron 1	C	29.5%	31.8%	7.9E-03	0.90[0.83-0.97]	0.02
I	rs584954	183303730	*NMNAT2* intron 1	C	29.2%	31.7%	3.3E-03	0.89[0.83-0.96]	0.02
I	rs596670	183304016	*NMNAT2* intron 1	C	29.2%	31.7%	2.9E-03	0.89[0.82-0.96]	0.03
I	rs597546	183304193	*NMNAT2* intron 1	C	29.2%	31.7%	2.9E-03	0.89[0.82-0.96]	0.03
I	rs518900	183304250	*NMNAT2* intron 1	G	29.2%	31.7%	2.9E-03	0.89[0.82-0.96]	0.03
I	rs516210	183304528	*NMNAT2* intron 1	T	29.2%	31.7%	3.3E-03	0.89[0.83-0.96]	0.02
I	rs2811553	183305435	*NMNAT2* intron 1	T	29.2%	31.7%	2.9E-03	0.89[0.82-0.96]	0.03
I	rs2788051	183305464	*NMNAT2* intron 1	G	29.2%	31.7%	3.3E-03	0.89[0.83-0.96]	0.02
I	rs644681	183306465	*NMNAT2* intron 1	G	29.2%	31.7%	2.8E-03	0.89[0.82-0.96]	0.03
I	rs644711	183306485	*NMNAT2* intron 1	C	29.2%	31.7%	2.8E-03	0.89[0.82-0.96]	0.03
I	rs530396	183306668	*NMNAT2* intron 1	C	29.2%	31.7%	2.9E-03	0.89[0.82-0.96]	0.02
I	rs658205	183307147	*NMNAT2* intron 1	T	29.2%	31.7%	2.7E-03	0.89[0.82-0.96]	0.02
I	rs2811554	183307874	*NMNAT2* intron 1	A	29.2%	31.7%	3.8E-03	0.89[0.83-0.96]	0.01
I	rs2788053	183307942	*NMNAT2* intron 1	A	29.2%	31.7%	3.6E-03	0.89[0.83-0.96]	0.01
I	rs2485928	183308479	*NMNAT2* intron 1	G	29.5%	31.8%	5.5E-03	0.90[0.83-0.97]	0.02
I	rs2492290	183308513	*NMNAT2* intron 1	A	29.2%	31.7%	3.8E-03	0.89[0.83-0.96]	0.01
I	rs2485930	183308787	*NMNAT2* intron 1	A	29.2%	31.7%	3.6E-03	0.89[0.83-0.96]	0.02
I	rs1536985	183308942	*NMNAT2* intron 1	C	29.3%	31.8%	3.4E-03	0.89[0.83-0.96]	0.02
I	rs2023245	183309023	*NMNAT2* intron 1	C	29.2%	31.7%	3.7E-03	0.89[0.83-0.96]	0.02
I	rs1536984	183309101	*NMNAT2* intron 1	A	29.2%	31.7%	3.7E-03	0.89[0.83-0.96]	0.02
I	rs1541170	183309818	*NMNAT2* intron 1	T	29.2%	31.7%	3.7E-03	0.89[0.83-0.96]	0.02

				Tested	**Frequency**				
Type	**SNP**	**Position**	**Annotation**	**Allele**	**SLE (n=3438)**	**CTRL (n=3417)**	***P***	**OR [95%CI]**	P_c
I	rs567842	183310136	*NMNAT2* intron 1	C	29.2%	31.7%	3.7E-03	0.89[0.83-0.96]	0.02
I	rs595164	183310176	*NMNAT2* intron 1	C	29.2%	31.7%	3.7E-03	0.89[0.83-0.96]	0.02
I	rs595684	183310300	*NMNAT2* intron 1	C	29.2%	31.7%	3.7E-03	0.89[0.83-0.96]	0.02
I	rs595742	183310326	*NMNAT2* intron 1	G	29.5%	31.9%	4.8E-03	0.89[0.83-0.97]	0.02
I	rs565959	183310334	*NMNAT2* intron 1	C	29.2%	31.7%	3.7E-03	0.89[0.83-0.96]	0.02
I	rs537630	183310981	*NMNAT2* intron 1	A	29.2%	31.7%	3.8E-03	0.89[0.83-0.96]	0.02
I	rs76436457	183312333	*NMNAT2* intron 1	T	11.0%	10.1%	0.15	1.09[0.97-1.22]	--
I	rs811886	183314011	*NMNAT2* intron 1	T	29.2%	31.6%	4.5E-03	0.89[0.83-0.97]	0.02
I	rs813293	183314026	*NMNAT2* intron 1	T	29.4%	31.9%	3.1E-03	0.89[0.82-0.96]	0.02
I	rs944190	183314293	*NMNAT2* intron 1	G	41.1%	42.8%	0.06	0.93[0.87-1.00]	--
I	rs1360277	183314641	*NMNAT2* intron 1	T	41.2%	42.8%	0.06	0.93[0.87-1.00]	--
I	rs509168	183315483	*NMNAT2* intron 1	A	29.2%	31.7%	3.2E-03	0.89[0.83-0.96]	0.02
I	rs3924298	183317819	*NMNAT2* intron 1	T	42.1%	43.3%	0.14	0.95[0.88-1.02]	--
I	rs649614	183320192	*NMNAT2* intron 1	C	36.9%	41.3%	***3.6E-07***	0.83[0.77-0.89]	ND
I	rs779152	183322317	*NMNAT2* intron 1	G	50.2%	46.5%	***2.1E-05***	1.17[1.09-1.25]	0.34
I	rs10911318	183323643	*NMNAT2* intron 1	T	49.8%	46.2%	***2.9E-05***	1.16[1.08-1.25]	0.25
I	rs564146	183323708	*NMNAT2* intron 1	A	36.9%	41.3%	***4.1E-07***	0.83[0.77-0.89]	*
I	rs12125953	183323804	*NMNAT2* intron 1	A	49.8%	46.2%	***2.9E-05***	1.16[1.08-1.25]	0.24
I	rs681054	183324354	*NMNAT2* intron 1	T	37.0%	41.3%	***4.7E-07***	0.83[0.77-0.89]	*
G	rs664422	183325722	*NMNAT2* intron 1	C	37.0%	41.4%	***4.3E-07***	0.83[0.77-0.89]	*
I	rs502870	183325796	*NMNAT2* intron 1	T	37.0%	41.3%	***5.0E-07***	0.83[0.77-0.89]	*
I	rs548292	183326828	*NMNAT2* intron 1	A	37.1%	41.6%	***3.2E-07***	0.83[0.77-0.89]	*
G	rs634375	183327866	*NMNAT2* intron 1	T	50.3%	46.8%	***4.3E-05***	1.16[1.08-1.24]	0.24
G	rs10494562	183327971	*NMNAT2* intron 1	T	7.5%	9.6%	***2.9E-05***	0.77[0.68-0.87]	0.01
G	rs12146097	183329261	*NMNAT2* intron 1	T	16.7%	12.9%	***1.5E-10***	1.38[1.25-1.53]	*
I	rs2811557	183330255	*NMNAT2* intron 1	T	28.9%	31.2%	5.5E-03	0.90[0.83-0.97]	0.01
I	rs2811558	183330413	*NMNAT2* intron 1	T	50.1%	46.6%	***3.6E-05***	1.16[1.08-1.25]	0.30
I	rs4465156	183331860	*NMNAT2* intron 1	T	11.1%	10.4%	0.24	1.07[0.96-1.20]	--
G	rs12757973	183333504	*NMNAT2* intron 1	T	5.3%	6.3%	5.4E-03	0.81[0.69-0.94]	0.01
I	rs554395	183333554	*NMNAT2* intron 1	C	38.0%	42.3%	***3.5E-07***	0.83[0.77-0.89]	0.54
I	rs2485931	183333785	*NMNAT2* intron 1	A	50.1%	46.4%	***2.8E-05***	1.16[1.08-1.25]	0.33
I	rs10911319	183334150	*NMNAT2* intron 1	G	8.7%	10.7%	***9.6E-05***	0.79[0.70-0.89]	0.06
I	rs502849	183335467	*NMNAT2* intron 1	T	38.0%	42.4%	***3.1E-07***	0.83[0.77-0.89]	0.54

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]	P_c
					SLE (n=3438)	CTRL (n=3417)			
I	rs502937	183335495	*NMNAT2* intron 1	C	38.0%	42.4%	***3.1E-07***	0.83[0.77-0.89]	0.54
I	rs542349	183337933	*NMNAT2* intron 1	A	28.9%	31.2%	5.1E-03	0.90[0.83-0.97]	0.01
I	rs673593	183338207	*NMNAT2* intron 1	T	50.1%	46.4%	***2.9E-05***	1.16[1.08-1.25]	0.32
I	rs2811559	183338826	*NMNAT2* intron 1	G	38.1%	42.4%	***3.7E-07***	0.83[0.77-0.89]	0.53
I	rs525138	183339985	*NMNAT2* intron 1	T	28.8%	31.3%	3.3E-03	0.89[0.83-0.96]	0.02
I	rs526845	183340129	*NMNAT2* intron 1	G	28.8%	31.3%	3.3E-03	0.89[0.83-0.96]	0.02
I	rs2485932	183343362	*NMNAT2* intron 1	A	37.3%	41.8%	***1.0E-07***	0.82[0.76-0.88]	0.42
G	rs2788058	183345203	*NMNAT2* intron 1	A	38.1%	42.3%	***4.8E-07***	0.83[0.77-0.89]	0.34
I	rs12409487	183345350	*NMNAT2* intron 1	G	8.0%	10.2%	***2.4E-05***	0.77[0.68-0.87]	0.02
I	rs2811562	183345452	*NMNAT2* intron 1	T	28.8%	31.2%	3.2E-03	0.89[0.83-0.96]	0.04
I	rs2788057	183345707	*NMNAT2* intron 1	A	38.1%	42.3%	***3.9E-07***	0.83[0.77-0.89]	0.52
I	rs2811563	183346669	*NMNAT2* intron 1	T	38.0%	42.3%	***3.1E-07***	0.83[0.77-0.89]	0.44
I	rs10911321	183347254	*NMNAT2* intron 1	T	8.9%	10.9%	***9.7E-05***	0.79[0.70-0.89]	0.04
I	rs1933540	183347324	*NMNAT2* intron 1	T	38.0%	42.3%	***2.7E-07***	0.83[0.77-0.89]	0.41
I	rs4351602	183348251	*NMNAT2* intron 1	A	9.0%	11.0%	***1.1E-04***	0.79[0.71-0.89]	0.05
I	rs116825143	183348393	*NMNAT2* intron 1	A	7.4%	9.6%	***1.9E-05***	0.76[0.67-0.86]	0.01
I	rs1338379	183349557	*NMNAT2* intron 1	C	38.1%	42.4%	***3.8E-07***	0.83[0.77-0.89]	0.43
I	rs1338378	183351256	*NMNAT2* intron 1	A	38.0%	42.3%	***2.6E-07***	0.83[0.77-0.89]	0.35
I	rs2811565	183351784	*NMNAT2* intron 1	T	28.9%	31.3%	2.9E-03	0.89[0.83-0.96]	0.04
I	rs10797876	183352051	*NMNAT2* intron 1	C	8.0%	10.1%	***5.4E-05***	0.77[0.68-0.88]	0.02
I	rs76009573	183352439	*NMNAT2* intron 1	A	11.8%	11.1%	0.24	1.07[0.96-1.20]	--
I	rs2225932	183352565	*NMNAT2* intron 1	A	8.3%	10.4%	***4.9E-05***	0.78[0.69-0.88]	0.01
I	rs75033236	183353183	*NMNAT2* intron 1	C	9.2%	11.1%	***3.6E-04***	0.81[0.72-0.91]	0.07
I	rs2185081	183353730	*NMNAT2* intron 1	C	28.8%	31.2%	2.8E-03	0.89[0.82-0.96]	0.05
I	rs7546142	183353769	*NMNAT2* intron 1	A	11.8%	11.0%	0.21	1.07[0.96-1.20]	--
G	rs2022013	183353853	*NMNAT2* intron 1	C	38.1%	42.4%	***3.9E-07***	0.83[0.77-0.89]	0.56
I	rs7551809	183355088	*NMNAT2* intron 1	T	11.8%	11.1%	0.25	1.07[0.96-1.19]	--
I	rs7529886	183355664	*NMNAT2* intron 1	C	21.2%	22.3%	0.09	0.93[0.85-1.01]	--
I	rs7552360	183355702	*NMNAT2* intron 1	G	21.2%	22.3%	0.09	0.93[0.85-1.01]	--
I	rs10911324	183356478	*NMNAT2* intron 1	C	20.9%	22.1%	0.09	0.93[0.85-1.01]	--
I	rs10911325	183356523	*NMNAT2* intron 1	A	20.9%	22.1%	0.09	0.93[0.85-1.01]	--
I	rs1122258	183356694	*NMNAT2* intron 1	C	21.0%	22.2%	0.08	0.93[0.85-1.01]	--
I	rs1122259	183356931	*NMNAT2* intron 1	A	9.3%	11.1%	***3.8E-04***	0.81[0.72-0.91]	0.07

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]	P_c
					SLE (n=3438)	CTRL (n=3417)			
I	rs1338376	183357817	*NMNAT2* intron 1	T	9.4%	11.2%	***6.7E-04***	0.82[0.73-0.92]	0.08
I	rs12410472	183358169	*NMNAT2* intron 1	C	7.4%	9.6%	***1.1E-05***	0.76[0.67-0.86]	0.01
G	rs2078087	183358405	*NMNAT2* intron 1	T	9.6%	11.4%	***7.1E-04***	0.82[0.73-0.92]	0.08
I	rs1819628	183358440	*NMNAT2* intron 1	T	29.0%	31.4%	3.1E-03	0.89[0.83-0.96]	0.04
I	rs7548141	183359514	*NMNAT2* intron 1	T	21.4%	22.5%	0.09	0.93[0.85-1.01]	--
I	rs78316688	183359879	*NMNAT2* intron 1	T	7.4%	9.6%	***1.1E-05***	0.75[0.67-0.86]	0.01
I	rs4428846	183360475	*NMNAT2* intron 1	G	11.8%	11.0%	0.20	1.08[0.96-1.20]	--
I	rs12123377	183361578	*NMNAT2* intron 1	T	21.4%	22.5%	0.09	0.93[0.85-1.01]	--
I	rs2788060	183362646	*NMNAT2* intron 1	T	49.1%	45.6%	***6.0E-05***	1.16[1.08-1.24]	0.19
I	1-183362847	183362847	*NMNAT2* intron 1	T	11.8%	11.0%	0.20	1.08[0.96-1.20]	--
I	rs10797879	183364016	*NMNAT2* intron 1	T	21.0%	22.1%	0.11	0.93[0.86-1.02]	--
I	rs7527227	183368916	*NMNAT2* intron 1	T	29.5%	31.6%	8.9E-03	0.90[0.84-0.97]	0.02
I	rs7529644	183369065	*NMNAT2* intron 1	G	21.5%	22.6%	0.09	0.93[0.85-1.01]	--
I	rs12406861	183371192	*NMNAT2* intron 1	A	9.5%	11.4%	***4.0E-04***	0.81[0.72-0.91]	0.05
I	rs3120798	183373665	*NMNAT2* intron 1	T	28.8%	31.0%	6.2E-03	0.90[0.83-0.97]	0.03
I	rs3120799	183373841	*NMNAT2* intron 1	A	28.8%	31.0%	6.0E-03	0.90[0.83-0.97]	0.04
I	rs2788061	183374040	*NMNAT2* intron 1	A	28.8%	31.0%	6.0E-03	0.90[0.83-0.97]	0.04
G	rs10732975	183374722	*NMNAT2* intron 1	C	29.4%	31.7%	5.5E-03	0.90[0.83-0.97]	0.05
I	rs78998082	183374838	*NMNAT2* intron 1	G	13.2%	12.4%	0.24	1.07[0.96-1.18]	--
I	rs2788063	183375311	*NMNAT2* intron 1	T	28.8%	31.0%	5.7E-03	0.90[0.83-0.97]	0.04
I	rs10752911	183375454	*NMNAT2* intron 1	A	7.5%	9.6%	***1.8E-05***	0.76[0.67-0.86]	0.01
I	rs2702183	183375601	*NMNAT2* intron 1	A	28.8%	31.0%	6.0E-03	0.90[0.83-0.97]	0.04
G	rs10797880	183376810	*NMNAT2* intron 1	A	7.5%	9.6%	***1.7E-05***	0.76[0.67-0.86]	0.01
G	rs10494563	183376980	*NMNAT2* intron 1	T	7.6%	9.6%	***2.7E-05***	0.77[0.68-0.87]	0.01
I	rs2788065	183377675	*NMNAT2* intron 1	T	28.8%	31.0%	5.7E-03	0.90[0.83-0.97]	0.04
I	rs55638901	183377972	*NMNAT2* intron 1	T	13.3%	12.5%	0.22	1.07[0.96-1.19]	--
I	rs12119966	183378051	*NMNAT2* intron 1	A	9.4%	11.3%	***3.5E-04***	0.81[0.72-0.91]	0.08
I	rs12407801	183379314	*NMNAT2* intron 1	T	7.5%	9.6%	***1.6E-05***	0.76[0.67-0.86]	0.01
I	rs12402878	183379362	*NMNAT2* intron 1	A	7.5%	9.6%	***1.6E-05***	0.76[0.67-0.86]	0.01
I	rs10911329	183379958	*NMNAT2* intron 1	C	7.5%	9.6%	***1.8E-05***	0.76[0.67-0.86]	0.01
G	rs1361197	183380407	*NMNAT2* intron 1	T	39.1%	43.2%	***2.0E-06***	0.84[0.78-0.90]	0.96
I	rs1361198	183380611	*NMNAT2* intron 1	G	46.8%	43.6%	***1.5E-04***	1.15[1.07-1.23]	0.23
I	rs2485935	183380702	*NMNAT2* intron 1	T	28.8%	31.0%	5.6E-03	0.90[0.83-0.97]	0.04

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]	P_c
					SLE (n=3438)	CTRL (n=3417)			
I	rs114395214	183381366	*NMNAT2* intron 1	A	13.3%	12.4%	0.19	1.07[0.97-1.19]	--
I	rs7539430	183381444	*NMNAT2* intron 1	C	30.8%	32.7%	0.02	0.91[0.85-0.98]	0.06
I	rs7539602	183381613	*NMNAT2* intron 1	C	31.5%	33.4%	0.02	0.91[0.84-0.98]	0.13
I	rs10911330	183382989	*NMNAT2* intron 1	G	31.3%	33.3%	0.02	0.91[0.85-0.98]	0.12
I	rs2788043	183383362	*NMNAT2* intron 1	T	30.7%	32.6%	0.02	0.91[0.85-0.99]	0.08
G	rs4652800	183383643	*NMNAT2* intron 1	C	47.6%	44.5%	***1.3E-04***	1.15[1.07-1.23]	0.28
I	rs12745288	183384395	*NMNAT2* intron 1	A	47.5%	44.4%	***2.0E-04***	1.14[1.07-1.23]	0.22
I	rs12035399	183386537	*NMNAT2* intron 1	G	47.8%	44.8%	***3.0E-04***	1.14[1.07-1.23]	0.19
I	rs1815590	183386828	*NMNAT2* intron 1	C	28.5%	30.8%	4.4E-03	0.89[0.83-0.97]	0.04
I	rs6689029	183387943	Intergenic	C	13.2%	12.4%	0.23	1.07[0.96-1.18]	--
I	rs12074508	183388259	Intergenic	C	47.8%	44.4%	***6.9E-05***	1.16[1.08-1.24]	0.24
I	rs2702189	183389150	Intergenic	C	28.5%	30.8%	5.8E-03	0.90[0.83-0.97]	0.06
I	rs2788047	183389460	Intergenic	A	28.5%	30.8%	5.5E-03	0.90[0.83-0.97]	0.06
I	rs2788048	183389877	Intergenic	A	28.5%	30.8%	5.5E-03	0.90[0.83-0.97]	0.06
I	rs2702191	183391524	Intergenic	T	28.5%	30.8%	5.2E-03	0.90[0.83-0.97]	0.06
I	rs6702692	183391954	Intergenic	T	13.3%	12.4%	0.20	1.07[0.96-1.19]	--
I	rs6680808	183392006	Intergenic	G	13.3%	12.4%	0.21	1.07[0.96-1.19]	--
I	rs12731807	183394037	Intergenic	T	47.8%	44.5%	***8.8E-05***	1.15[1.07-1.24]	0.38
I	rs10797882	183394478	Intergenic	T	8.1%	10.2%	***4.0E-05***	0.77[0.69-0.88]	0.01
I	rs2485937	183394535	Intergenic	T	28.5%	30.8%	4.6E-03	0.89[0.83-0.97]	0.06
I	rs75245837	183394862	Intergenic	A	13.3%	12.5%	0.23	1.07[0.96-1.18]	--
I	rs12032353	183396066	Intergenic	A	8.1%	10.2%	***3.7E-05***	0.77[0.69-0.87]	0.01
I	rs2485939	183396610	Intergenic	A	28.6%	30.8%	5.7E-03	0.90[0.83-0.97]	0.06
I	rs2702197	183397041	Intergenic	A	30.5%	32.7%	6.0E-03	0.90[0.83-0.97]	0.12
I	rs2702198	183397087	Intergenic	A	29.0%	31.2%	6.1E-03	0.90[0.83-0.97]	0.05
I	rs2811551	183397589	Intergenic	C	28.6%	30.8%	6.2E-03	0.90[0.83-0.97]	0.05
G	rs2993476	183398233	Intergenic	G	28.1%	30.2%	9.8E-03	0.90[0.83-0.98]	0.07
G	rs12130057	183398487	Intergenic	A	3.6%	3.2%	0.46	1.08[0.89-1.31]	--
I	rs2788056	183400890	Intergenic	T	28.7%	30.9%	6.6E-03	0.90[0.83-0.97]	0.05
I	rs2702199	183401880	Intergenic	T	29.0%	31.3%	5.1E-03	0.90[0.83-0.97]	0.06
G	rs12129543	183402792	Intergenic	T	3.6%	3.2%	0.41	1.09[0.89-1.32]	--
I	rs6424897	183419203	Intergenic	T	41.3%	37.0%	***1.1E-07***	1.22[1.13-1.31]	0.02
G	rs12024309	183419981	Intergenic	A	41.2%	37.0%	***4.3E-07***	1.21[1.12-1.30]	0.01

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]	P_c
					SLE (n=3438)	CTRL (n=3417)			
I	rs4047798	183421406	Intergenic	C	41.2%	36.8%	***5.8E-08***	1.22[1.14-1.31]	0.02
G	rs9286848	183426249	Intergenic	C	41.2%	36.8%	***5.8E-08***	1.22[1.14-1.31]	0.02
I	rs7518244	183434807	*SMG7-AS1* intron 3	C	41.2%	36.8%	***6.3E-08***	1.22[1.14-1.31]	0.02
I	rs6669960	183436577	*SMG7-AS1* intron 3	C	41.2%	36.8%	***6.3E-08***	1.22[1.14-1.31]	0.02
I	rs2275675	183439483	*SMG7-AS1* intron 2	C	41.1%	36.7%	***5.7E-08***	1.22[1.14-1.31]	0.01
I	rs10911339	183442097	*SMG7* intron 1	T	41.2%	36.9%	***1.0E-07***	1.22[1.13-1.31]	0.02
I	rs12742245	183446922	*SMG7* intron 1	A	40.6%	36.1%	***7.4E-08***	1.22[1.14-1.31]	0.01
I	rs2702177	183450622	*SMG7* intron 1	C	41.2%	36.8%	***5.3E-08***	1.22[1.14-1.31]	0.02
I	rs2702178	183452545	*SMG7* intron 1	A	40.8%	36.2%	***2.4E-08***	1.23[1.14-1.32]	0.01
I	rs2702205	183457198	*SMG7* intron 1	G	41.2%	36.8%	***5.3E-08***	1.22[1.14-1.31]	0.02
I	rs2702204	183457396	*SMG7* intron 1	G	41.2%	36.8%	***4.6E-08***	1.22[1.14-1.31]	0.02
I	rs2794619	183459670	*SMG7* intron 1	A	41.2%	36.8%	***5.3E-08***	1.22[1.14-1.31]	0.02
I	rs2761581	183474850	*SMG7* intron 1	C	41.2%	36.8%	***5.3E-08***	1.22[1.14-1.31]	0.02
I	rs2782411	183476929	*SMG7* intron 1	A	40.1%	35.7%	***5.5E-08***	1.23[1.14-1.32]	0.02
I	rs10797886	183479090	*SMG7* intron 1	C	40.3%	35.8%	***2.9E-08***	1.23[1.14-1.33]	0.01
I	rs10911353	183489203	*SMG7* intron 3	A	40.3%	35.8%	***2.9E-08***	1.23[1.14-1.33]	0.01
I	rs10911354	183489278	*SMG7* intron 3	A	40.3%	35.8%	***2.9E-08***	1.23[1.14-1.33]	0.01
I	rs12117885	183494214	*SMG7* intron 3	G	41.2%	36.8%	***5.6E-08***	1.22[1.14-1.31]	0.02
I	rs2702182	183516440	*SMG7* intron 17	A	40.5%	36.0%	***4.6E-08***	1.23[1.14-1.32]	0.01

If *P* reached the Bonferroni-corrected significance level of 1.0×10^{-3}, it is highlighted in bold and italic. Position of each SNP is based on GRch37/hg19.

21 SNPs within the *SMG7* region that showed strong association with SLE with P values around the GWAS significance level (named as group 2) are shaded in gray.

G, genotyped SNP; I, imputed SNP; ND, non-distinguishable in conditional testing; *Pc*, P value after conditioning on six SNPs (named as group 1) shown as '*'. For SNPs that were not tested in conditional testing (*P*>0.05), the *Pc* value is denoted as '--'.

Table S2. Allelic association of *NMNAT2/SMG7* SNPs with SLE in Amerindian/Hispanics

Type	**SNP**	**Position**	**Annotation**	**Tested Allele**	**Frequency**		***P***	**OR [95%CI]**	***P***
					SLE (n=1492)	**CTRL (n=807)**			
I	rs3768593	183212548	*LAMC2* 3'UTR	G	33.5%	30.4%	0.66	1.03[0.90-1.18]	--
I	rs563015	183215236	Intergenic	C	33.5%	31.4%	0.89	0.99[0.87-1.13]	--
G	rs539443	183215457	Intergenic	C	34.4%	32.0%	0.94	1.01[0.88-1.15]	--
I	rs504895	183215522	Intergenic	C	34.6%	32.2%	0.93	1.01[0.88-1.15]	--
I	rs649954	183216448	Intergenic	A	34.6%	32.2%	0.93	1.01[0.88-1.15]	--
I	rs549191	183220937	*NMNAT2* 3'UTR	G	34.2%	31.4%	0.75	1.02[0.89-1.17]	--
I	rs4652787	183225089	*NMNAT2* intron 10	A	33.9%	31.3%	0.85	1.01[0.89-1.16]	--
I	rs2105160	183226129	*NMNAT2* intron 10	C	33.3%	30.9%	0.99	1.00[0.87-1.14]	--
I	rs599303	183227761	*NMNAT2* intron 10	G	33.7%	30.9%	0.80	1.02[0.89-1.17]	--
I	rs473189	183229872	*NMNAT2* intron 10	T	33.8%	31.1%	0.86	1.01[0.88-1.16]	--
I	rs659712	183232058	*NMNAT2* intron 8	G	33.5%	30.6%	0.76	1.02[0.89-1.17]	--
I	rs10911291	183233815	*NMNAT2* intron 8	A	14.7%	15.3%	0.22	0.90[0.75-1.07]	--
I	rs10911294	183238100	*NMNAT2* intron 8	T	14.7%	15.3%	0.25	0.90[0.76-1.07]	--
I	rs16860727	183241781	*NMNAT2* intron 8	A	14.4%	15.0%	0.18	0.89[0.75-1.06]	--
G	rs10911295	183245285	*NMNAT2* intron 8	A	14.4%	14.9%	0.22	0.90[0.75-1.07]	--
I	rs12404011	183247022	*NMNAT2* intron 8	C	12.0%	13.0%	0.11	0.86[0.71-1.04]	--
G	rs10494561	183247090	*NMNAT2* intron 8	T	14.4%	14.9%	0.22	0.90[0.75-1.07]	--
I	rs10911297	183250163	*NMNAT2* intron 7	A	13.9%	14.4%	0.19	0.89[0.74-1.06]	--
G	rs607332	183253213	*NMNAT2* intron 6	A	29.0%	34.0%	4.7E-03	0.83[0.73-0.94]	0.01
G	rs603850	183253959	*NMNAT2* intron 5	G	39.8%	40.6%	0.85	0.99[0.87-1.12]	--
I	rs500530	183254972	*NMNAT2* intron 5	T	29.1%	34.1%	4.3E-03	0.83[0.73-0.94]	0.01
G	rs588492	183255067	*NMNAT2* intron 5	G	39.1%	37.5%	0.36	1.06[0.93-1.21]	--
I	rs685575	183255232	*NMNAT2* intron 5	G	49.4%	43.7%	1.1E-03	1.23[1.09-1.39]	0.23
I	rs17541993	183258673	*NMNAT2* intron 4	C	7.0%	7.2%	0.12	0.83[0.65-1.05]	--
I	rs946173	183260659	*NMNAT2* intron 3	G	8.3%	8.1%	0.38	1.11[0.88-1.38]	--
I	rs944189	183261710	*NMNAT2* intron 3	A	39.8%	40.1%	0.67	0.97[0.86-1.10]	--
I	rs2301876	183262006	*NMNAT2* intron 2	C	6.9%	7.2%	0.09	0.81[0.63-1.03]	--
G	rs10797864	183262569	*NMNAT2* intron 2	T	41.2%	41.4%	0.75	0.98[0.87-1.11]	--
G	rs10752907	183263356	*NMNAT2* intron 1	G	40.4%	38.4%	0.02	1.17[1.03-1.32]	0.76
G	rs10797865	183263629	*NMNAT2* intron 1	C	31.6%	29.8%	0.05	1.15[1.00-1.31]	0.60
I	rs115872210	183263797	*NMNAT2* intron 1	T	8.9%	8.6%	0.34	1.11[0.89-1.38]	--
G	rs10752908	18326409	*NMNAT2* intron 1	C	31.4%	29.5%	0.04	1.15[1.01-	0.6

Type	SNP	Position	Annotation	Tested Allele	Frequency		P	OR [95%CI]	P_c
					SLE (n=1492)	CTRL (n=807)			
		3						1.32]	7
I	rs61811578	183264343	*NMNAT2* intron 1	T	8.9%	8.6%	0.39	1.10[0.89-1.36]	--
I	rs10911298	183264510	*NMNAT2* intron 1	G	40.9%	41.5%	0.60	0.97[0.85-1.10]	--
I	rs12077208	183264654	*NMNAT2* intron 1	T	40.6%	41.3%	0.55	0.96[0.85-1.09]	--
I	rs10797866	183264742	*NMNAT2* intron 1	T	40.9%	41.5%	0.60	0.97[0.85-1.10]	--
I	rs10797867	183264849	*NMNAT2* intron 1	T	40.9%	41.5%	0.59	0.97[0.85-1.09]	--
I	rs10797868	183264906	*NMNAT2* intron 1	C	40.9%	41.5%	0.60	0.97[0.85-1.10]	--
I	rs11810250	183265024	*NMNAT2* intron 1	T	29.5%	28.8%	0.19	1.10[0.95-1.27]	--
I	rs10797869	183265044	*NMNAT2* intron 1	C	40.9%	41.5%	0.60	0.97[0.85-1.10]	--
I	rs11805583	183265160	*NMNAT2* intron 1	C	31.6%	30.0%	0.05	1.14[1.00-1.31]	0.59
I	rs12072223	183265263	*NMNAT2* intron 1	A	8.8%	8.6%	0.43	1.09[0.88-1.35]	--
I	rs12092487	183265280	*NMNAT2* intron 1	T	8.8%	8.5%	0.38	1.10[0.89-1.37]	--
I	rs7545564	183265381	*NMNAT2* intron 1	A	40.9%	41.5%	0.60	0.97[0.85-1.10]	--
I	rs12077549	183265406	*NMNAT2* intron 1	C	8.1%	7.7%	0.27	1.14[0.91-1.43]	--
I	rs7535453	183265670	*NMNAT2* intron 1	T	40.2%	40.4%	0.77	0.98[0.86-1.11]	--
I	rs7535467	183265710	*NMNAT2* intron 1	T	41.0%	41.5%	0.63	0.97[0.86-1.10]	--
I	rs7523495	183265736	*NMNAT2* intron 1	C	40.9%	41.5%	0.60	0.97[0.85-1.10]	--
I	rs12046529	183265801	*NMNAT2* intron 1	T	10.1%	11.2%	0.13	0.86[0.70-1.05]	--
I	rs7523677	183265903	*NMNAT2* intron 1	T	31.1%	29.7%	0.07	1.13[0.99-1.30]	--
I	rs4652794	183266096	*NMNAT2* intron 1	C	40.9%	41.5%	0.61	0.97[0.86-1.10]	--
G	rs4652795	183266182	*NMNAT2* intron 1	C	40.9%	41.5%	0.60	0.97[0.85-1.10]	--
I	rs4652796	183266278	*NMNAT2* intron 1	G	41.0%	41.5%	0.62	0.97[0.86-1.10]	--
I	1-183266611	183266611	*NMNAT2* intron 1	A	10.2%	11.4%	0.11	0.85[0.70-1.04]	--
I	rs6672141	183266643	*NMNAT2* intron 1	A	49.0%	48.6%	0.87	1.01[0.89-1.15]	--
I	rs6696287	183266731	*NMNAT2* intron 1	A	39.6%	40.0%	0.65	0.97[0.85-1.10]	--
I	rs6672163	183266814	*NMNAT2* intron 1	C	40.9%	41.5%	0.64	0.97[0.86-1.10]	--
I	rs6672269	183266884	*NMNAT2* intron 1	C	40.9%	41.4%	0.65	0.97[0.86-1.10]	--
G	rs10752910	183267183	*NMNAT2* intron 1	T	40.6%	38.6%	0.02	1.16[1.02-1.32]	0.79
I	rs6669787	183267249	*NMNAT2* intron 1	C	31.5%	29.9%	0.05	1.14[1.00-1.31]	0.60
I	rs12134014	183267520	*NMNAT2* intron 1	C	31.6%	30.0%	0.06	1.14[1.00-1.31]	--
I	rs12096687	183267920	*NMNAT2* intron 1	A	8.5%	7.9%	0.20	1.16[0.92-1.45]	--
I	rs12081719	183268041	*NMNAT2* intron 1	A	8.5%	7.9%	0.23	1.15[0.92-1.44]	--
I	rs12076412	183268127	*NMNAT2* intron 1	A	8.5%	7.9%	0.23	1.15[0.92-1.44]	--

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]	P_c
					SLE (n=1492)	CTRL (n=807)			
I	rs12076457	183268236	*NMNAT2* intron 1	A	8.3%	7.7%	0.22	1.15[0.92-1.44]	--
I	rs12076462	183268267	*NMNAT2* intron 1	A	8.3%	7.6%	0.19	1.16[0.93-1.46]	--
I	1-183268483	183268483	*NMNAT2* intron 1	T	9.8%	11.0%	0.12	0.85[0.69-1.04]	--
I	rs115650090	183269218	*NMNAT2* intron 1	T	5.9%	6.6%	0.03	0.75[0.58-0.98]	0.02
I	rs61811580	183269660	*NMNAT2* intron 1	A	8.2%	7.7%	0.26	1.14[0.91-1.44]	--
I	rs16860763	183270797	*NMNAT2* intron 1	T	19.3%	20.5%	0.16	0.89[0.77-1.05]	--
I	rs16860767	183271536	*NMNAT2* intron 1	C	18.4%	19.6%	0.15	0.89[0.76-1.04]	--
G	rs6687056	183272295	*NMNAT2* intron 1	C	22.8%	26.3%	0.01	0.84[0.73-0.96]	0.74
G	rs2276879	183273751	*NMNAT2* intron 1	T	19.4%	20.6%	0.15	0.89[0.77-1.04]	--
I	rs10911300	183274239	*NMNAT2* intron 1	G	10.1%	10.8%	0.19	0.87[0.71-1.07]	--
I	rs529558	183275110	*NMNAT2* intron 1	A	25.0%	28.2%	0.05	0.87[0.76-1.00]	0.95
I	rs60404994	183275147	*NMNAT2* intron 1	A	10.1%	10.9%	0.17	0.87[0.71-1.06]	--
I	rs76293603	183276090	*NMNAT2* intron 1	A	5.2%	6.3%	0.02	0.72[0.55-0.94]	0.01
I	rs869740	183276903	*NMNAT2* intron 1	T	9.5%	10.4%	0.13	0.85[0.69-1.05]	--
I	rs869741	183277081	*NMNAT2* intron 1	A	9.5%	10.5%	0.11	0.84[0.69-1.04]	--
G	rs536586	183278553	*NMNAT2* intron 1	A	44.2%	39.2%	***2.7E-04***	1.26[1.11-1.43]	0.07
I	rs12566804	183278682	*NMNAT2* intron 1	T	18.9%	20.1%	0.17	0.90[0.77-1.05]	--
I	rs602182	183279029	*NMNAT2* intron 1	T	44.0%	39.2%	***4.7E-04***	1.25[1.10-1.42]	0.09
I	rs10911303	183284987	*NMNAT2* intron 1	T	9.8%	10.9%	0.12	0.85[0.69-1.04]	--
I	rs10911307	183289710	*NMNAT2* intron 1	T	9.9%	11.0%	0.11	0.85[0.69-1.04]	--
I	rs1338371	183293267	*NMNAT2* intron 1	T	26.4%	30.1%	0.02	0.85[0.74-0.97]	0.83
I	rs10911309	183293707	*NMNAT2* intron 1	G	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.42
I	rs687392	183294416	*NMNAT2* intron 1	T	26.5%	30.1%	0.02	0.85[0.74-0.97]	0.82
I	rs4651152	183294430	*NMNAT2* intron 1	G	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.39
I	rs4549998	183295930	*NMNAT2* intron 1	G	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.41
I	rs4630090	183296270	*NMNAT2* intron 1	T	50.3%	46.7%	0.02	1.16[1.02-1.31]	0.42
I	rs12033696	183297422	*NMNAT2* intron 1	T	50.1%	46.7%	0.03	1.15[1.02-1.30]	0.36
I	rs12750586	183297476	*NMNAT2* intron 1	A	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.41
I	rs12122499	183297613	*NMNAT2* intron 1	C	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.41
I	rs12122568	183297826	*NMNAT2* intron 1	C	50.2%	46.6%	0.02	1.15[1.02-1.30]	0.42
I	rs12130199	183298008	*NMNAT2* intron 1	T	50.3%	46.7%	0.02	1.16[1.02-1.31]	0.39
I	rs12145095	183298049	*NMNAT2* intron 1	A	50.3%	46.7%	0.02	1.16[1.02-1.31]	0.39
I	rs616545	183298150	*NMNAT2* intron 1	G	26.6%	30.2%	0.02	0.85[0.74-0.97]	0.82

					Frequency				
Type	**SNP**	**Position**	**Annotation**	**Tested Allele**	**SLE (n=1492)**	**CTRL (n=807)**	***P***	**OR [95%CI]**	**P_c**
I	rs10911310	183298219	*NMNAT2* intron 1	C	50.2%	46.6%	0.02	1.16[1.02-1.31]	0.42
I	rs10797873	183298463	*NMNAT2* intron 1	C	50.3%	46.7%	0.02	1.16[1.02-1.31]	0.40
I	rs10797874	183298495	*NMNAT2* intron 1	C	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.40
G	rs10797875	183298502	*NMNAT2* intron 1	C	50.0%	46.4%	0.02	1.16[1.02-1.31]	0.32
I	rs4651153	183298610	*NMNAT2* intron 1	C	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.42
I	rs10911312	183299013	*NMNAT2* intron 1	G	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.42
I	rs10911313	183299153	*NMNAT2* intron 1	A	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.42
I	rs1330224	183299502	*NMNAT2* intron 1	A	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.42
I	rs953273	183299611	*NMNAT2* intron 1	G	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.42
I	rs485677	183299623	*NMNAT2* intron 1	T	26.6%	30.2%	0.02	0.85[0.74-0.97]	0.83
G	rs953274	183299881	*NMNAT2* intron 1	C	50.3%	46.7%	0.02	1.16[1.03-1.31]	0.42
I	rs16860810	183299974	*NMNAT2* intron 1	G	10.0%	11.0%	0.14	0.86[0.70-1.05]	--
I	rs67820432	183300112	*NMNAT2* intron 1	C	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.40
I	rs952446	183300311	*NMNAT2* intron 1	G	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.40
I	rs2020986	183300515	*NMNAT2* intron 1	A	50.4%	46.7%	0.02	1.16[1.03-1.31]	0.40
I	rs675220	183302111	*NMNAT2* intron 1	C	21.8%	21.5%	0.92	1.01[0.87-1.17]	--
I	rs677475	183302605	*NMNAT2* intron 1	C	22.0%	21.7%	0.94	1.01[0.86-1.17]	--
I	rs12034392	183303443	*NMNAT2* intron 1	A	9.9%	11.0%	0.09	0.84[0.69-1.03]	--
I	rs12048443	183303467	*NMNAT2* intron 1	T	9.9%	11.0%	0.09	0.84[0.69-1.03]	--
I	rs530396	183306668	*NMNAT2* intron 1	C	26.4%	30.0%	0.02	0.85[0.74-0.97]	0.88
I	rs658205	183307147	*NMNAT2* intron 1	T	26.4%	30.0%	0.02	0.85[0.74-0.97]	0.90
I	rs2811554	183307874	*NMNAT2* intron 1	A	26.5%	30.0%	0.02	0.85[0.74-0.98]	0.86
I	rs2788053	183307942	*NMNAT2* intron 1	A	26.4%	30.0%	0.02	0.85[0.74-0.97]	0.87
I	rs2492290	183308513	*NMNAT2* intron 1	A	26.4%	29.9%	0.02	0.85[0.74-0.98]	0.84
I	rs944190	183314293	*NMNAT2* intron 1	G	38.6%	40.5%	0.39	0.95[0.83-1.07]	--
I	rs1360277	183314641	*NMNAT2* intron 1	T	38.6%	40.7%	0.34	0.94[0.83-1.07]	--
I	rs509168	183315483	*NMNAT2* intron 1	A	26.3%	29.5%	0.04	0.87[0.76-1.00]	0.65
I	rs10911317	183316328	*NMNAT2* intron 1	A	44.4%	41.2%	0.02	1.16[1.03-1.32]	0.68
I	rs55901929	183317470	*NMNAT2* intron 1	A	9.6%	8.3%	0.13	1.19[0.95-1.48]	--
I	rs649614	183320192	*NMNAT2* intron 1	C	37.3%	41.9%	1.1E-03	0.81[0.71-0.92]	ND
I	rs779152	183322317	*NMNAT2* intron 1	G	49.2%	45.8%	0.03	1.15[1.01-1.30]	0.25
I	rs10911318	183323643	*NMNAT2* intron 1	T	48.3%	45.5%	0.06	1.13[0.99-1.27]	--
I	rs564146	183323708	*NMNAT2* intron 1	A	37.3%	42.0%	***9.9E-04***	0.81[0.71-0.92]	*

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]	P_c
					SLE (n=1492)	CTRL (n=807)			
I	rs12125953	183323804	*NMNAT2* intron 1	A	48.3%	45.5%	0.06	1.13[0.99-1.27]	--
I	rs681054	183324354	*NMNAT2* intron 1	T	37.4%	42.1%	***8.2E-04***	0.81[0.71-0.91]	*
G	rs664422	183325722	*NMNAT2* intron 1	C	37.5%	42.2%	***9.5E-04***	0.81[0.71-0.92]	*
I	rs502870	183325796	*NMNAT2* intron 1	T	37.4%	42.1%	***8.2E-04***	0.81[0.71-0.91]	*
I	rs548292	183326828	*NMNAT2* intron 1	A	37.6%	42.5%	***7.2E-04***	0.81[0.71-0.91]	*
G	rs634375	183327866	*NMNAT2* intron 1	T	49.3%	46.6%	0.07	1.12[0.99-1.26]	--
G	rs10494562	183327971	*NMNAT2* intron 1	T	10.1%	11.5%	0.04	0.82[0.67-0.99]	0.66
G	rs12146097	183329261	*NMNAT2* intron 1	T	9.5%	7.4%	***9.3E-04***	1.47[1.17-1.84]	*
I	rs2811557	183330255	*NMNAT2* intron 1	T	26.5%	29.7%	0.04	0.86[0.75-0.99]	0.54
I	rs2811558	183330413	*NMNAT2* intron 1	T	49.1%	46.6%	0.10	1.11[0.98-1.26]	--
I	rs4465156	183331860	*NMNAT2* intron 1	T	10.4%	9.2%	0.15	1.17[0.95-1.44]	--
G	rs12757973	183333504	*NMNAT2* intron 1	T	2.8%	2.4%	0.25	1.26[0.85-1.88]	--
I	rs554395	183333554	*NMNAT2* intron 1	C	39.5%	43.1%	0.01	0.85[0.75-0.96]	0.02
I	rs2485931	183333785	*NMNAT2* intron 1	A	49.0%	46.6%	0.12	1.10[0.98-1.25]	--
I	rs10911319	183334150	*NMNAT2* intron 1	G	11.9%	12.5%	0.34	0.91[0.76-1.10]	--
I	rs542349	183337933	*NMNAT2* intron 1	A	26.4%	29.5%	0.05	0.87[0.76-1.00]	0.51
I	rs673593	183338207	*NMNAT2* intron 1	T	48.9%	46.7%	0.13	1.10[0.97-1.24]	--
I	rs525138	183339985	*NMNAT2* intron 1	T	26.7%	29.5%	0.07	0.88[0.77-1.01]	--
I	rs526845	183340129	*NMNAT2* intron 1	G	26.7%	29.5%	0.07	0.88[0.77-1.01]	--
I	rs2485932	183343362	*NMNAT2* intron 1	A	40.5%	43.1%	0.05	0.88[0.78-1.00]	0.01
G	rs2788058	183345203	*NMNAT2* intron 1	A	40.9%	43.5%	0.06	0.89[0.78-1.00]	--
I	rs12409487	183345350	*NMNAT2* intron 1	G	13.0%	12.9%	0.74	0.97[0.81-1.17]	--
I	rs2811562	183345452	*NMNAT2* intron 1	T	27.3%	29.8%	0.11	0.90[0.78-1.03]	--
I	rs2788057	183345707	*NMNAT2* intron 1	A	40.8%	43.4%	0.06	0.89[0.78-1.01]	--
I	rs2811563	183346669	*NMNAT2* intron 1	T	40.7%	43.0%	0.08	0.89[0.79-1.01]	--
I	rs10911321	183347254	*NMNAT2* intron 1	T	13.3%	13.4%	0.60	0.95[0.80-1.14]	--
I	rs1933540	183347324	*NMNAT2* intron 1	T	40.7%	43.0%	0.08	0.89[0.79-1.01]	--
I	rs3122177	183348252	*NMNAT2* intron 1	C	47.2%	46.0%	0.43	1.05[0.93-1.19]	--
I	rs116825143	183348393	*NMNAT2* intron 1	A	10.5%	11.9%	0.05	0.82[0.68-1.00]	0.58
I	rs1338379	183349557	*NMNAT2* intron 1	C	41.2%	43.5%	0.09	0.90[0.79-1.02]	--
I	rs1338378	183351256	*NMNAT2* intron 1	A	40.9%	43.4%	0.07	0.89[0.78-1.01]	--
I	rs2811565	183351784	*NMNAT2* intron 1	T	27.1%	29.4%	0.12	0.90[0.78-1.03]	--
I	rs10797876	183352051	*NMNAT2* intron 1	C	13.2%	13.1%	0.78	0.97[0.81-1.17]	--

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]	P_c
					SLE (n=1492)	CTRL (n=807)			
I	rs76009573	183352439	*NMNAT2* intron 1	A	11.1%	9.8%	0.14	1.17[0.95-1.43]	--
I	rs2225932	183352565	*NMNAT2* intron 1	A	12.9%	13.0%	0.55	0.95[0.79-1.14]	--
I	rs75033236	183353183	*NMNAT2* intron 1	C	13.6%	13.5%	0.71	0.97[0.81-1.16]	--
I	rs2185081	183353730	*NMNAT2* intron 1	C	27.4%	29.8%	0.12	0.90[0.78-1.03]	--
I	rs7546142	183353769	*NMNAT2* intron 1	A	11.0%	9.8%	0.14	1.17[0.95-1.43]	--
G	rs2022013	183353853	*NMNAT2* intron 1	C	41.0%	43.2%	0.11	0.90[0.80-1.02]	--
I	rs7551809	183355088	*NMNAT2* intron 1	T	11.0%	9.7%	0.14	1.17[0.95-1.43]	--
I	rs7529886	183355664	*NMNAT2* intron 1	C	24.8%	23.2%	0.32	1.08[0.93-1.25]	--
I	rs7552360	183355702	*NMNAT2* intron 1	G	24.8%	23.2%	0.32	1.08[0.93-1.25]	--
I	rs1122258	183356694	*NMNAT2* intron 1	C	24.6%	23.3%	0.46	1.06[0.91-1.22]	--
I	rs1122259	183356931	*NMNAT2* intron 1	A	13.6%	13.6%	0.69	0.96[0.81-1.15]	--
I	rs1338376	183357817	*NMNAT2* intron 1	T	13.8%	13.8%	0.67	0.96[0.81-1.15]	--
I	rs12410472	183358169	*NMNAT2* intron 1	C	10.5%	11.9%	0.04	0.82[0.67-0.99]	0.56
G	rs2078087	183358405	*NMNAT2* intron 1	T	13.9%	13.8%	0.77	0.97[0.82-1.16]	--
I	rs1819628	183358440	*NMNAT2* intron 1	T	27.6%	29.9%	0.14	0.90[0.79-1.03]	--
I	rs7548141	183359514	*NMNAT2* intron 1	T	25.0%	23.5%	0.38	1.07[0.92-1.23]	--
I	rs78316688	183359879	*NMNAT2* intron 1	T	10.5%	11.9%	0.04	0.82[0.67-0.99]	0.54
I	rs4428846	183360475	*NMNAT2* intron 1	G	11.1%	9.8%	0.13	1.17[0.96-1.44]	--
I	rs12123377	183361578	*NMNAT2* intron 1	T	24.9%	23.7%	0.48	1.05[0.91-1.22]	--
I	rs2788060	183362646	*NMNAT2* intron 1	T	47.0%	46.1%	0.54	1.04[0.92-1.18]	--
I	1-183362847	183362847	*NMNAT2* intron 1	T	11.0%	9.8%	0.15	1.16[0.95-1.43]	--
I	rs7529644	183369065	*NMNAT2* intron 1	G	25.1%	23.7%	0.40	1.06[0.92-1.23]	--
I	rs12406861	183371192	*NMNAT2* intron 1	A	13.5%	13.9%	0.41	0.93[0.78-1.11]	--
I	rs3120798	183373665	*NMNAT2* intron 1	T	26.9%	29.1%	0.16	0.91[0.79-1.04]	--
I	rs3120799	183373841	*NMNAT2* intron 1	A	26.9%	29.1%	0.16	0.91[0.79-1.04]	--
I	rs2788061	183374040	*NMNAT2* intron 1	A	27.0%	29.3%	0.13	0.90[0.78-1.03]	--
G	rs10732975	183374722	*NMNAT2* intron 1	C	27.9%	30.6%	0.08	0.89[0.78-1.02]	--
I	rs78998082	183374838	*NMNAT2* intron 1	G	12.2%	10.8%	0.10	1.18[0.97-1.43]	--
I	rs2788063	183375311	*NMNAT2* intron 1	T	27.0%	29.3%	0.13	0.90[0.78-1.03]	--
I	rs10752911	183375454	*NMNAT2* intron 1	A	10.7%	12.2%	0.04	0.82[0.67-0.99]	0.57
I	rs2702183	183375601	*NMNAT2* intron 1	A	27.0%	29.3%	0.13	0.90[0.79-1.03]	--
G	rs10797880	183376810	*NMNAT2* intron 1	A	10.2%	11.8%	0.02	0.80[0.66-0.97]	0.51
G	rs10494563	183376980	*NMNAT2* intron 1	T	10.9%	12.2%	0.05	0.83[0.68-1.00]	0.68

Type	SNP	Position	Annotation	Tested Allele	Frequency		P	OR [95%CI]	P_c
					SLE (n=1492)	CTRL (n=807)			
I	rs2788065	183377675	*NMNAT2* intron 1	T	27.0%	29.3%	0.13	0.90[0.79-1.03]	--
I	rs55638901	183377972	*NMNAT2* intron 1	T	12.3%	11.0%	0.13	1.16[0.96-1.41]	--
I	rs12119966	183378051	*NMNAT2* intron 1	A	13.6%	13.8%	0.51	0.94[0.79-1.13]	--
I	rs12407801	183379314	*NMNAT2* intron 1	T	10.6%	12.2%	0.03	0.81[0.67-0.98]	0.51
I	rs12402878	183379362	*NMNAT2* intron 1	A	10.7%	12.2%	0.04	0.82[0.67-0.99]	0.57
I	rs10911329	183379958	*NMNAT2* intron 1	C	10.6%	12.2%	0.03	0.81[0.67-0.98]	0.51
G	rs1361197	183380407	*NMNAT2* intron 1	T	42.3%	44.8%	0.09	0.90[0.79-1.02]	--
I	rs1361198	183380611	*NMNAT2* intron 1	G	44.4%	43.1%	0.37	1.06[0.93-1.20]	--
I	rs2485935	183380702	*NMNAT2* intron 1	T	27.0%	29.3%	0.13	0.90[0.79-1.03]	--
I	rs114395214	183381366	*NMNAT2* intron 1	A	12.0%	10.9%	0.17	1.15[0.94-1.40]	--
I	rs7539430	183381444	*NMNAT2* intron 1	C	29.3%	30.6%	0.48	0.95[0.83-1.09]	--
I	rs7539602	183381613	*NMNAT2* intron 1	C	30.4%	32.0%	0.36	0.94[0.82-1.07]	--
G	rs4652800	183383643	*NMNAT2* intron 1	C	45.8%	44.1%	0.30	1.07[0.94-1.21]	--
I	rs12745288	183384395	*NMNAT2* intron 1	A	45.7%	44.1%	0.31	1.07[0.94-1.21]	--
I	rs2788045	183384796	*NMNAT2* intron 1	G	29.5%	30.6%	0.58	0.96[0.84-1.10]	--
I	rs12035399	183386537	*NMNAT2* intron 1	G	46.1%	44.8%	0.40	1.06[0.93-1.20]	--
I	rs1815590	183386828	*NMNAT2* intron 1	C	26.7%	28.8%	0.15	0.90[0.79-1.04]	--
I	rs6689029	183387943	Intergenic	C	12.0%	10.8%	0.17	1.15[0.94-1.39]	--
I	rs2702189	183389150	Intergenic	C	26.6%	28.7%	0.18	0.91[0.79-1.04]	--
I	rs2788047	183389460	Intergenic	A	26.6%	28.7%	0.16	0.91[0.79-1.04]	--
I	rs2788048	183389877	Intergenic	A	26.7%	28.7%	0.19	0.91[0.80-1.05]	--
I	rs2702191	183391524	Intergenic	T	26.6%	28.7%	0.17	0.91[0.79-1.04]	--
I	rs6702692	183391954	Intergenic	T	11.9%	10.8%	0.16	1.15[0.95-1.40]	--
I	rs6680808	183392006	Intergenic	G	11.9%	10.8%	0.16	1.15[0.95-1.40]	--
I	rs10797882	183394478	Intergenic	T	11.5%	13.3%	0.02	0.81[0.67-0.97]	0.67
I	rs2485937	183394535	Intergenic	T	26.6%	28.8%	0.14	0.90[0.79-1.04]	--
I	rs75245837	183394862	Intergenic	A	12.0%	10.9%	0.17	1.15[0.94-1.39]	--
I	rs12032353	183396066	Intergenic	A	11.5%	13.3%	0.03	0.81[0.67-0.97]	0.68
I	rs2485939	183396610	Intergenic	A	26.5%	28.9%	0.12	0.90[0.78-1.03]	--
I	rs2702197	183397041	Intergenic	A	28.1%	30.7%	0.10	0.89[0.78-1.02]	--
I	rs2811551	183397589	Intergenic	C	26.6%	28.9%	0.13	0.90[0.79-1.03]	--
G	rs2993476	183398233	Intergenic	G	26.3%	28.4%	0.17	0.91[0.79-1.04]	--
G	rs12130057	183398487	Intergenic	A	4.0%	3.5%	0.25	1.22[0.87-1.70]	--

Type	SNP	Position	Annotation	Tested Allele	Frequency		P	OR [95%CI]	P_c
					SLE (n=1492)	CTRL (n=807)			
I	rs2702199	183401880	Intergenic	T	26.8%	28.9%	0.15	0.91[0.79-1.04]	--
G	rs12129543	183402792	Intergenic	T	3.9%	3.5%	0.33	1.18[0.85-1.65]	--
I	rs6424897	183419203	Intergenic	T	46.4%	41.9%	0.01	1.17[1.03-1.32]	0.64
G	rs12024309	183419981	Intergenic	A	46.4%	41.6%	7.8E-03	1.19[1.05-1.35]	0.76
I	rs4047798	183421406	Intergenic	C	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.74
G	rs9286848	183426249	Intergenic	C	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.74
I	rs7518244	183434807	*SMG7-AS1* intron 3	C	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.74
I	rs6669960	183436577	*SMG7-AS1* intron 3	C	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.74
I	rs2275675	183439483	*SMG7-AS1* intron 2	C	46.2%	41.7%	0.01	1.17[1.04-1.33]	0.73
I	rs10911339	183442097	*SMG7* intron 1	T	46.3%	41.7%	0.01	1.18[1.04-1.33]	0.74
I	rs12742245	183446922	*SMG7* intron 1	A	45.9%	41.1%	7.5E-03	1.19[1.05-1.35]	0.76
I	rs2702177	183450622	*SMG7* intron 1	C	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.74
I	rs2702178	183452545	*SMG7* intron 1	A	45.9%	41.1%	8.3E-03	1.19[1.05-1.34]	0.79
I	rs2702205	183457198	*SMG7* intron 1	G	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.74
I	rs2702204	183457396	*SMG7* intron 1	G	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.74
I	rs2794619	183459670	*SMG7* intron 1	A	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.74
I	rs2761581	183474850	*SMG7* intron 1	C	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.74
I	rs2782411	183476929	*SMG7* intron 1	A	44.9%	40.8%	0.02	1.16[1.02-1.32]	0.89
I	rs10797886	183479090	*SMG7* intron 1	C	46.0%	41.6%	0.01	1.17[1.03-1.33]	0.76
I	rs10911353	183489203	*SMG7* intron 3	A	46.0%	41.6%	0.01	1.17[1.03-1.33]	0.76
I	rs10911354	183489278	*SMG7* intron 3	A	46.0%	41.6%	0.01	1.17[1.03-1.33]	0.76
I	rs12117885	183494214	*SMG7* intron 3	G	46.2%	41.7%	0.01	1.18[1.04-1.33]	0.78

If *P* reached the Bonferroni-corrected significance level of 1.0×10^{-3}, it is highlighted in bold and italic. Position of each SNP is based on GRch37/hg19.

G, genotyped SNP; I, imputed SNP; ND, non-distinguishable in conditional testing; *Pc*, P value after conditioning on six SNPs (named as group 1) shown as ‘*’. For SNPs that were not tested in conditional testing (*P*>0.05), the *Pc* value is denoted as ‘--’.

Table S3. Allelic association of *NMNAT2/SMG7* SNPs with SLE in African American

Type	**SNP**	**Position**	**Annotation**	**Tested Allele**	**Frequency**		***P***	**OR [95%CI]**
					SLE (n=1679)	**CTRL (n=1934)**		
I	rs563015	183215236	Intergenic	C	49.5%	48.9%	0.54	1.03[0.93-1.14]
G	rs539443	183215457	Intergenic	C	48.9%	48.1%	0.33	1.05[0.95-1.16]
I	rs649954	183216448	Intergenic	A	49.8%	49.0%	0.47	1.04[0.94-1.15]
G	rs10911295	183245285	*NMNAT2* intron 8	A	3.6%	4.0%	0.61	0.94[0.73-1.20]
G	rs10494561	183247090	*NMNAT2* intron 8	T	2.2%	2.3%	0.82	1.04[0.75-1.44]
G	rs607332	183253213	*NMNAT2* intron 6	A	38.7%	42.5%	3.1E-03	0.86[0.78-0.95]
G	rs603850	183253959	*NMNAT2* intron 5	T	42.2%	38.6%	0.01	1.13[1.02-1.25]
G	rs588492	183255067	*NMNAT2* intron 5	G	36.9%	33.4%	0.01	1.14[1.03-1.26]
G	rs10797864	183262569	*NMNAT2* intron 2	C	33.6%	32.6%	0.61	1.03[0.93-1.14]
G	rs10752907	183263356	*NMNAT2* intron 1	G	22.2%	21.2%	0.49	1.04[0.93-1.17]
G	rs10797865	183263629	*NMNAT2* intron 1	C	12.5%	12.1%	0.58	1.04[0.90-1.21]
G	rs10752908	183264093	*NMNAT2* intron 1	C	12.5%	12.1%	0.70	1.03[0.89-1.19]
I	rs10911298	183264510	*NMNAT2* intron 1	A	33.6%	32.6%	0.64	1.03[0.93-1.14]
I	rs10797866	183264742	*NMNAT2* intron 1	C	33.6%	32.6%	0.64	1.03[0.93-1.14]
I	rs10797867	183264849	*NMNAT2* intron 1	A	33.6%	32.6%	0.64	1.03[0.93-1.14]
I	rs10797868	183264906	*NMNAT2* intron 1	G	33.6%	32.6%	0.64	1.03[0.93-1.14]
I	rs11810250	183265024	*NMNAT2* intron 1	T	12.6%	12.2%	0.68	1.03[0.89-1.19]
I	rs10797869	183265044	*NMNAT2* intron 1	T	33.6%	32.6%	0.64	1.03[0.93-1.14]
I	rs10797870	183265055	*NMNAT2* intron 1	T	33.6%	32.6%	0.64	1.03[0.93-1.14]
I	rs11805583	183265160	*NMNAT2* intron 1	C	10.0%	9.2%	0.41	1.07[0.91-1.26]
I	rs12072223	183265263	*NMNAT2* intron 1	A	9.7%	9.1%	0.64	1.04[0.88-1.22]
I	rs12092487	183265280	*NMNAT2* intron 1	T	9.6%	9.0%	0.65	1.04[0.88-1.22]
I	rs7545564	183265381	*NMNAT2* intron 1	G	33.6%	32.6%	0.63	1.03[0.93-1.14]
I	rs12077549	183265406	*NMNAT2* intron 1	C	9.6%	9.0%	0.69	1.03[0.88-1.22]
I	rs7545584	183265445	*NMNAT2* intron 1	G	33.6%	32.6%	0.63	1.03[0.93-1.14]
I	rs7535467	183265710	*NMNAT2* intron 1	C	33.6%	32.6%	0.63	1.03[0.93-1.14]
I	rs7523495	183265736	*NMNAT2* intron 1	T	33.6%	32.6%	0.63	1.03[0.93-1.14]
I	rs7523677	183265903	*NMNAT2* intron 1	T	12.3%	11.9%	0.72	1.03[0.89-1.19]
I	rs4652794	183266096	*NMNAT2* intron 1	G	33.6%	32.6%	0.62	1.03[0.93-1.14]
G	rs4652795	183266182	*NMNAT2* intron 1	T	33.7%	32.6%	0.56	1.03[0.93-1.14]
I	rs4652796	183266278	*NMNAT2* intron 1	T	33.6%	32.6%	0.62	1.03[0.93-1.14]
I	rs6672141	18326664	*NMNAT2* intron 1	A	23.8%	23.1%	0.65	1.03[0.92-

Type	SNP	Position	Annotation	Tested Allele	Frequency		P	OR [95%CI]
					SLE (n=1679)	CTRL (n=1934)		
		3						1.15]
I	rs6672163	183266814	*NMNAT2* intron 1	T	33.4%	32.3%	0.54	1.03[0.93-1.15]
I	rs6672269	183266884	*NMNAT2* intron 1	T	33.0%	31.9%	0.55	1.03[0.93-1.15]
G	rs10752910	183267183	*NMNAT2* intron 1	T	22.6%	21.5%	0.47	1.04[0.93-1.17]
I	rs6669787	183267249	*NMNAT2* intron 1	C	12.3%	11.7%	0.55	1.05[0.90-1.22]
I	rs12134014	183267520	*NMNAT2* intron 1	C	9.9%	9.1%	0.35	1.08[0.92-1.28]
I	rs10797871	183268466	*NMNAT2* intron 1	A	11.9%	11.3%	0.51	1.05[0.90-1.23]
G	rs6687056	183272295	*NMNAT2* intron 1	C	33.9%	33.2%	0.48	1.04[0.94-1.15]
G	rs2276879	183273751	*NMNAT2* intron 1	T	13.3%	13.7%	0.55	0.96[0.83-1.10]
G	rs536586	183278553	*NMNAT2* intron 1	A	44.7%	44.6%	0.96	1.00[0.91-1.11]
I	rs12566804	183278682	*NMNAT2* intron 1	T	13.5%	13.6%	0.85	0.99[0.86-1.14]
I	rs602182	183279029	*NMNAT2* intron 1	T	45.0%	44.6%	0.77	1.02[0.92-1.12]
I	rs16860790	183279325	*NMNAT2* intron 1	T	13.2%	13.5%	0.68	0.97[0.84-1.12]
I	rs951420	183279912	*NMNAT2* intron 1	T	12.4%	12.5%	0.75	0.98[0.84-1.13]
I	rs10911309	183293707	*NMNAT2* intron 1	G	28.6%	31.2%	0.04	0.90[0.81-0.99]
I	rs4651152	183294430	*NMNAT2* intron 1	G	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs4549998	183295930	*NMNAT2* intron 1	G	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs4630090	183296270	*NMNAT2* intron 1	T	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs12033696	183297422	*NMNAT2* intron 1	T	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs12750586	183297476	*NMNAT2* intron 1	A	28.7%	31.3%	0.04	0.90[0.81-0.99]
I	rs12122499	183297613	*NMNAT2* intron 1	C	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs12122568	183297826	*NMNAT2* intron 1	C	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs12130199	183298008	*NMNAT2* intron 1	T	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs12145095	183298049	*NMNAT2* intron 1	A	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs10911310	183298219	*NMNAT2* intron 1	C	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs10911311	183298342	*NMNAT2* intron 1	T	28.6%	31.3%	0.03	0.89[0.81-0.99]
I	rs10797873	183298463	*NMNAT2* intron 1	C	28.6%	31.4%	0.03	0.89[0.80-0.99]
I	rs10797874	183298495	*NMNAT2* intron 1	C	28.9%	31.5%	0.04	0.89[0.81-0.99]
G	rs10797875	183298502	*NMNAT2* intron 1	C	28.7%	31.2%	0.04	0.90[0.81-1.00]
I	rs4651153	183298610	*NMNAT2* intron 1	C	28.5%	31.2%	0.03	0.90[0.80-0.99]
I	rs10911312	183299013	*NMNAT2* intron 1	G	28.5%	31.2%	0.03	0.89[0.81-0.99]
I	rs10911313	183299153	*NMNAT2* intron 1	A	28.5%	31.2%	0.03	0.89[0.81-0.99]
I	rs1330224	183299502	*NMNAT2* intron 1	A	28.5%	31.2%	0.03	0.89[0.81-0.99]

				Tested	Frequency			
Type	SNP	Position	Annotation	Allele	SLE (n=1679)	CTRL (n=1934)	*P*	OR [95%CI]
I	rs953273	183299611	*NMNAT2* intron 1	G	28.5%	31.2%	0.03	0.89[0.81-0.99]
G	rs953274	183299881	*NMNAT2* intron 1	C	28.6%	31.3%	0.04	0.89[0.81-0.99]
I	rs2020986	183300515	*NMNAT2* intron 1	A	27.4%	29.7%	0.08	0.91[0.82-1.01]
I	rs10911316	183313912	*NMNAT2* intron 1	C	17.5%	18.3%	0.27	0.93[0.82-1.06]
I	rs779152	183322317	*NMNAT2* intron 1	G	31.1%	32.8%	0.07	0.91[0.82-1.01]
I	rs10911318	183323643	*NMNAT2* intron 1	T	16.5%	17.2%	0.34	0.94[0.83-1.07]
I	rs12125953	183323804	*NMNAT2* intron 1	A	17.0%	18.2%	0.16	0.91[0.81-1.04]
I	rs681054	183324354	*NMNAT2* intron 1	T	48.2%	46.5%	0.09	1.09[0.99-1.20]
G	rs664422	183325722	*NMNAT2* intron 1	C	48.0%	46.2%	0.09	1.09[0.99-1.20]
I	rs548292	183326828	*NMNAT2* intron 1	A	48.1%	46.2%	0.07	1.09[0.99-1.20]
G	rs634375	183327866	*NMNAT2* intron 1	T	31.2%	32.8%	0.09	0.92[0.83-1.01]
G	rs10494562	183327971	*NMNAT2* intron 1	T	1.8%	1.8%	0.99	1.00[0.69-1.45]
G	rs12146097	183329261	*NMNAT2* intron 1	T	3.8%	3.7%	0.90	0.98[0.77-1.26]
G	rs12757973	183333504	*NMNAT2* intron 1	T	1.1%	0.9%	0.86	1.04[0.64-1.69]
G	rs2788058	183345203	*NMNAT2* intron 1	G	30.1%	31.1%	0.23	0.94[0.85-1.04]
I	rs2811563	183346669	*NMNAT2* intron 1	C	31.4%	32.6%	0.14	0.93[0.84-1.03]
I	rs10911321	183347254	*NMNAT2* intron 1	T	20.2%	20.7%	0.81	0.99[0.87-1.11]
I	rs4630091	183347913	*NMNAT2* intron 1	C	11.4%	12.0%	0.64	0.96[0.83-1.12]
I	rs3122177	183348252	*NMNAT2* intron 1	C	26.9%	28.3%	0.11	0.91[0.82-1.02]
I	rs2225932	183352565	*NMNAT2* intron 1	A	20.7%	21.1%	1.00	1.00[0.89-1.13]
I	rs75033236	183353183	*NMNAT2* intron 1	C	20.6%	20.9%	0.96	1.00[0.89-1.13]
G	rs2022013	183353853	*NMNAT2* intron 1	T	30.2%	32.0%	0.05	0.90[0.81-1.00]
I	rs1122258	183356694	*NMNAT2* intron 1	C	22.3%	22.5%	0.85	1.01[0.90-1.14]
I	rs1122259	183356931	*NMNAT2* intron 1	A	20.5%	20.9%	0.90	0.99[0.88-1.12]
I	rs12139593	183357563	*NMNAT2* intron 1	T	11.5%	12.0%	0.69	0.97[0.84-1.13]
I	rs1338376	183357817	*NMNAT2* intron 1	T	20.7%	21.2%	0.79	0.98[0.87-1.11]
G	rs2078087	183358405	*NMNAT2* intron 1	T	21.7%	22.1%	0.94	1.00[0.89-1.12]
I	rs78316688	183359879	*NMNAT2* intron 1	T	8.6%	8.6%	0.91	1.01[0.85-1.20]
I	rs2185082	183361025	*NMNAT2* intron 1	A	11.5%	12.0%	0.69	0.97[0.84-1.13]
I	1-183370910	183370910	*NMNAT2* intron 1	C	10.2%	10.7%	0.61	0.96[0.82-1.13]
I	rs12406861	183371192	*NMNAT2* intron 1	A	20.5%	20.9%	0.96	1.00[0.89-1.13]
I	rs74914001	183372675	*NMNAT2* intron 1	C	11.6%	12.2%	0.74	0.98[0.84-1.13]
I	rs2702184	183374718	*NMNAT2* intron 1	T	9.3%	9.7%	0.35	0.92[0.78-1.09]

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]
					SLE (n=1679)	**CTRL (n=1934)**		
G	rs10732975	183374722	*NMNAT2* intron 1	T	47.4%	47.8%	0.82	0.99[0.90-1.09]
I	rs2788064	183375619	*NMNAT2* intron 1	T	9.3%	9.7%	0.34	0.92[0.78-1.09]
G	rs10797880	183376810	*NMNAT2* intron 1	A	3.9%	3.9%	0.87	0.98[0.76-1.26]
I	rs2702186	183376886	*NMNAT2* intron 1	G	9.3%	9.7%	0.34	0.92[0.78-1.09]
G	rs10494563	183376980	*NMNAT2* intron 1	T	8.9%	8.8%	0.76	1.03[0.87-1.21]
I	rs2702187	183377227	*NMNAT2* intron 1	T	9.3%	9.7%	0.34	0.92[0.78-1.09]
I	rs12127454	183378308	*NMNAT2* intron 1	G	11.7%	12.1%	0.81	0.98[0.85-1.14]
I	rs2485934	183379129	*NMNAT2* intron 1	A	9.3%	9.7%	0.34	0.92[0.78-1.09]
I	rs12407801	183379314	*NMNAT2* intron 1	T	10.2%	9.9%	0.54	1.05[0.90-1.23]
I	rs2492287	183380278	*NMNAT2* intron 1	A	9.2%	9.6%	0.30	0.91[0.77-1.08]
G	rs1361197	183380407	*NMNAT2* intron 1	C	18.7%	19.2%	0.48	0.96[0.85-1.08]
I	rs2492288	183381758	*NMNAT2* intron 1	A	9.2%	9.6%	0.30	0.91[0.77-1.08]
G	rs4652800	183383643	*NMNAT2* intron 1	C	16.4%	17.1%	0.40	0.95[0.83-1.08]
I	rs2788044	183384325	*NMNAT2* intron 1	C	9.2%	9.6%	0.29	0.91[0.77-1.08]
I	rs946169	183387172	*NMNAT2* intron 1	A	9.2%	9.6%	0.29	0.91[0.77-1.08]
I	rs78232289	183394705	Intergenic	G	11.4%	11.7%	0.95	1.00[0.86-1.17]
I	1-183396823	183396823	Intergenic	T	9.9%	9.3%	0.21	1.11[0.94-1.32]
G	rs2993476	183398233	Intergenic	G	41.8%	39.3%	0.01	1.13[1.03-1.25]
G	rs12130057	183398487	Intergenic	A	11.8%	12.1%	0.97	1.00[0.86-1.16]
G	rs12129543	183402792	Intergenic	T	8.9%	9.4%	0.64	0.96[0.81-1.14]
G	rs12024309	183419981	Intergenic	A	15.5%	16.8%	0.14	0.90[0.79-1.03]
G	rs9286848	183426249	Intergenic	C	15.3%	16.6%	0.13	0.90[0.79-1.03]
I	rs7518244	183434807	*SMG7-AS1* intron 3	C	15.5%	16.8%	0.16	0.91[0.79-1.04]

Position of each SNP is based on GRch37/hg19. G, genotyped SNP; I, imputed SNP.

Table S4. Allelic association of *NMNAT2/SMG7* SNPs with SLE in Asian

				Tested	**Frequency**			
Type	**SNP**	**Position**	**Annotation**	**Allele**	**SLE (n=1265)**	**CTRL (n=1260)**	***P***	**OR [95%CI]**
I	rs648809	183208842	*LAMC2* intron 20	G	18.7%	20.2%	0.17	0.90[0.78-1.04]
I	rs2477436	183209086	*LAMC2* intron 20	A	36.0%	37.6%	0.25	0.93[0.83-1.05]
I	rs7525417	183211052	*LAMC2* intron 22	A	28.2%	30.2%	0.10	0.90[0.80-1.02]
I	rs3768594	183212171	*LAMC2* intron 22	A	40.5%	42.3%	0.22	0.93[0.83-1.04]
I	rs3768593	183212548	*LAMC2* 3'UTR	G	39.7%	41.3%	0.25	0.94[0.84-1.05]
I	rs10797863	183213410	*LAMC2* 3'UTR	T	20.9%	22.2%	0.22	0.92[0.80-1.05]
I	rs10429829	183214883	Intergenic	C	20.9%	22.2%	0.22	0.92[0.80-1.05]
I	rs10429830	183214927	Intergenic	A	20.9%	22.2%	0.22	0.92[0.80-1.05]
I	rs563015	183215236	Intergenic	C	39.2%	40.5%	0.39	0.95[0.85-1.07]
G	rs539443	183215457	Intergenic	C	40.4%	42.2%	0.22	0.93[0.83-1.04]
I	rs504895	183215522	Intergenic	C	40.4%	42.1%	0.23	0.93[0.84-1.05]
I	rs75394497	183215798	Intergenic	A	28.3%	30.3%	0.10	0.90[0.80-1.02]
I	rs649954	183216448	Intergenic	A	36.8%	38.6%	0.18	0.92[0.82-1.04]
I	rs2021320	183219348	*NMNAT2* 3'UTR	T	21.0%	22.2%	0.24	0.92[0.82-1.06]
I	rs503243	183222013	*NMNAT2* intron 10	A	37.2%	38.9%	0.21	0.93[0.82-1.04]
I	rs77767132	183222678	*NMNAT2* intron 10	G	8.1%	8.8%	0.45	0.92[0.75-1.13]
I	rs79353094	183222982	*NMNAT2* intron 10	A	21.0%	22.2%	0.25	0.92[0.81-1.06]
I	rs4652787	183225089	*NMNAT2* intron 10	A	32.5%	33.6%	0.41	0.95[0.84-1.07]
I	rs77664727	183225361	*NMNAT2* intron 10	T	20.5%	21.9%	0.21	0.92[0.80-1.05]
I	1-183225475	183225475	*NMNAT2* intron 10	T	21.0%	22.2%	0.25	0.92[0.81-1.06]
I	1-183225509	183225509	*NMNAT2* intron 10	T	6.9%	7.7%	0.28	0.89[0.72-1.10]
I	rs2105160	183226129	*NMNAT2* intron 10	C	40.6%	42.3%	0.27	0.94[0.84-1.05]
I	rs78539389	183226726	*NMNAT2* intron 10	G	6.9%	7.7%	0.28	0.89[0.72-1.10]
I	rs599303	183227761	*NMNAT2* intron 10	G	40.8%	42.4%	0.25	0.94[0.84-1.05]
I	rs12565393	183228306	*NMNAT2* intron 10	T	21.0%	22.2%	0.24	0.92[0.80-1.06]
I	rs79157659	183228375	*NMNAT2* intron 10	A	21.0%	22.2%	0.26	0.92[0.81-1.06]
I	rs79583958	183229061	*NMNAT2* intron 10	T	6.9%	7.7%	0.28	0.89[0.72-1.10]
I	rs659712	183232058	*NMNAT2* intron 8	G	40.0%	41.8%	0.22	0.93[0.83-1.04]
I	rs12027380	183232704	*NMNAT2* intron 8	G	20.8%	22.1%	0.22	0.92[0.80-1.05]
I	rs12024028	183232982	*NMNAT2* intron 8	C	20.8%	22.1%	0.22	0.92[0.80-1.05]
I	rs10911291	183233815	*NMNAT2* intron 8	A	20.8%	22.1%	0.22	0.92[0.80-1.05]
I	rs58734925	18323417	*NMNAT2* intron 8	G	20.8%	22.1%	0.2	0.92[0.80-

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]
					SLE (n=1265)	CTRL (n=1260)		
		7					2	1.05]
I	rs609648	183234329	*NMNAT2* intron 8	C	39.8%	41.7%	0.20	0.93[0.83-1.04]
I	rs10911294	183238100	*NMNAT2* intron 8	T	20.8%	22.1%	0.22	0.92[0.80-1.05]
I	rs498993	183240470	*NMNAT2* intron 8	C	40.1%	41.7%	0.25	0.94[0.83-1.05]
I	rs594488	183241262	*NMNAT2* intron 8	G	40.1%	41.6%	0.30	0.94[0.84-1.06]
I	rs16860727	183241781	*NMNAT2* intron 8	A	20.9%	22.2%	0.22	0.92[0.80-1.05]
I	rs16860731	183245215	*NMNAT2* intron 8	G	6.9%	7.7%	0.29	0.89[0.72-1.10]
G	rs10911295	183245285	*NMNAT2* intron 8	A	21.0%	22.4%	0.21	0.92[0.80-1.05]
I	rs12404011	183247022	*NMNAT2* intron 8	C	21.0%	22.4%	0.19	0.91[0.80-1.04]
G	rs10494561	183247090	*NMNAT2* intron 8	T	21.0%	22.4%	0.21	0.92[0.80-1.05]
I	rs10911297	183250163	*NMNAT2* intron 7	A	21.0%	22.1%	0.28	0.93[0.80-1.06]
I	rs1330223	183251080	*NMNAT2* intron 7	G	26.6%	27.0%	0.71	0.98[0.86-1.11]
G	rs607332	183253213	*NMNAT2* intron 6	A	25.6%	26.3%	0.53	0.96[0.85-1.09]
G	rs603850	183253959	*NMNAT2* intron 5	G	33.7%	34.8%	0.40	0.95[0.85-1.07]
I	rs500530	183254972	*NMNAT2* intron 5	T	25.4%	26.1%	0.52	0.96[0.84-1.09]
G	rs588492	183255067	*NMNAT2* intron 5	G	45.4%	42.9%	0.05	1.12[1.00-1.25]
I	rs685575	183255232	*NMNAT2* intron 5	A	45.3%	47.4%	0.10	0.91[0.81-1.02]
I	rs2480767	183257218	*NMNAT2* intron 4	T	25.2%	25.8%	0.64	0.97[0.85-1.10]
I	rs944189	183261710	*NMNAT2* intron 3	G	49.3%	49.2%	0.96	1.00[0.90-1.12]
I	rs3815208	183262375	*NMNAT2* intron 2	C	5.6%	5.5%	0.93	1.01[0.79-1.29]
G	rs10797864	183262569	*NMNAT2* intron 2	C	49.6%	49.7%	1.00	1.00[0.89-1.12]
G	rs10752907	183263356	*NMNAT2* intron 1	G	31.1%	30.1%	0.36	1.06[0.94-1.19]
G	rs10797865	183263629	*NMNAT2* intron 1	C	25.5%	24.2%	0.26	1.08[0.95-1.22]
G	rs10752908	183264093	*NMNAT2* intron 1	C	25.5%	24.2%	0.28	1.08[0.95-1.22]
I	rs10911298	183264510	*NMNAT2* intron 1	A	47.7%	47.8%	0.94	1.00[0.89-1.11]
I	rs12077208	183264654	*NMNAT2* intron 1	A	49.6%	49.7%	0.97	1.00[0.89-1.12]
I	rs10797866	183264742	*NMNAT2* intron 1	C	49.6%	49.7%	0.97	1.00[0.89-1.12]
I	rs10797868	183264906	*NMNAT2* intron 1	G	47.6%	47.7%	0.95	1.00[0.89-1.11]
I	rs11810250	183265024	*NMNAT2* intron 1	T	25.6%	24.3%	0.28	1.07[0.95-1.22]
I	rs10797869	183265044	*NMNAT2* intron 1	T	47.6%	47.7%	0.95	1.00[0.89-1.11]
I	rs10797870	183265055	*NMNAT2* intron 1	T	47.6%	47.7%	0.95	1.00[0.89-1.11]
I	rs12035340	183265158	*NMNAT2* intron 1	G	5.6%	5.6%	0.99	1.00[0.78-1.28]
I	rs11805583	183265160	*NMNAT2* intron 1	C	25.6%	24.4%	0.29	1.07[0.94-1.22]

Type	SNP	Position	Annotation	Tested Allele	Frequency SLE (n=1265)	Frequency CTRL (n=1260)	*P*	OR [95%CI]
I	rs7545584	183265445	*NMNAT2* intron 1	G	47.6%	47.7%	0.95	1.00[0.89-1.11]
I	rs7535453	183265670	*NMNAT2* intron 1	C	46.8%	46.4%	0.78	1.02[0.91-1.14]
I	rs7535467	183265710	*NMNAT2* intron 1	C	47.6%	47.7%	0.95	1.00[0.89-1.11]
I	rs7523495	183265736	*NMNAT2* intron 1	T	47.6%	47.7%	0.95	1.00[0.89-1.11]
I	rs12046524	183265755	*NMNAT2* intron 1	T	5.6%	5.6%	0.99	1.00[0.78-1.28]
I	rs12046529	183265801	*NMNAT2* intron 1	T	12.5%	14.1%	0.07	0.86[0.73-1.01]
I	rs7523677	183265903	*NMNAT2* intron 1	T	25.5%	24.3%	0.30	1.07[0.94-1.21]
I	rs4652794	183266096	*NMNAT2* intron 1	G	47.6%	47.7%	0.95	1.00[0.89-1.11]
G	rs4652795	183266182	*NMNAT2* intron 1	T	47.7%	47.7%	0.97	1.00[0.89-1.12]
I	rs4652796	183266278	*NMNAT2* intron 1	T	47.6%	47.7%	0.95	1.00[0.89-1.11]
I	rs12047459	183266669	*NMNAT2* intron 1	A	5.6%	5.4%	0.84	1.03[0.80-1.31]
I	rs6696287	183266731	*NMNAT2* intron 1	G	47.6%	47.7%	0.95	1.00[0.89-1.11]
I	rs6672269	183266884	*NMNAT2* intron 1	T	47.6%	47.7%	0.95	1.00[0.89-1.11]
G	rs10752910	183267183	*NMNAT2* intron 1	T	31.2%	30.0%	0.31	1.07[0.94-1.20]
I	rs12134014	183267520	*NMNAT2* intron 1	C	25.2%	24.3%	0.42	1.05[0.93-1.20]
I	rs12145136	183268261	*NMNAT2* intron 1	A	24.7%	24.0%	0.56	1.04[0.91-1.18]
I	rs10797871	183268466	*NMNAT2* intron 1	A	24.7%	24.1%	0.56	1.04[0.91-1.18]
I	rs12037564	183270738	*NMNAT2* intron 1	G	25.9%	25.4%	0.66	1.03[0.91-1.17]
I	rs16860763	183270797	*NMNAT2* intron 1	T	41.9%	40.2%	0.20	1.08[0.96-1.21]
I	rs16860767	183271536	*NMNAT2* intron 1	C	41.3%	39.6%	0.22	1.08[0.96-1.21]
I	rs6673931	183272048	*NMNAT2* intron 1	A	6.6%	7.9%	0.07	0.82[0.66-1.02]
G	rs6687056	183272295	*NMNAT2* intron 1	C	10.3%	11.5%	0.15	0.88[0.73-1.05]
I	rs12748895	183272486	*NMNAT2* intron 1	T	26.9%	26.0%	0.40	1.05[0.93-1.19]
I	rs12037899	183272560	*NMNAT2* intron 1	C	4.9%	5.2%	0.70	0.95[0.73-1.23]
G	rs2276879	183273751	*NMNAT2* intron 1	T	40.4%	38.8%	0.22	1.07[0.96-1.20]
I	rs60404994	183275147	*NMNAT2* intron 1	A	15.3%	16.5%	0.22	0.91[0.78-1.06]
I	rs869741	183277081	*NMNAT2* intron 1	A	15.5%	16.6%	0.23	0.91[0.78-1.06]
G	rs536586	183278553	*NMNAT2* intron 1	A	27.9%	26.7%	0.30	1.07[0.94-1.21]
I	rs12566804	183278682	*NMNAT2* intron 1	T	40.6%	38.6%	0.14	1.09[0.97-1.23]
I	rs602182	183279029	*NMNAT2* intron 1	T	27.8%	26.7%	0.31	1.07[0.94-1.21]
I	rs10911303	183284987	*NMNAT2* intron 1	T	6.2%	6.5%	0.59	0.94[0.74-1.18]
I	rs10911307	183289710	*NMNAT2* intron 1	T	6.2%	6.5%	0.59	0.94[0.75-1.18]
I	rs12046401	183292291	*NMNAT2* intron 1	G	7.6%	8.0%	0.57	0.94[0.76-1.16]

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]
					SLE (n=1265)	CTRL (n=1260)		
I	rs12045638	183295069	*NMNAT2* intron 1	T	6.4%	6.7%	0.58	0.94[0.75-1.18]
I	rs12033696	183297422	*NMNAT2* intron 1	C	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs12750586	183297476	*NMNAT2* intron 1	G	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs12122499	183297613	*NMNAT2* intron 1	A	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs12122568	183297826	*NMNAT2* intron 1	A	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs12130199	183298008	*NMNAT2* intron 1	C	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs12145095	183298049	*NMNAT2* intron 1	G	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs10911310	183298219	*NMNAT2* intron 1	G	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs10911311	183298342	*NMNAT2* intron 1	C	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs10797873	183298463	*NMNAT2* intron 1	G	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs10797874	183298495	*NMNAT2* intron 1	T	22.8%	24.1%	0.25	0.93[0.82-1.05]
G	rs10797875	183298502	*NMNAT2* intron 1	T	22.5%	23.9%	0.23	0.92[0.81-1.05]
I	rs4651153	183298610	*NMNAT2* intron 1	T	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs10911312	183299013	*NMNAT2* intron 1	A	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs10911313	183299153	*NMNAT2* intron 1	G	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs1330224	183299502	*NMNAT2* intron 1	G	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs953273	183299611	*NMNAT2* intron 1	A	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs485677	183299623	*NMNAT2* intron 1	T	10.0%	10.4%	0.60	0.95[0.79-1.15]
G	rs953274	183299881	*NMNAT2* intron 1	T	22.8%	24.1%	0.24	0.93[0.81-1.05]
I	rs16860810	183299974	*NMNAT2* intron 1	G	6.4%	6.7%	0.58	0.94[0.75-1.18]
I	rs67820432	183300112	*NMNAT2* intron 1	T	22.8%	24.1%	0.24	0.93[0.82-1.05]
I	rs952447	183300170	*NMNAT2* intron 1	T	6.4%	6.7%	0.58	0.94[0.75-1.18]
I	rs952446	183300311	*NMNAT2* intron 1	A	22.8%	24.1%	0.26	0.93[0.82-1.06]
I	rs2020986	183300515	*NMNAT2* intron 1	G	22.8%	24.1%	0.25	0.93[0.82-1.05]
I	rs675220	183302111	*NMNAT2* intron 1	C	11.1%	11.9%	0.35	0.92[0.77-1.10]
I	rs677475	183302605	*NMNAT2* intron 1	C	11.1%	11.9%	0.35	0.92[0.77-1.10]
I	rs581606	183302979	*NMNAT2* intron 1	C	11.1%	11.9%	0.38	0.92[0.77-1.10]
I	rs12034392	183303443	*NMNAT2* intron 1	A	6.4%	6.7%	0.58	0.94[0.75-1.18]
I	rs12048443	183303467	*NMNAT2* intron 1	T	6.4%	6.7%	0.58	0.94[0.75-1.18]
I	rs944190	183314293	*NMNAT2* intron 1	G	15.8%	17.0%	0.24	0.91[0.79-1.06]
I	rs1360277	183314641	*NMNAT2* intron 1	T	14.9%	16.0%	0.26	0.91[0.78-1.07]
I	rs649614	183320192	*NMNAT2* intron 1	C	21.5%	23.1%	0.14	0.91[0.79-1.03]
I	rs481157	183323001	*NMNAT2* intron 1	T	10.0%	10.6%	0.36	0.92[0.76-1.11]

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]
					SLE (n=1265)	CTRL (n=1260)		
I	rs10911318	183323643	*NMNAT2* intron 1	C	35.1%	36.3%	0.34	0.94[0.84-1.06]
I	rs564146	183323708	*NMNAT2* intron 1	A	21.6%	23.2%	0.13	0.90[0.79-1.03]
I	rs12125953	183323804	*NMNAT2* intron 1	G	35.2%	36.4%	0.37	0.95[0.84-1.07]
I	rs681054	183324354	*NMNAT2* intron 1	T	21.5%	22.9%	0.17	0.91[0.80-1.04]
I	rs76147160	183324749	*NMNAT2* intron 1	G	6.5%	6.6%	0.73	0.96[0.77-1.21]
G	rs664422	183325722	*NMNAT2* intron 1	C	21.6%	22.9%	0.18	0.91[0.80-1.04]
I	rs502870	183325796	*NMNAT2* intron 1	T	21.5%	22.9%	0.17	0.91[0.80-1.04]
I	1-183326488	183326488	*NMNAT2* intron 1	G	10.8%	11.1%	0.79	0.98[0.82-1.16]
I	rs548292	183326828	*NMNAT2* intron 1	A	22.0%	23.3%	0.22	0.92[0.80-1.05]
G	rs634375	183327866	*NMNAT2* intron 1	C	35.5%	36.6%	0.36	0.95[0.84-1.06]
G	rs10494562	183327971	*NMNAT2* intron 1	T	7.4%	7.2%	0.90	1.01[0.82-1.26]
G	rs12146097	183329261	*NMNAT2* intron 1	T	1.0%	1.1%	0.73	0.91[0.52-1.59]
I	rs2811558	183330413	*NMNAT2* intron 1	G	34.2%	35.6%	0.26	0.93[0.83-1.05]
G	rs12757973	183333504	*NMNAT2* intron 1	T	0.04%	0.12%	0.27	0.28[0.03-2.72]
I	rs554395	183333554	*NMNAT2* intron 1	C	32.4%	33.9%	0.22	0.93[0.82-1.05]
I	rs2485931	183333785	*NMNAT2* intron 1	G	35.2%	36.3%	0.37	0.95[0.84-1.07]
I	rs10911319	183334150	*NMNAT2* intron 1	G	18.2%	18.3%	0.92	0.99[0.86-1.15]
I	rs502937	183335495	*NMNAT2* intron 1	C	33.4%	34.6%	0.30	0.94[0.83-1.06]
I	rs542349	183337933	*NMNAT2* intron 1	A	9.9%	10.5%	0.40	0.92[0.76-1.12]
I	rs673593	183338207	*NMNAT2* intron 1	G	35.0%	36.1%	0.36	0.95[0.84-1.07]
I	rs2811559	183338826	*NMNAT2* intron 1	G	34.7%	36.1%	0.25	0.93[0.83-1.05]
I	rs525138	183339985	*NMNAT2* intron 1	T	11.0%	11.9%	0.23	0.90[0.75-1.07]
I	rs526845	183340129	*NMNAT2* intron 1	G	11.0%	11.9%	0.23	0.90[0.75-1.07]
I	rs527825	183340238	*NMNAT2* intron 1	A	33.5%	34.7%	0.31	0.94[0.83-1.06]
I	rs2485932	183343362	*NMNAT2* intron 1	A	38.0%	39.6%	0.21	0.93[0.83-1.04]
G	rs2788058	183345203	*NMNAT2* intron 1	A	38.1%	39.7%	0.19	0.93[0.83-1.04]
I	rs2788057	183345707	*NMNAT2* intron 1	A	38.1%	39.6%	0.21	0.93[0.83-1.04]
I	rs2811563	183346669	*NMNAT2* intron 1	T	38.1%	39.6%	0.21	0.93[0.83-1.04]
I	rs10911321	183347254	*NMNAT2* intron 1	T	24.3%	24.1%	0.88	1.01[0.89-1.15]
I	rs1933540	183347324	*NMNAT2* intron 1	T	38.1%	39.6%	0.21	0.93[0.83-1.04]
I	rs4630091	183347913	*NMNAT2* intron 1	C	18.7%	17.9%	0.48	1.05[0.91-1.22]
I	rs3122177	183348252	*NMNAT2* intron 1	T	39.6%	41.1%	0.24	0.93[0.83-1.05]
I	rs116825143	183348393	*NMNAT2* intron 1	A	5.5%	5.9%	0.45	0.90[0.71-1.16]

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]
					SLE (n=1265)	CTRL (n=1260)		
I	rs1338379	183349557	*NMNAT2* intron 1	C	38.1%	39.6%	0.21	0.93[0.83-1.04]
I	rs1338378	183351256	*NMNAT2* intron 1	A	38.1%	39.6%	0.21	0.93[0.83-1.04]
I	rs10797876	183352051	*NMNAT2* intron 1	C	26.7%	27.2%	0.71	0.98[0.86-1.11]
I	rs2225932	183352565	*NMNAT2* intron 1	A	26.7%	27.2%	0.73	0.98[0.86-1.11]
I	rs75033236	183353183	*NMNAT2* intron 1	C	26.6%	27.0%	0.75	0.98[0.86-1.11]
G	rs2022013	183353853	*NMNAT2* intron 1	C	38.1%	39.6%	0.23	0.93[0.83-1.05]
I	rs7529886	183355664	*NMNAT2* intron 1	C	25.9%	25.4%	0.73	1.02[0.90-1.16]
I	rs7552360	183355702	*NMNAT2* intron 1	G	25.9%	25.4%	0.73	1.02[0.90-1.16]
I	rs10911324	183356478	*NMNAT2* intron 1	C	25.9%	25.4%	0.73	1.02[0.90-1.16]
I	rs10911325	183356523	*NMNAT2* intron 1	A	25.9%	25.4%	0.73	1.02[0.90-1.16]
I	rs1122258	183356694	*NMNAT2* intron 1	C	25.9%	25.4%	0.73	1.02[0.90-1.16]
I	rs1122259	183356931	*NMNAT2* intron 1	A	24.4%	24.0%	0.77	1.02[0.89-1.16]
I	rs12139593	183357563	*NMNAT2* intron 1	T	18.7%	17.8%	0.39	1.07[0.92-1.23]
I	rs12410472	183358169	*NMNAT2* intron 1	C	5.5%	5.9%	0.45	0.91[0.71-1.16]
I	rs998784	183358263	*NMNAT2* intron 1	G	25.9%	25.4%	0.73	1.02[0.90-1.16]
G	rs2078087	183358405	*NMNAT2* intron 1	T	24.4%	23.9%	0.71	1.03[0.90-1.17]
I	rs1819628	183358440	*NMNAT2* intron 1	T	11.0%	12.0%	0.20	0.89[0.75-1.06]
I	rs7548141	183359514	*NMNAT2* intron 1	T	25.9%	25.4%	0.73	1.02[0.90-1.16]
I	rs78316688	183359879	*NMNAT2* intron 1	T	5.5%	5.9%	0.45	0.91[0.71-1.16]
I	rs2185082	183361025	*NMNAT2* intron 1	A	18.7%	17.8%	0.39	1.07[0.92-1.23]
I	rs12123377	183361578	*NMNAT2* intron 1	T	25.9%	25.4%	0.73	1.02[0.90-1.16]
I	rs2811566	183362544	*NMNAT2* intron 1	G	36.9%	37.9%	0.40	0.95[0.85-1.07]
I	rs2788060	183362646	*NMNAT2* intron 1	C	39.7%	41.0%	0.29	0.94[0.84-1.05]
I	rs10797879	183364016	*NMNAT2* intron 1	T	25.9%	25.4%	0.72	1.02[0.90-1.17]
I	rs9425595	183369036	*NMNAT2* intron 1	C	37.1%	37.9%	0.44	0.95[0.85-1.07]
I	rs7529644	183369065	*NMNAT2* intron 1	G	25.7%	25.3%	0.76	1.02[0.90-1.16]
I	rs80087059	183369250	*NMNAT2* intron 1	G	39.5%	40.7%	0.33	0.94[0.84-1.06]
I	rs6690052	183370057	*NMNAT2* intron 1	A	39.8%	40.9%	0.35	0.95[0.84-1.06]
I	rs12406861	183371192	*NMNAT2* intron 1	A	24.4%	23.9%	0.71	1.03[0.90-1.17]
I	rs74914001	183372675	*NMNAT2* intron 1	C	18.8%	17.8%	0.39	1.07[0.92-1.23]
I	rs3120798	183373665	*NMNAT2* intron 1	T	13.8%	15.6%	0.06	0.86[0.74-1.01]
I	rs3120799	183373841	*NMNAT2* intron 1	A	11.0%	12.0%	0.21	0.89[0.75-1.07]
I	rs2788061	183374040	*NMNAT2* intron 1	A	11.0%	12.0%	0.21	0.89[0.75-1.07]

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]
					SLE (n=1265)	CTRL (n=1260)		
G	rs10732975	183374722	*NMNAT2* intron 1	C	13.8%	15.5%	0.07	0.87[0.74-1.01]
I	rs2788063	183375311	*NMNAT2* intron 1	T	11.0%	12.0%	0.21	0.89[0.75-1.07]
I	rs10752911	183375454	*NMNAT2* intron 1	A	5.5%	6.1%	0.34	0.89[0.70-1.13]
I	rs2702183	183375601	*NMNAT2* intron 1	A	11.0%	12.0%	0.21	0.89[0.75-1.07]
G	rs10797880	183376810	*NMNAT2* intron 1	A	5.7%	6.1%	0.44	0.91[0.71-1.16]
G	rs10494563	183376980	*NMNAT2* intron 1	T	5.7%	6.1%	0.46	0.91[0.72-1.16]
I	rs2788065	183377675	*NMNAT2* intron 1	T	11.0%	12.0%	0.21	0.89[0.75-1.07]
I	rs12119966	183378051	*NMNAT2* intron 1	A	24.4%	23.9%	0.72	1.02[0.90-1.17]
I	rs12127454	183378308	*NMNAT2* intron 1	G	18.6%	17.8%	0.43	1.06[0.92-1.23]
I	rs12407801	183379314	*NMNAT2* intron 1	T	5.3%	6.0%	0.24	0.87[0.68-1.10
I	rs12402878	183379362	*NMNAT2* intron 1	A	5.5%	6.1%	0.37	0.90[0.71-1.14]
I	rs10911329	183379958	*NMNAT2* intron 1	C	5.5%	6.1%	0.37	0.90[0.71-1.14]
G	rs1361197	183380407	*NMNAT2* intron 1	T	38.5%	39.9%	0.28	0.94[0.84-1.05]
I	rs1361198	183380611	*NMNAT2* intron 1	T	40.8%	42.0%	0.34	0.95[0.85-1.06]
I	rs2485935	183380702	*NMNAT2* intron 1	T	14.1%	15.5%	0.12	0.88[0.75-1.03]
I	rs7539430	183381444	*NMNAT2* intron 1	C	17.6%	18.9%	0.24	0.92[0.79-1.06]
I	rs11577151	183381795	*NMNAT2* intron 1	A	5.5%	6.1%	0.37	0.89[0.71-1.14]
G	rs4652800	183383643	*NMNAT2* intron 1	T	39.8%	41.1%	0.31	0.94[0.84-1.06]
I	rs12745288	183384395	*NMNAT2* intron 1	G	39.6%	40.7%	0.35	0.95[0.84-1.06]
I	rs2788045	183384796	*NMNAT2* intron 1	G	17.6%	18.8%	0.26	0.92[0.79-1.06]
I	rs12035399	183386537	*NMNAT2* intron 1	A	39.7%	40.9%	0.34	0.95[0.84-1.06]
I	rs1815590	183386828	*NMNAT2* intron 1	C	11.2%	12.1%	0.21	0.89[0.75-1.07]
I	rs2702189	183389150	Intergenic	C	10.4%	11.1%	0.36	0.92[0.77-1.10]
I	rs2788047	183389460	Intergenic	A	11.0%	12.1%	0.17	0.88[0.74-1.06]
I	rs2788048	183389877	Intergenic	A	11.0%	12.0%	0.17	0.89[0.74-1.06]
I	rs12128348	183392567	Intergenic	C	18.3%	17.5%	0.45	1.06[0.91-1.22]
I	rs12731807	183394037	Intergenic	G	38.6%	40.3%	0.18	0.92[0.82-1.04]
I	rs2485937	183394535	Intergenic	T	11.0%	12.0%	0.18	0.89[0.74-1.06]
I	rs78232289	183394705	Intergenic	G	17.6%	16.9%	0.55	1.05[0.90-1.22]
I	rs7521864	183395226	Intergenic	T	17.1%	16.3%	0.43	1.06[0.91-1.24]
I	rs2464366	183396401	Intergenic	T	11.1%	12.2%	0.17	0.88[0.74-1.05]
I	rs61130991	183396513	Intergenic	A	17.6%	16.6%	0.38	1.07[0.92-1.24]
I	rs2485939	183396610	Intergenic	A	11.2%	12.4%	0.15	0.88[0.73-1.05]

Type	SNP	Position	Annotation	Tested Allele	Frequency		*P*	OR [95%CI]
					SLE (n=1265)	CTRL (n=1260)		
I	rs2702198	183397087	Intergenic	A	11.2%	12.5%	0.14	0.87[0.73-1.04]
I	rs2811551	183397589	Intergenic	C	11.0%	12.1%	0.17	0.88[0.74-1.05]
I	rs12144629	183397899	Intergenic	T	18.4%	17.5%	0.41	1.06[0.92-1.23]
G	rs2993476	183398233	Intergenic	G	11.0%	12.3%	0.10	0.86[0.72-1.03]
G	rs12130057	183398487	Intergenic	A	18.4%	17.6%	0.45	1.06[0.91-1.22]
I	rs12130903	183398868	Intergenic	C	18.4%	17.5%	0.41	1.06[0.92-1.23]
I	rs12143386	183402224	Intergenic	T	18.3%	17.5%	0.44	1.06[0.92-1.23]
G	rs12129543	183402792	Intergenic	T	19.6%	18.2%	0.19	1.10[0.95-1.27]
I	rs4047801	183415318	Intergenic	G	44.5%	43.7%	0.60	1.03[0.92-1.16]
I	rs6424897	183419203	Intergenic	C	45.0%	44.2%	0.64	1.03[0.92-1.15]
G	rs12024309	183419981	Intergenic	G	44.9%	44.1%	0.63	1.03[0.92-1.15]
I	rs4047798	183421406	Intergenic	T	44.2%	43.5%	0.67	1.03[0.91-1.15]
G	rs9286848	183426249	Intergenic	G	45.0%	44.3%	0.71	1.02[0.91-1.15]
I	rs7518244	183434807	*SMG7-AS1* intron 3	T	45.0%	44.3%	0.64	1.03[0.92-1.15]
I	rs2275675	183439483	*SMG7-AS1* intron 2	T	44.6%	43.7%	0.58	1.03[0.92-1.16]
I	rs10911339	183442097	*SMG7* intron 1	C	44.6%	43.7%	0.58	1.03[0.92-1.16]
I	rs12742245	183446922	*SMG7* intron 1	T	44.7%	44.0%	0.65	1.03[0.92-1.15]

Position of each SNP is based on GRch37/hg19. G, genotyped SNP; I, imputed SNP.

Table S5. Significant association of SNPs with SLE in European American and Amerindian/Hispanics

					EA		HS		Meta-analysis	
Type	**SNP**	**Gene**	**Annotation**	**Tested Allele**	**P**	**OR [95%CI]**	**P**	**OR [95%CI]**	**P**	**OR**
G	rs536586	*NMNAT2*	intron 1	A	7.2E-05	1.15[1.08-1.24]	2.7E-04	1.26[1.11-1.43]	1.5E-07	1.18
I	rs602182	*NMNAT2*	intron 1	T	1.4E-04	1.15[1.07-1.23]	4.7E-04	1.25[1.10-1.42]	4.5E-07	1.17
I	rs564146	*NMNAT2*	intron 1	A	4.1E-07	0.83[0.77-0.89]	9.9E-04	0.81[0.71-0.92]	1.6E-09	0.82
I	rs681054	*NMNAT2*	intron 1	T	4.7E-07	0.83[0.77-0.89]	8.2E-04	0.81[0.71-0.91]	1.6E-09	0.82
G	rs664422	*NMNAT2*	intron 1	C	4.3E-07	0.83[0.77-0.89]	9.5E-04	0.81[0.71-0.92]	1.6E-09	0.82
I	rs502870	*NMNAT2*	intron 1	T	5.0E-07	0.83[0.77-0.89]	8.2E-04	0.81[0.71-0.91]	1.7E-09	0.82
I	rs548292	*NMNAT2*	intron 1	A	3.2E-07	0.83[0.77-0.89]	7.2E-04	0.80[0.71-0.91]	9.8E-10	0.82
G	rs12146097	*NMNAT2*	intron 1	T	1.5E-10	1.38[1.25-1.53]	9.3E-04	1.47[1.17-1.84]	6.4E-13	1.40

Only SNPs that remain significant associations with SLE after Bonferroni correction in both EA and HS are listed in this table. SNPs that show a combined P_{meta}<5×10^{-8} in the trans-ancestral meta-analysis (named as group 1) are highlighted in gray.
EA, European American; G, genotyped SNP; HS, Amerindian/Hispanics; I, imputed SNP.

Table S6. Association between low *SMG7* mRNA levels and the SLE-risk allele of tag SNPs in eQTL databases

Study	SNP Group	Tag SNP	SLE-Risk Allele	*P* value for each *SMG7* Probe			Cells
				ILMN_1690469	ILMN_1706553	ILMN_2368597	
Dimas et al, 2009 [16]	1	rs12146097	T	NS	NS	10^{-4}	F
	2	rs10911353	A	NS	NS	10^{-5}~10^{-9}	L, T
Nica et al, 2011 [17]	1	rs502870	G	NS	NS	10^{-5}	L
	2	rs2275675	C	NS	NS	10^{-7}~10^{-10}	L, A
	2	rs10911353	A	NS	NS	10^{-7}~10^{-10}	L, A
Stranger et al, 2012 [18]	1	rs12146097	T	NS	NS	NA	L
	1	rs502870	G	NS	10^{-4}	NA	L
	2	rs2275675	C	NS	10^{-4}	NA	L
	2	rs10911353	A	NS	10^{-4}	NA	L
Fairfax et al, 2012 [19]	1	rs664422	T	NA	NS	10^{-8}~10^{-9}	B, M
	2	rs2275675	C	NA	10^{-8}~10^{-13}	10^{-32}~10^{-47}	B, M
Westra et al, 2013 [20]	1	rs12146097	T	NA	10^{-17}	10^{-34}	P
	1	rs502870	G	NA	10^{-32}	10^{-80}	P
	2	rs2275675	C	NA	10^{-198}	10^{-198}	P
	2	rs10911353	A	NA	10^{-198}	10^{-198}	P

A, adipocytes; B, primary B cells; F, fibroblasts; L, lymphoblastoid cell lines; M, primary monocytes; P, peripheral blood cells; T, primary T cells. NA, not available; NS, not significant.