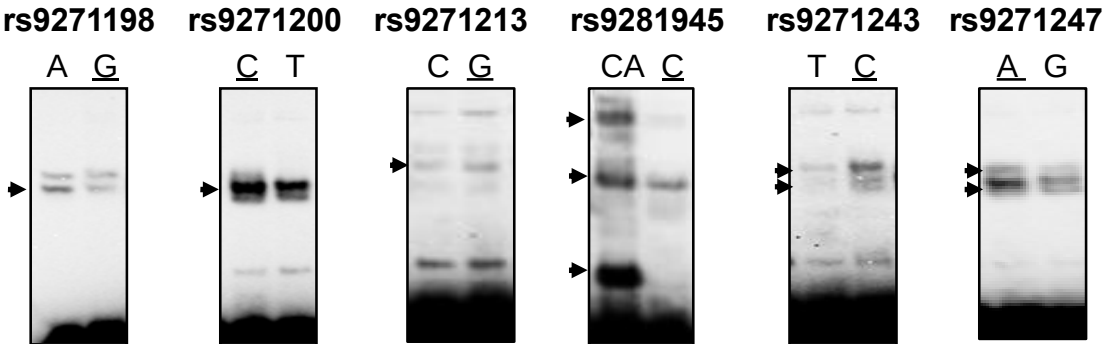
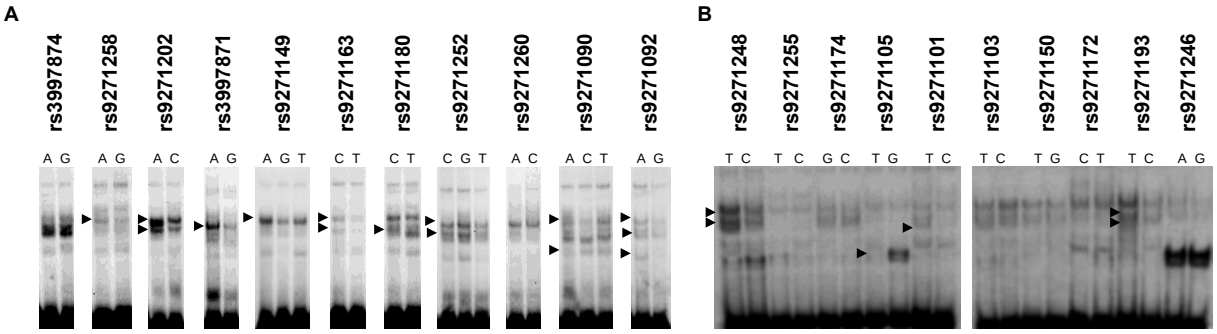
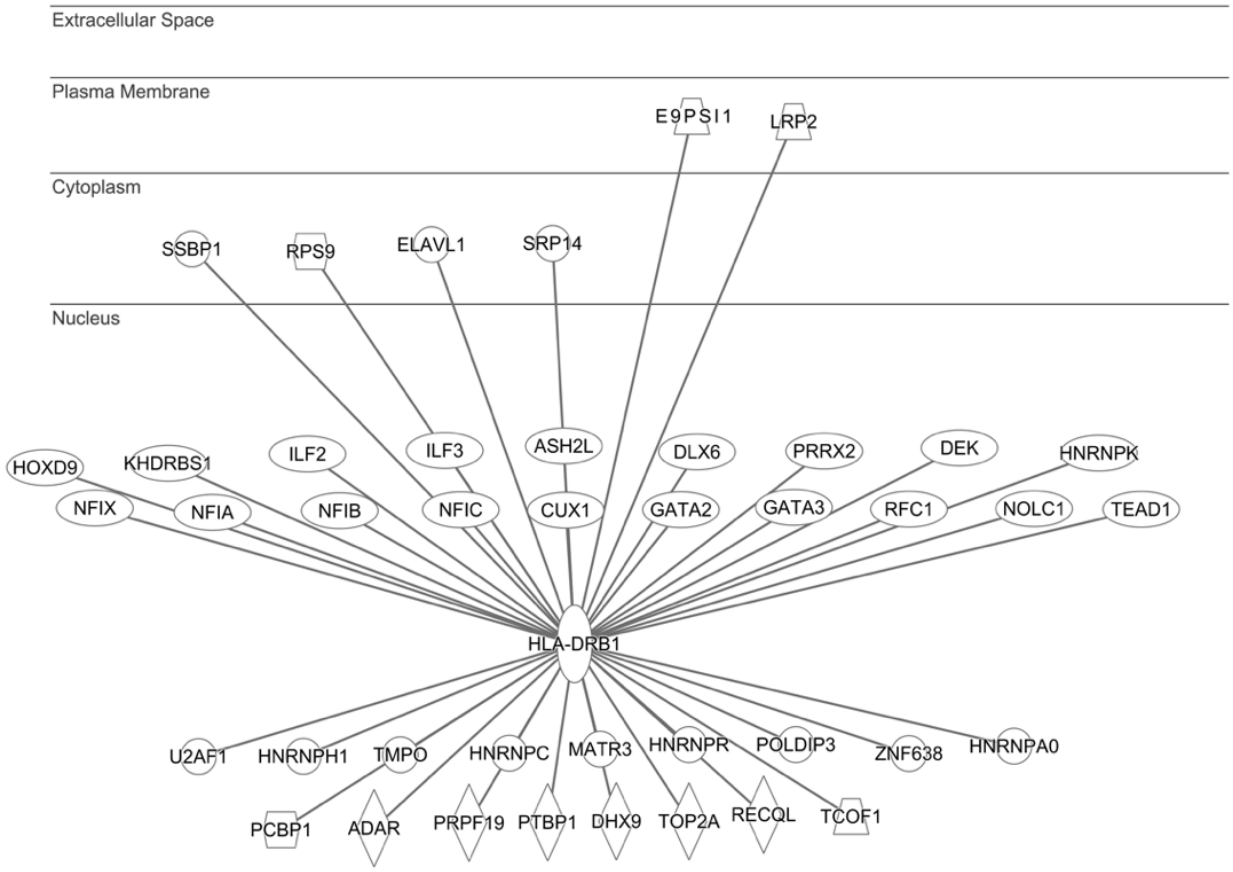
Supplementary Figure 1. EMSA showing allele-imbalanced gel shifting with the 6 candidate fSNPs on the *HLA-DRB1/DQA1* locus using NE from human frontal cortex. Arrow indicating the allele-imbalanced gel shifting. Risk alleles are underlined.



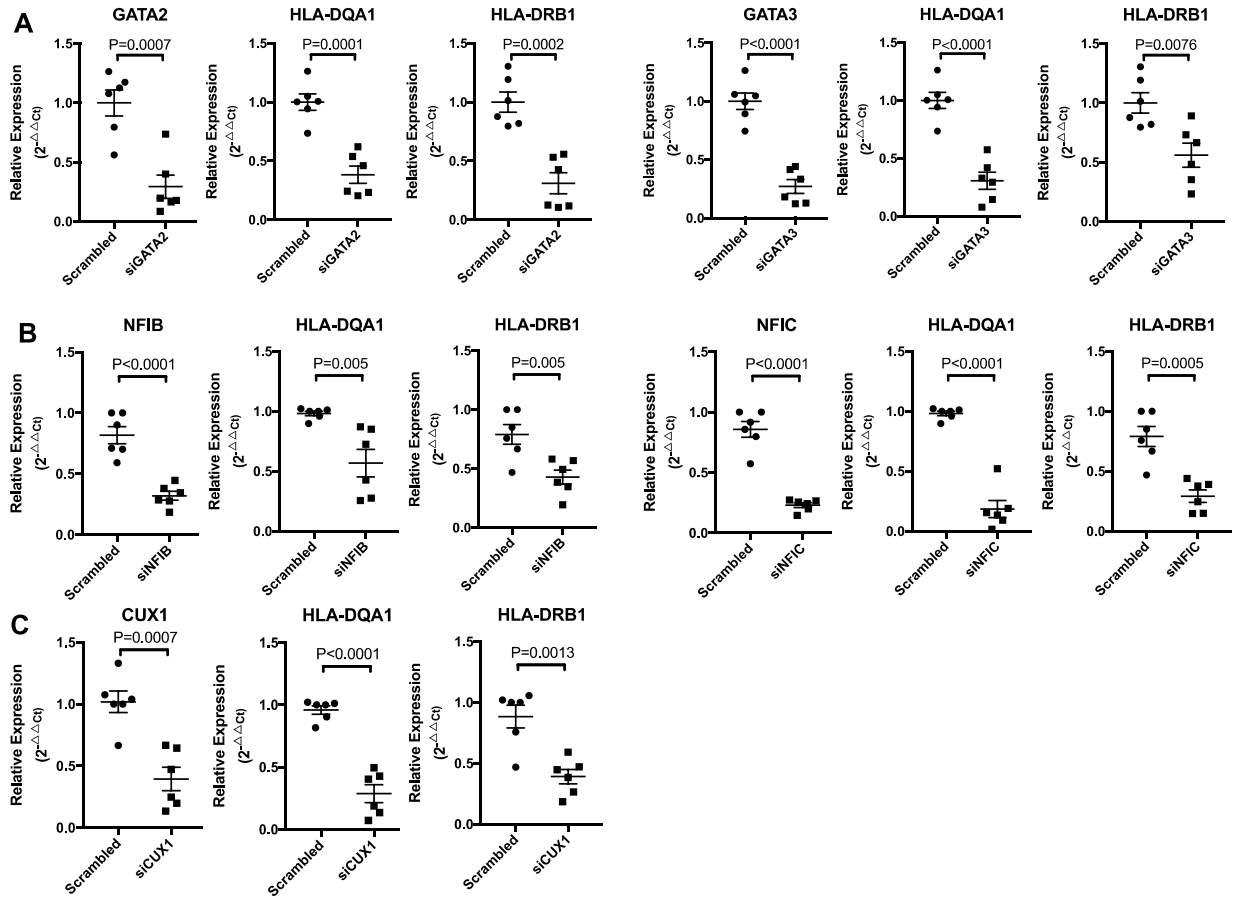
Supplementary Figure 2. EMSA showing allele-imbalanced gel shifting with the 11 putative fSNPs (A) and 10 SNPs randomly selected from the 42 non-fSNPs (B). At least 8 putative fSNPs and 4 non-fSNPs showed allele-imbalanced gel shifting (indicated by arrows), demonstrating that they are functional. The data together with the data from **Fig. 1** also suggest a ~83% positive recovery rate and a 40% false negative rate for this Reel-seq screen. Arrow indicating the allele-imbalanced gel shifting.



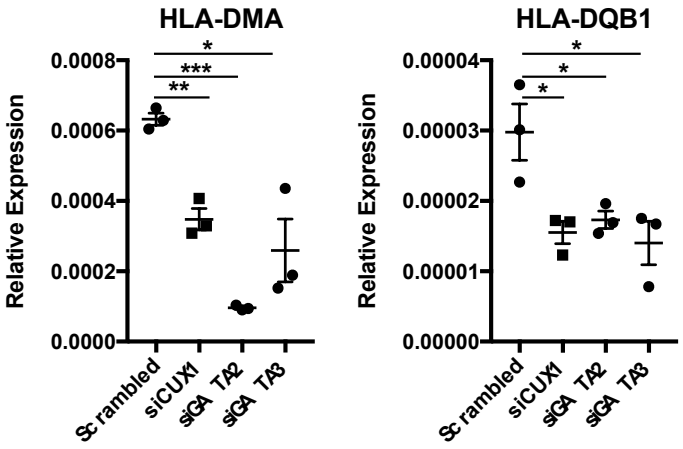
Supplementary Figure 3. Ingenuity pathway analysis on the 42 proteins identified by SDCP-MS.



Supplementary Figure 4. qPCR showing a significant alteration of the *HLA-DQA1* and *HLA-DRB1* expression by downregulating GATA2 (A), GATA3 (B), NFIB (C), NFIC (D) and CUX1 (E) in the siRNA knockdown HMC3 cells. Data for qPCR represents the combination of three biologically independent experiments (n=3), each in duplicate. GAPDH was used as control for qPCR.



Supplementary Figure 5. qPCR showing a significant downregulation of *HLA-DMA* (left) and *HLA-DQB1* (right) expression in the CUX1, GATA2, and GATA3 shRNA knockdown HMC3 cells. Data for qPCR represents a combination of three biologically independent experiments (n=3). GAPDH was used as control for qPCR. * *p*-value < 0.05; ** *p*-value < 0.001; and *** *p*-value < 0.0001;



Supplementary Table 1. 58 SNPs on the *HLA-DRB1/DQA1* locus in LD (R^2 > 0.8) with rs9271192 associated with LOAD with an overall OR = 1.11 and P < 2.9 x 10^{-12}.

	SeqID		SeqID		SeqID
Candidate fSNP	rs9271189	**non-fSNPs**	rs202092830	**non-fSNPs**	rs9271179
-0.05 > slope > 0.05 and a p-value < 0.05	rs9271200	**p-value > 0.05**	rs2894378	**p-value > 0.05**	rs9271182
	rs9271213		rs79267592		rs9271186
	rs9271243		rs9271094		rs9271192
	rs9271247		rs9271096		rs9271193
			rs9271100		rs9271194
			rs9271101		rs9271198
			rs9271103		rs9271199
			rs9271104		rs9271201
			rs9271105		rs9271239
			rs9271146		rs9271240
			rs9271150		rs9271246
putative fSNPs	rs3997874		rs9271151		rs9271247
-0.05 < slope < 0.05 and a p-value < 0.05	rs9271258		rs9271153		rs9271248
	rs9271202		rs9271156		rs9271251
	rs3997871		rs9271170		rs9271255
	rs9271149		rs9271171		rs9271257
	rs9271163		rs9271172		rs927174
	rs9271180		rs9271173		rs9281945
	rs9271252		rs9271174		rs9281946
	rs9271260		rs9271178		rs9271205
	rs9271090		rs9271179		rs9271242
	rs9271092		rs9271182		rs9271162

Supplementary Table 2. Epigenetic and functional annotations of the 6 SNPs on the LOAD associated *HLA-DRB1/DQA1* locus using HaploReg 4.1.

	SNP	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	Score
Candidate fSNPs	**rs9271189**	ESC, BLD	IPSC, BLD, THYM	BLD,BLD		Hoxa13,Mef2	**4**
	rs9271200	BLD	IPSC, BLD, THYM	BLD,BLD,BLD	BATF,MEF2A,MEF2C		**4**
	rs9271213		BLD	BLD		5 altered motifs	**3**
	rs9271243		BLD			Mef2	**2**
	rs9281945		BLD			EBF,Hsf,Myf	**2**
	rs9271247					CEBPA	**1**

Supplementary Table 3. Primers used in this work.

Applications	Primer Name	Sequence (5'→3')
Q-PCR	ELAVL1-F	GGGTGACATCGGGAGAACG
	ELAVL1-R	CTGAACAGGCTTCGTAACTCAT
	HNRNPA0-F	GCGACCTGATCGAGCACTTC
	HNRNPA0-F	CGCGTCGTGATTCTGGAAATAC
	ILF2-F	CGCTGCTTGCAGATTCTGG
	ILF2-R	TGTGTGTACTCTAAAGTTGCCAC
	ILF3-F	TTAGCTGGAGAAACGCTATCAGT
	ILF3-R	AATGACACAAGACTTCAGCCC
	DQA-F	CAGTTGGTGCTTCCAGACA
	DQA-R	GTCCATTCTTCTGCTCCTGTAG
	DRB1-F	TCATCTACTTCAGGAATCAGAAAGG
	DRB1-R	TGTCATCTGCACTTCAGCTC
	NFIB-F	GCTGTGTCTTATCCAATCCCG
	NFIB-R	TGCCTTTGAACAGGATGACCA
	NFIC-F	CGCCTCTCCAGCTTCAC
	NFIC-R	ATGGACGTCGTAGGGAAATG
	CUX1-F	CCATGGAGTTTGCACCGT
	CUX1-R	CAGCGAGCGGTTCTTCTC
	GAPDH-F	CGACCACTTTGTCAAGCTCA
	GAPDH-R	AGGGGTCTACATGGCAACTG
shRNA lentivirus	shGATA2-F	CCGGCCGGCACCTGTTGTGCAAATTCTCGAGAATTTGCACAACAGGTGCCGGTTTTTG
	shGATA2-R	AATTCAAAAACCGGCACCTGTTGTGCAAATTCTCGAGAATTTGCACAACAGGTGCCGG
	shGATA3-F	CCGGCCCAAGAACAGCTCGTTTAACCTCGAGGTTAAACGAGCTGTTCTTGGGTTTTTG
	shGATA3-R	AATTCAAAAACCCAAGAACAGCTCGTTTAACCTCGAGGTTAAACGAGCTGTTCTTGGG
	shELAVL1-F	CCGGGAGAACGAATTTGATCGTCAACTCGAGTTGACGATCAAATTCGTTCTCTTTTTG
	shELAVL1-R	AATTCAAAAAGAGAACGAATTTGATCGTCAACTCGAGTTGACGATCAAATTCGTTCTC
	shHNRNPA0-F	CCGGCGGCTTCGTGTATTTCCAGAACTCGAGTTCTGGAAATACACGAAGCCGTTTTTG
	shHNRNPA0-R	AATTCAAAAACGGCTTCGTGTATTTCCAGAACTCGAGTTCTGGAAATACACGAAGCCG
	shILF2-F	CCGGGCTATCTTGCTTCTGAAATATCTCGAGATATTTCAGAAGCAAGATAGCTTTTTG
	shILF2-R	AATTCAAAAAGCTATCTTGCTTCTGAAATATCTCGAGATATTTCAGAAGCAAGATAGC
	shILF3-F	CCGGGGTCTTCCTAGAGCGTCTAAACTCGAGTTTAGACGCTCTAGGAAGACCTTTTTG
	shILF3-R	AATTCAAAAAGGTCTTCCTAGAGCGTCTAAACTCGAGTTTAGACGCTCTAGGAAGACC
	shNFIB-F	CCGGGCAGCACTTACAATCACTAATCTCGAGCGTCGTGAATGTTAGTGATTATTTTTG
	shNFIB-R	AATTCAAAAAGCAGCACTTACAATCACTAATCTCGAGCGTCGTGAATGTTAGTGATTA
	shNFIC-F	CCGGCCCGGTGAAGAAGACAGAGATCTCGAGATCTCTGTCTTCTTCACCGGGTTTTTG
	shNFIC-R	AATTCAAAAACCCGGTGAAGAAGACAGAGATCTCGAGATCTCTGTCTTCTTCACCGGG
	shCUX1-F	CCGGGCACGATATTGAAACAGAGAACTCGAGTTCTCTGTTTCAATATCGTGCTTTTTG
	shCUX1-R	AATTCAAAAAGCACGATATTGAAACAGAGAACTCGAGTTCTCTGTTTCAATATCGTGC
SDCP-MS	rs9271198/G-F	5'Biosg/GTCTGTGTTCCGTTGTCCGTGCTGAATGGATCCGGATCCAGGGTTGAATTGCATGATCTCTCAAGTTAATGAATTCGAATTCGC
	rs9271198/G-R	GCGAATTCGAATTCATTAACTTGAAGAATCATGCAATTCAACCCTGGATCCGGATCCATT
	rs9271200/C-F	5'Biosg/GTCTGTGTTCCGTTGTCCGTGCTGAATGGATCCGGATCCTACTTAACTCATTCCCGGACCATGATAAATAGAATTCGAATTCGC
	rs9271200/C-R	GCGAATTCGAATTCTATTTATCATGGTCCGGGAATGAGTTAAGTAGGATCCGGATCCATT
	rs9271213/T-F	GTCTGTGTTCCGTTGTCCGTGCTGAATGGATCCGGATCCATCTTCTTTCCTTTCTAGGTCTTTCCCTTGAGAATTCGAATTCGC
	rs9271213/T-R	GCGAATTCGAATTCTCAAGGGAAAGACCTAGAAAGGAAAGAAGATGGATCCGGATCCATT
	rs9271243/T-F	5'Biosg/GTCTGTGTTCCGTTGTCCGTGCTGAATGGATCCGGATCCGCCATTGGTCACTCATATTTGGCTCAAAATAGAATTCGAATTCGC
	rs9271243/T-R	GCGAATTCGAATTCTATTTTGAGCCAAATATGAGTGACCAATGGCGGATCCGGATCCATT
	rs9271247/T-F	5'Biosg/GTCTGTGTTCCGTTGTCCGTGCTGAATGGATCCGGATCCCTACTGTTGACCAGATGTTTTACCAATAACAGAATTCGAATTCGC
	rs9271247/T-R	GCGAATTCGAATTCTGTTATTGGTAAAACATCTGGTCAACAGTAGGGATCCGGATCCATT
	rs9281945/CAT-F	5'Biosg/GTCTGTGTTCCGTTGTCCGTGCTGAATGGATCCGGATCCAACCACCTTGGGCACGTGTTCTCAGGATCTTGAATTCGAATTCGC
	rs9281945/CAT-R	GCGAATTCGAATTCAAGATCCTGAGAACACGTGCCCAAGGTGGTTGGATCCGGATCCATT
AIDP-Wb	sidpl/rs9271198-A-F	5'Biosg/AGGGTTGAATTGCATAATCTCTCAAGTTAAT
	sidpl/rs9271198-A-R	ATTAACTTGAGAGATTATGCAATTCAACCCT
	sidpl/rs9271198-G-F	5'Biosg/AGGGTTGAATTGCATGATCTCTCAAGTTAAT
	sidpl/rs9271198-G-R	ATTAACTTGAGAGATCATGCAATTCAACCCT
	sidpl/rs9271200-C-F	5'Biosg/TACTTAACTCATTCCCGGACCATGATAAATA
	sidpl/rs9271200-C-R	TATTTATCATGGTCCGGGAATGAGTTAAGTA
	sidpl/rs9271200-T-F	5'Biosg/TACTTAACTCATTCCTGGACCATGATAAATA
	sidpl/rs9271200-T-R	TATTTATCATGGTCCAGGAATGAGTTAAGTA
	sidpl/rs9271243-C-F	5'Biosg/GCCATTGGTCACTCACATTTGGCTCAAAATA
	sidpl/rs9271243-C-R	TATTTTGAGCCAAATGTGAGTGACCAATGGC
	sidpl/rs9271243-T-F	5'Biosg/GCCATTGGTCACTCATATTTGGCTCAAAATA
	sidpl/rs9271243-T-R	TATTTTGAGCCAAATATGAGTGACCAATGGC
	sidpl/rs9281945-C-F	5'Biosg/AACCACCTTGGGCACGTTCTCAGGATCTTCT
	sidpl/rs9281945-C-R	AGAAGATCCTGAGAACGTGCCCAAGGTGGTT
	dpl/rs9281945-CAT-F	5'Biosg/AACCACCTTGGGCACATGTTCTCAGGATCTT
	dpl/rs9281945-CAT-R	AAGATCCTGAGAACATGTGCCCAAGGTGGTT
	sidpl/rs9271247-A-F	5'Biosg/CTACTGTTGACCAGAAGTTTTACCAATAAC
	sidpl/rs9271247-A-R	TGTTATTGGTAAAACTTCTGGTCAACAGTA
	sidpl/rs9271247-G-F	5'Biosg/CTACTGTTGACCAGAGGTTTTACCAATAAC
	sidpl/rs9271247-G-R	TGTTATTGGTAAAACCTCTGGTCAACAGTA
Luciferase Reporter	LRA198-G-F	CAGGGTTGAATTGCATGATCTCTCAAGTTAATC
	LRA198-G-R	TCGAGATTAACTTGAGAGATCATGCAATTCAACCCTGAGCT
	LRA198-A-F	CAGGGTTGAATTGCATAATCTCTCAAGTTAATC
	LRA198-A-R	TCGAGATTAACTTGAGAGATTATGCAATTCAACCCTGAGCT
	LRA200-C-F	CTACTTAACTCATTCCCGGACCATGATAAATAC
	LRA200-C-R	TCGAGTATTTATCATGGTCCGGGAATGAGTTAAGTAGAGCT
	LRA200-T-F	CTACTTAACTCATTCCTGGACCATGATAAATAC
	LRA200-T-R	TCGAGTATTTATCATGGTCCAGGAATGAGTTAAGTAGAGCT
	LRA213-G-F	CATCTTCTTTCCTTTCGAGGTCTTTCCCTTGAC
	LRA213-G-R	TCGAGTCAAGGGAAAGACCTCGAAAGGAAAGAAGATGAGCT
	LRA213-C-F	CATCTTCTTTCCTTTCCAGGTCTTTCCCTTGAC
	LRA213-C-R	TCGAGTCAAGGGAAAGACCTGGAAAGGAAAGAAGATGAGCT
	LRA213-T-F	CATCTTCTTTCCTTTCTAGGTCTTTCCCTTGAC
	LRA213-T-R	TCGAGTCAAGGGAAAGACCTAGAAAGGAAAGAAGATGAGCT
	LRA243-C-F	CGCCATTGGTCACTCACATTTGGCTCAAAATAC
	LRA243-C-R	TCGAGTATTTTGAGCCAAATGTGAGTGACCAATGGCGAGCT
	LRA243-T-F	CGCCATTGGTCACTCATATTTGGCTCAAAATAC
	LRA243-T-R	TCGAGTATTTTGAGCCAAATATGAGTGACCAATGGCGAGCT
	LRA247-A-F	CCTACTGTTGACCAGAAGTTTTACCAATAACAC
	LRA247-A-R	TCGAGTGTTATTGGTAAAACTTCTGGTCAACAGTAGGAGCT
	LRA247-G-F	CCTACTGTTGACCAGAGGTTTTACCAATAACAC
	LRA247-G-R	TCGAGTGTTATTGGTAAAACCTCTGGTCAACAGTAGGAGCT
	LRA247-T-F	CCTACTGTTGACCAGATGTTTTACCAATAACAC
	LRA247-T-R	TCGAGTGTTATTGGTAAAACATCTGGTCAACAGTAGGAGCT
	LRA945-G-F	CACCGGCATGTATTGGGTAGAGGCCAGGGGTGC
	LRA945-G-R	TCGAGCACCCCTGGCCTCTACCCAATACATGCCGGTGAGCT
	LRA945-A-F	CACCGGCATGTATTGGATAGAGGCCAGGGGTGC
	LRA945-A-R	TCGAGCACCCCTGGCCTCTATCCAATACATGCCGGTGAGCT

Supplementary Table 4. Antibodies used in this work.

Antibody	Manufacturer	Cat#	Source	Website for validation and dilution
GATA2	ABclonal	A0677	Rabbit	https://abclonal.com.cn/catalog/A0677
GATA3	ABclonal	A1638	Rabbit	https://abclonal.com.cn/catalog/A1638
HNRNPA0	Proteintech	10848-1-AP	mouse	https://www.ptgcn.com/products/HNRNPA0-Antibody-10848-1-AP.htm
ELAVL1	Proteintech	11910-1-AP	Rabbit	https://www.ptglab.com/products/HuR-Antibody-11910-1-AP.htm
ILF2/NF45	Proteintech	14714-1-AP	Rabbit	https://www.ptglab.com/products/NF45-Antibody-14714-1-AP.htm
ILF3	Proteintech	19887-1-AP	Rabbit	https://www.ptglab.com/products/NF90,ILF3-Antibody-19887-1-AP.htm
NFIB antibody	abclonal	A15294	Rabbit	https://abclonal.com.cn/catalog/A15294
NFIC antibody	abclonal	A15074	Rabbit	https://abclonal.com.cn/catalog/A15074
HLA-DQA1	Abclonal	A2168	Rabbit	https://abclonal.com.cn/catalog/A2168
HLA-DRB1	Abclconal	A7685	Rabbit	https://abclonal.com.cn/catalog/A7685
CUX1	Sigma	ABE217	Rabbit	https://www.sigmaaldrich.cn/CN/en/product/mm/abe217?context=product
PARP-1(H-250)	Santa Cruz	sc-7150	Rabbit	https://www.scbt.com/scbt/zh/product/parp-1-antibody-h-250
α-Tubulin	Sigma	T6074	Mouse	https://www.sigmaaldrich.com/catalog/product/sigma/t6074?lang=en&region=US