

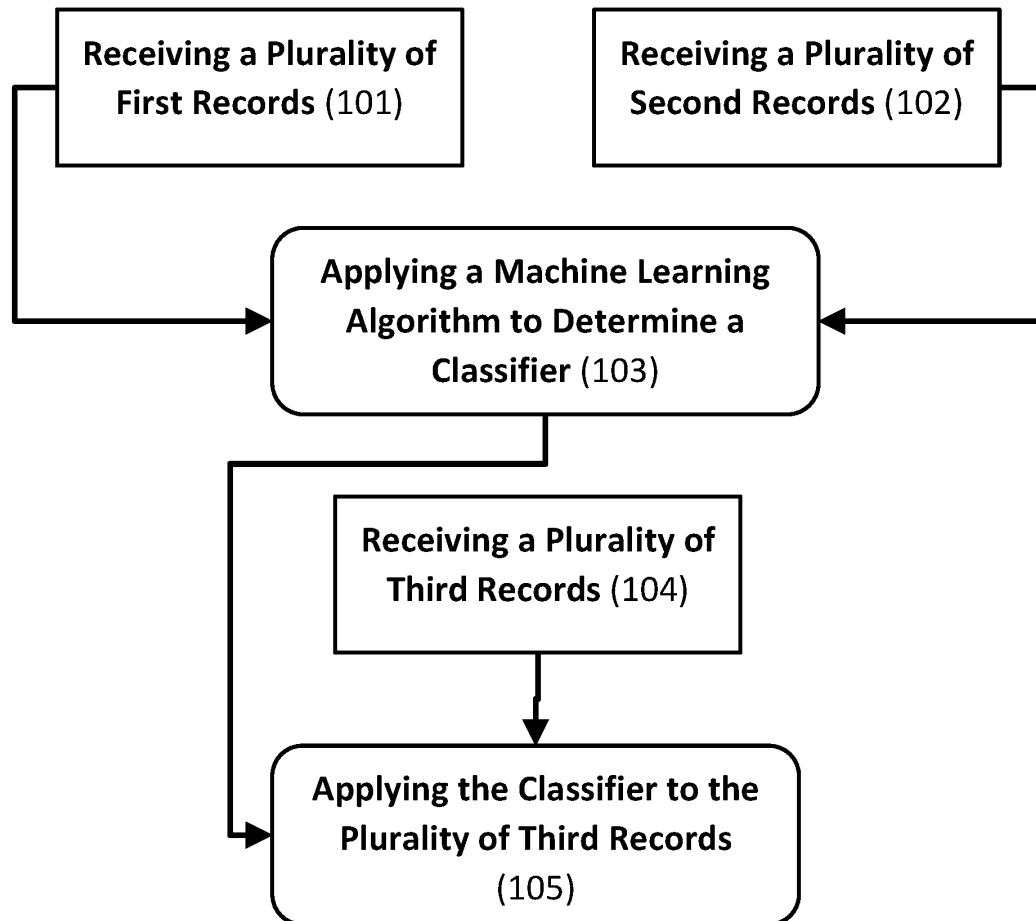


FIG. 1

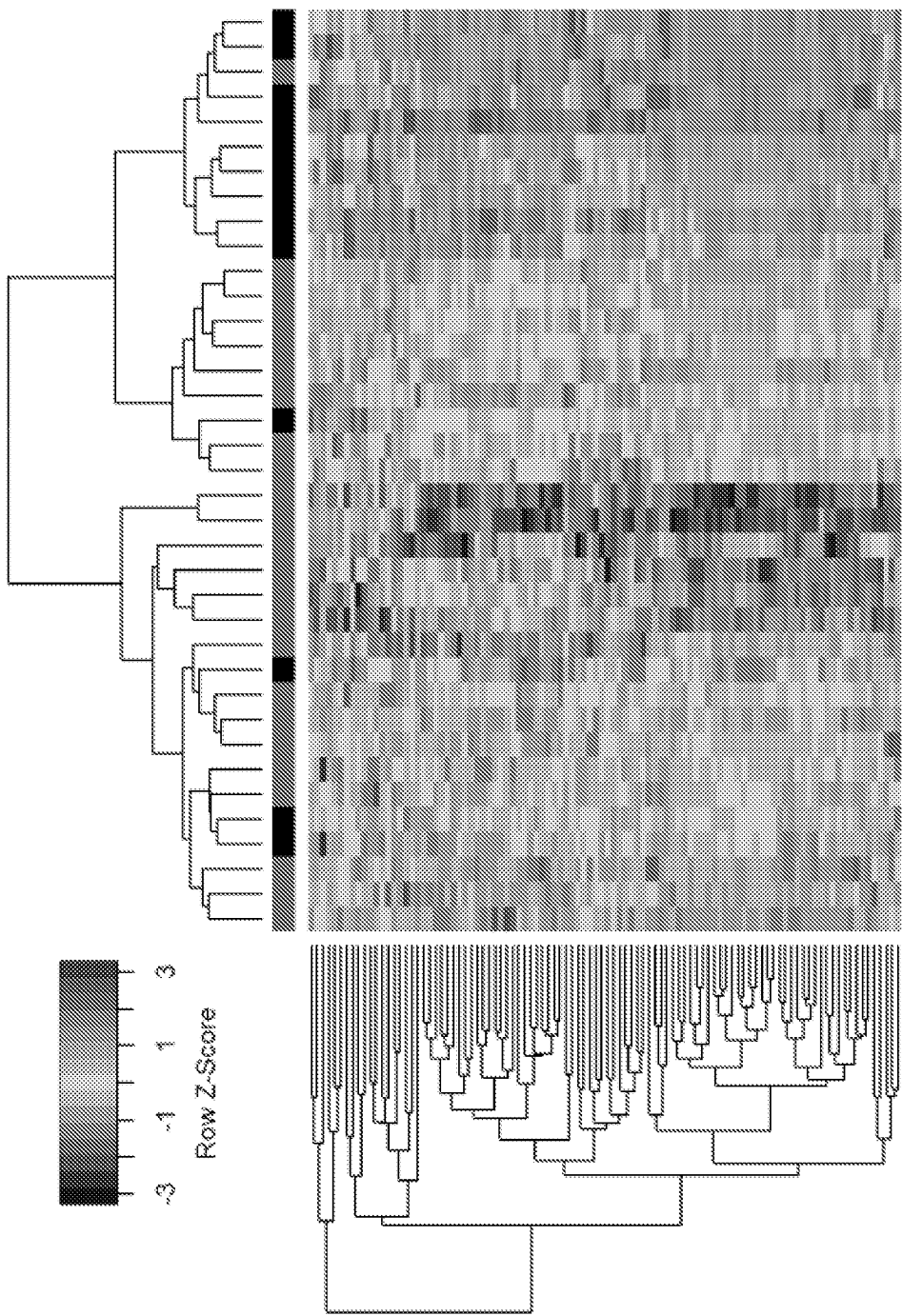


FIG. 2A

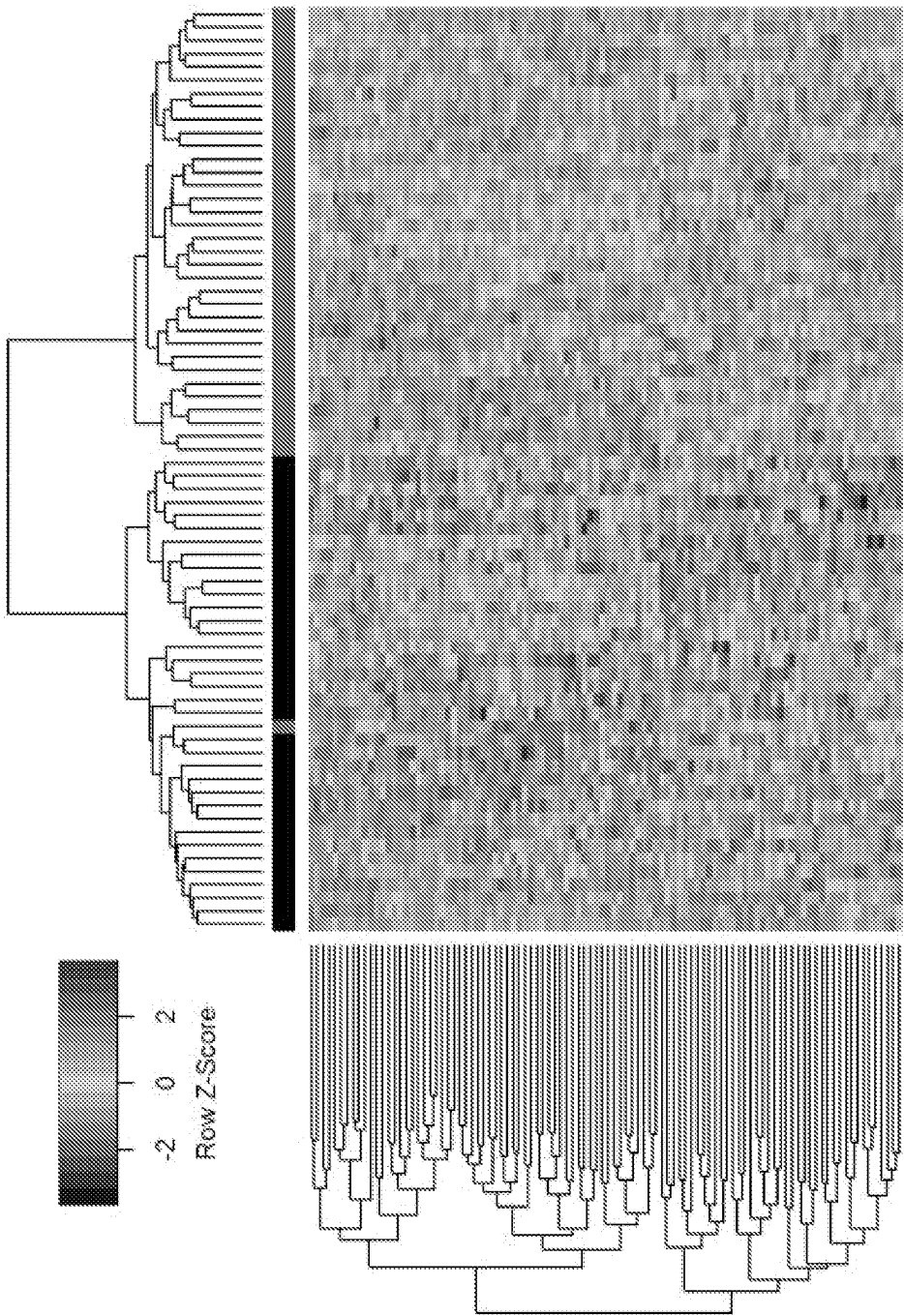


FIG. 2B

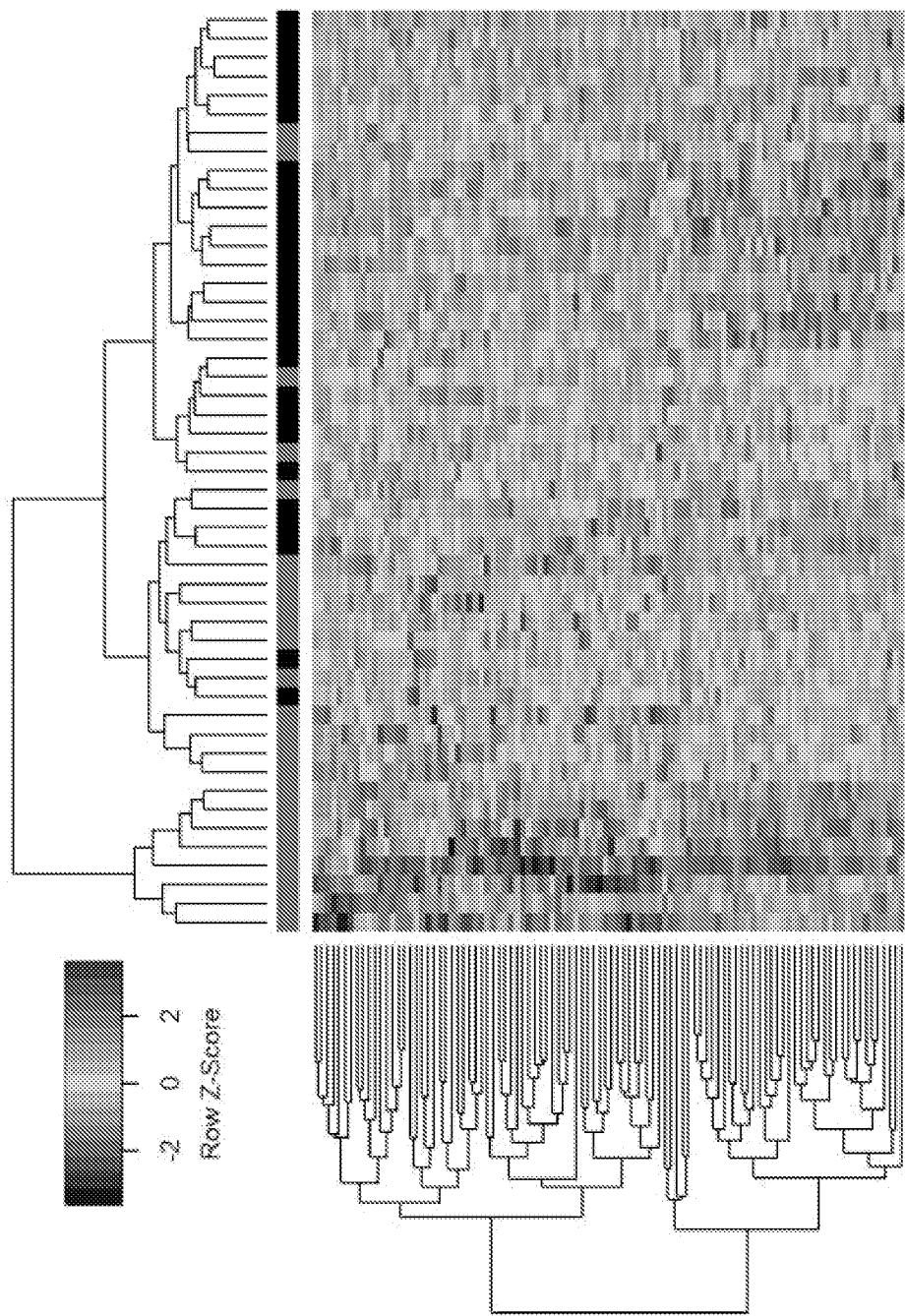


FIG. 2C

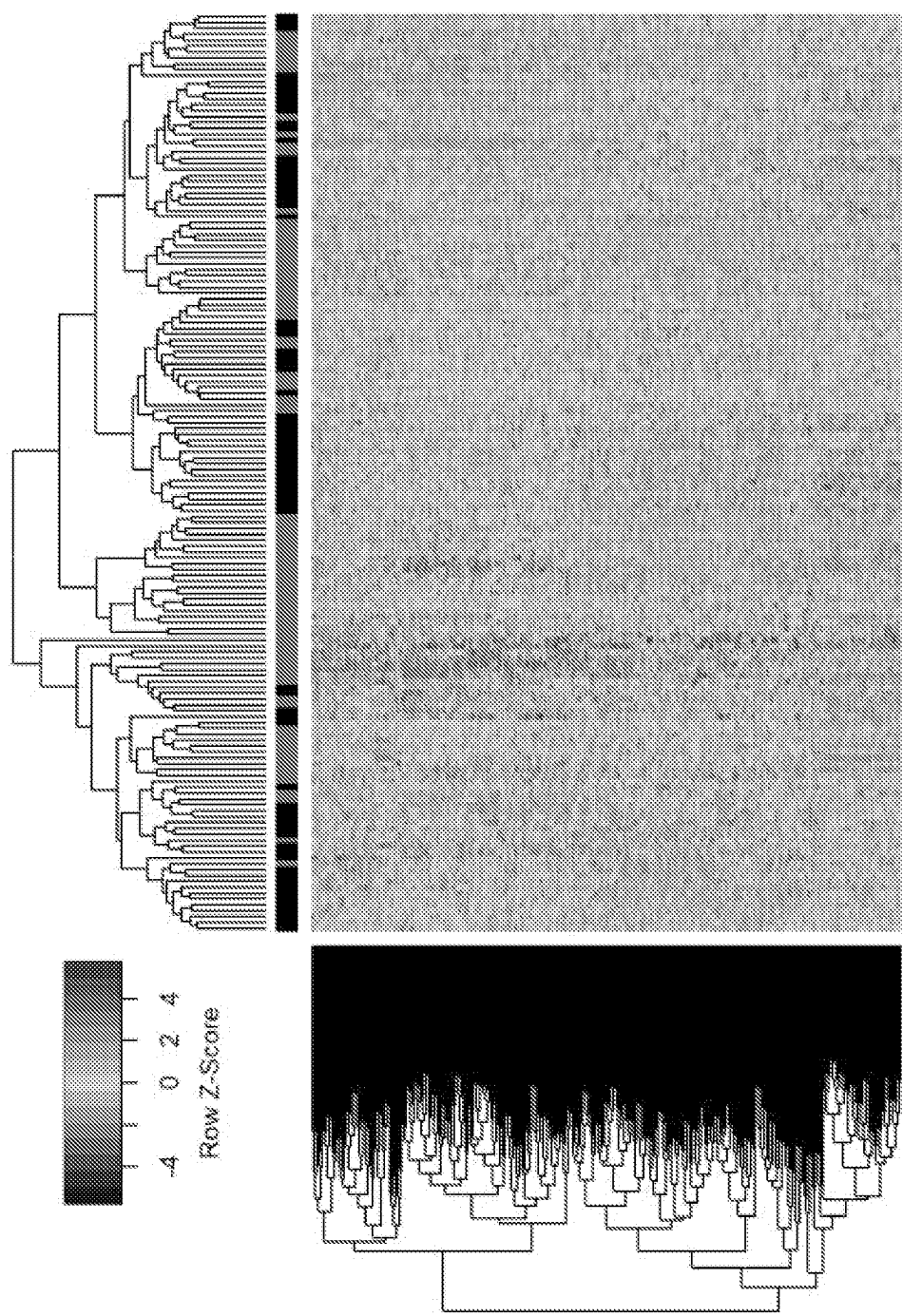
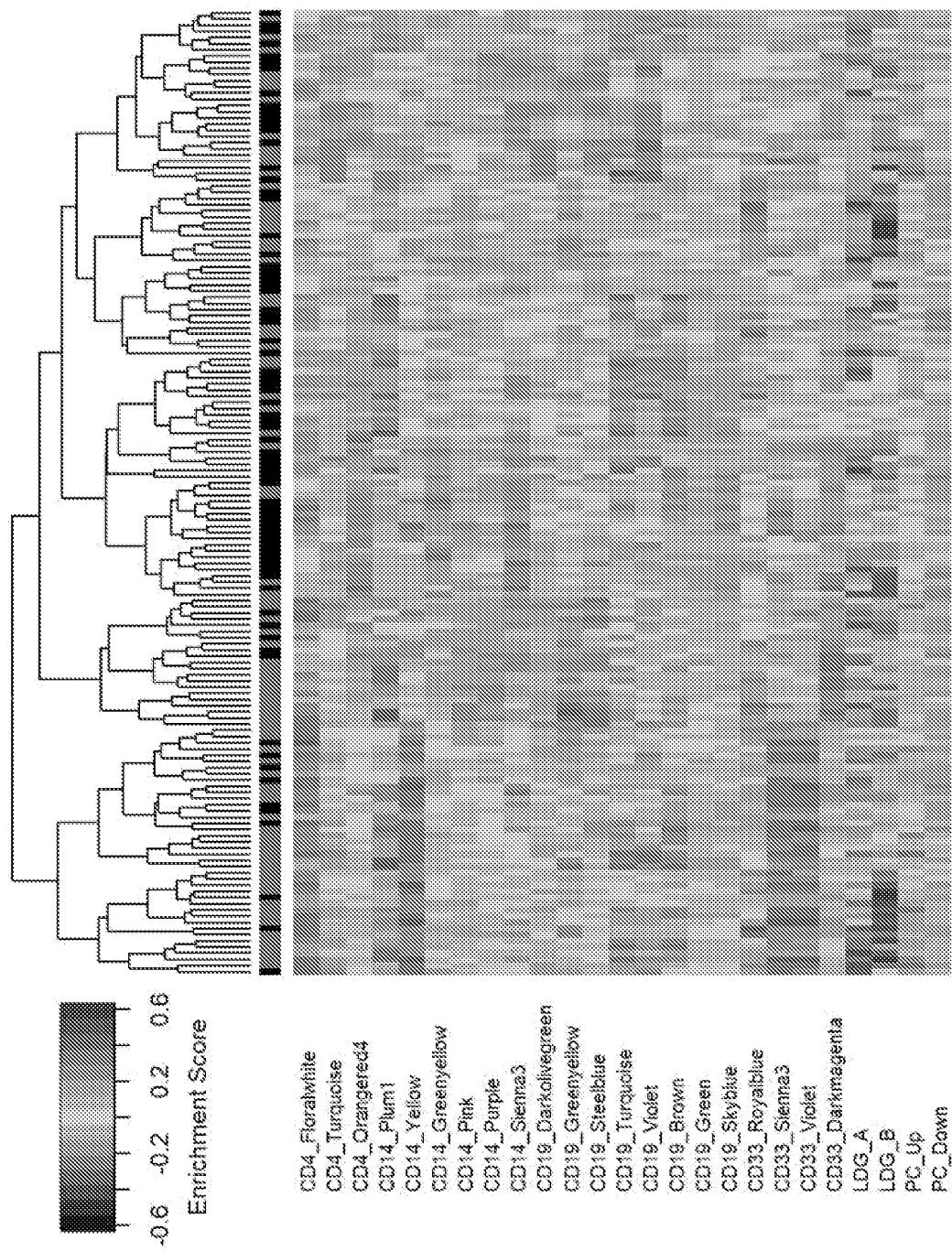


FIG. 2D



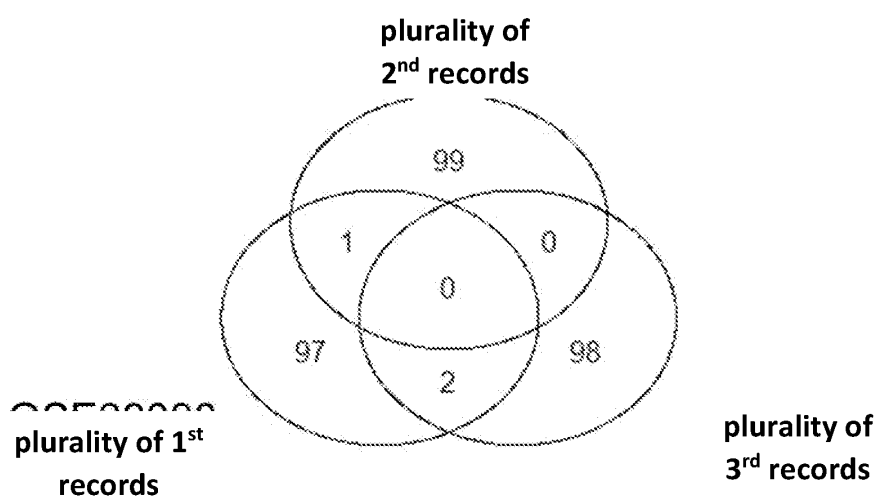


FIG. 3

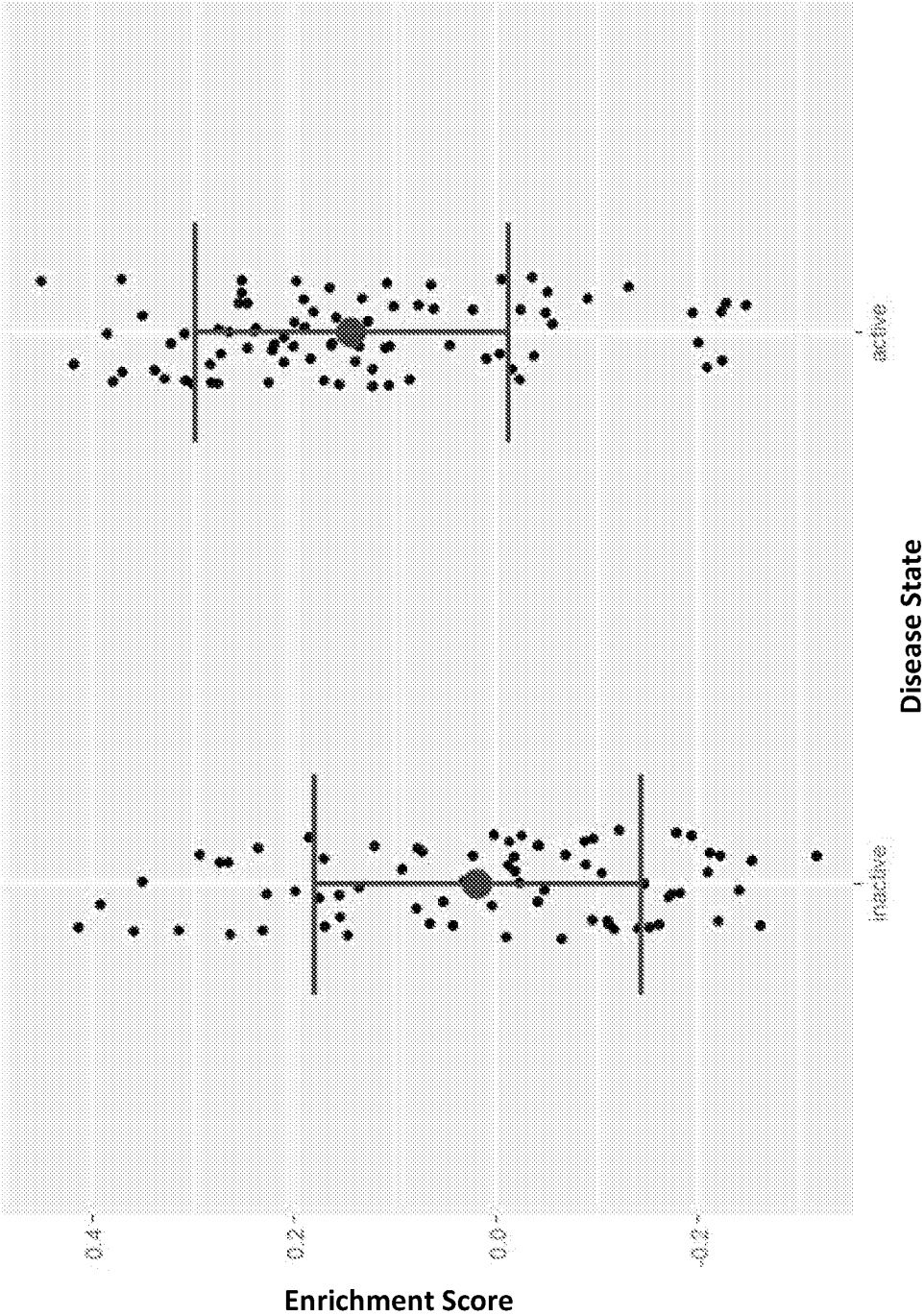


FIG. 4A

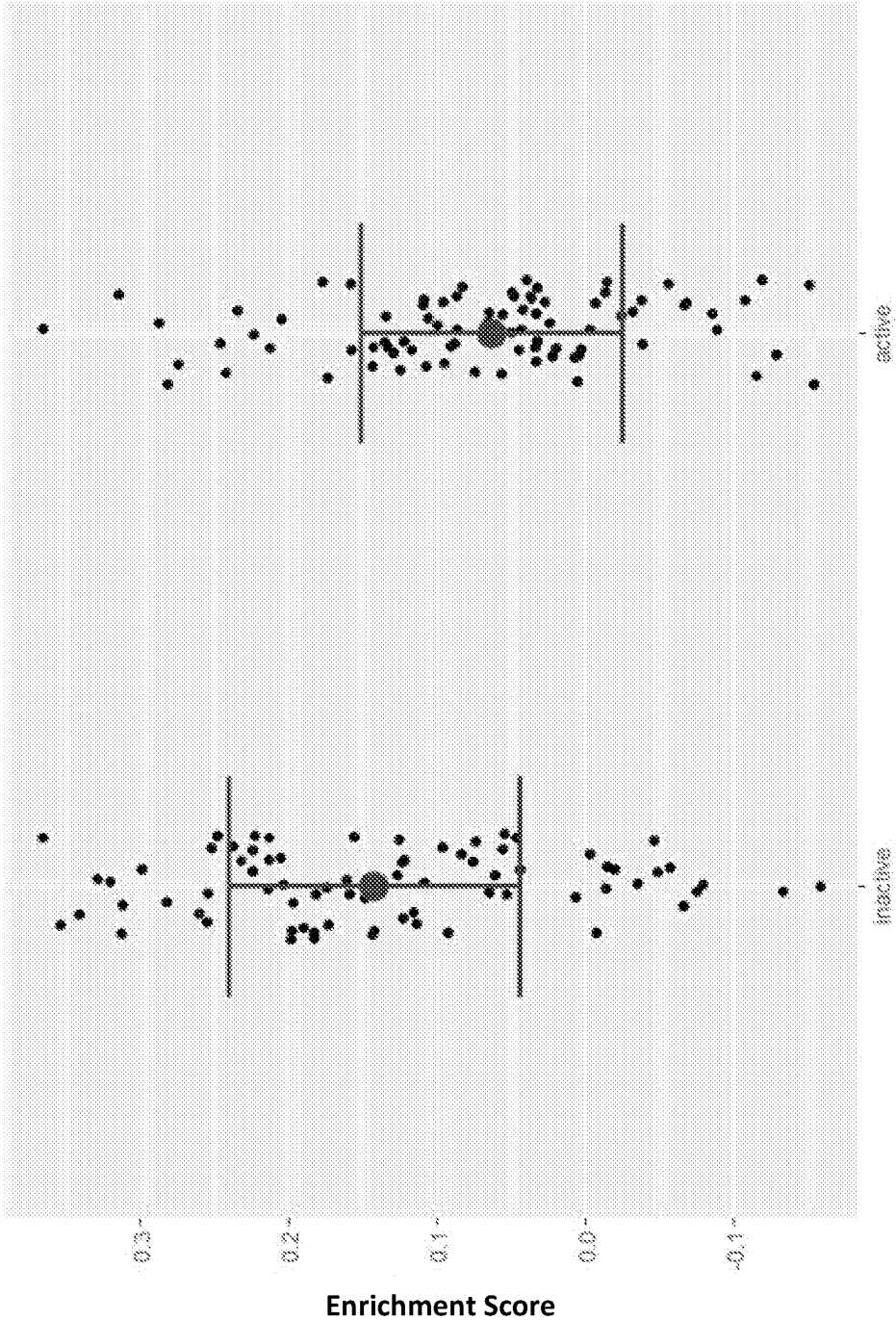


FIG. 4B

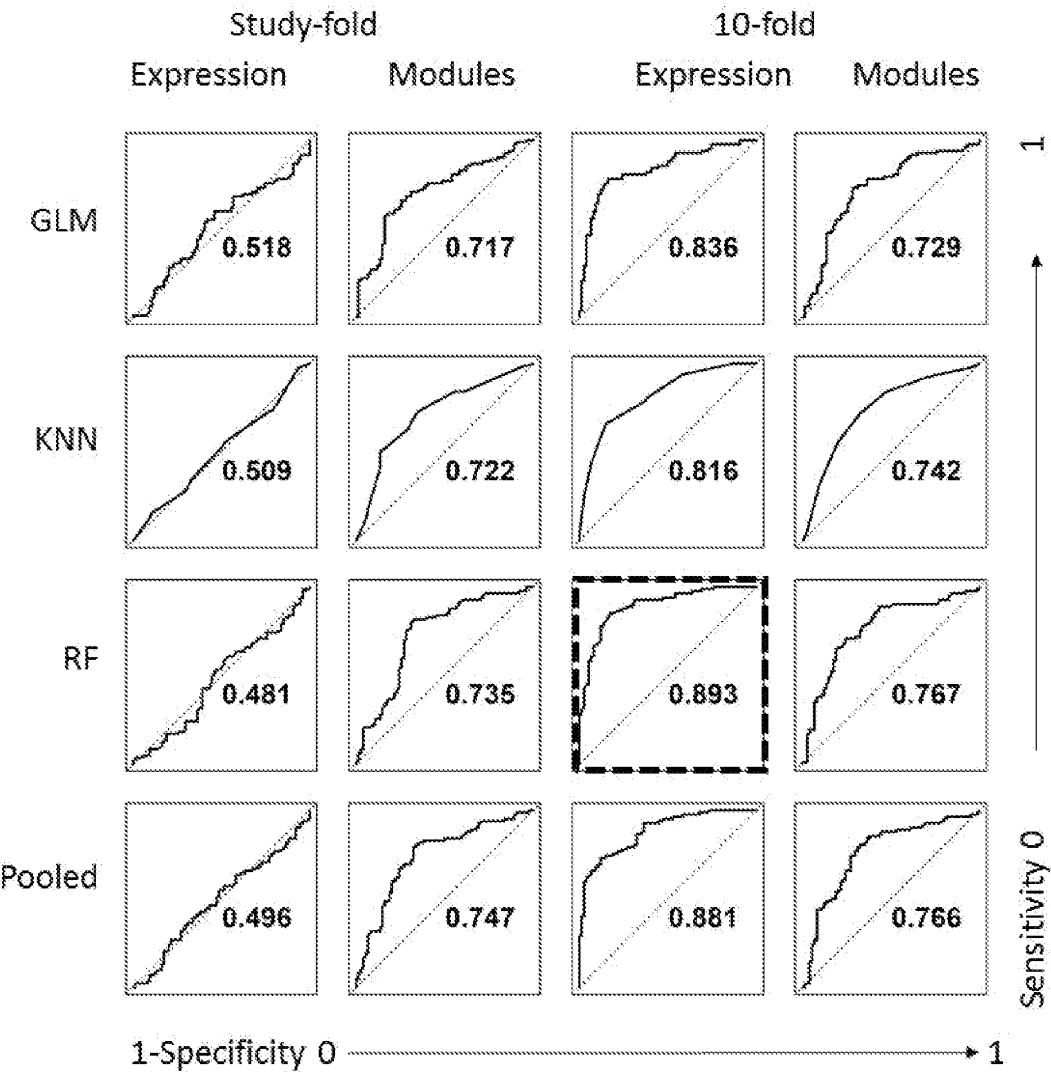


FIG. 5

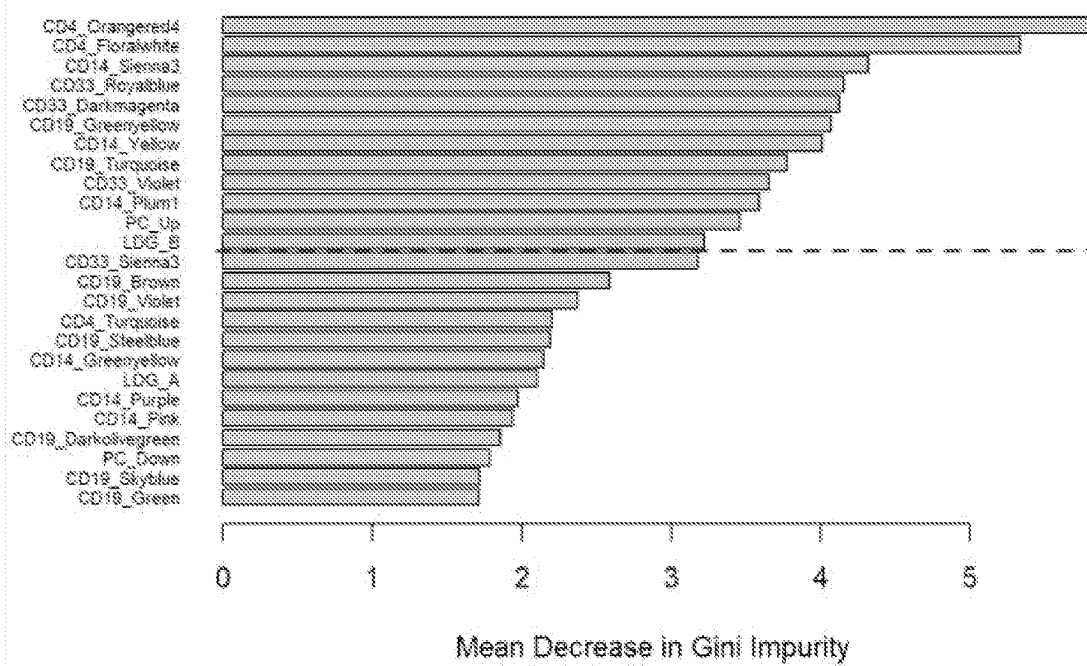


FIG. 6A

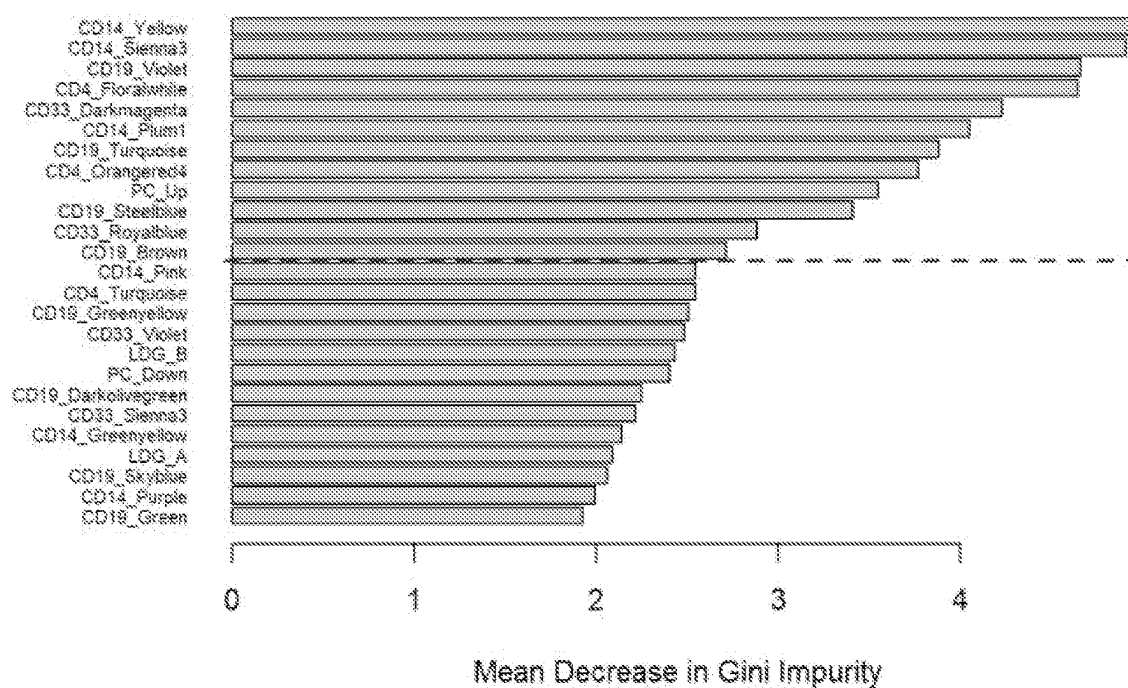


FIG. 6B

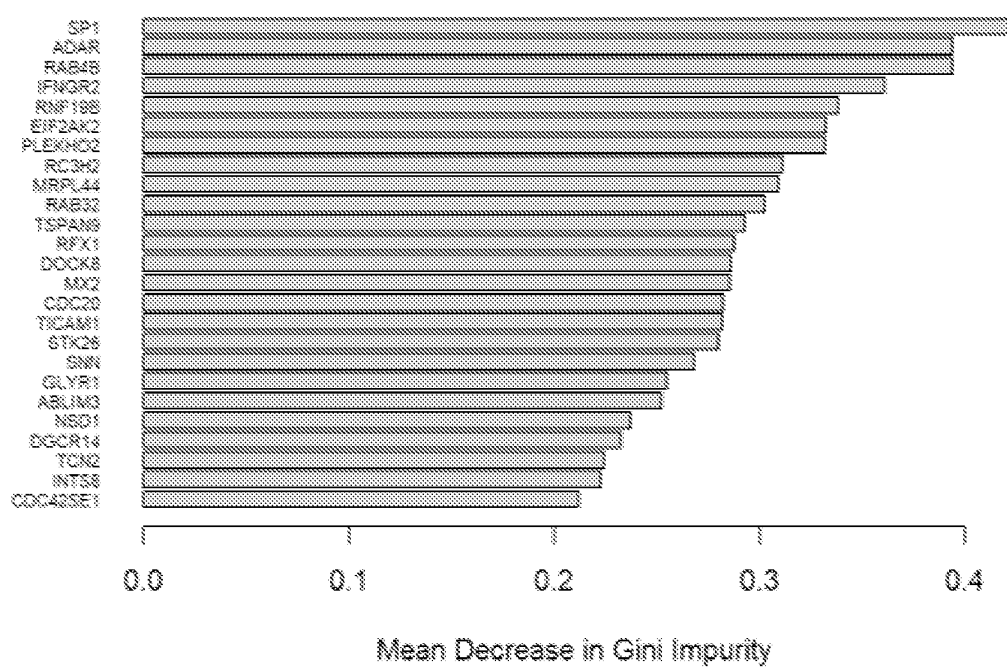


FIG. 6C

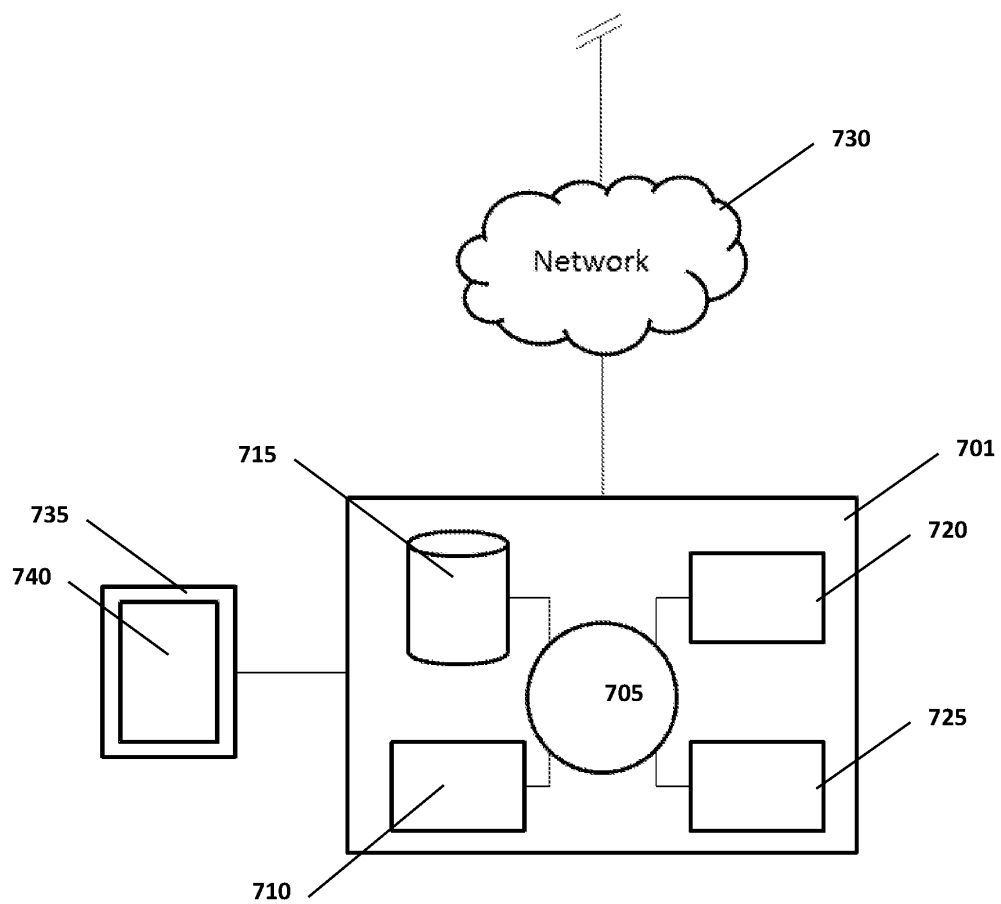


FIG. 7

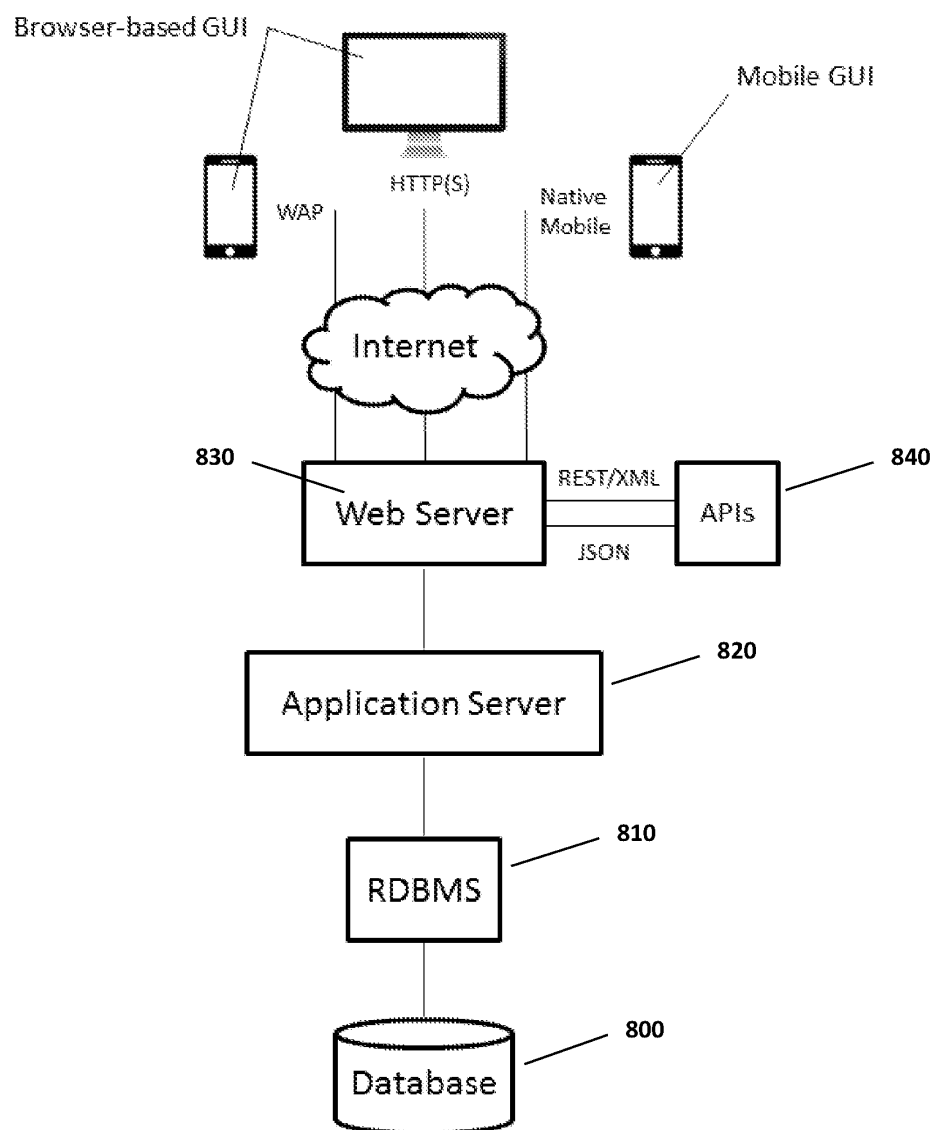


FIG. 8

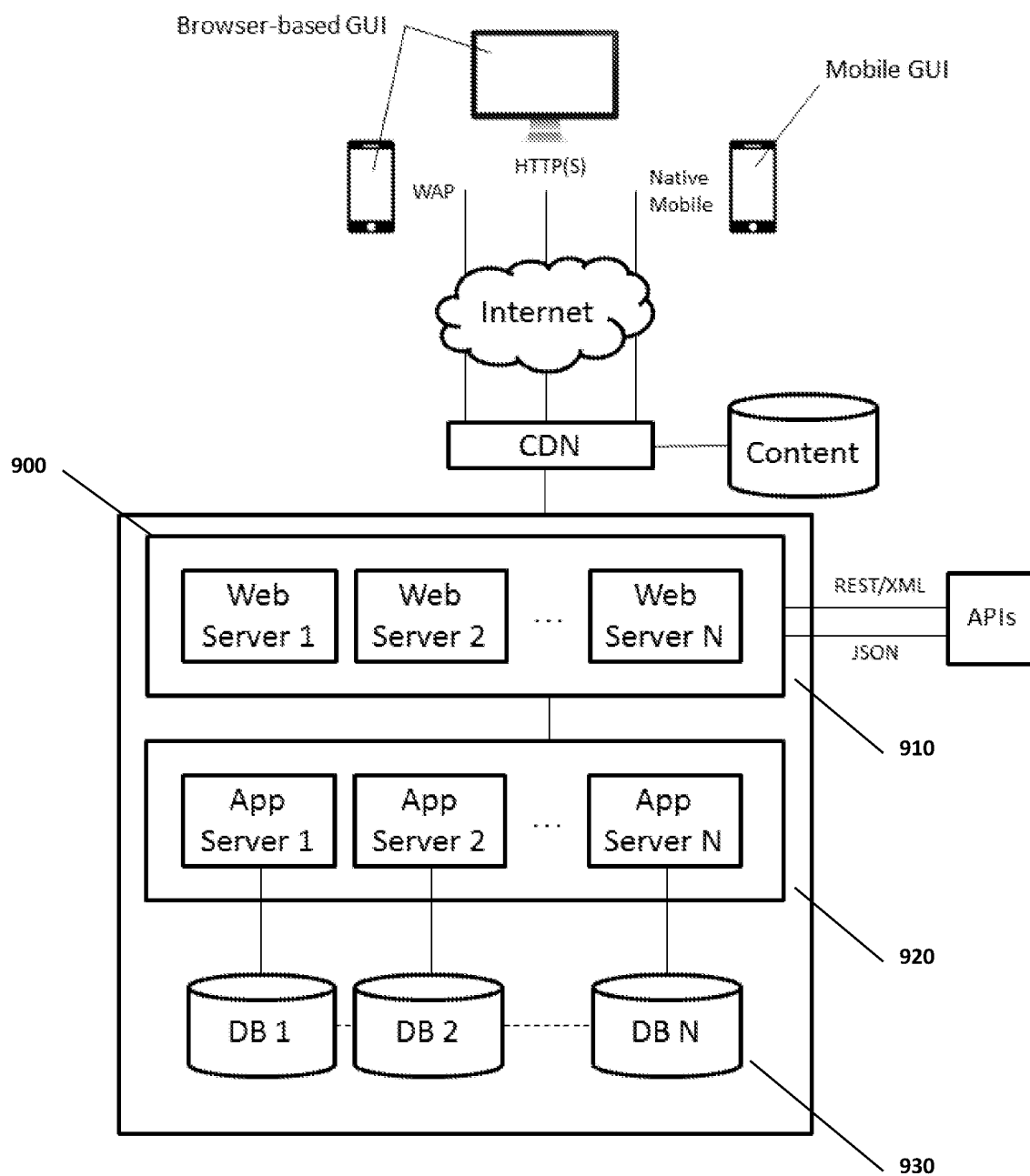


FIG. 9

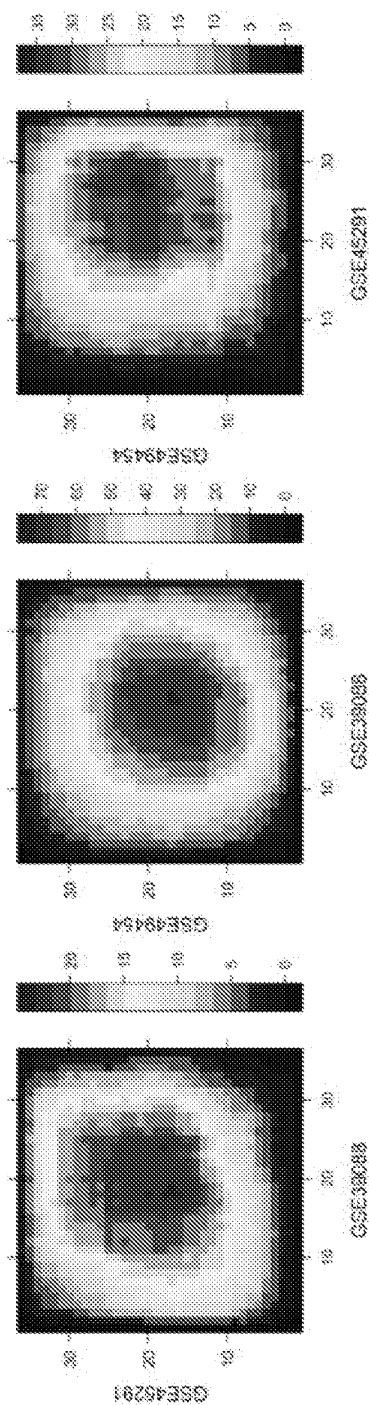


FIG. 10A

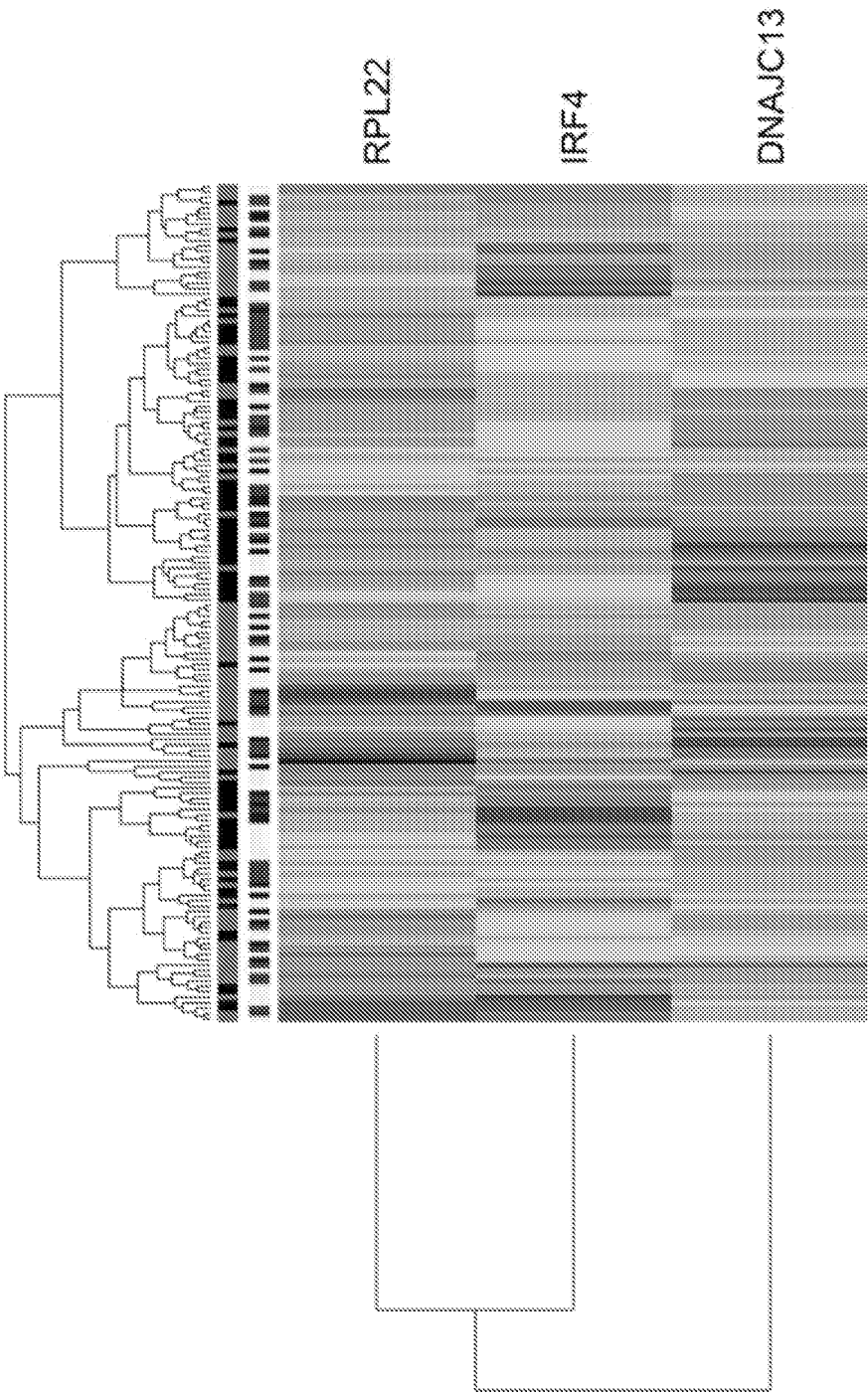


FIG. 10B

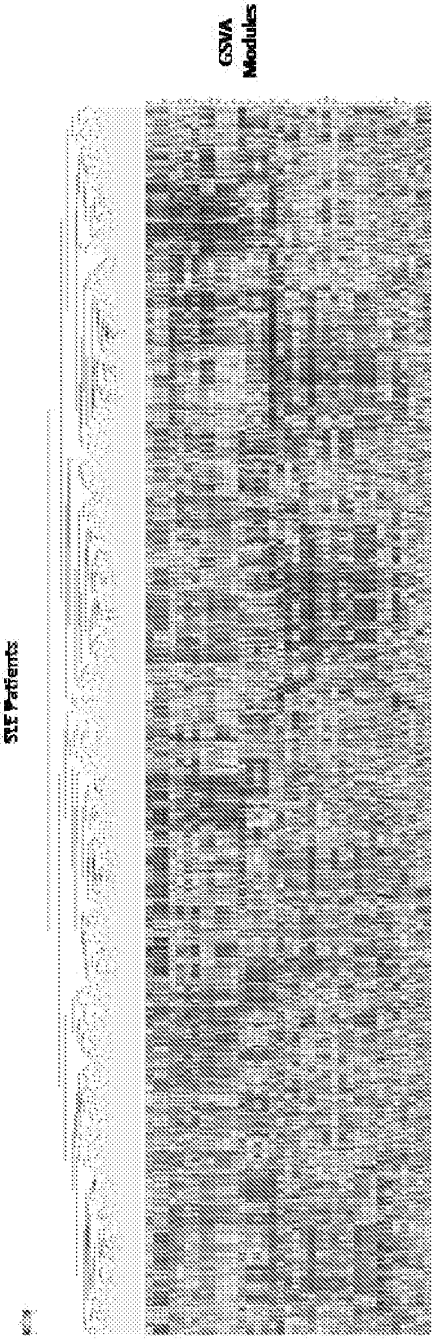


FIG. 11

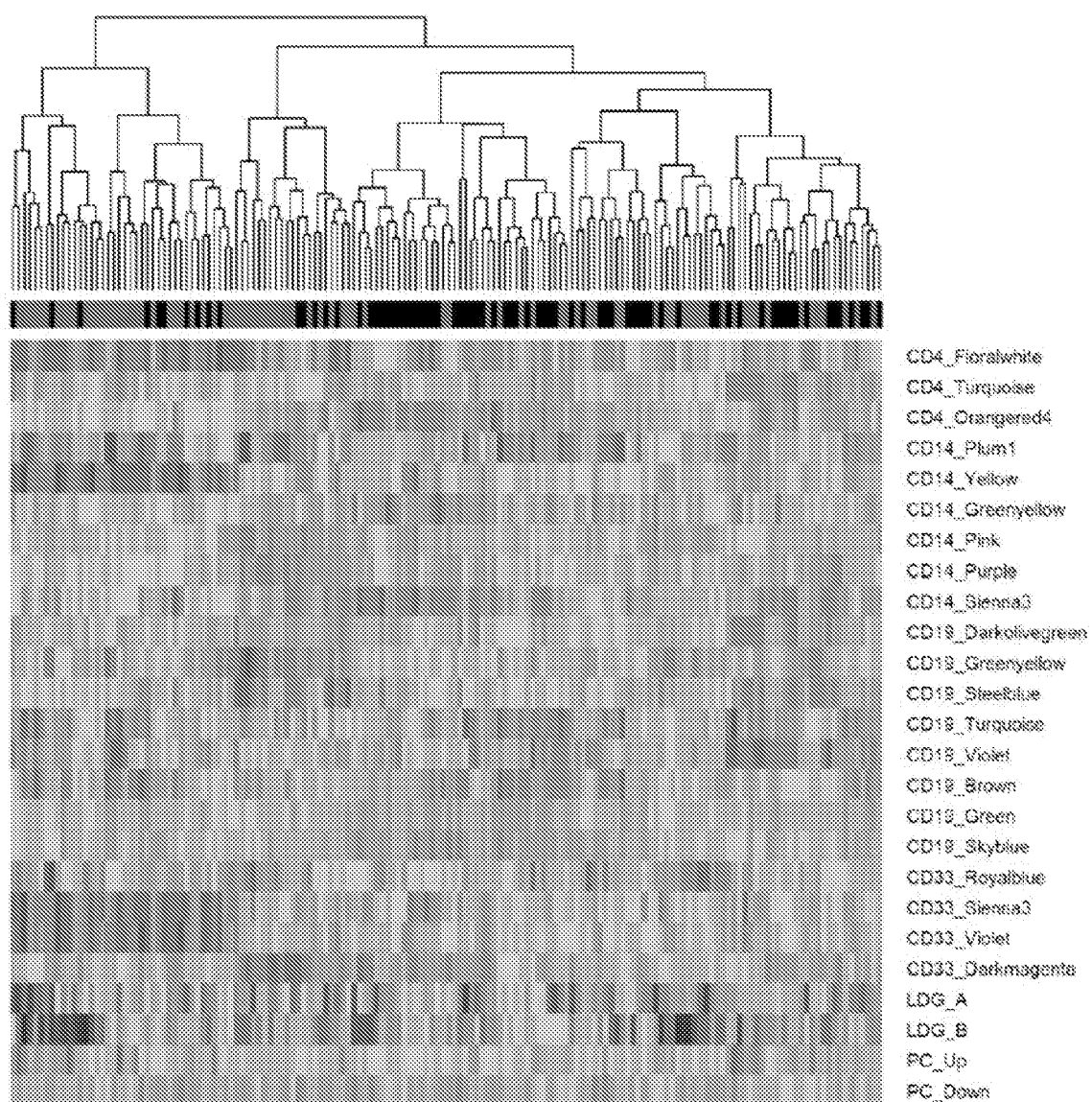


FIG. 12

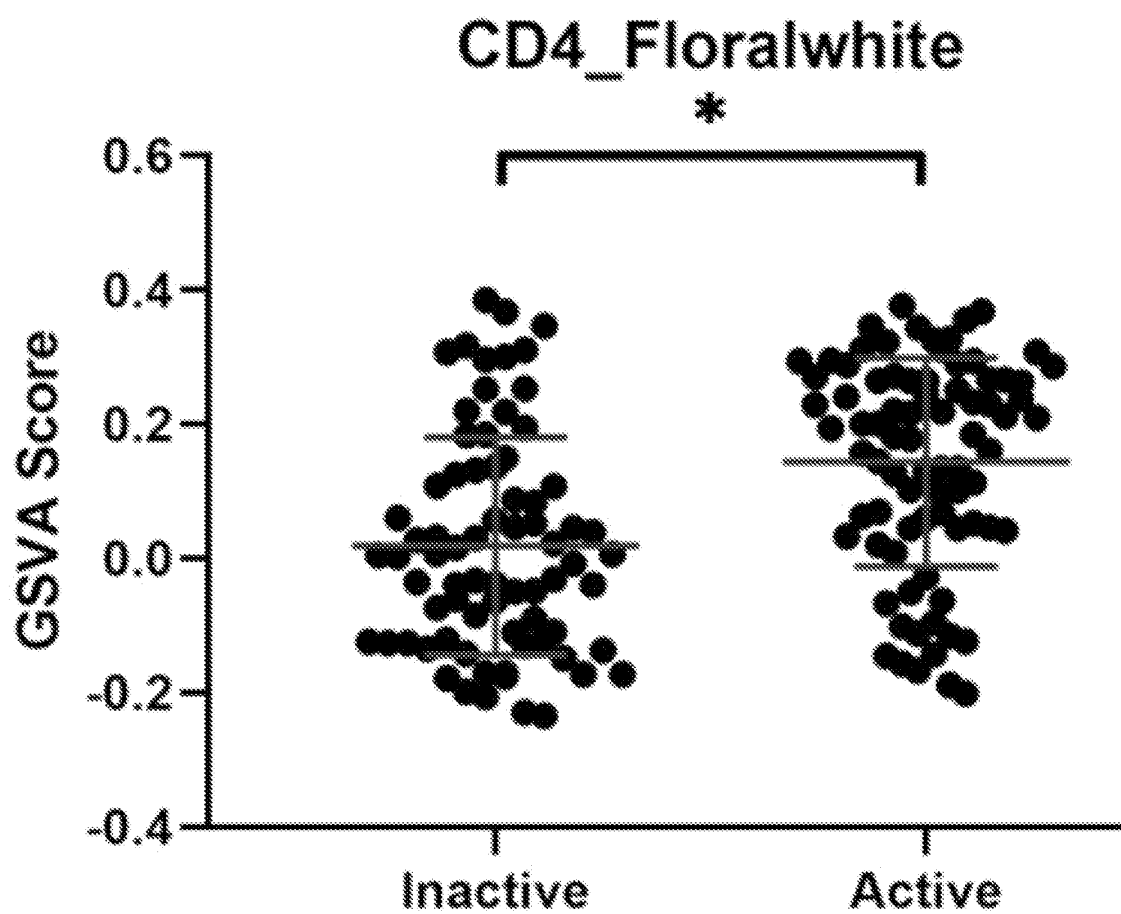


FIG. 13A

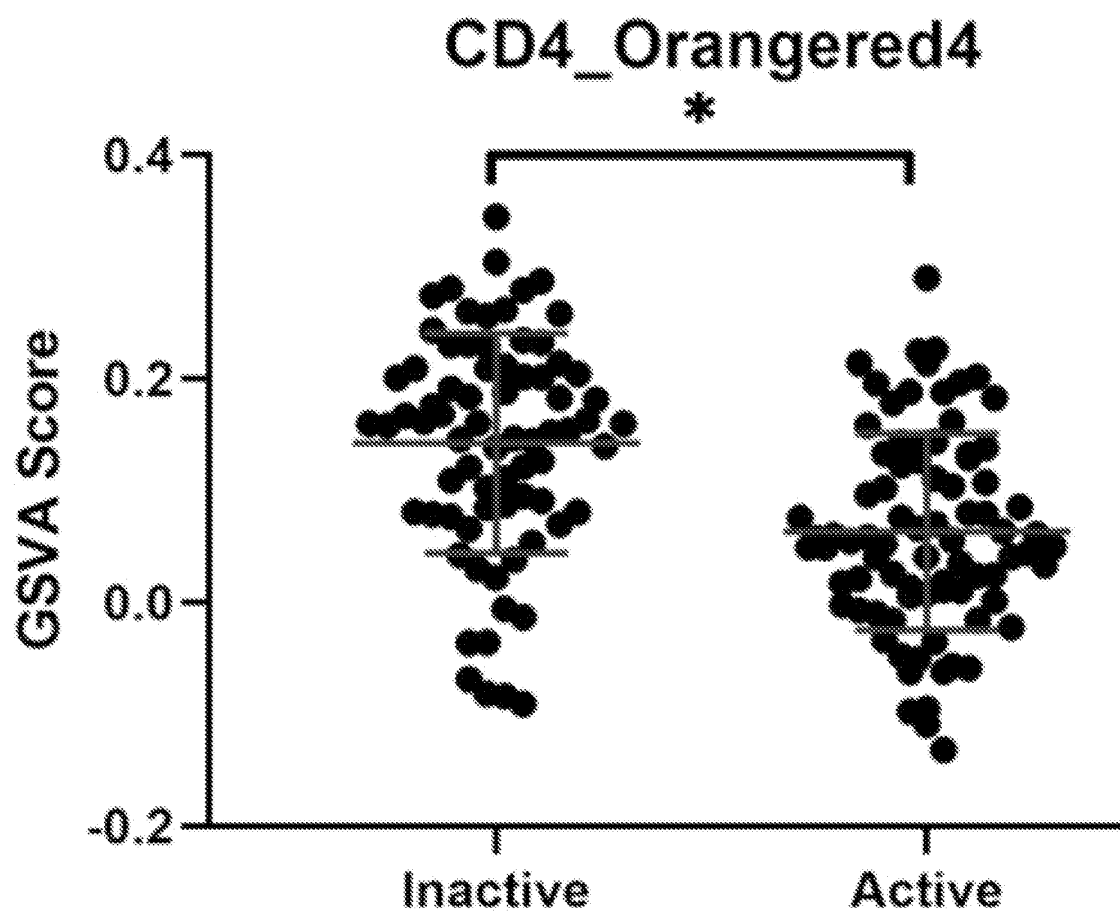


FIG. 13B

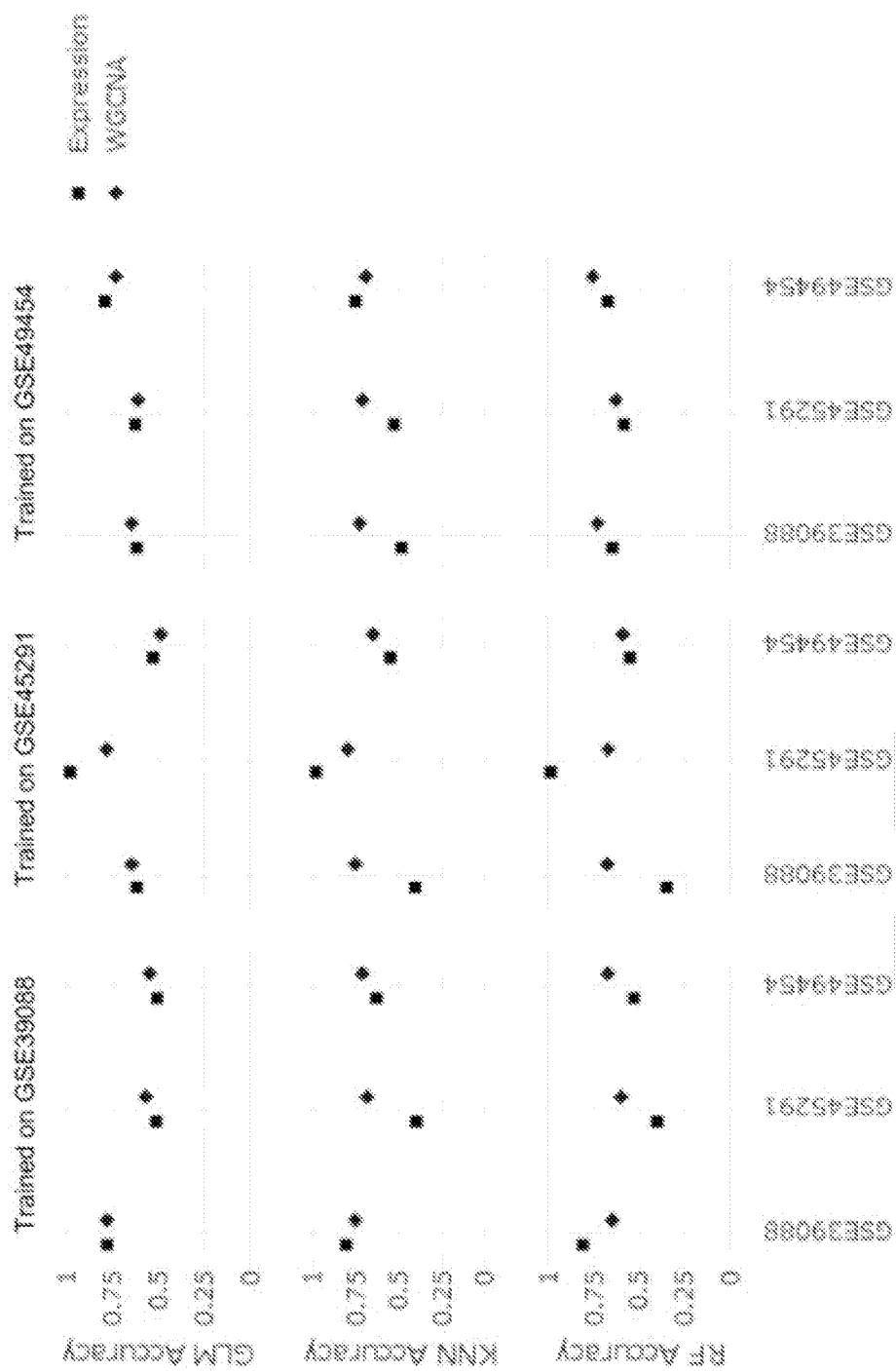


FIG. 14

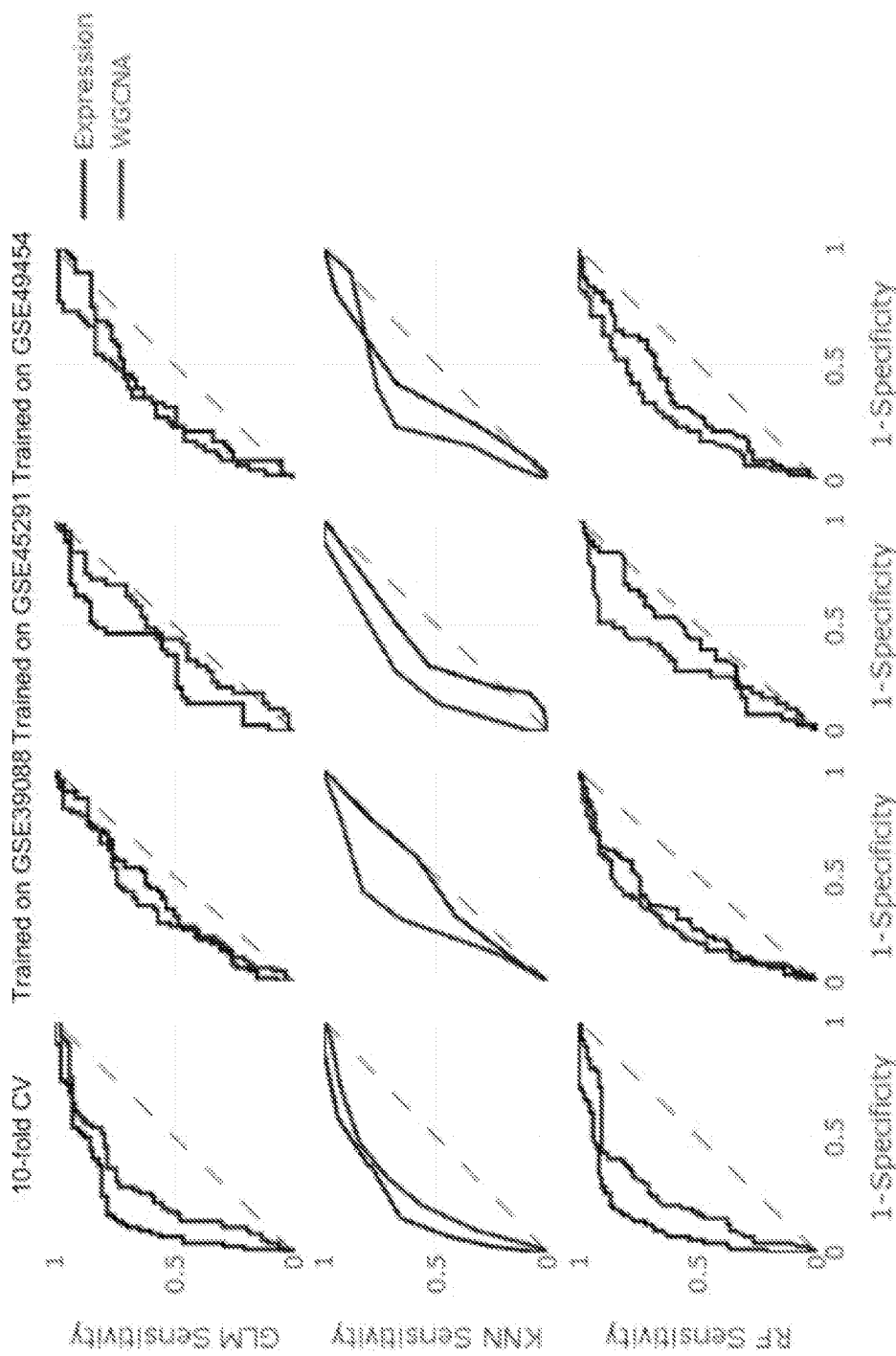


FIG. 15

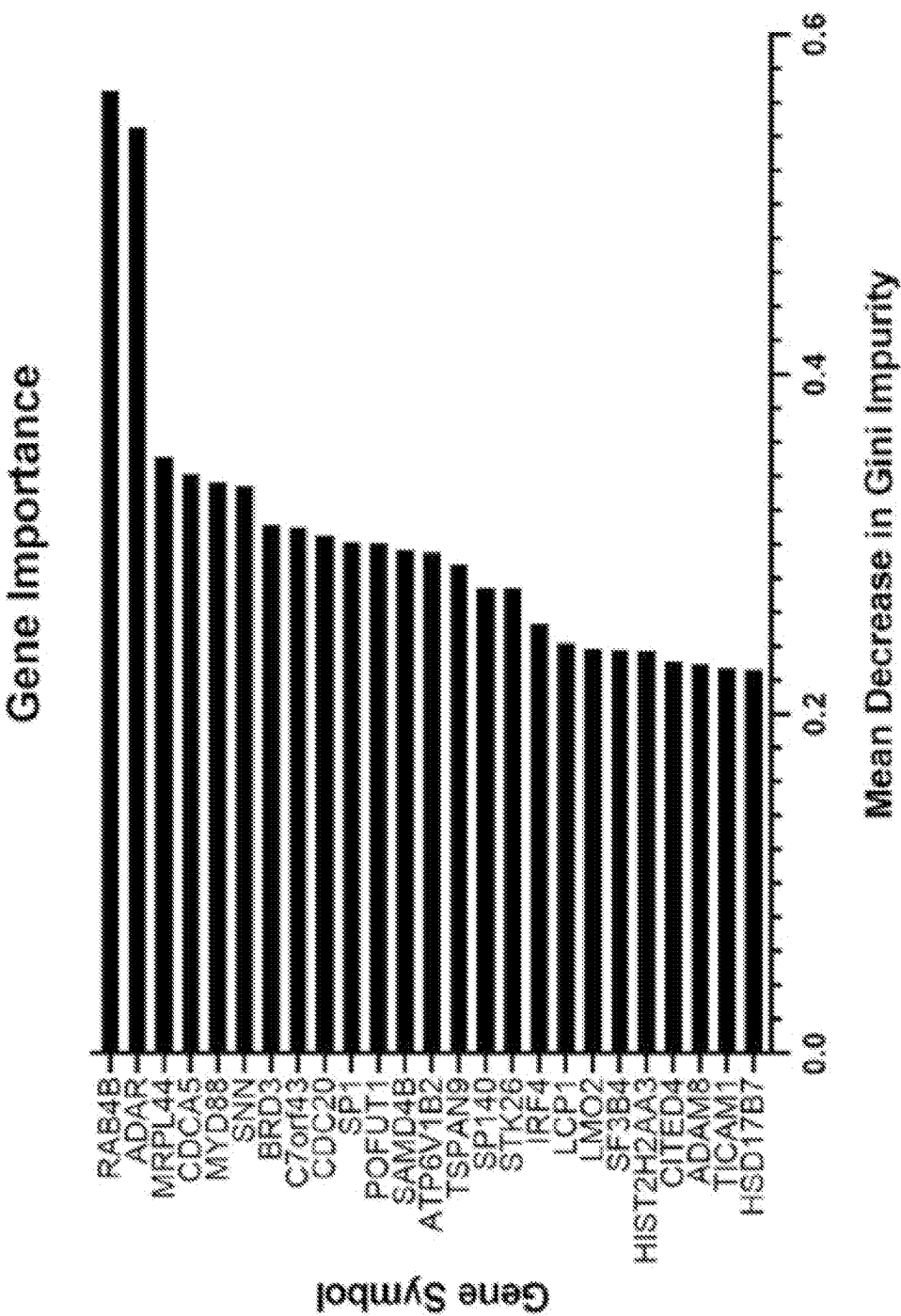


FIG. 16A

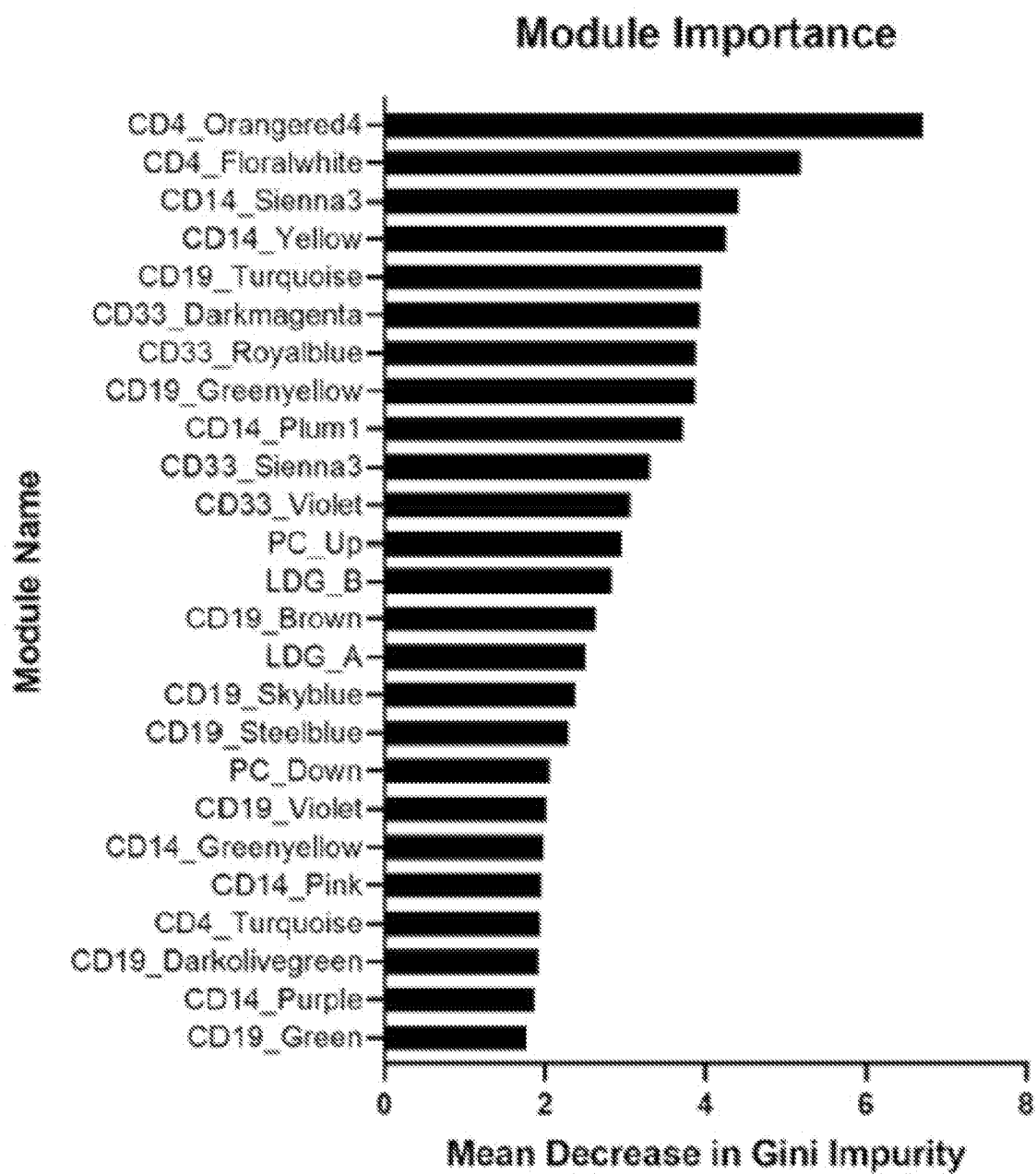


FIG. 16B

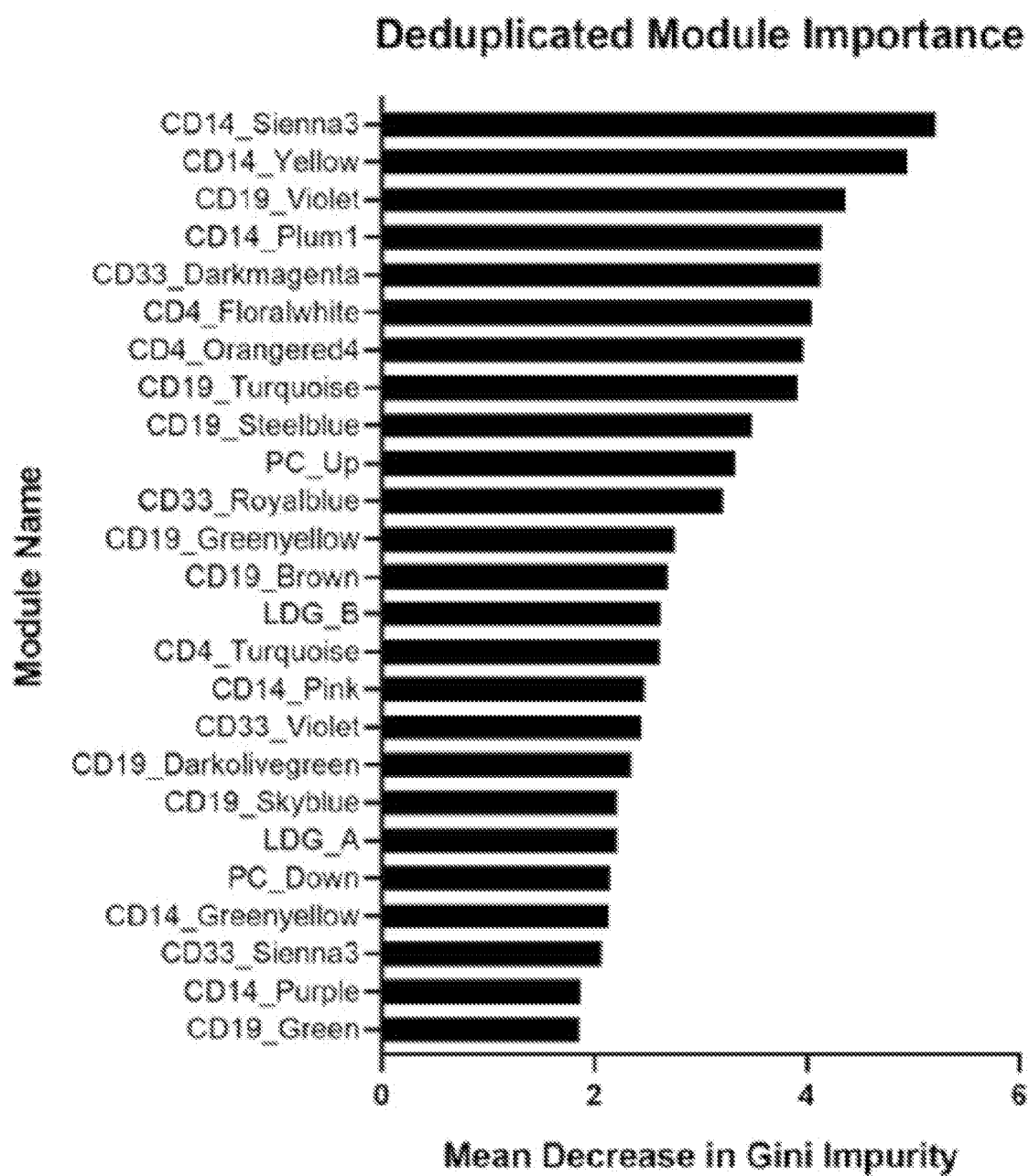


FIG. 16C

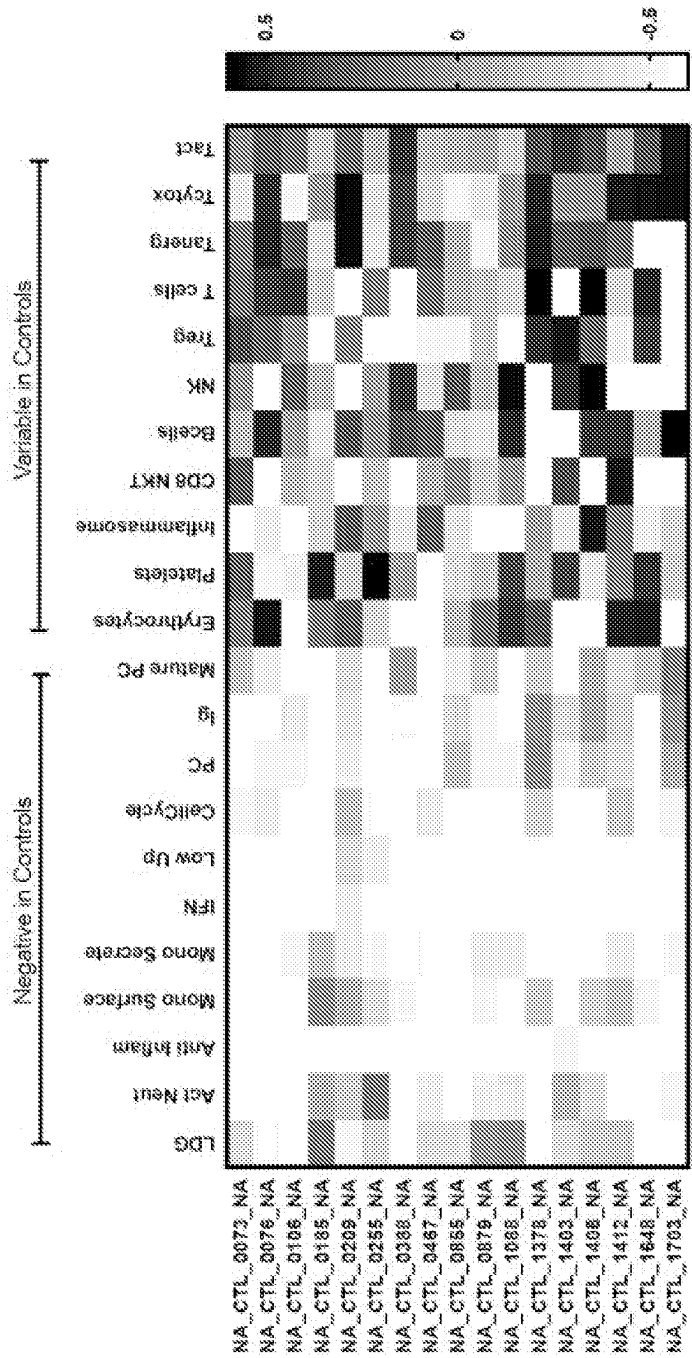
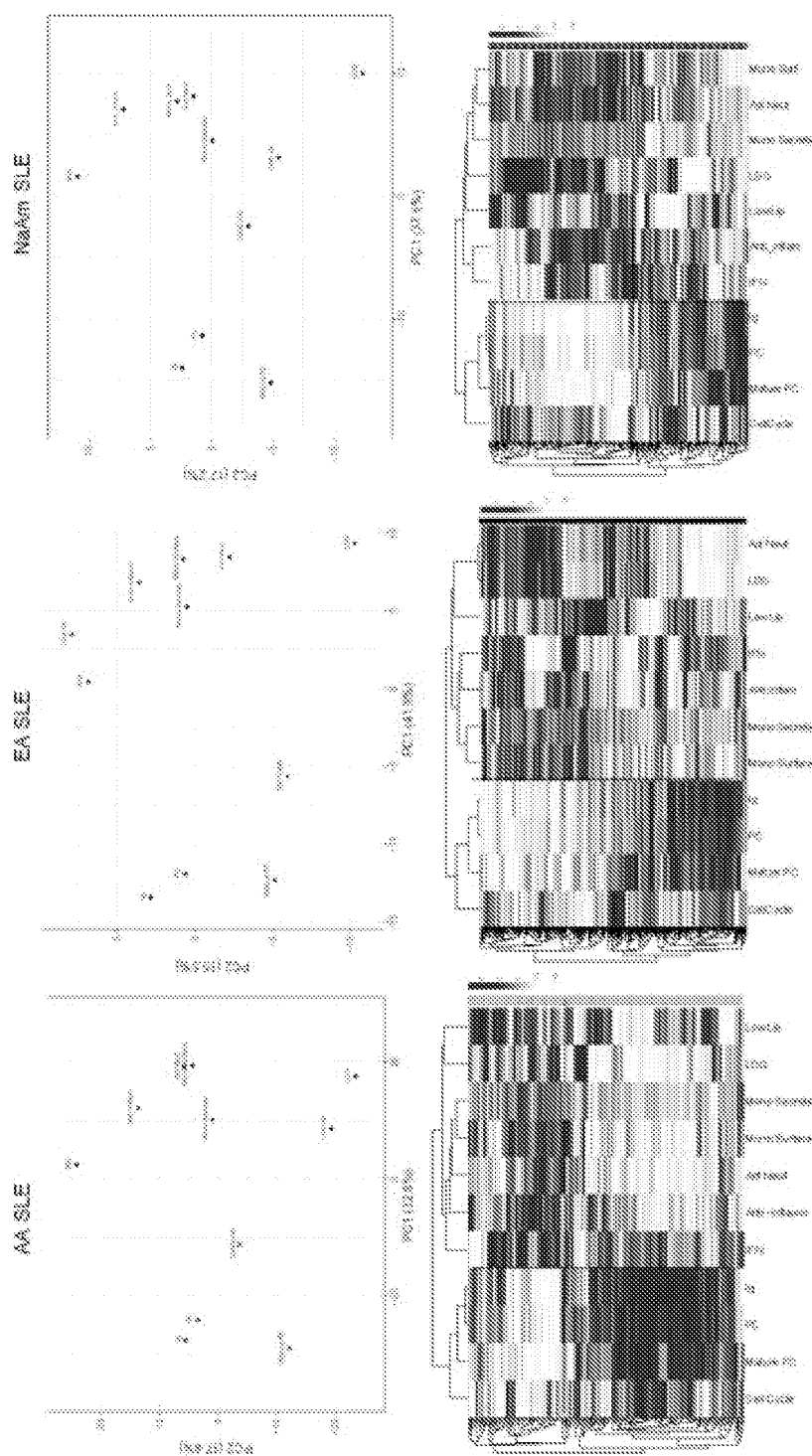


FIG. 17



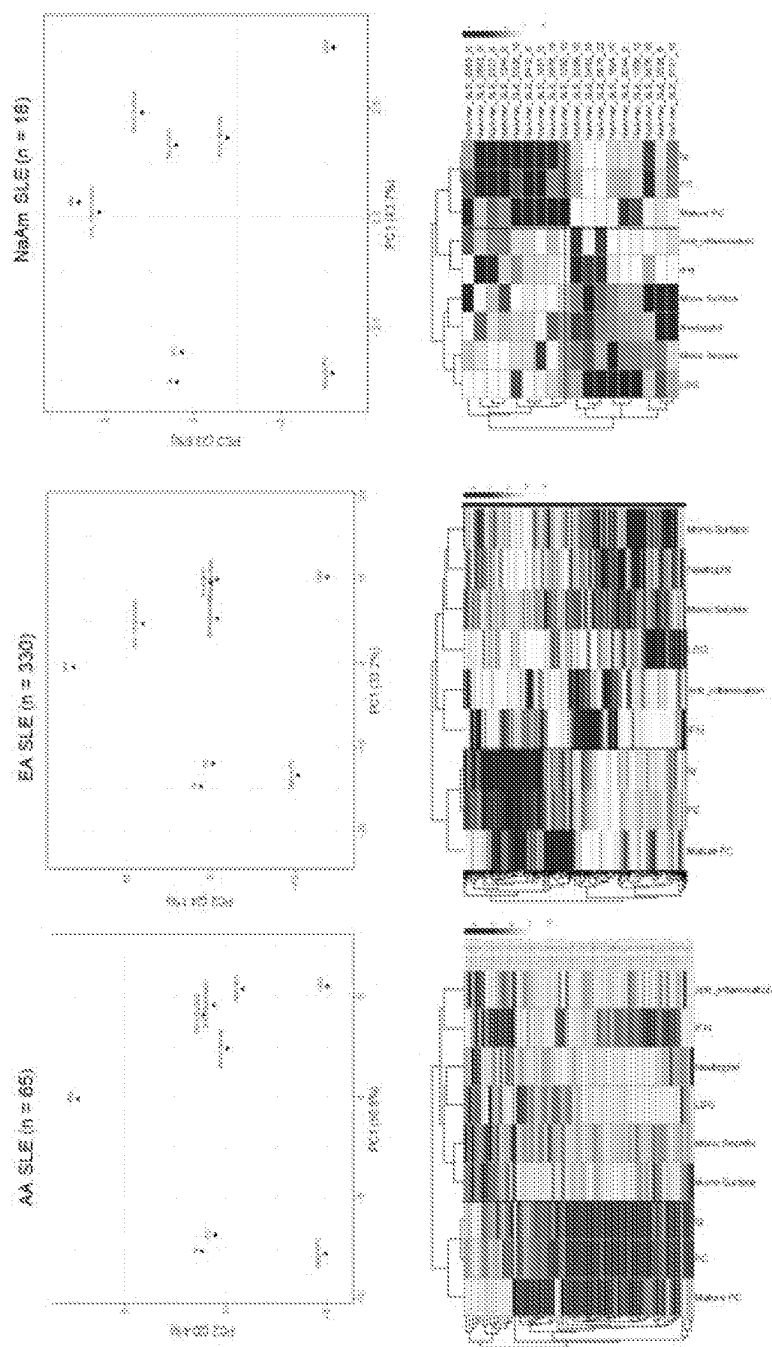


FIG. 19

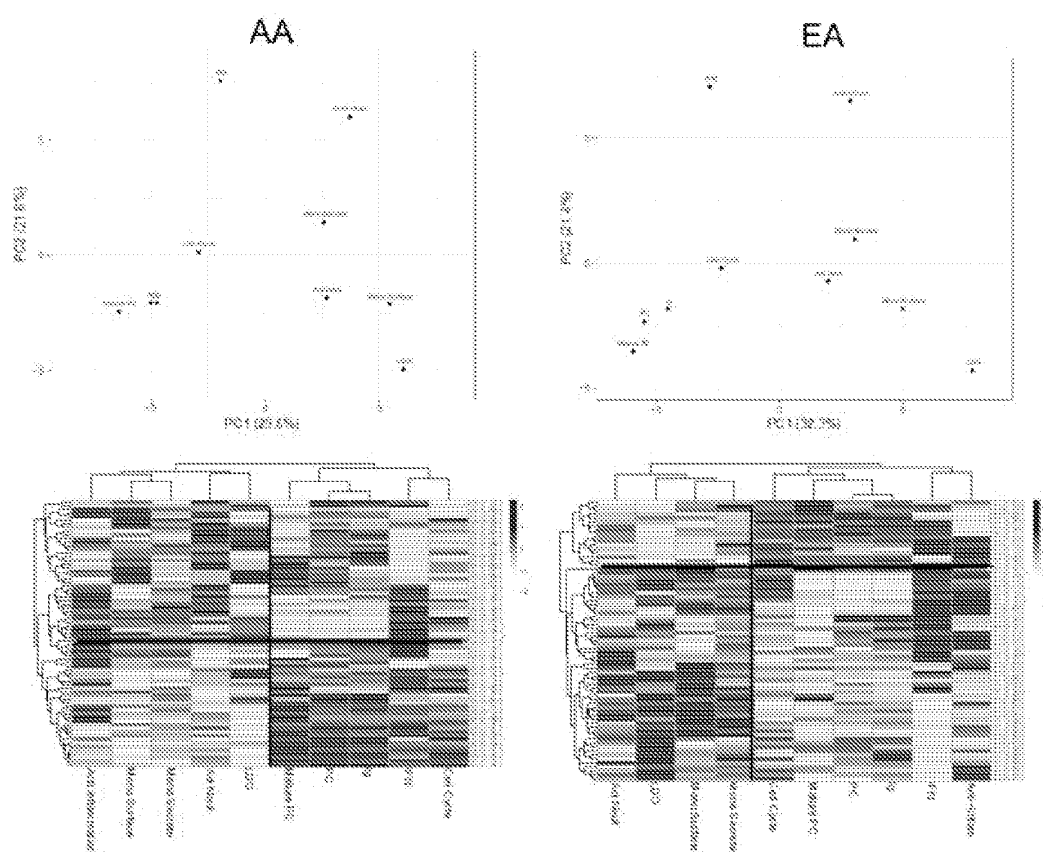


FIG. 20

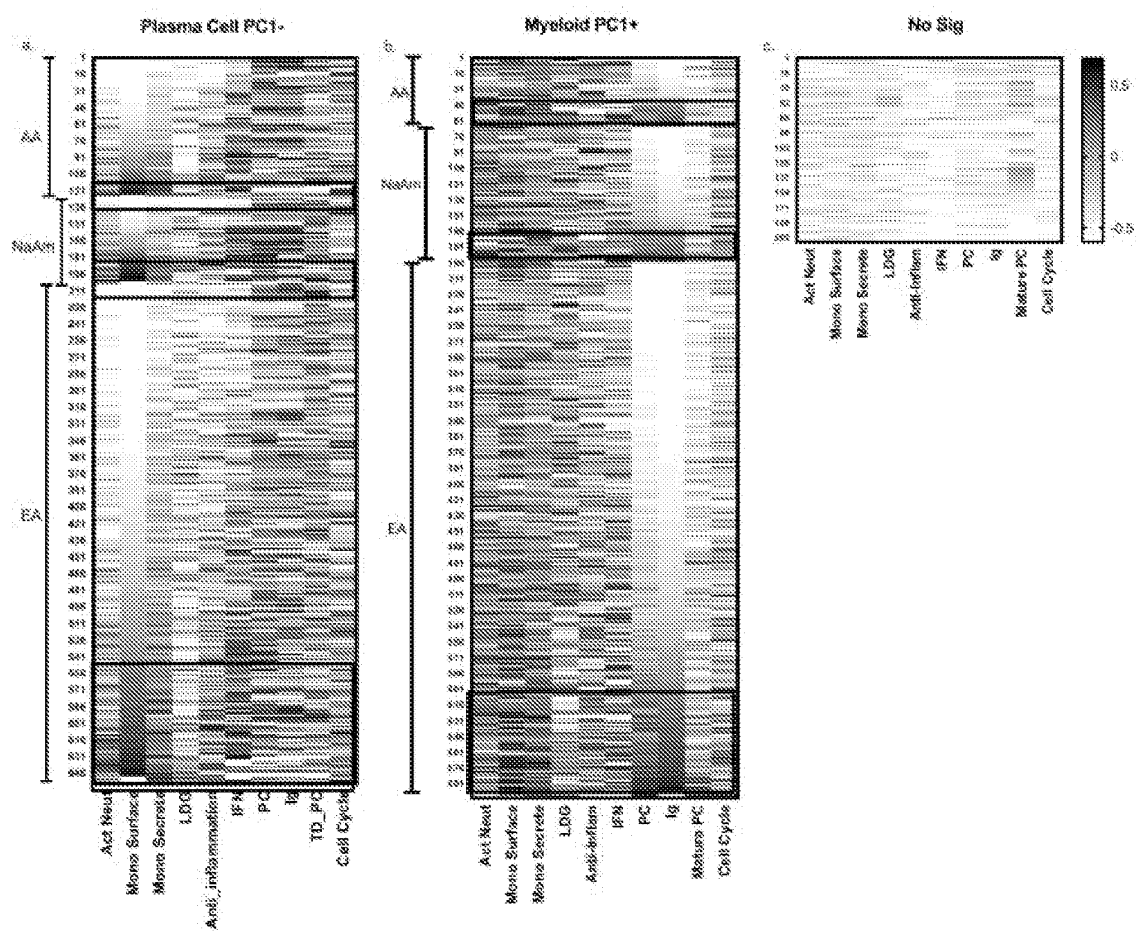


FIG. 21

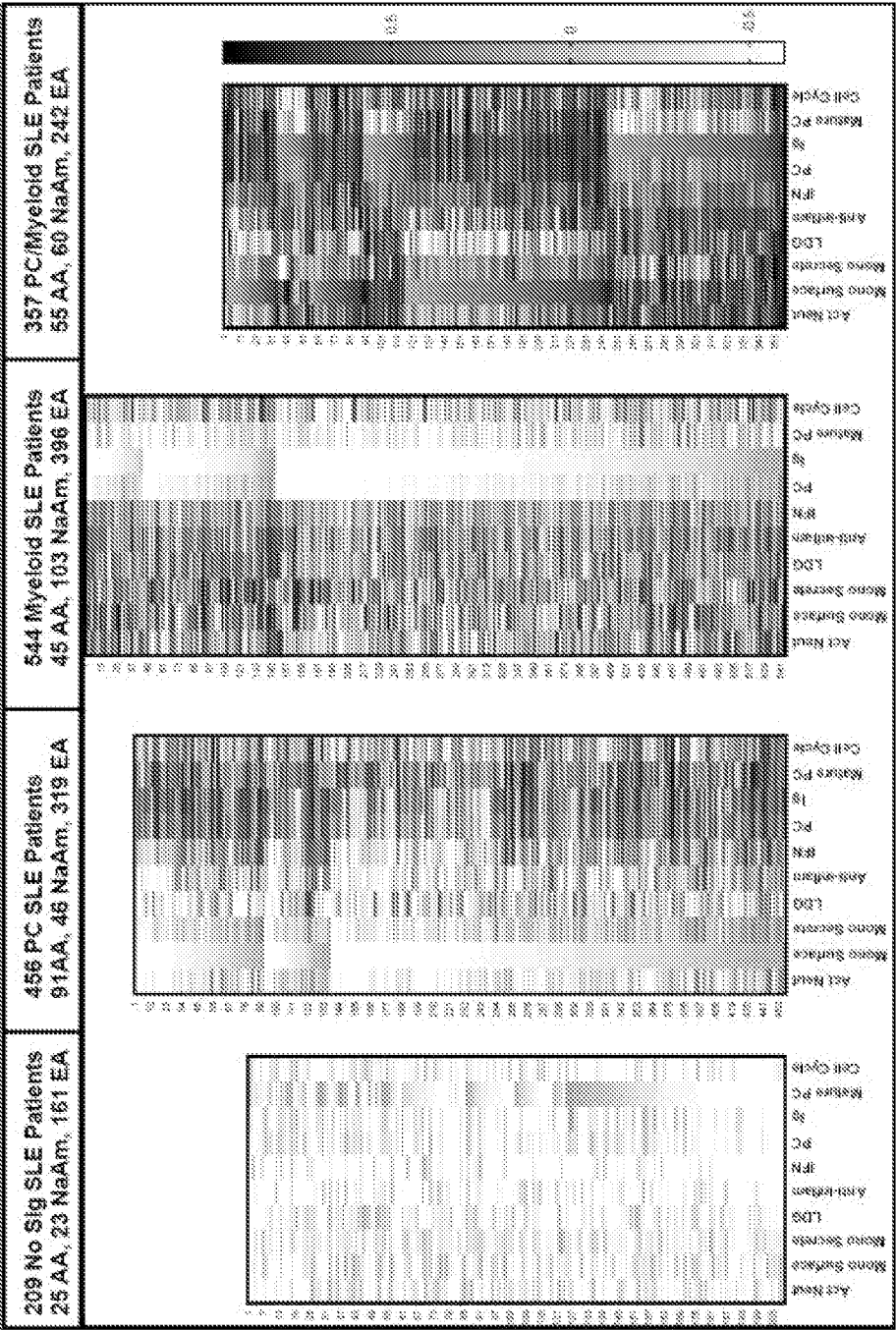


FIG. 22A

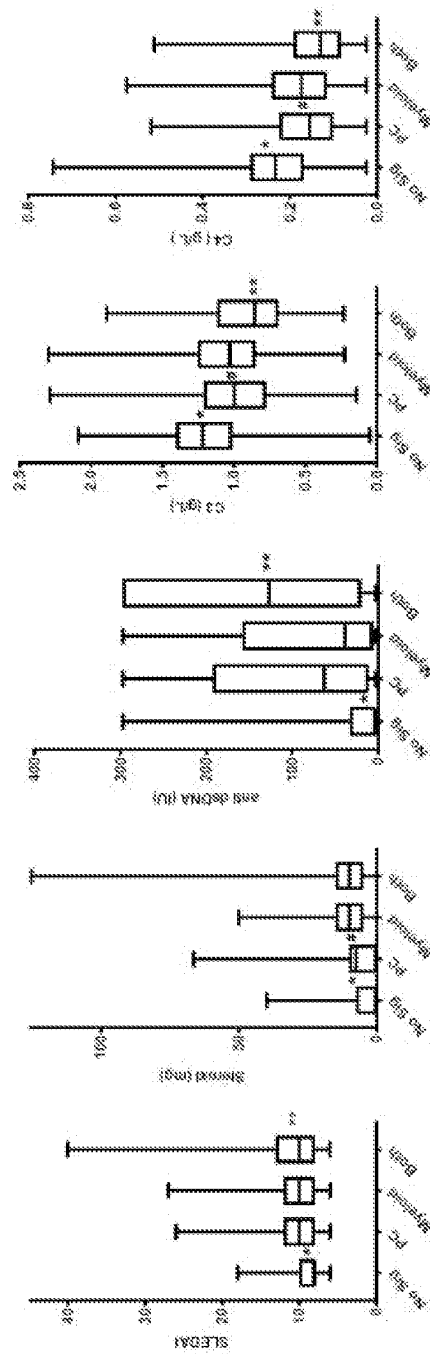


FIG. 22B

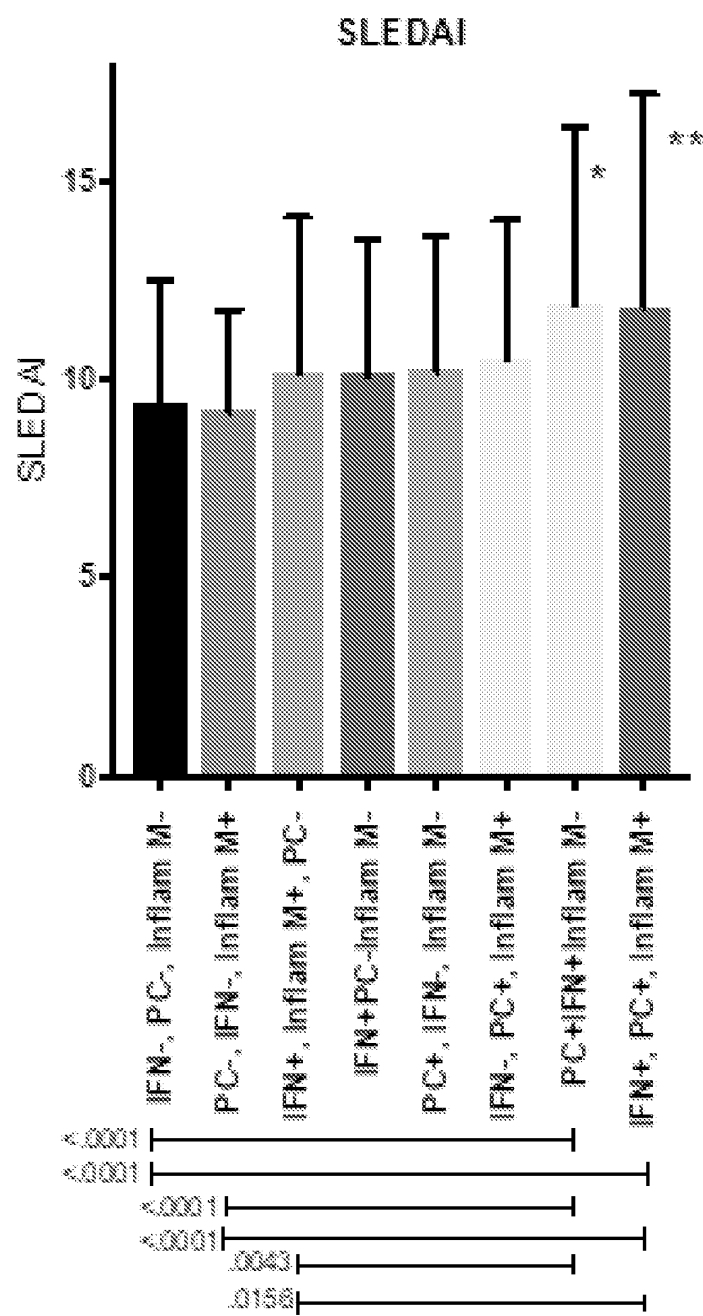


FIG. 23A

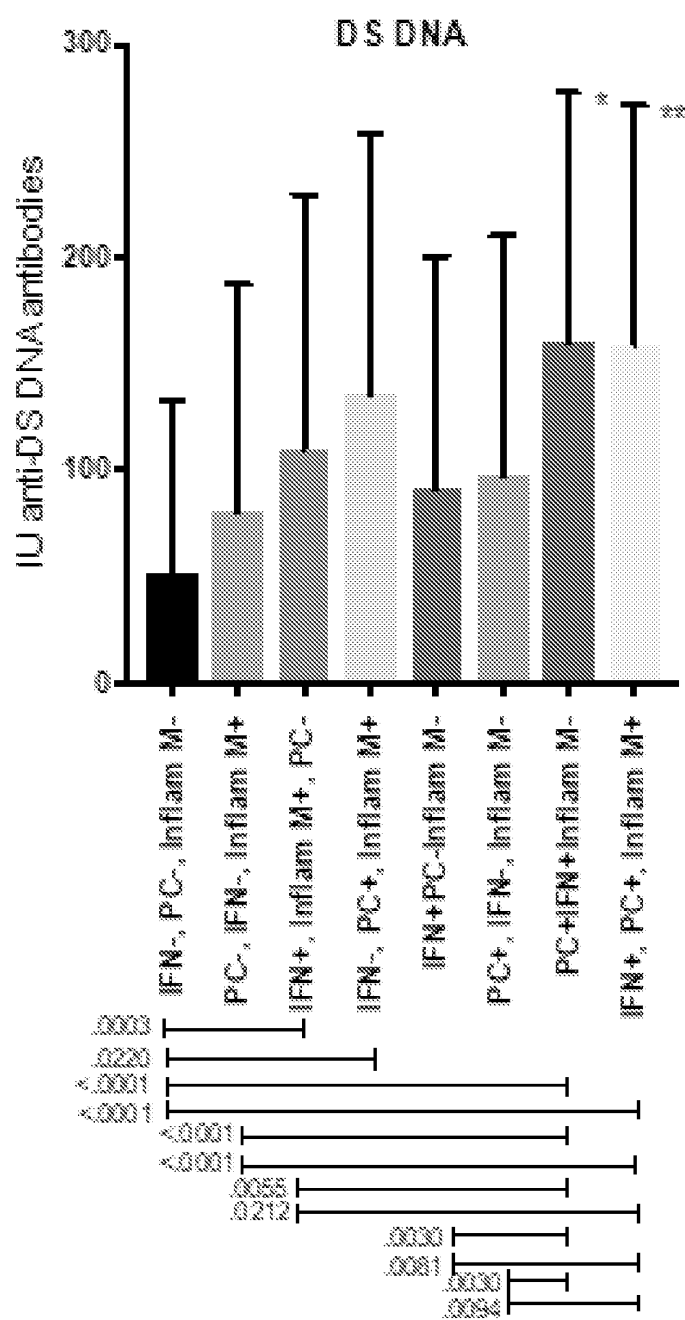


FIG. 23B

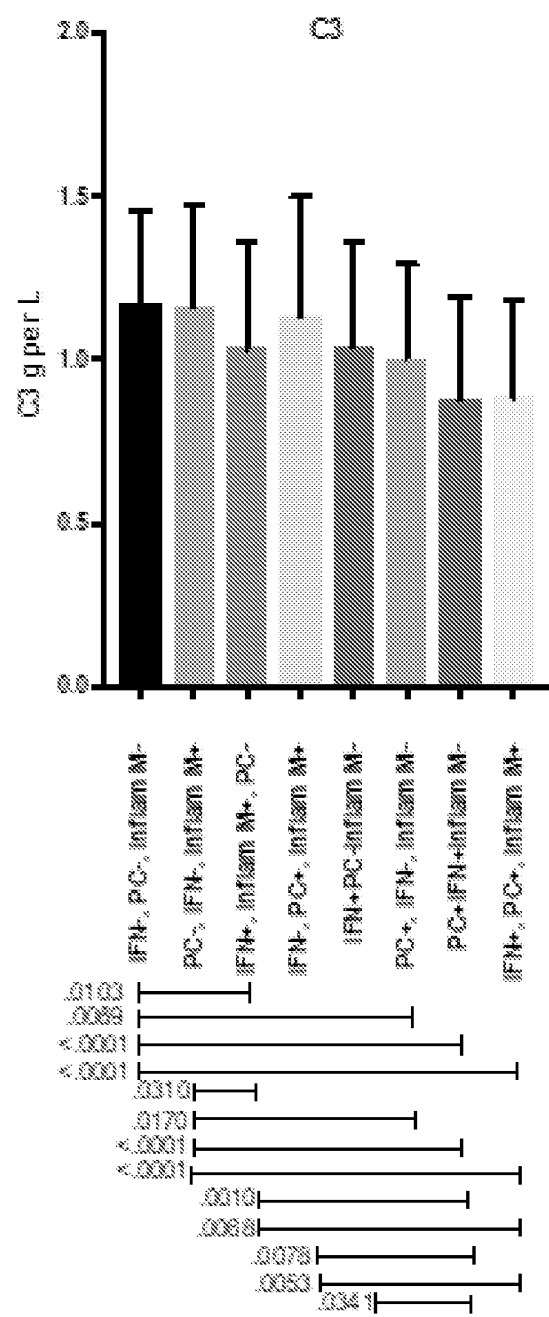


FIG. 23C

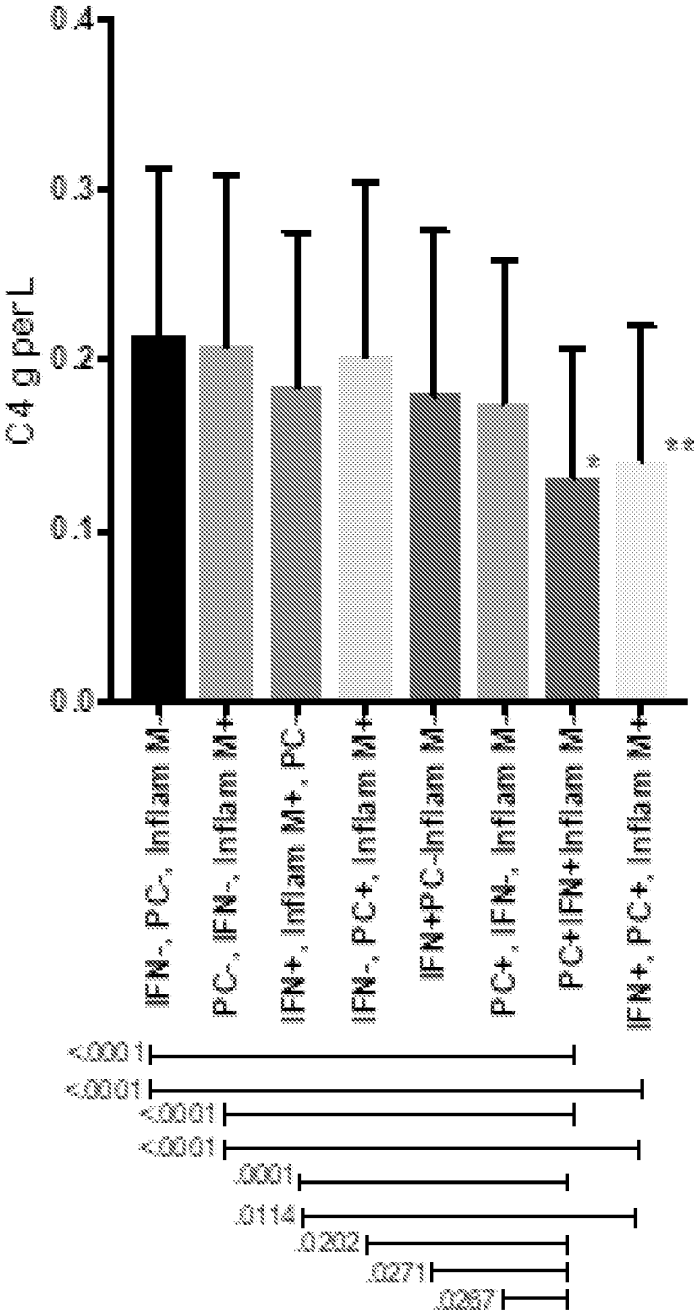


FIG. 23D

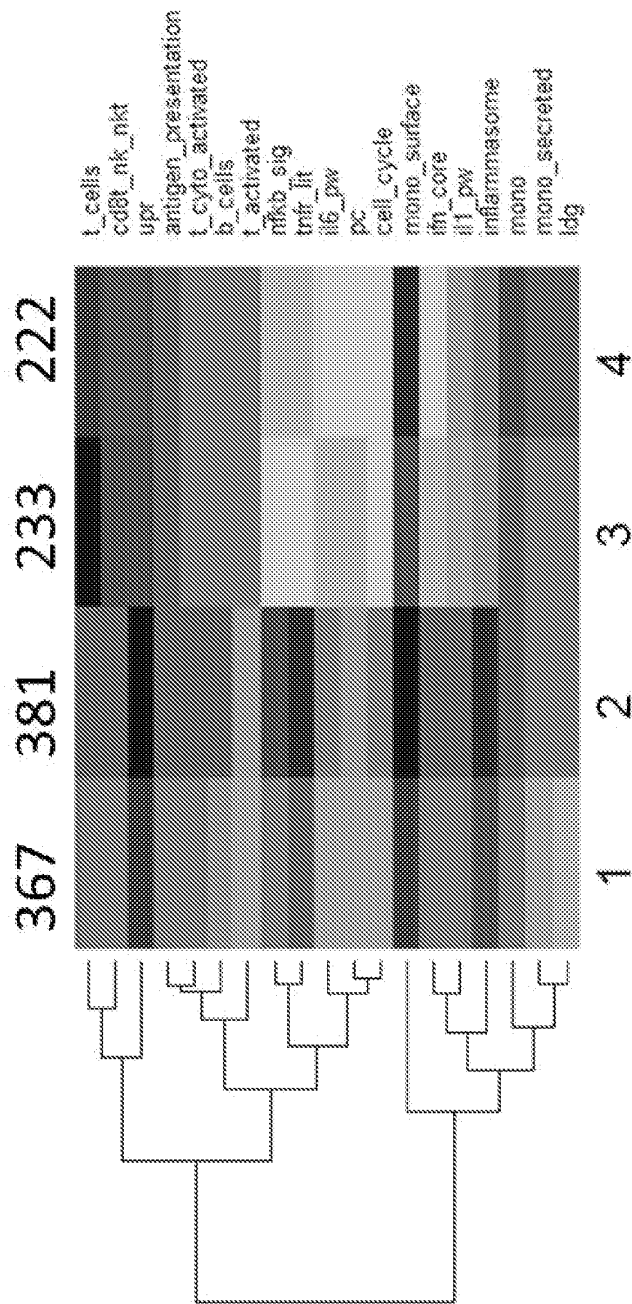
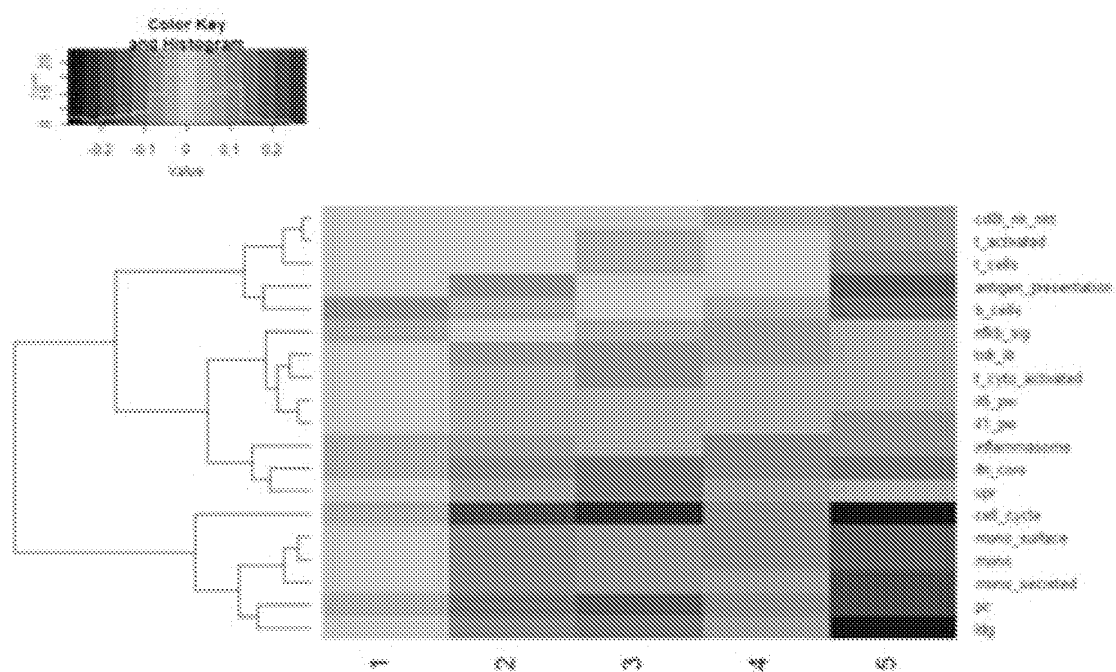


FIG. 24



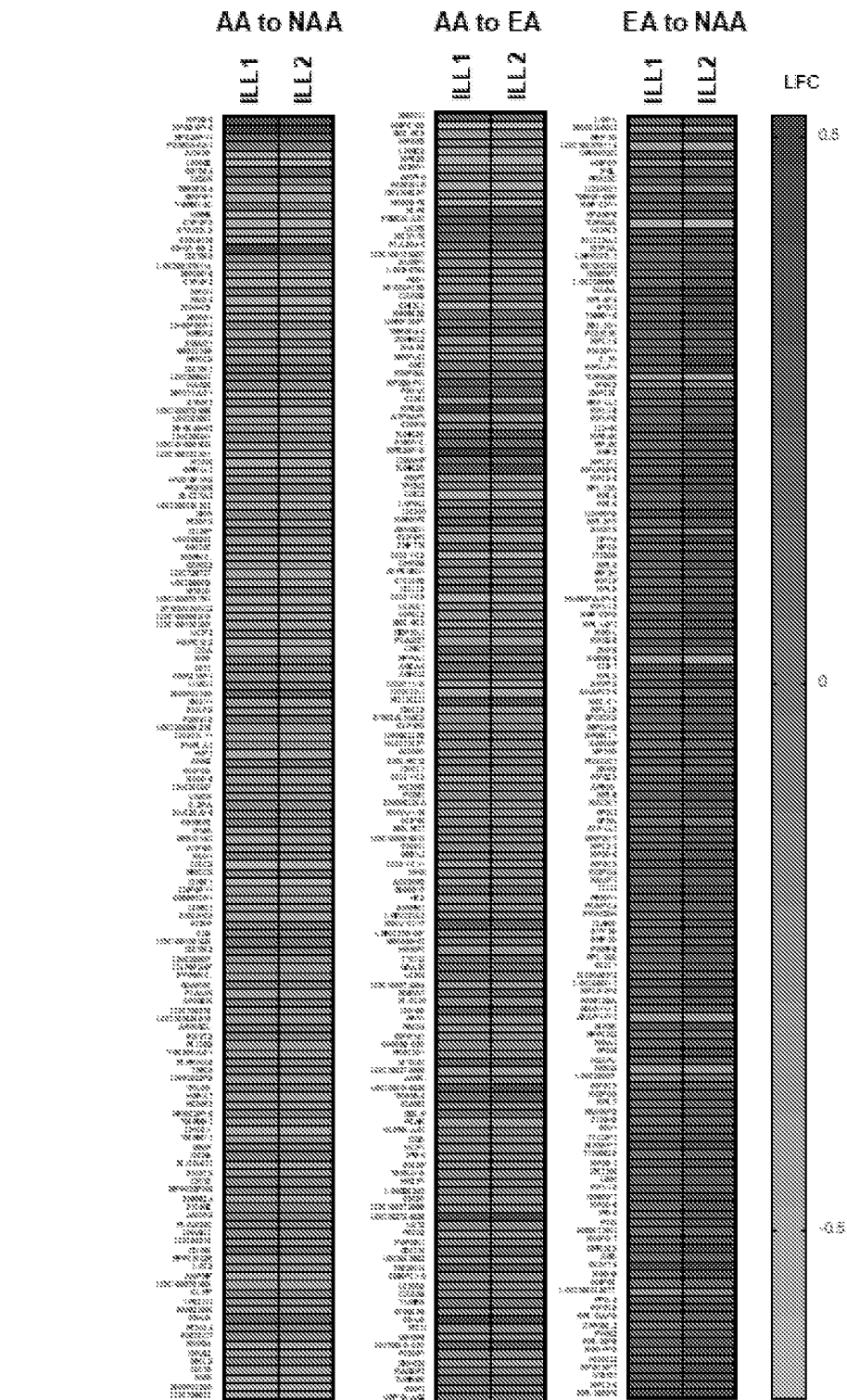


FIG. 26A

AA to NAA

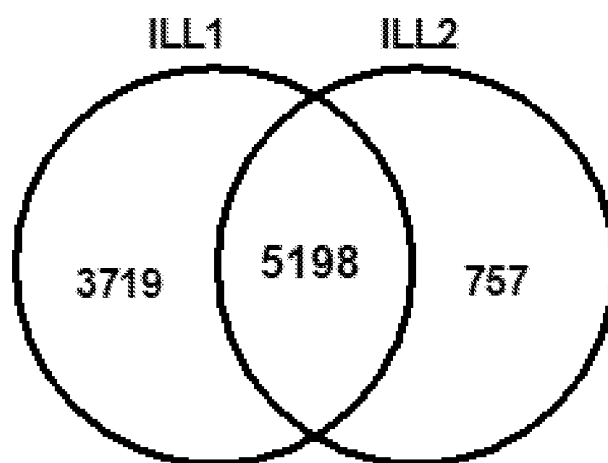


FIG. 26B

AA to EA

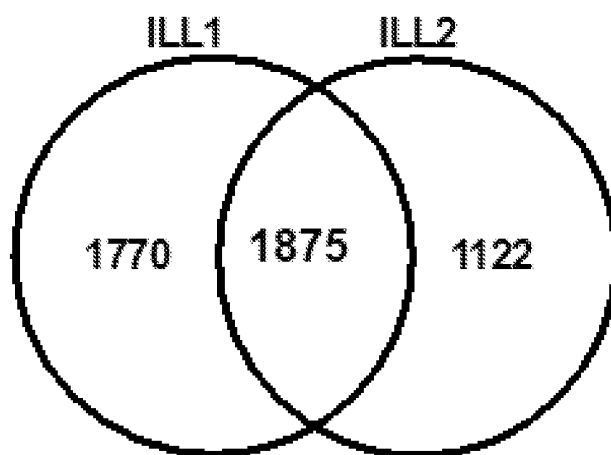


FIG. 26C

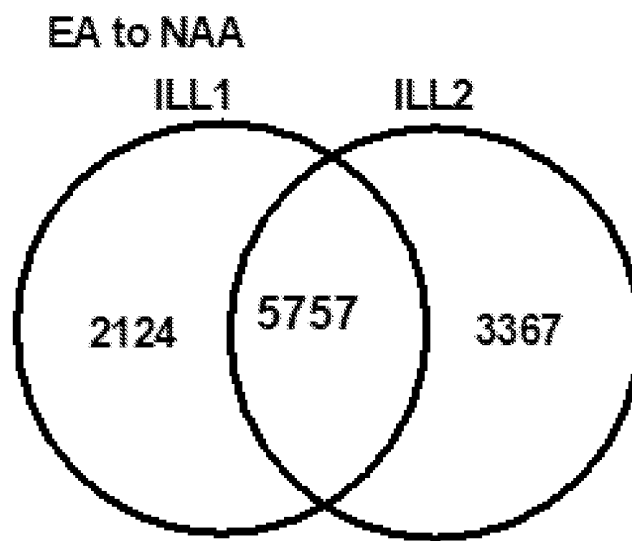


FIG. 26D

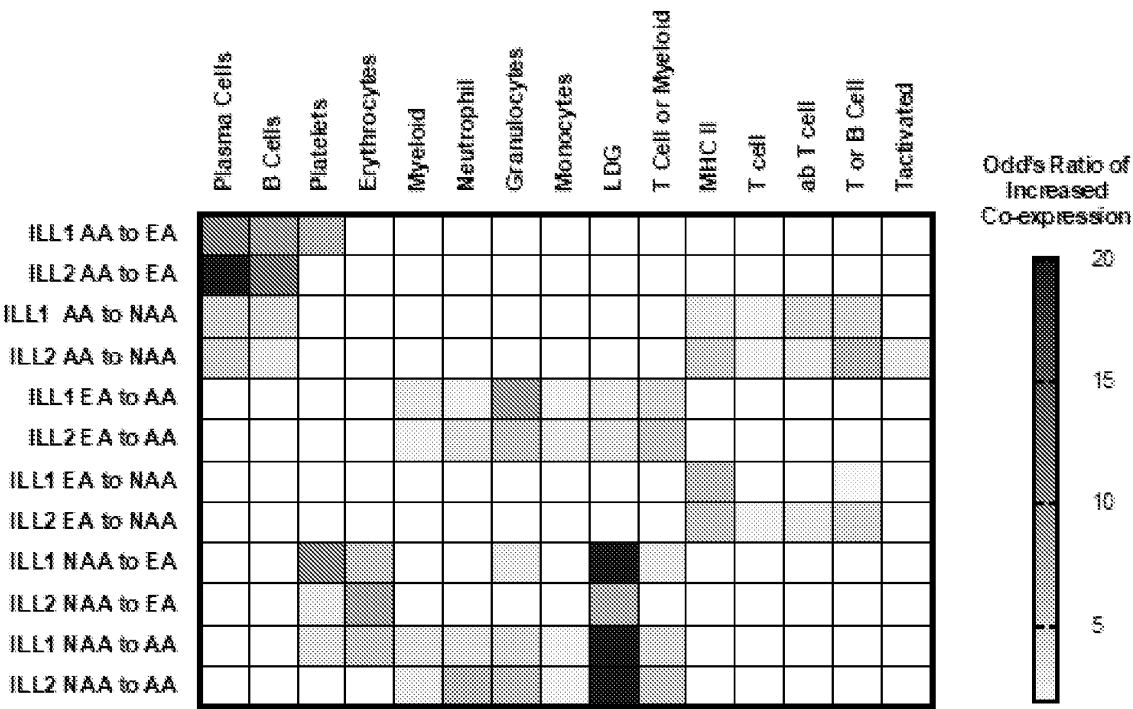


FIG. 27A

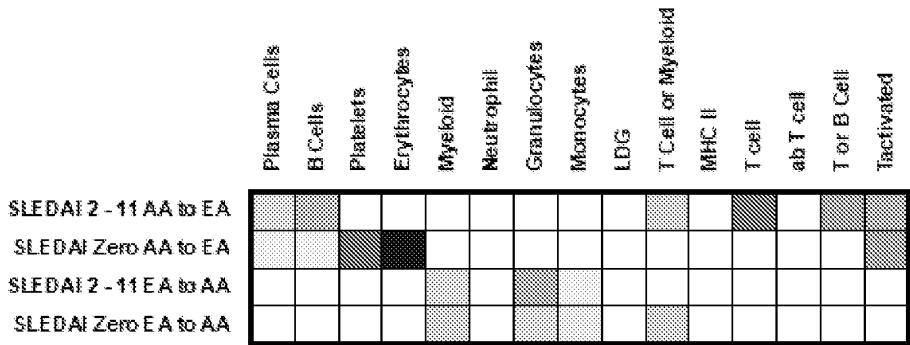


FIG. 27B

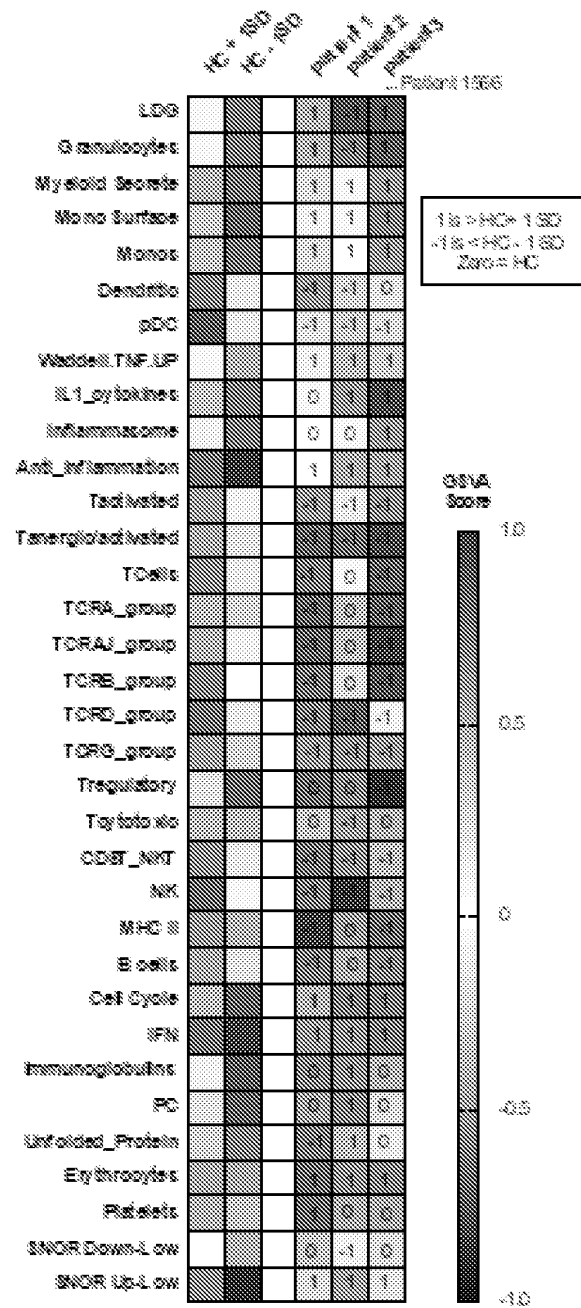


FIG. 28A

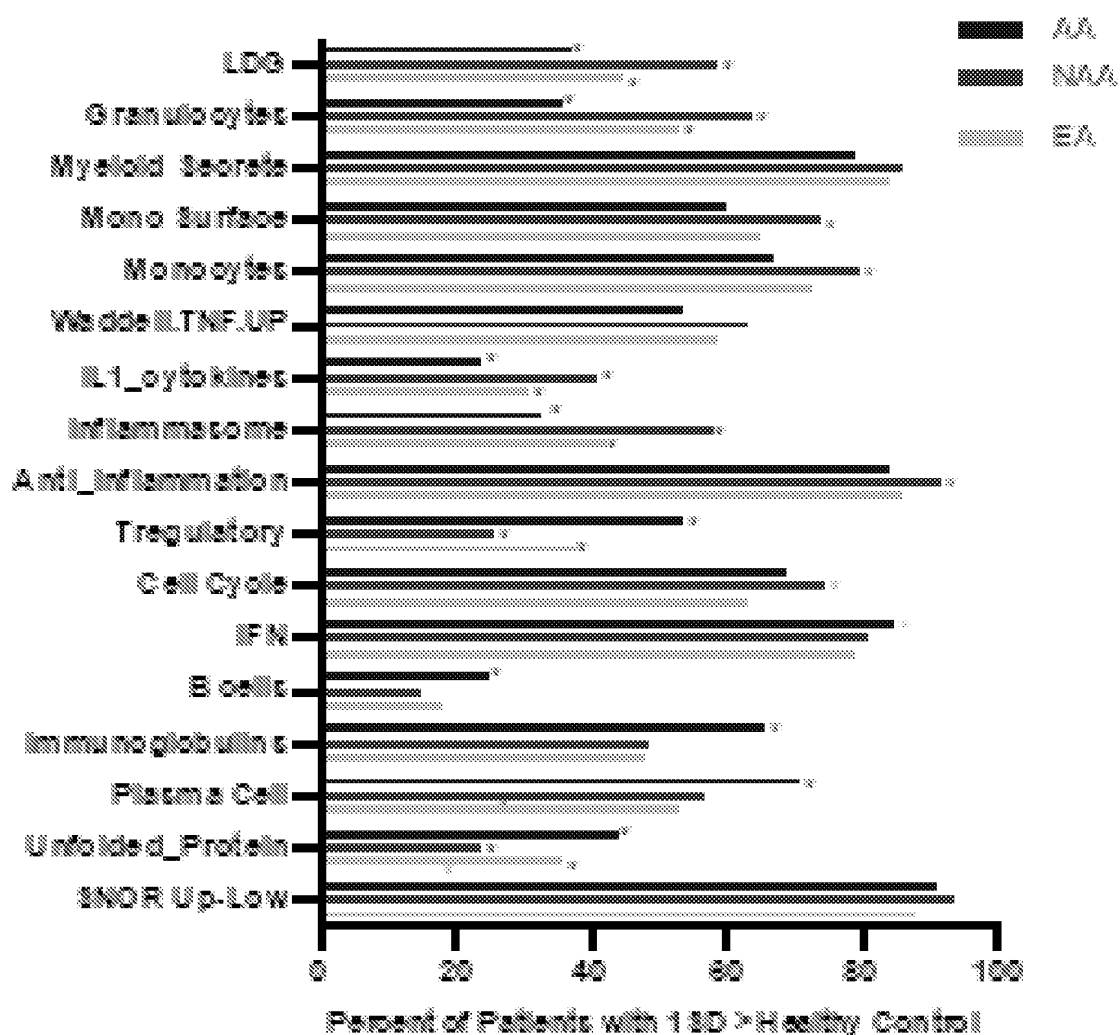


FIG. 28B

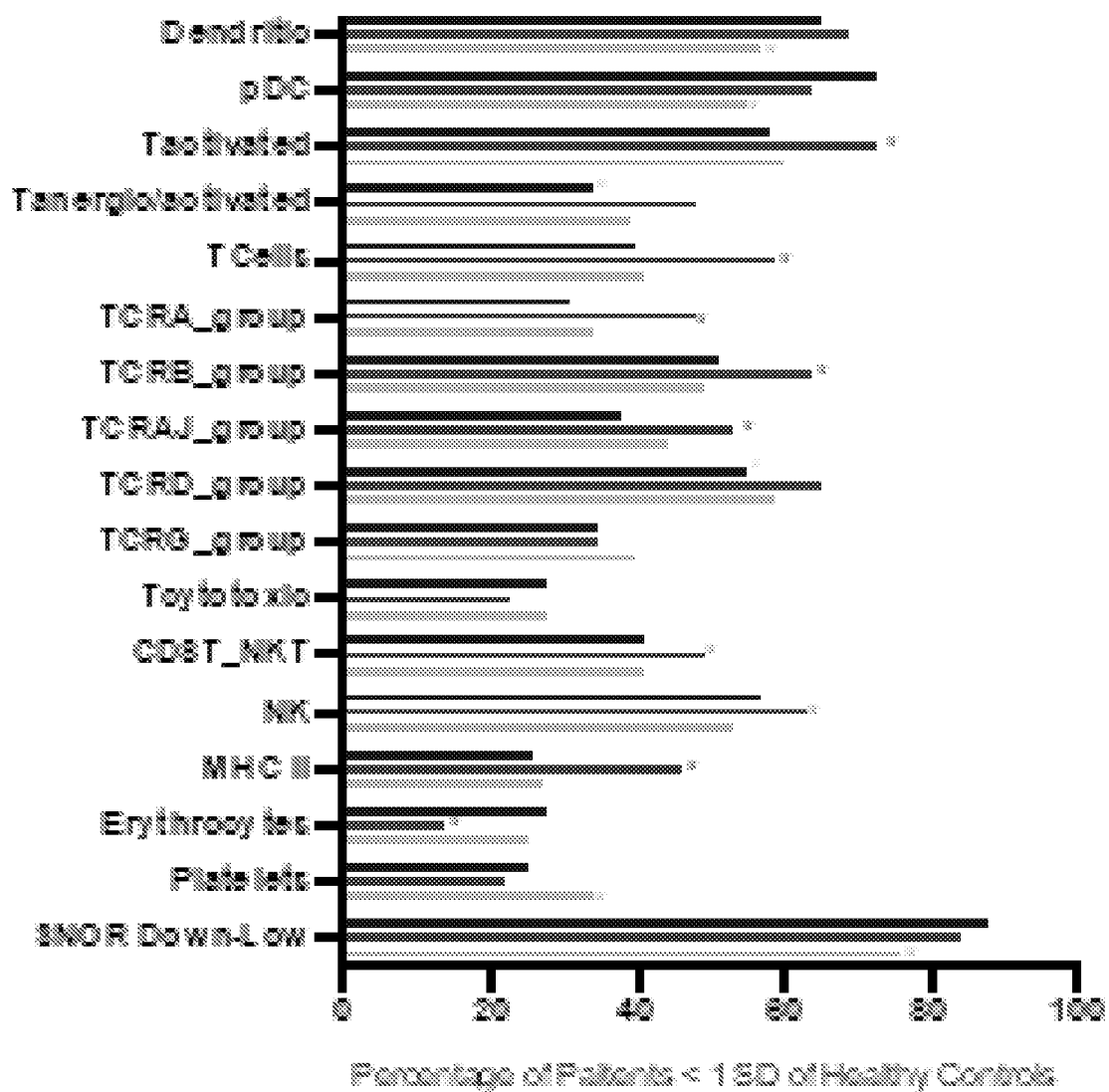


FIG. 28C

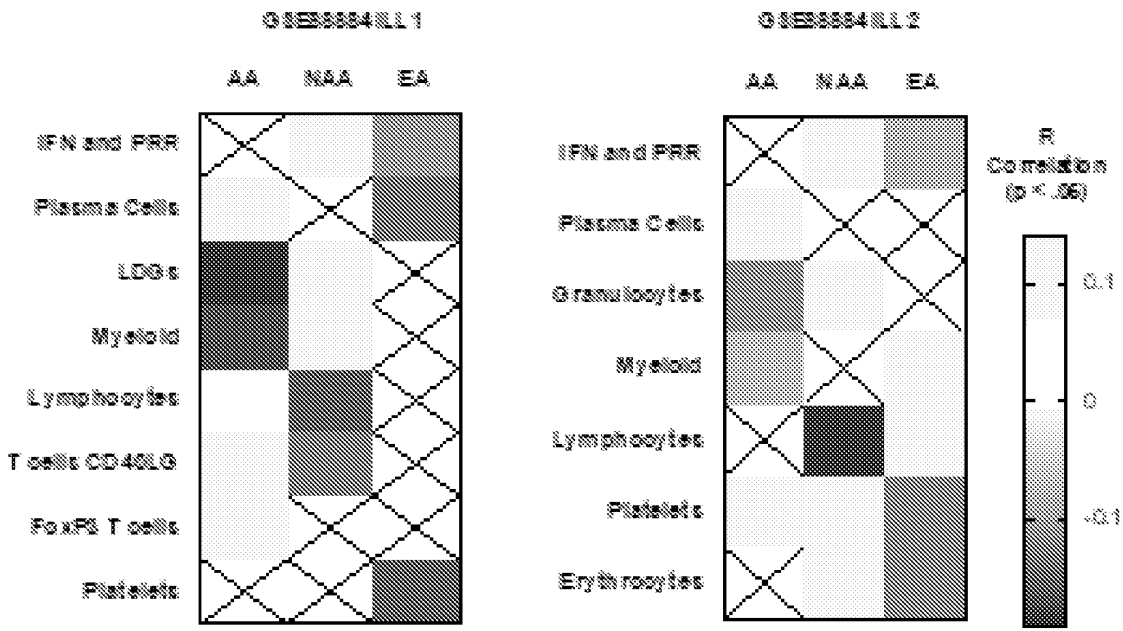


FIG. 28D

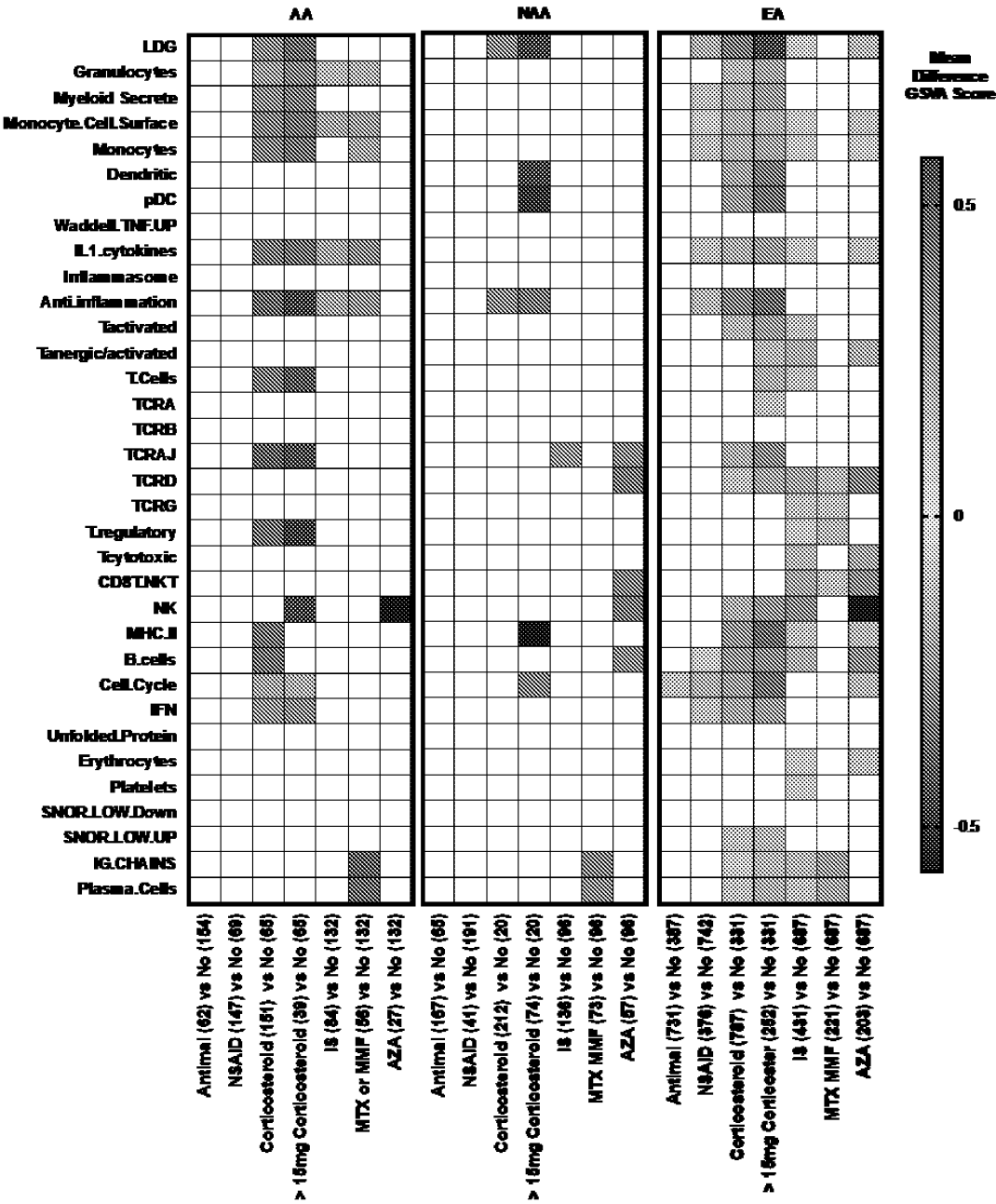


FIG. 29

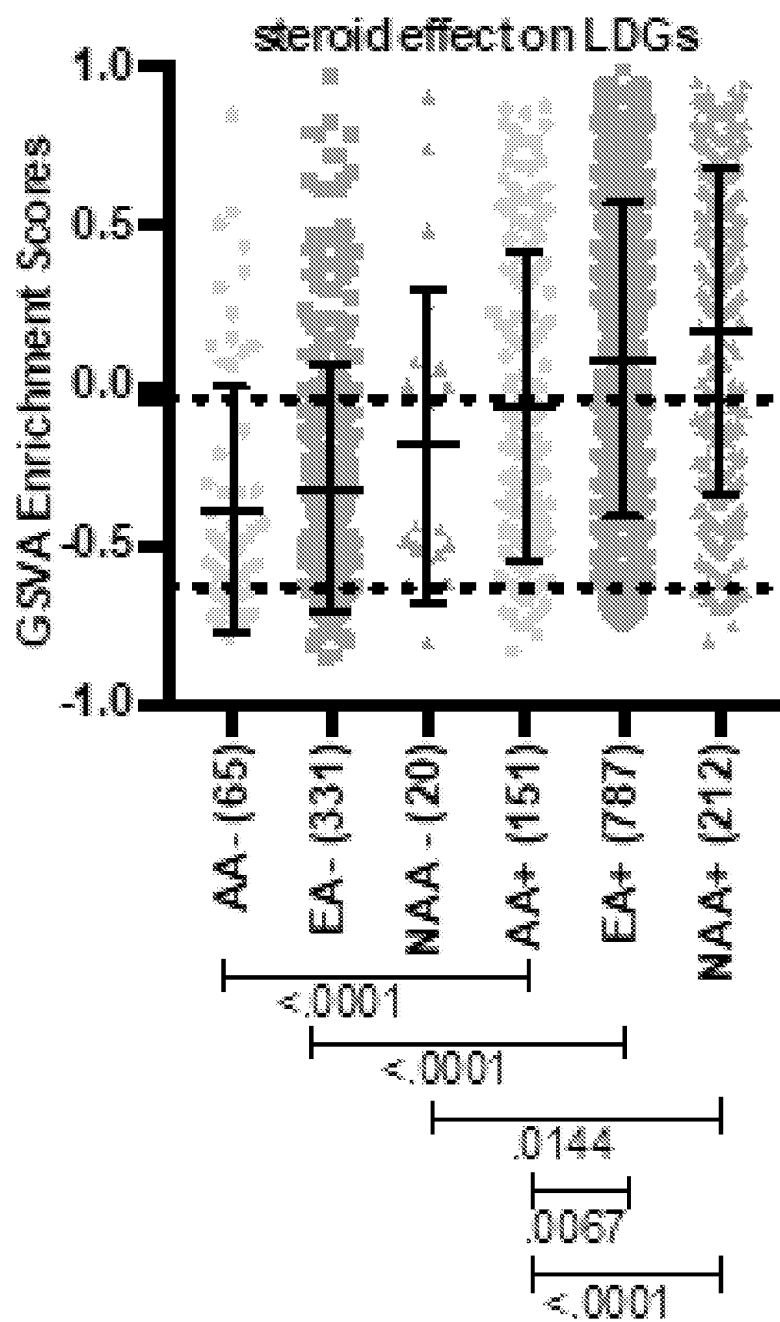


FIG. 30A

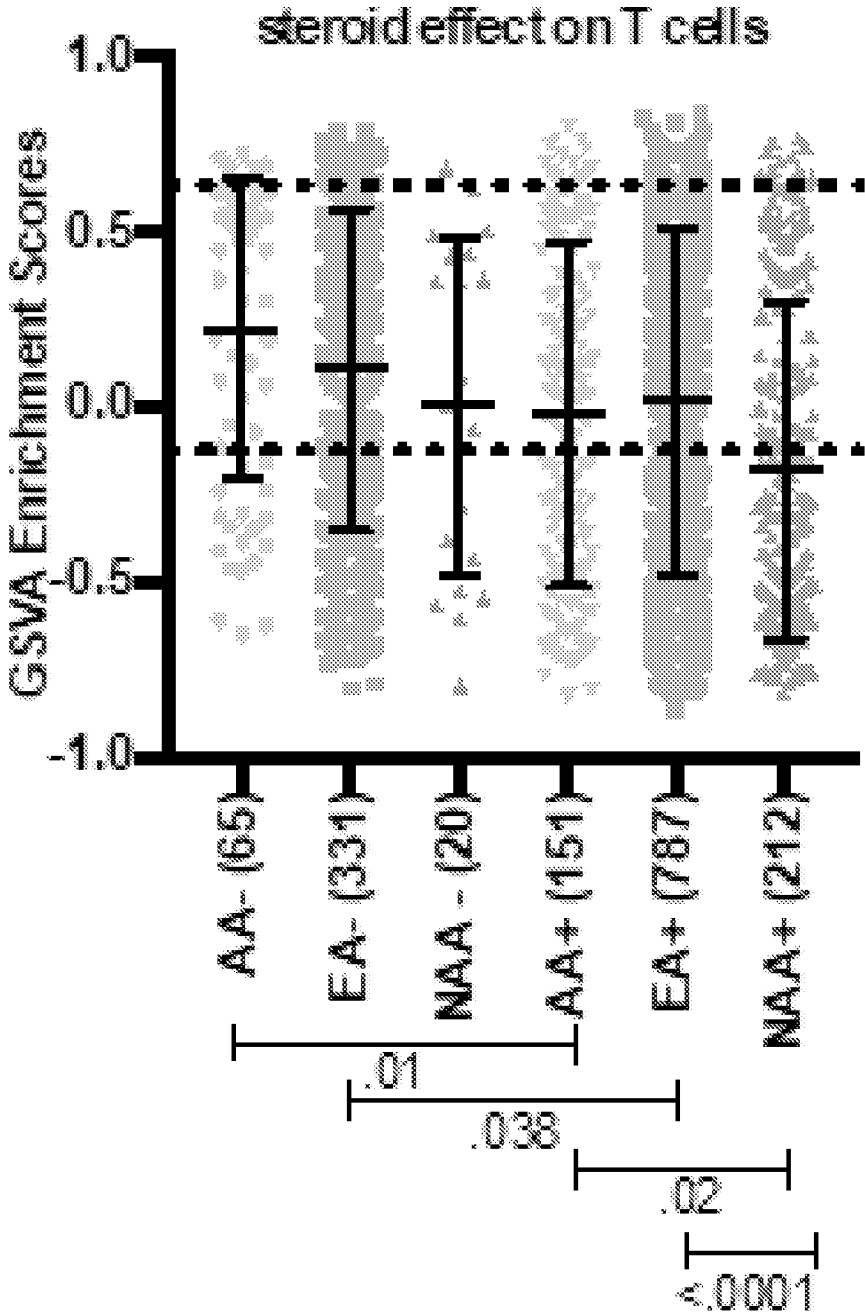


FIG. 30B

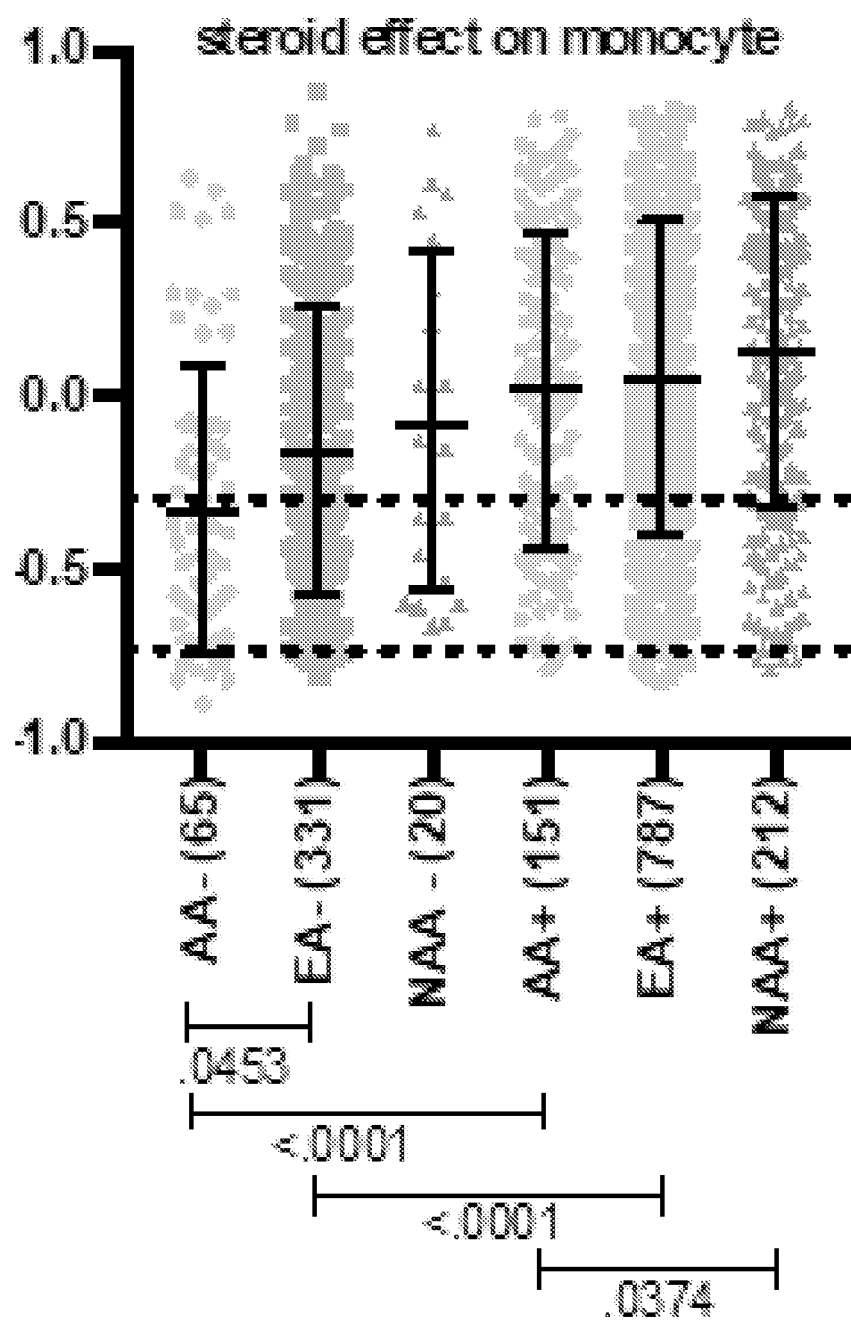


FIG. 30C

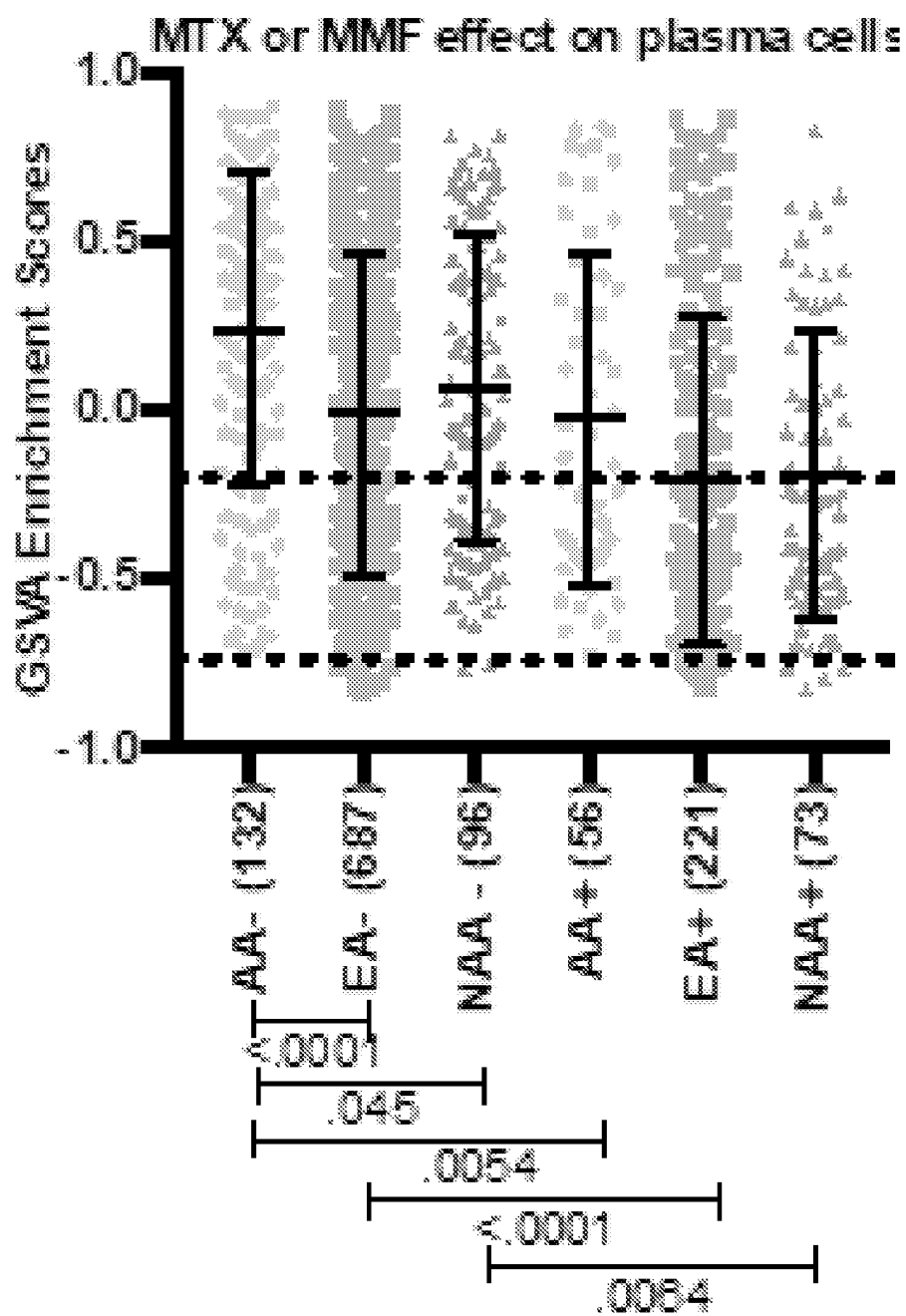


FIG. 30D

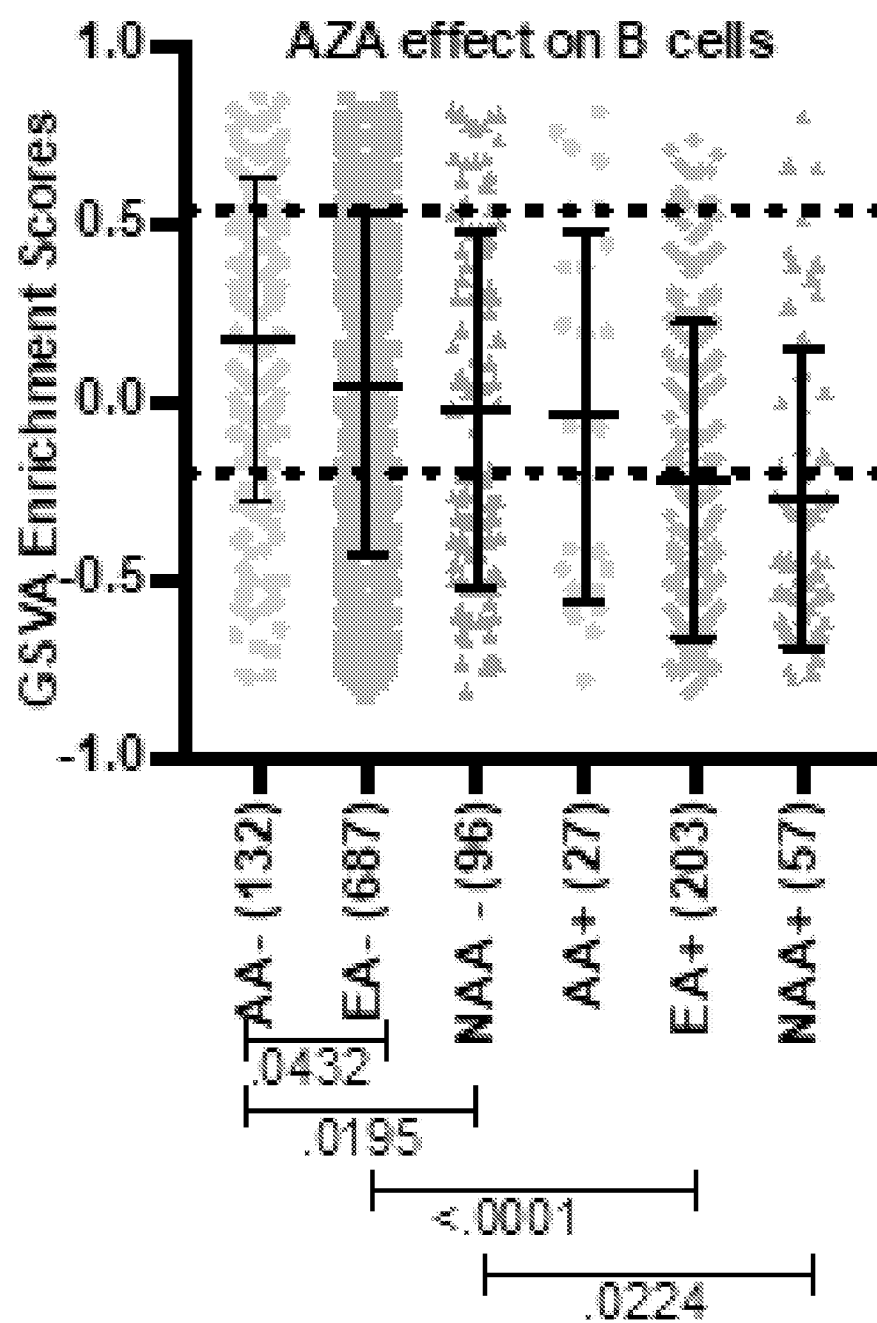


FIG. 30E

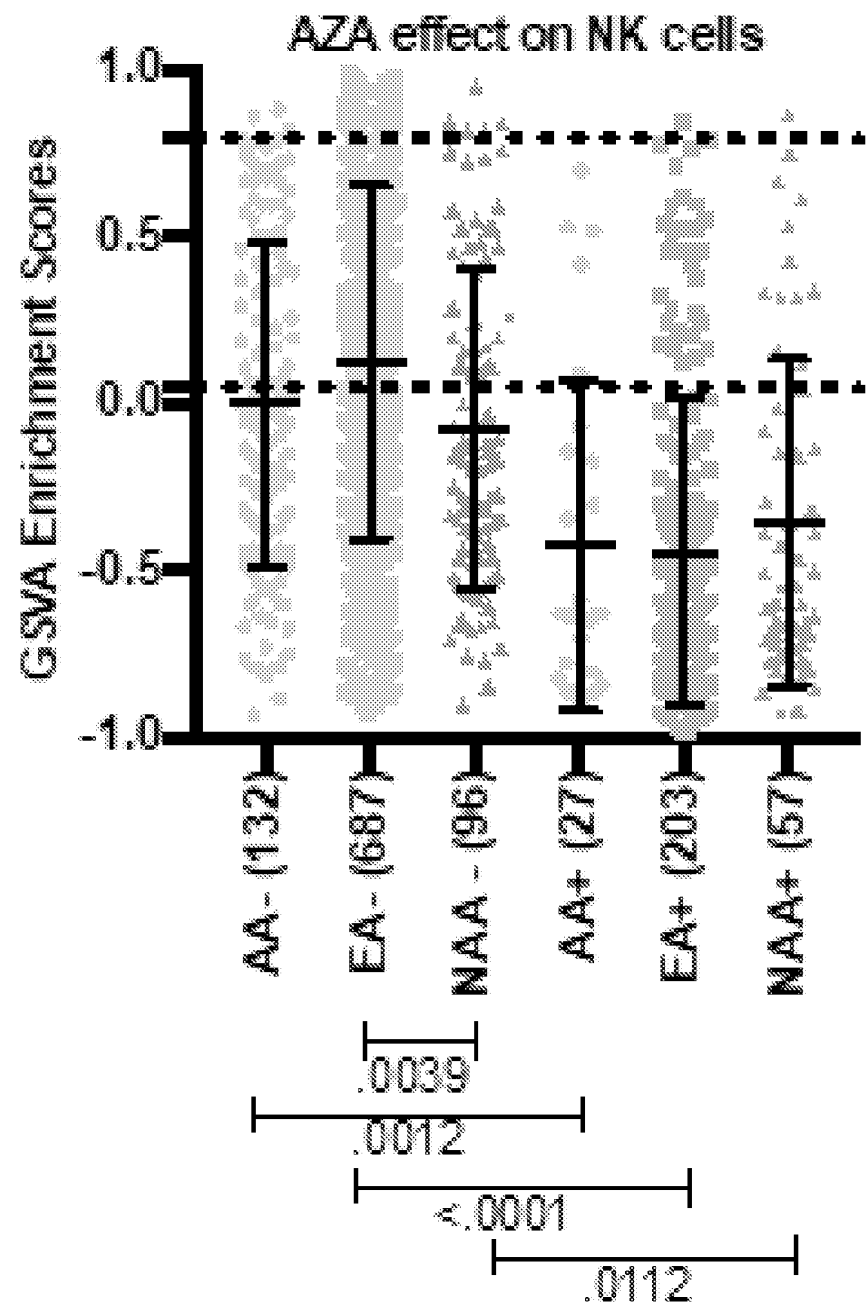


FIG. 30F

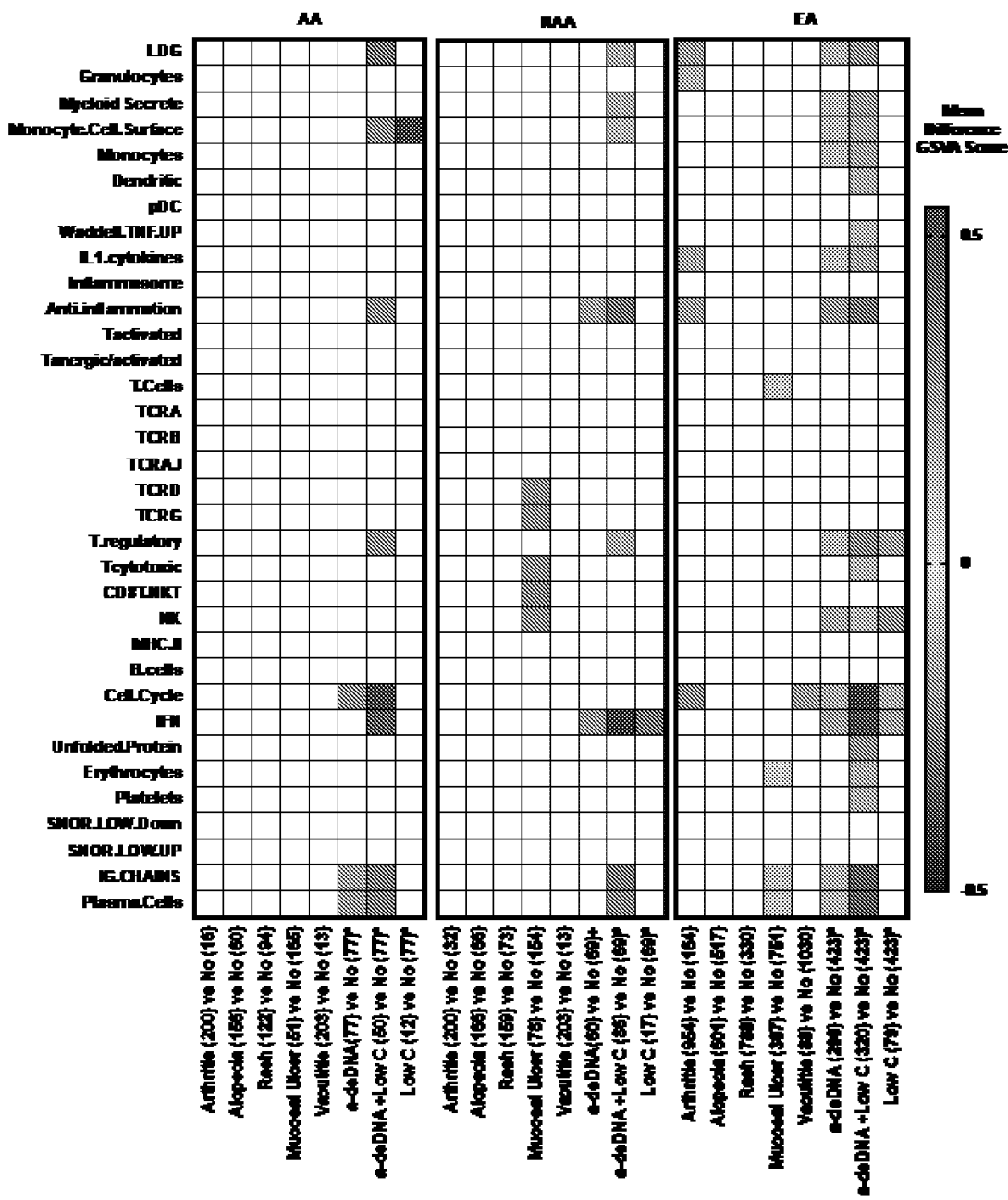


FIG. 31A

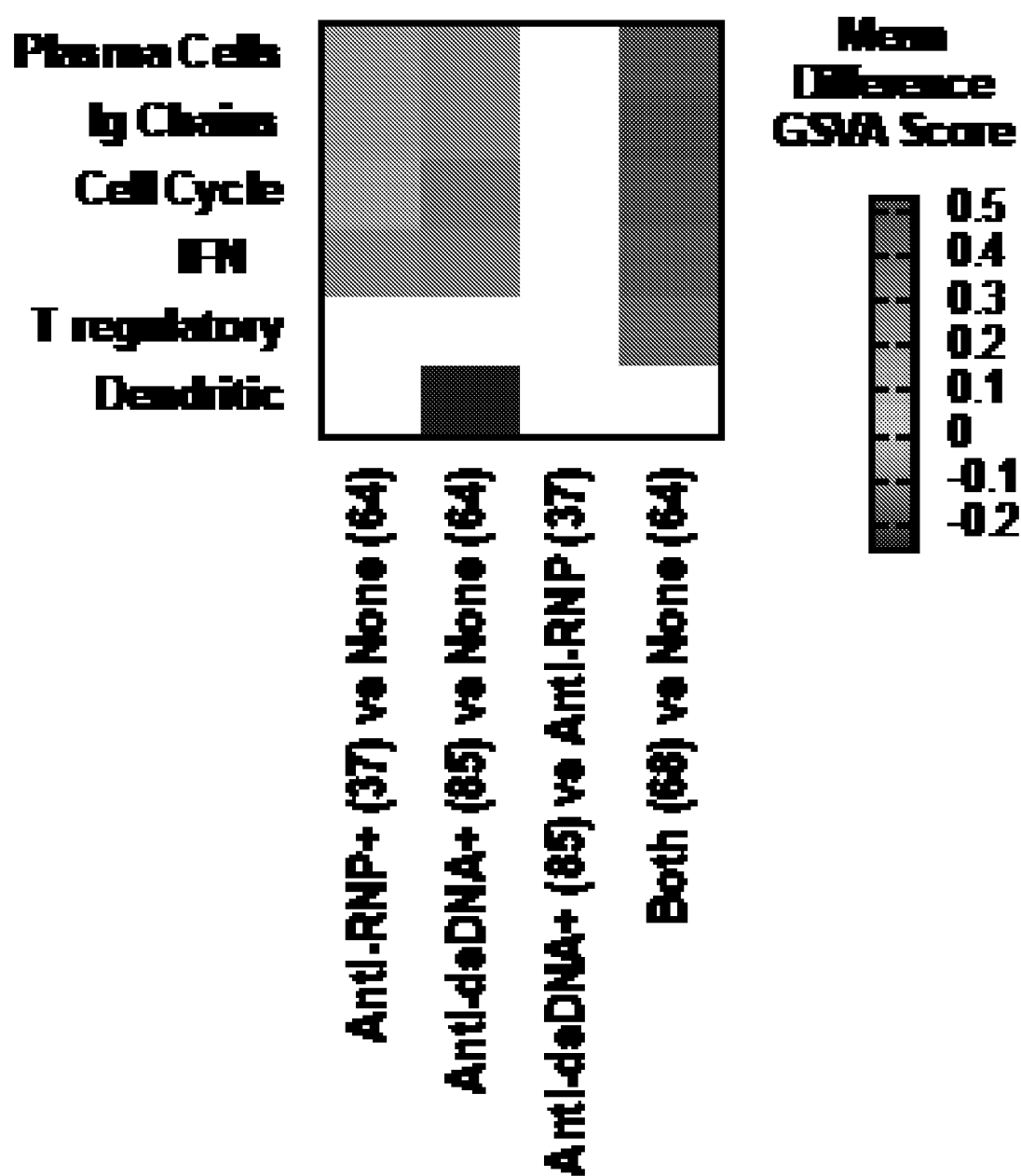


FIG. 31B

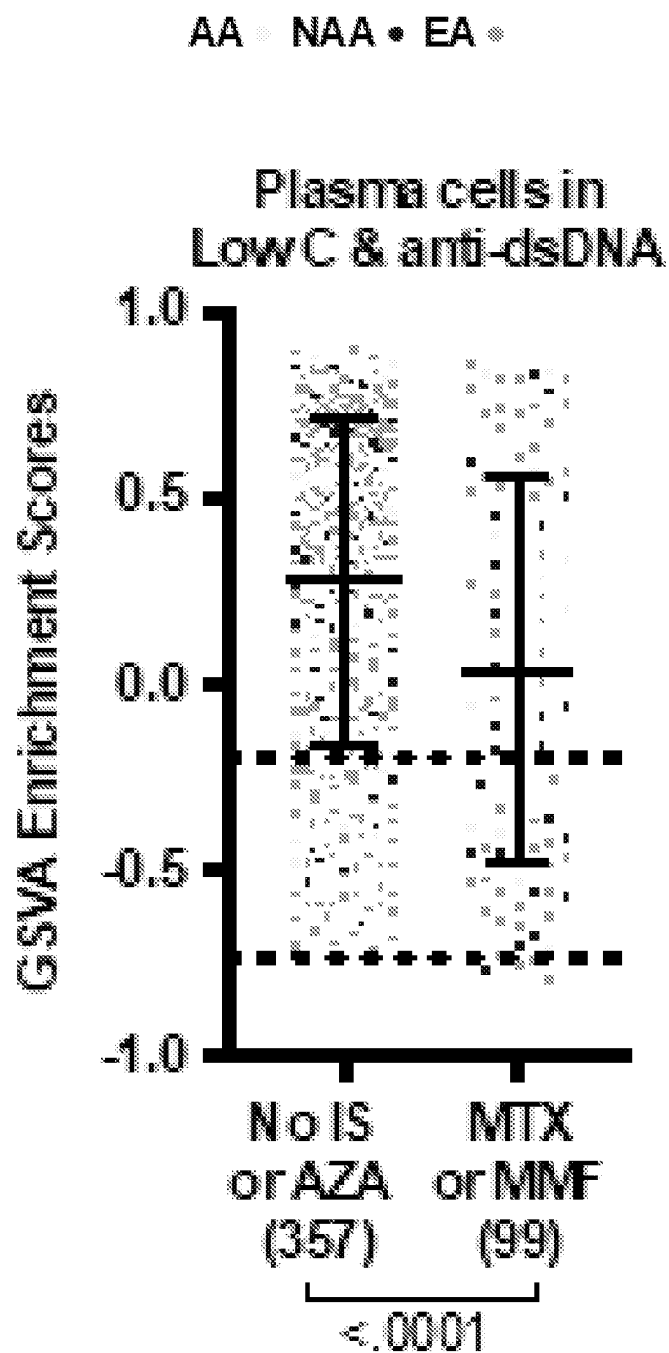


FIG. 32A

AA • NAA • EA •

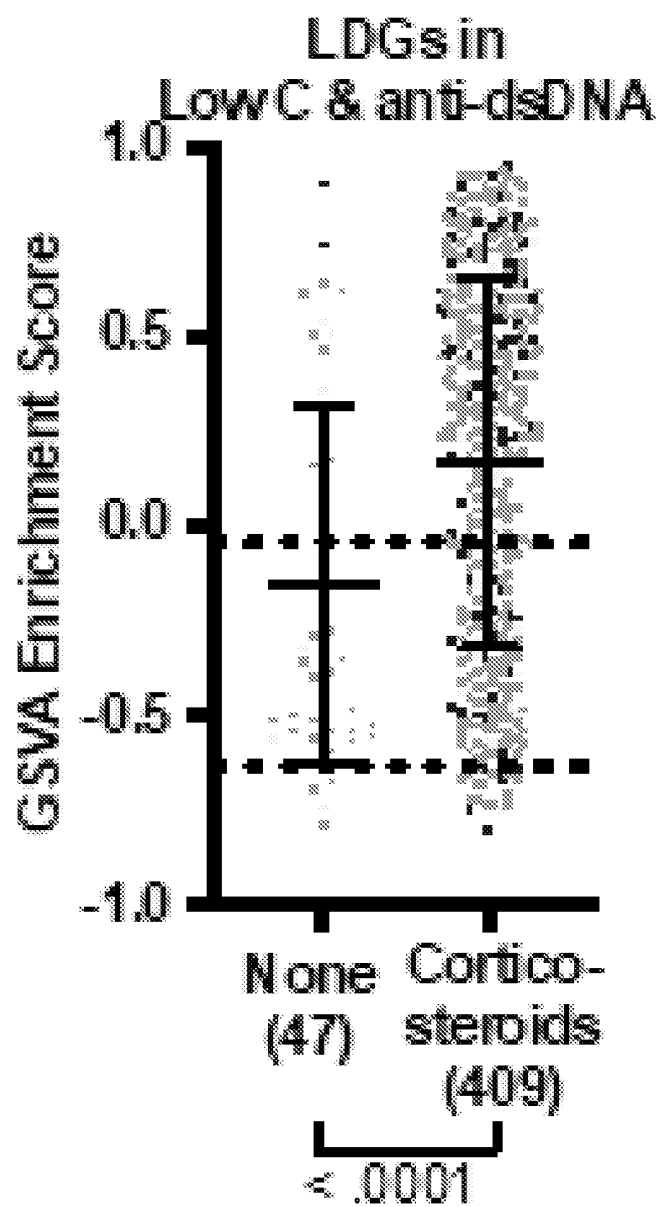


FIG. 32B

AA • NAA • EA •

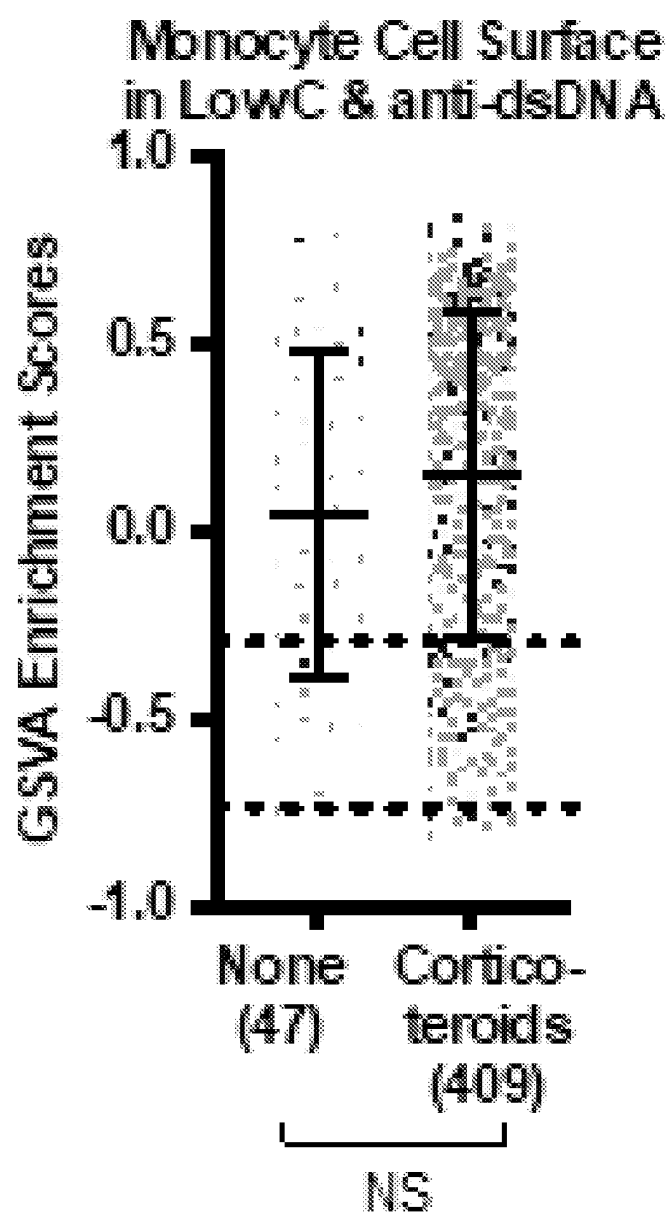


FIG. 32C

AA • NAA • EA •

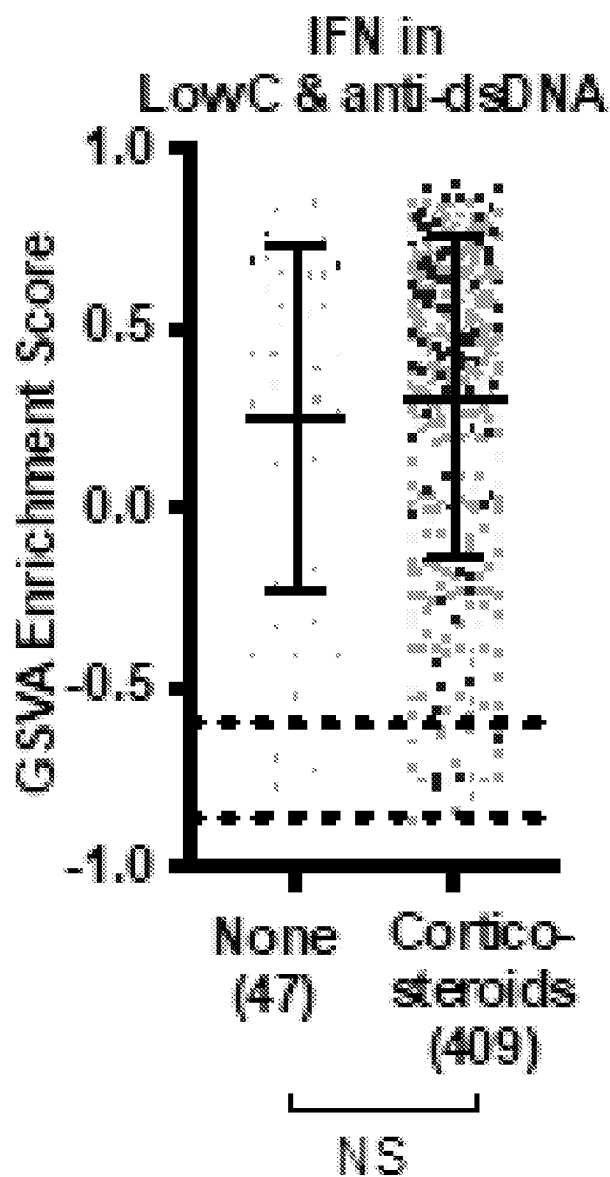


FIG. 32D

AA • NAA • EA •

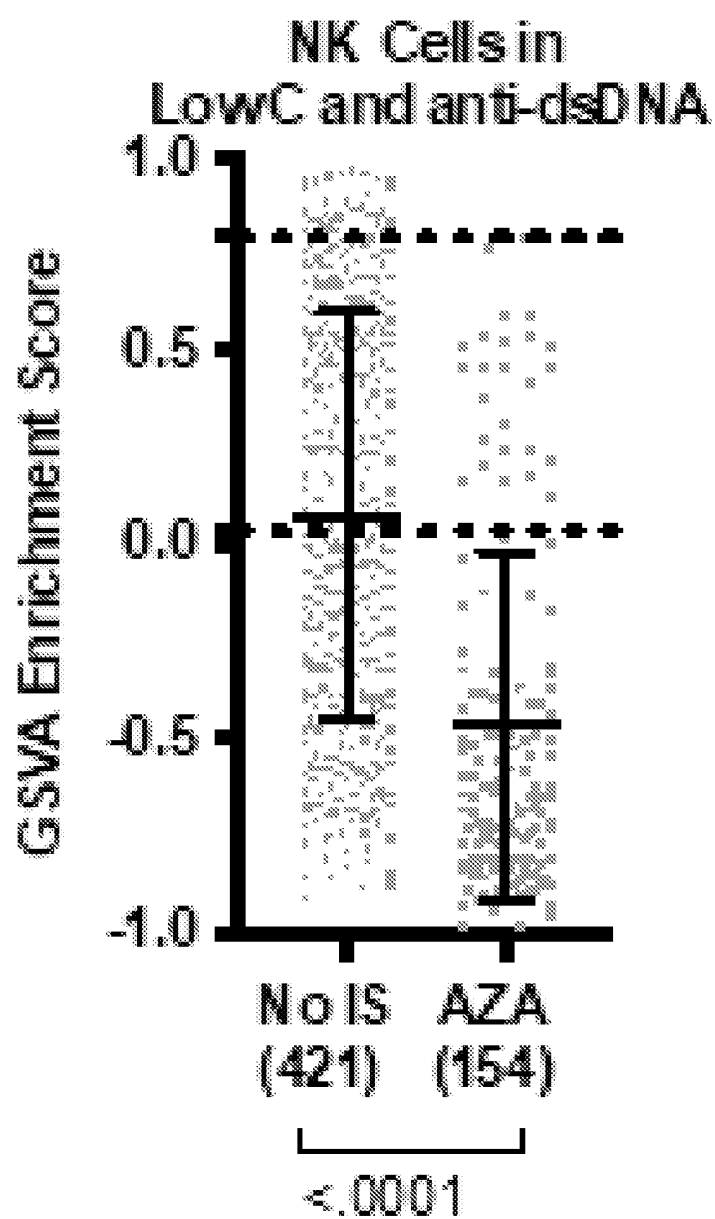


FIG. 32E

AA • NAA • EA •

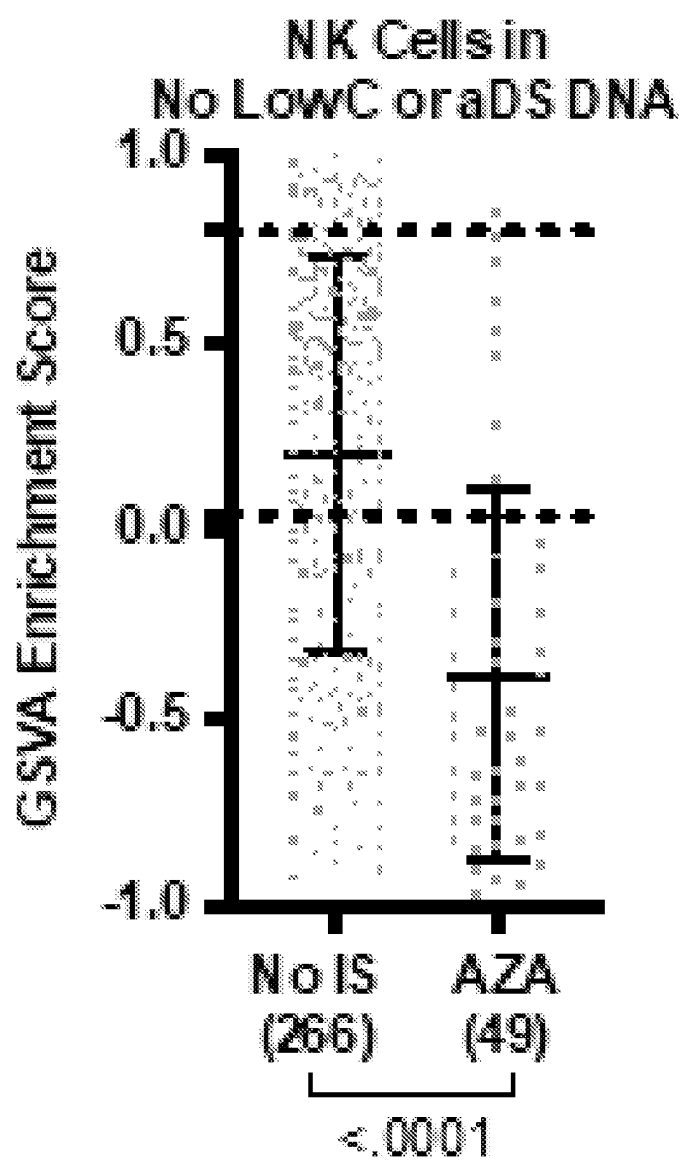


FIG. 32F

AA • NAA • EA •

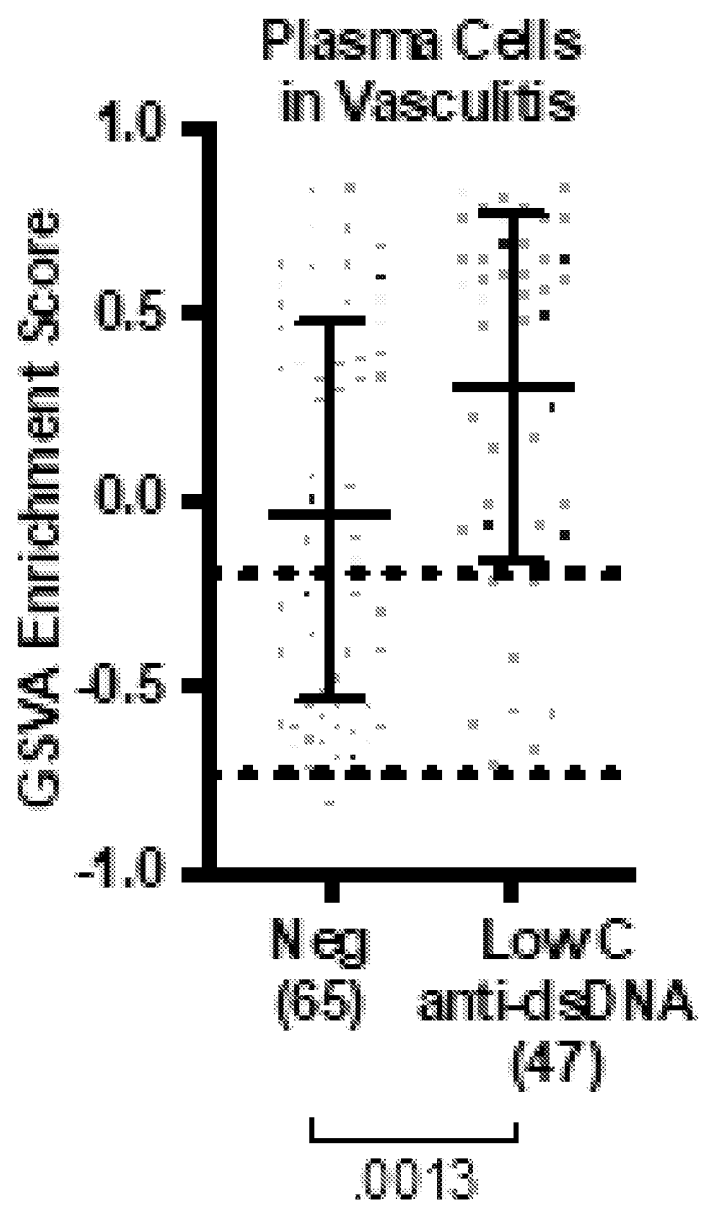


FIG. 32G

AA • NAA • EA •

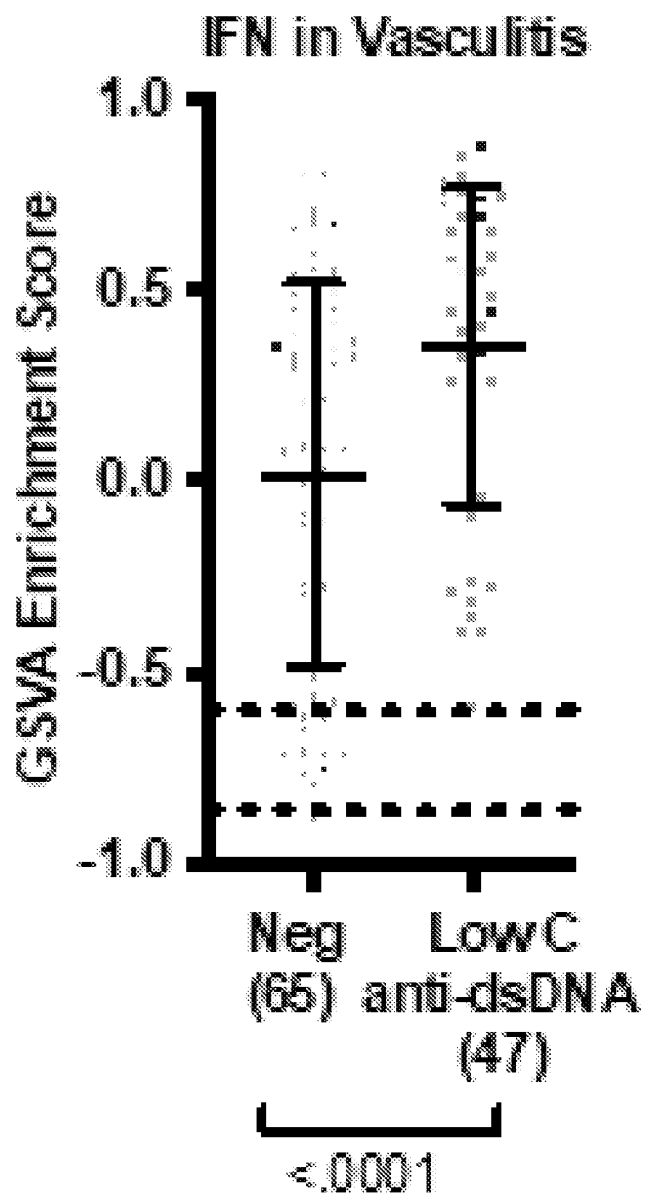


FIG. 32H

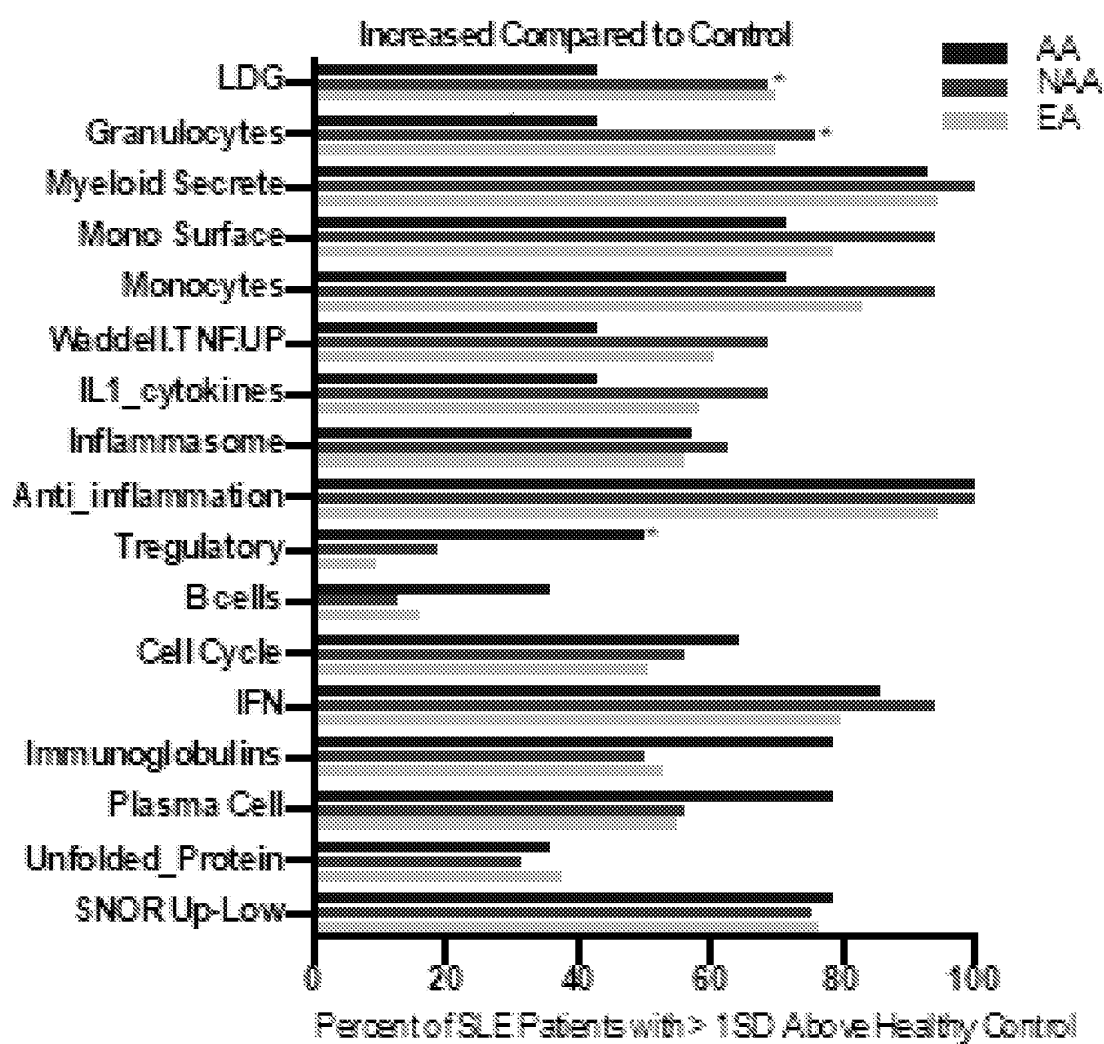


FIG. 33A

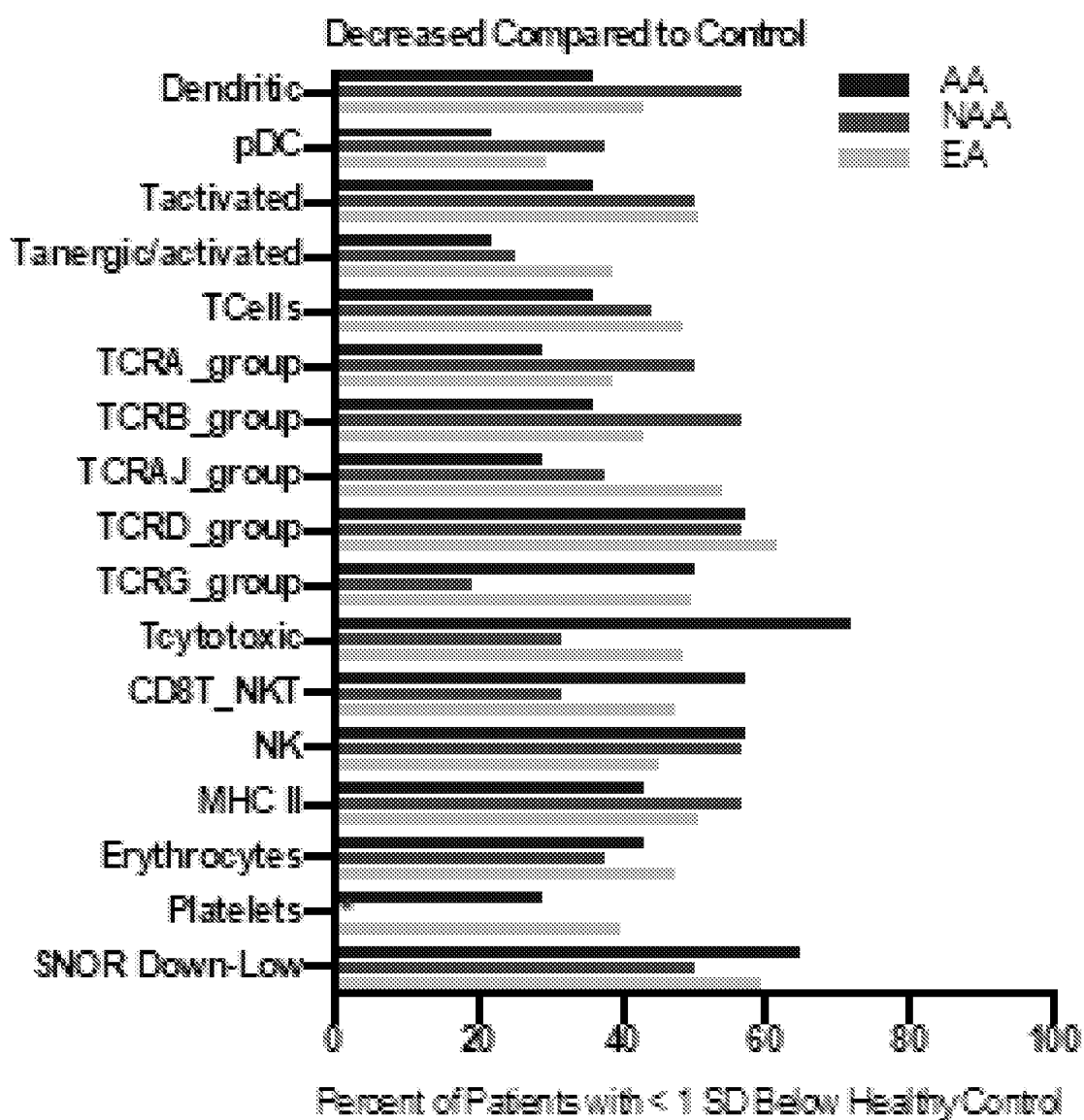


FIG. 33B

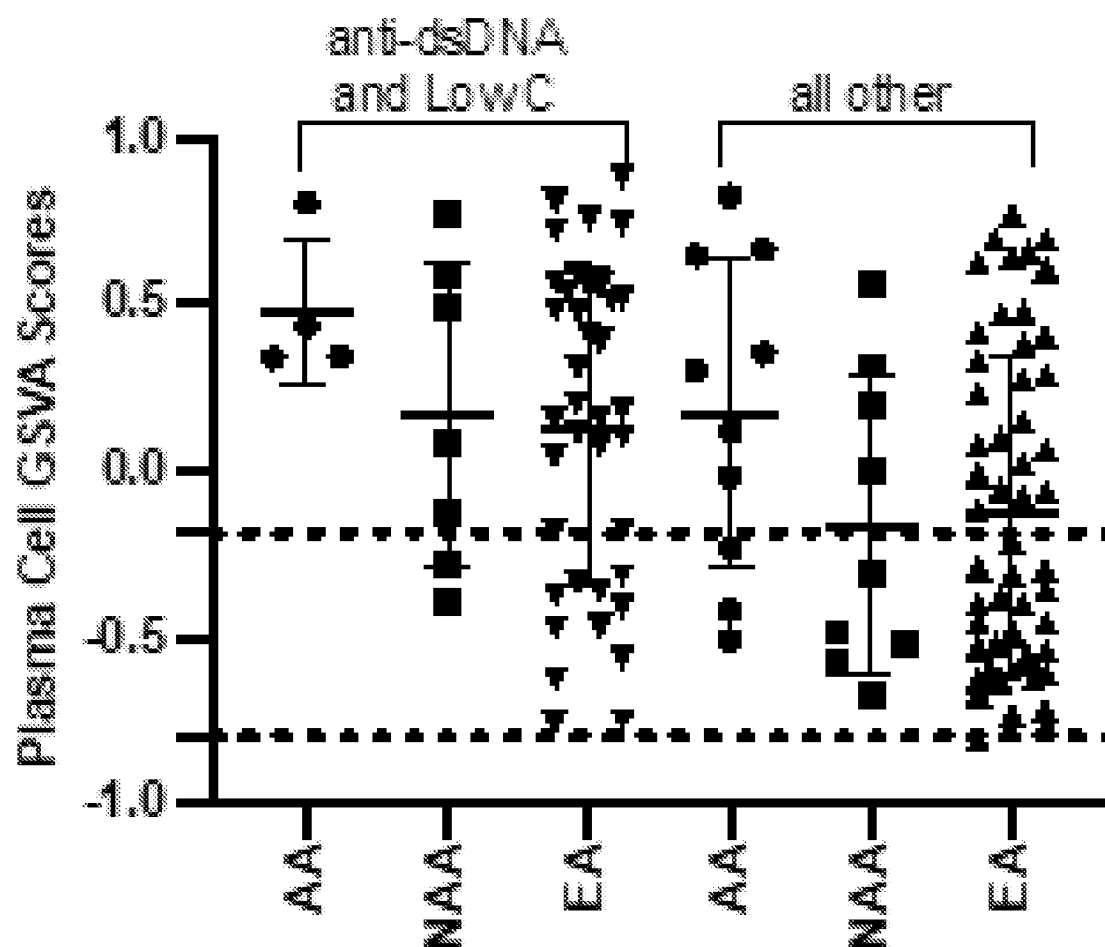
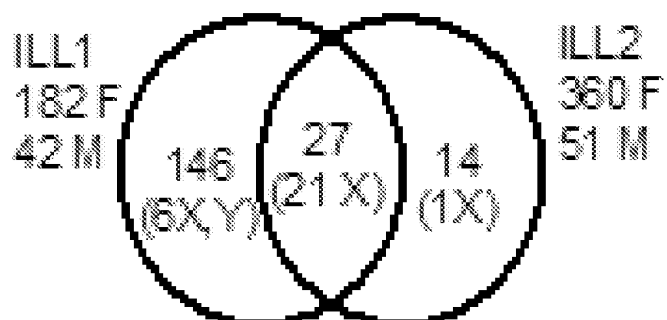


FIG. 33C

EAFemales Age 25 -49 DE to Male

Increased in Male



Increased in Female

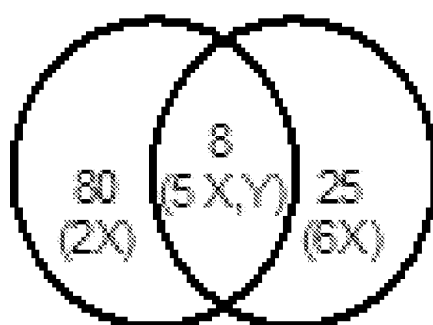
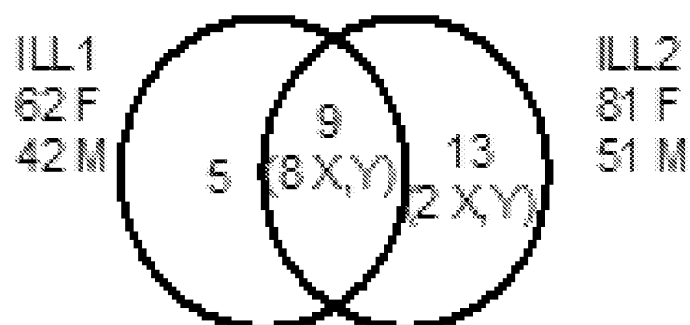


FIG. 33D

EAFemales > Age 50 DE to Male

Increased in Male



Increased in Female

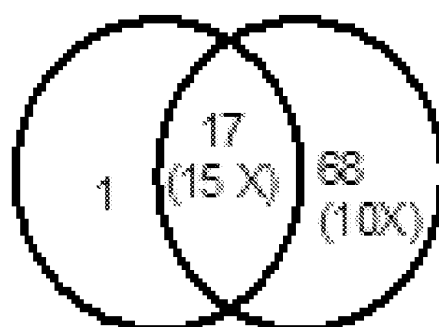


FIG. 33E

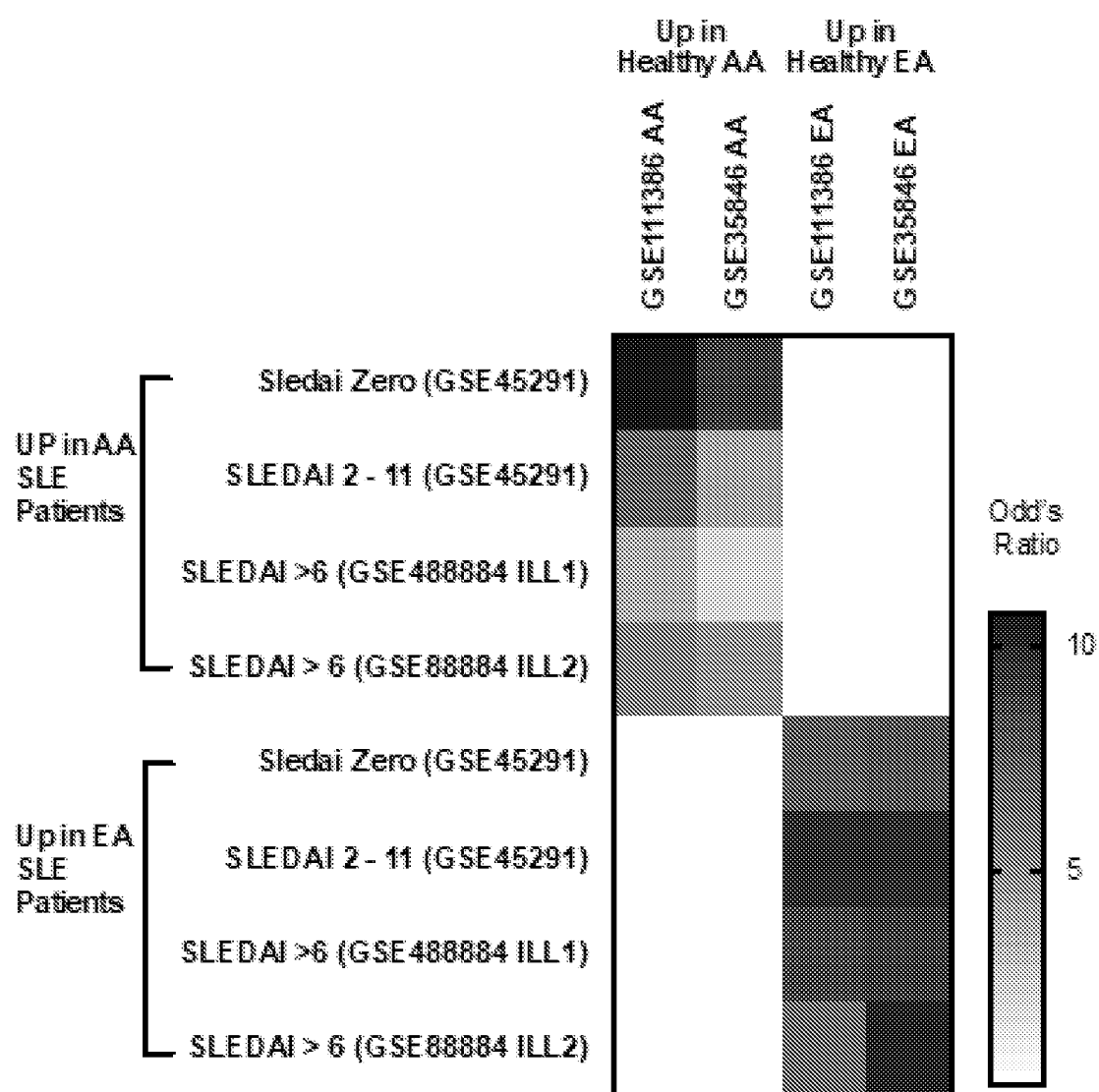


FIG. 34A

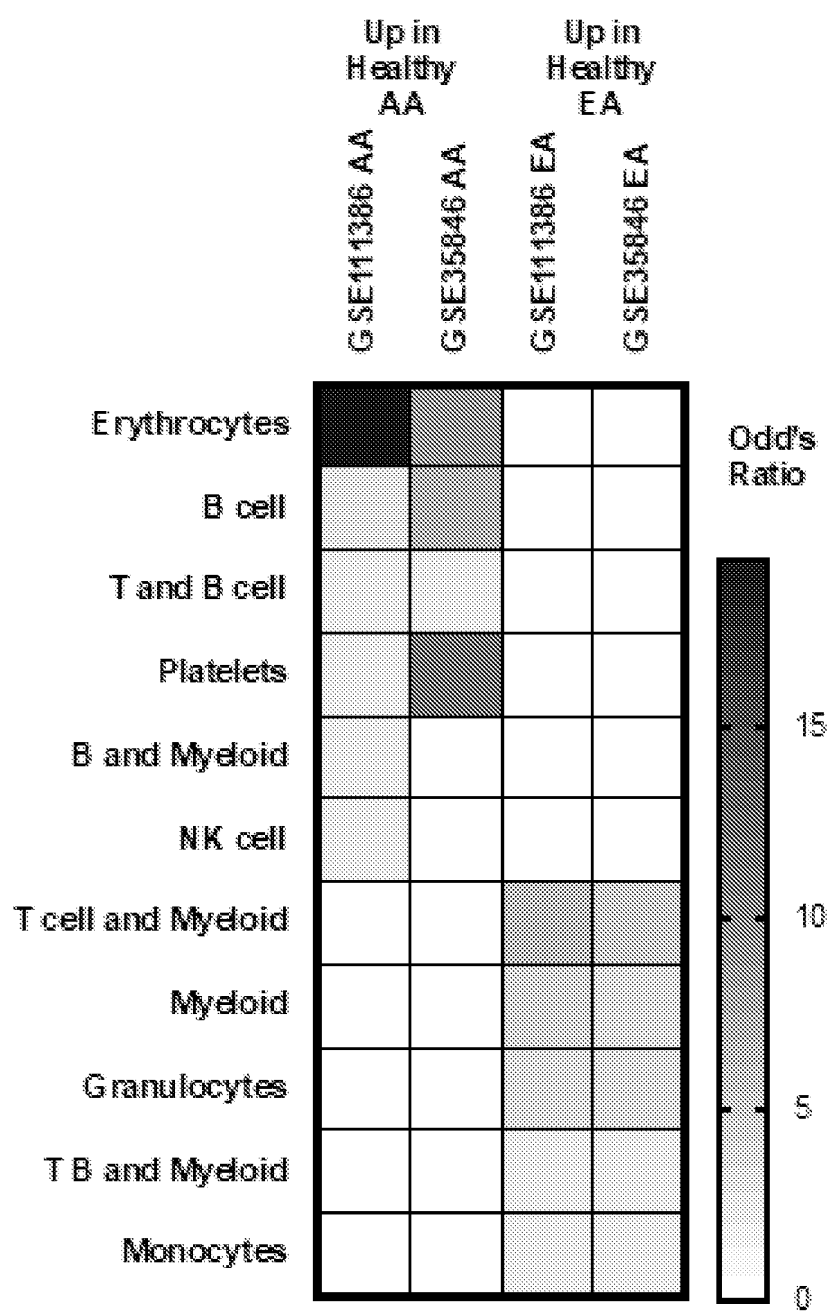


FIG. 34B

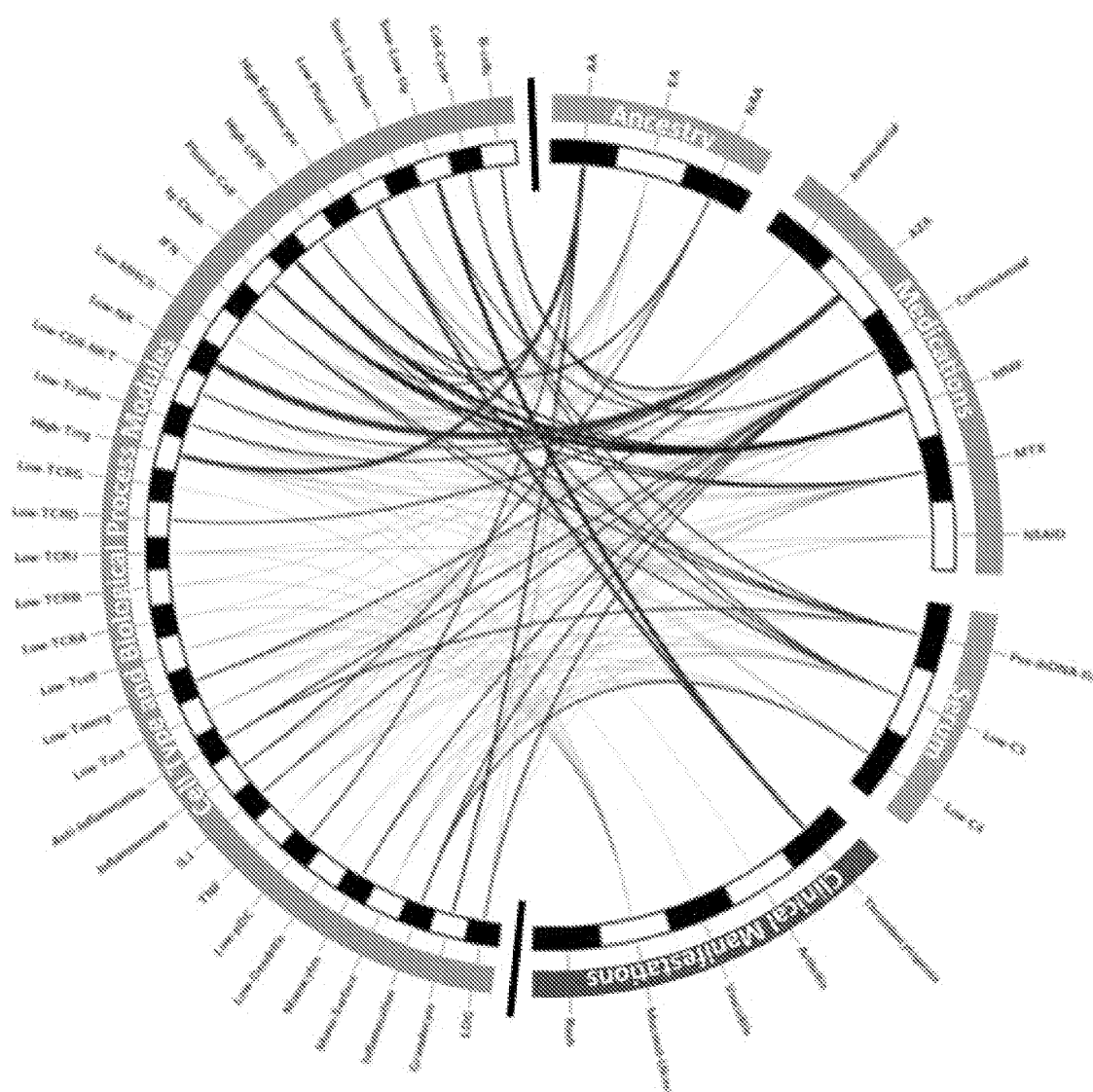


FIG. 35

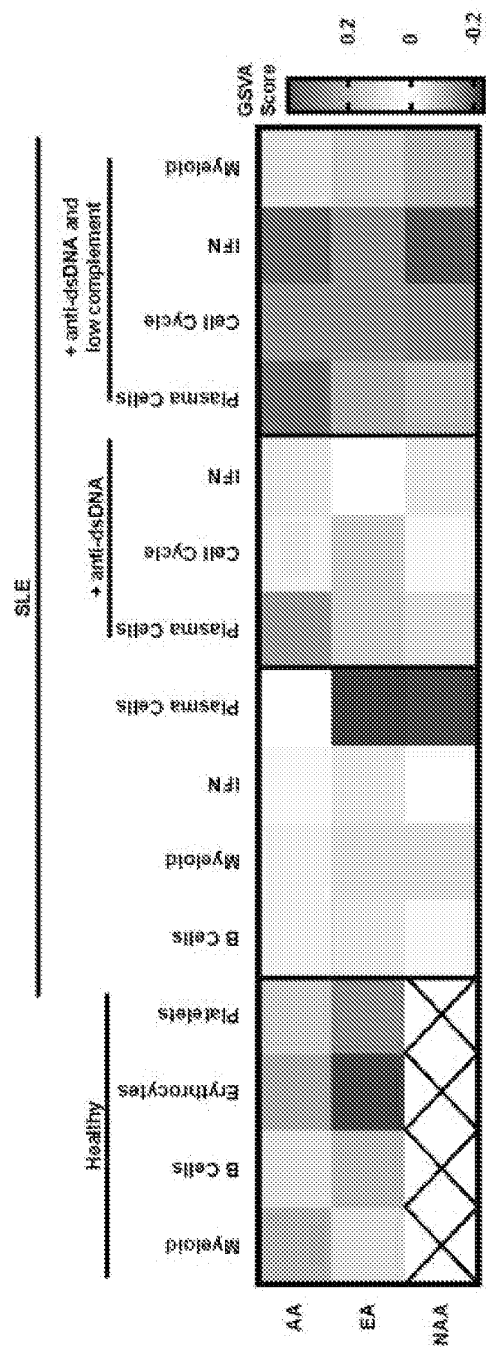


FIG. 36

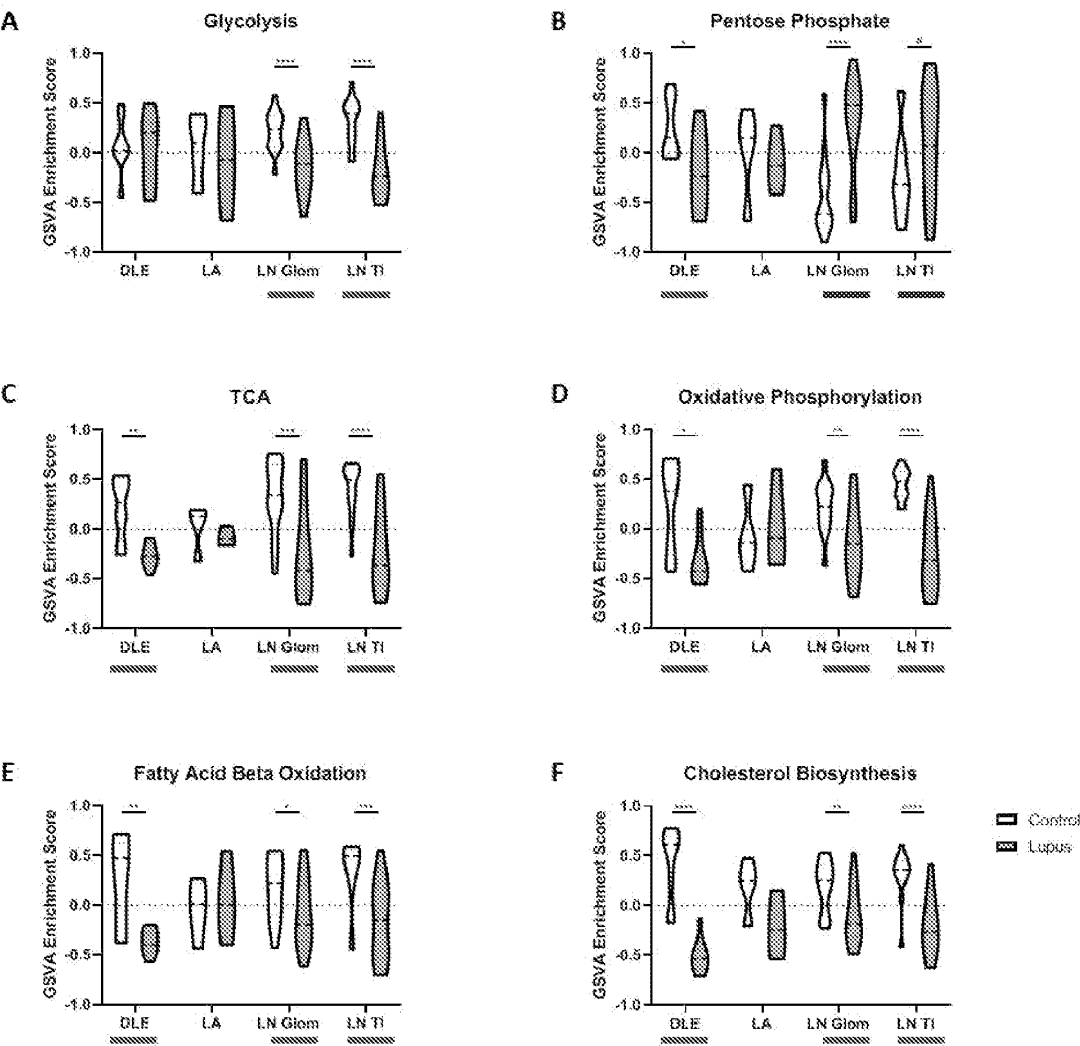
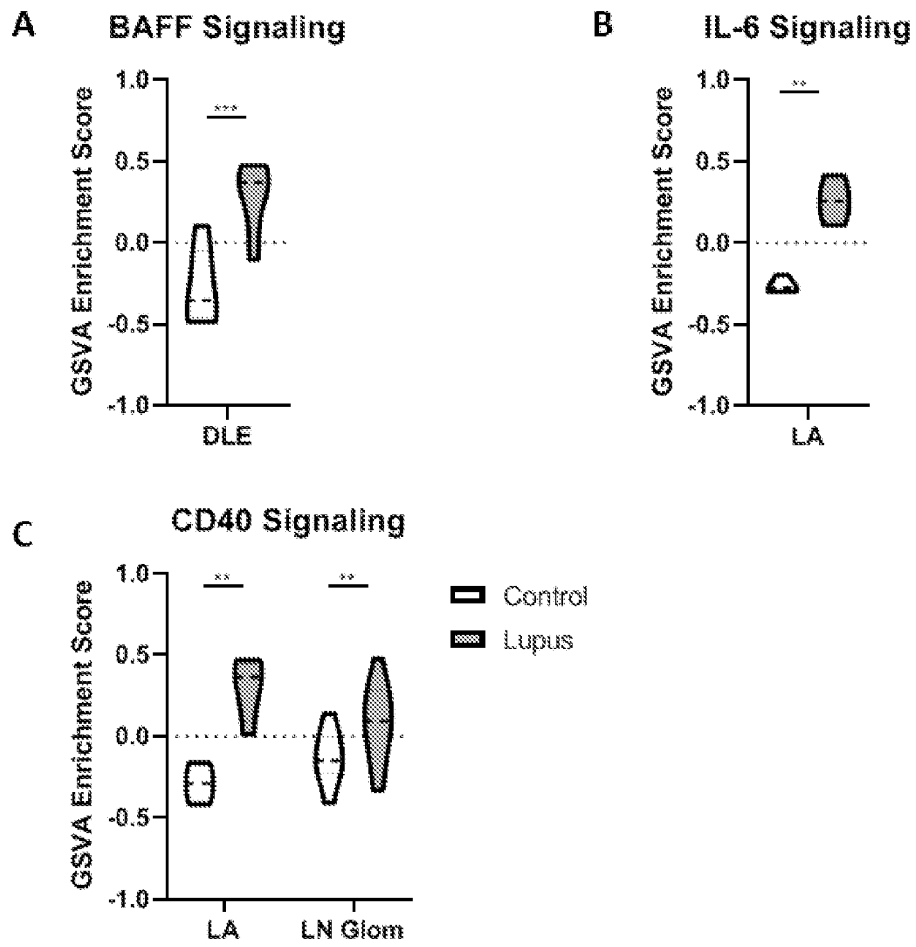


FIG. 37



FIGs. 38A-38C

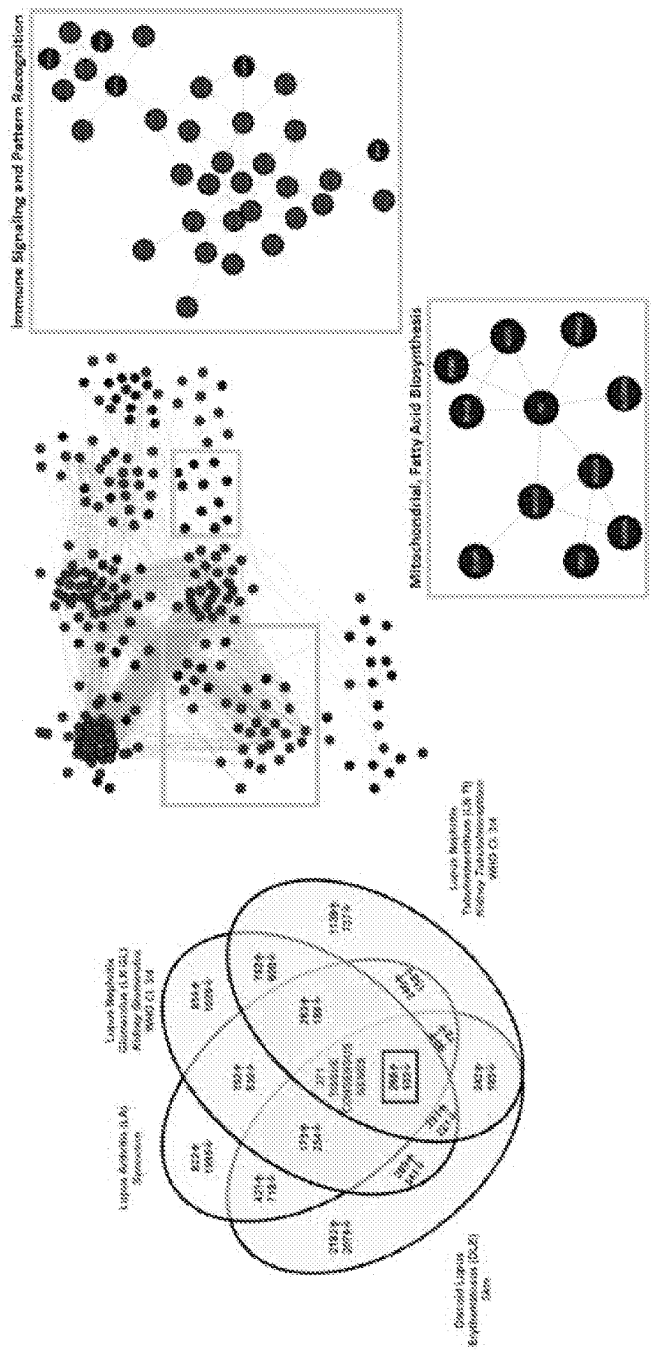


FIG. 38D

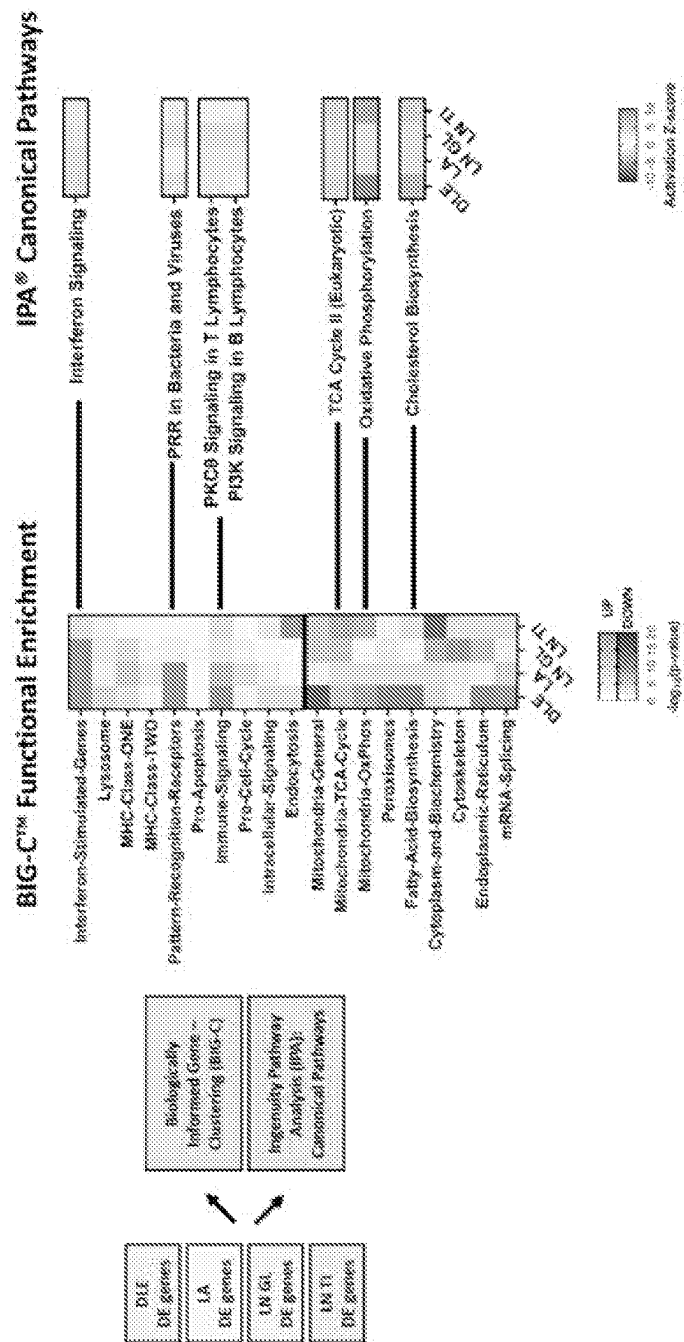


FIG. 38E

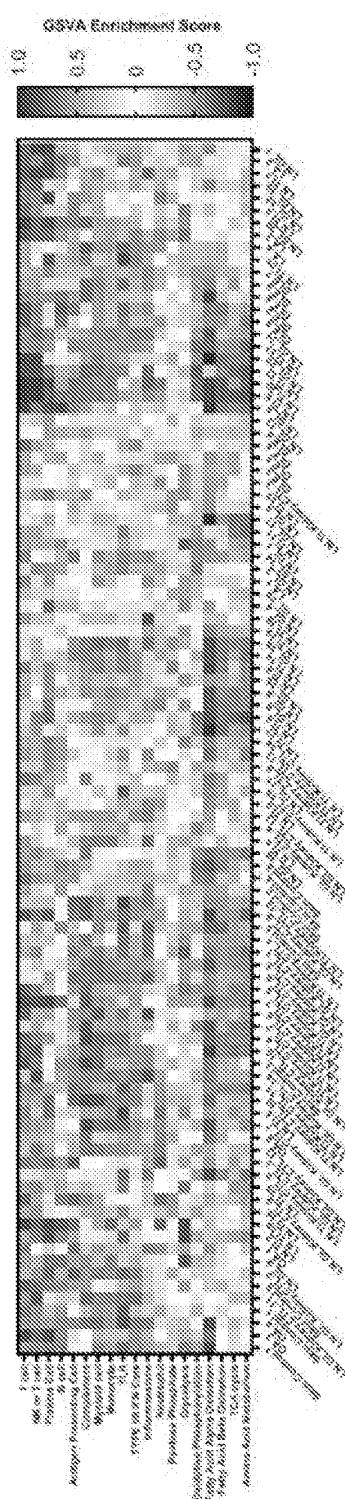


FIG. 38F

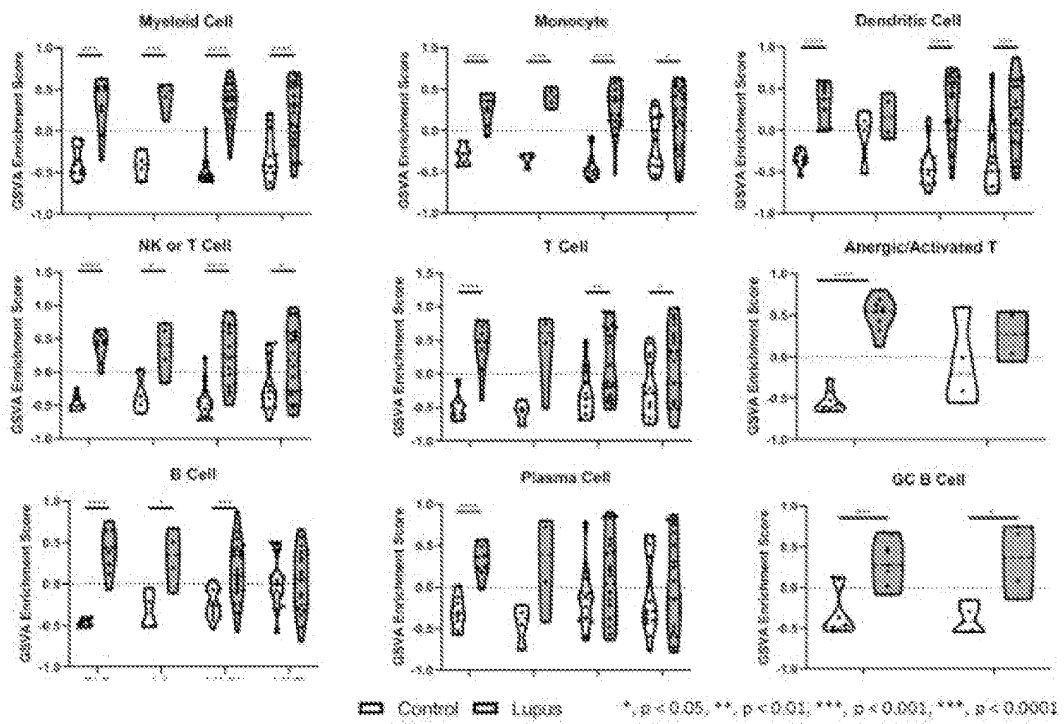


FIG. 38G

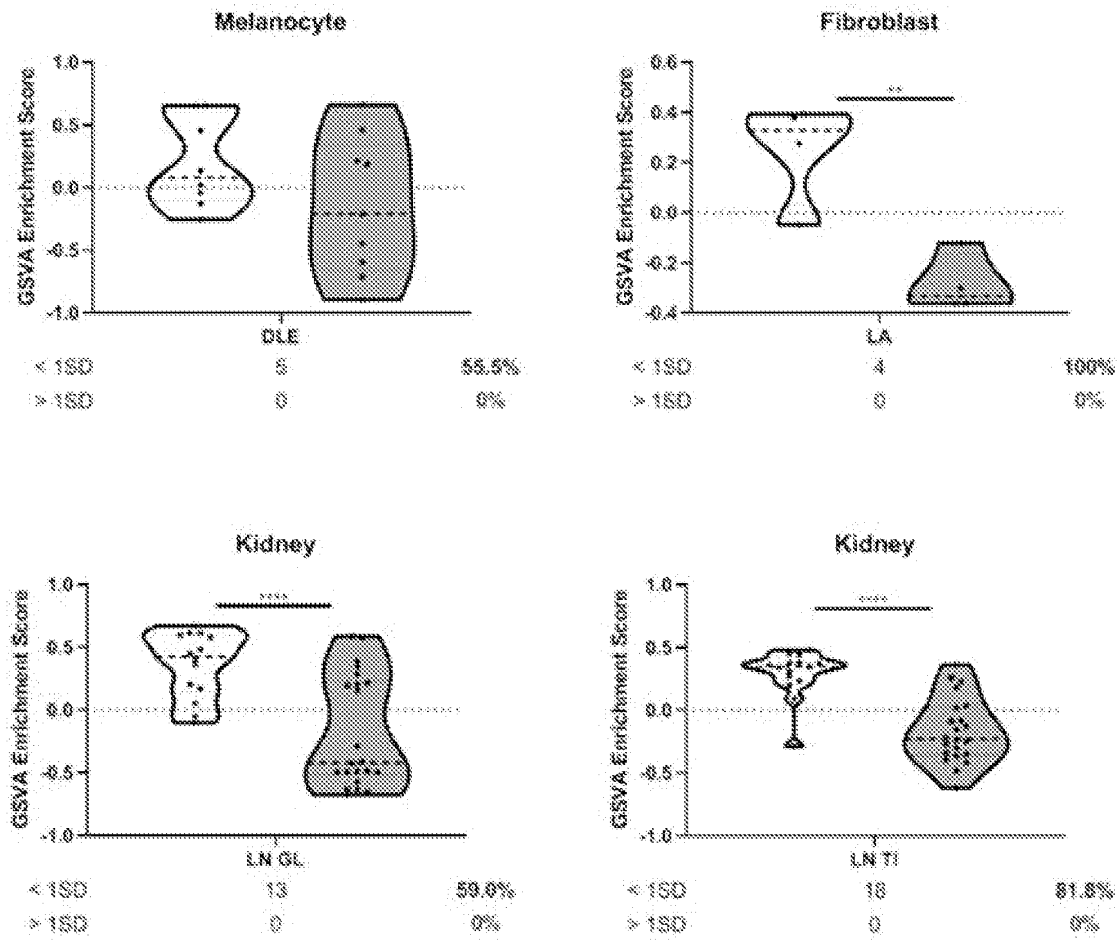


FIG. 38H

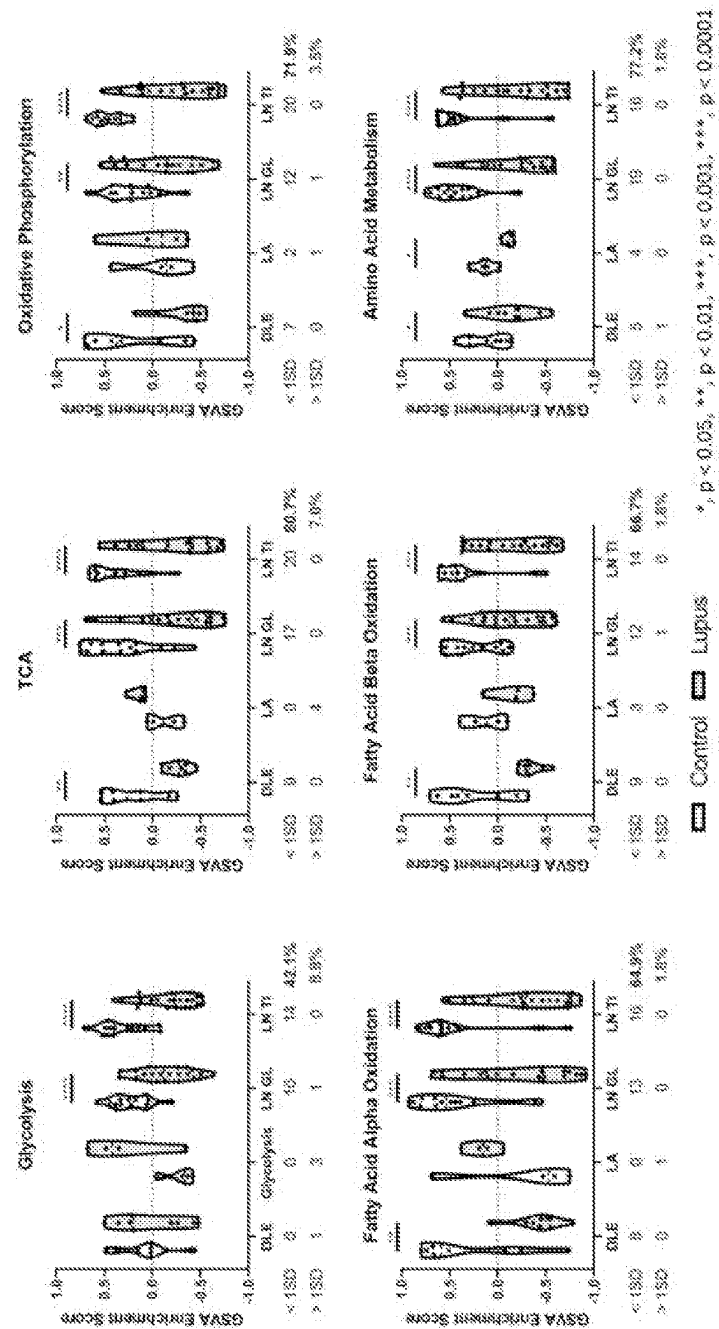


FIG. 38I

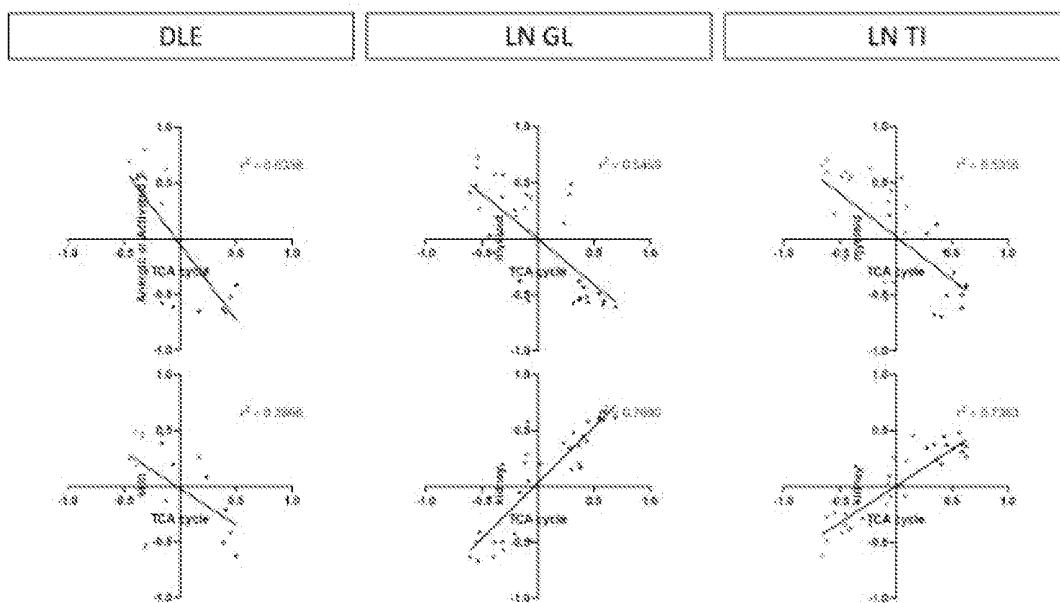


FIG. 38J

Immune and tissue cell GSVA scores for glomerulus

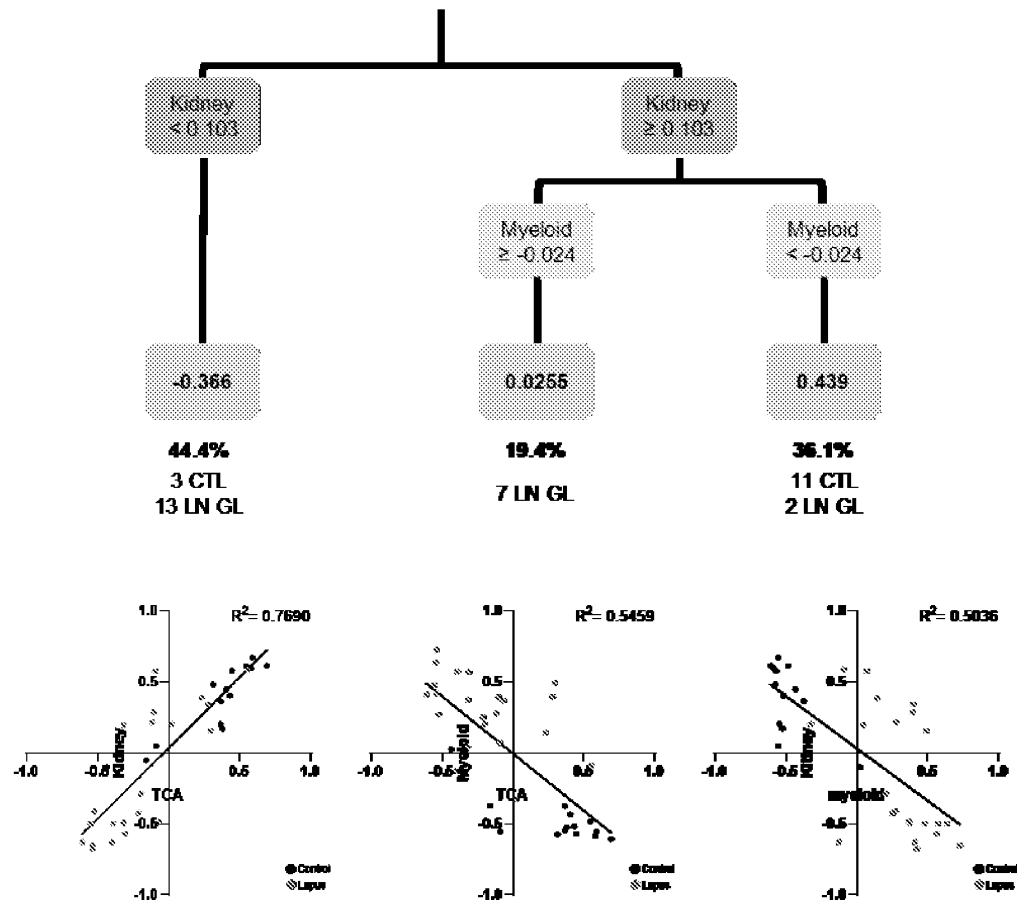


FIG. 38K

Immune and tissue cell GSVA scores for tubulointerstitium

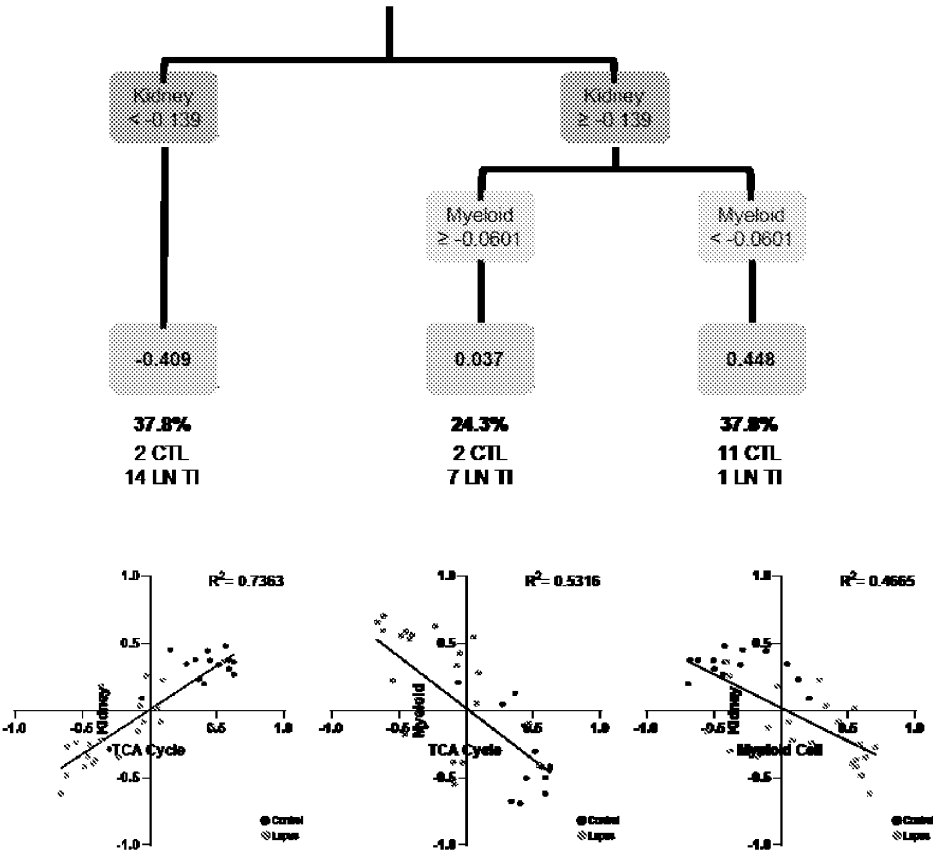


FIG. 38L

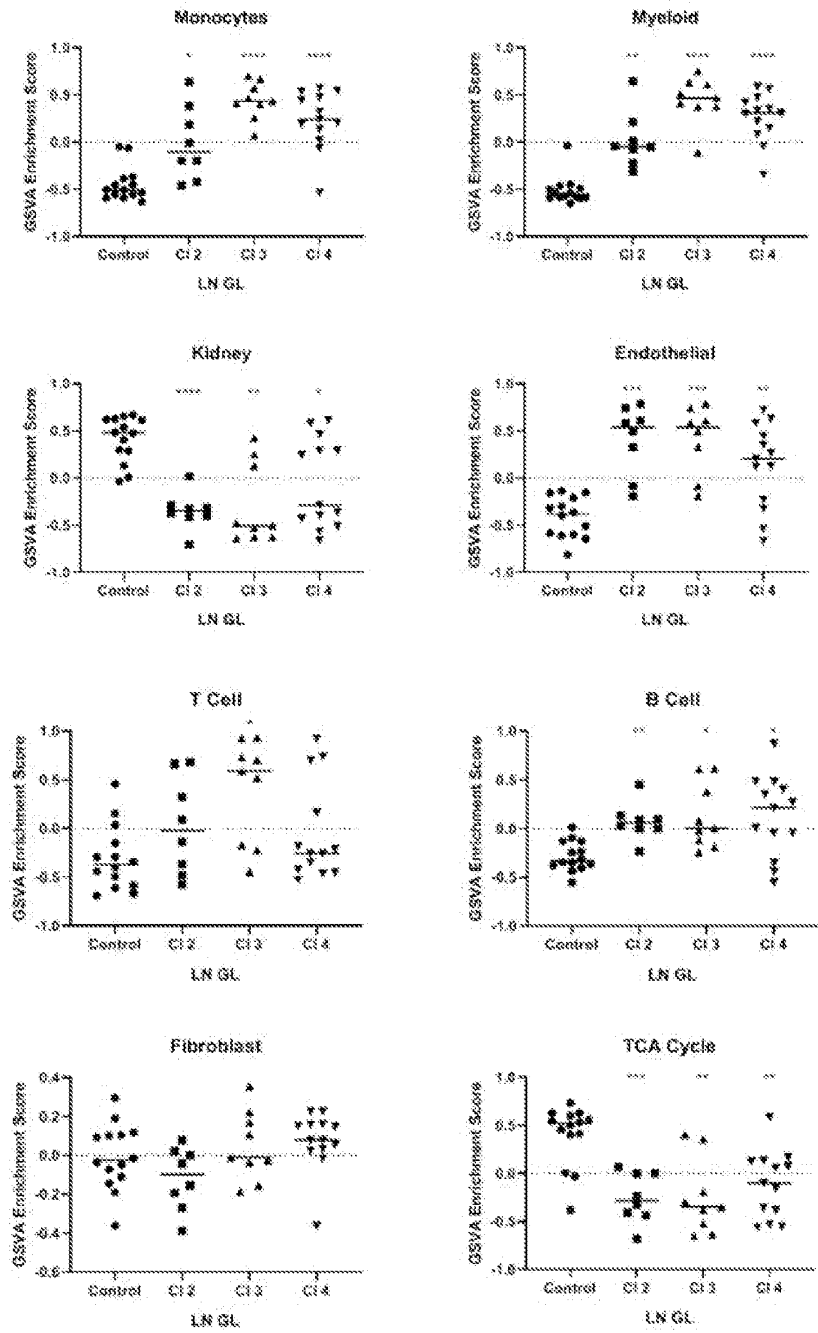


FIG. 38M

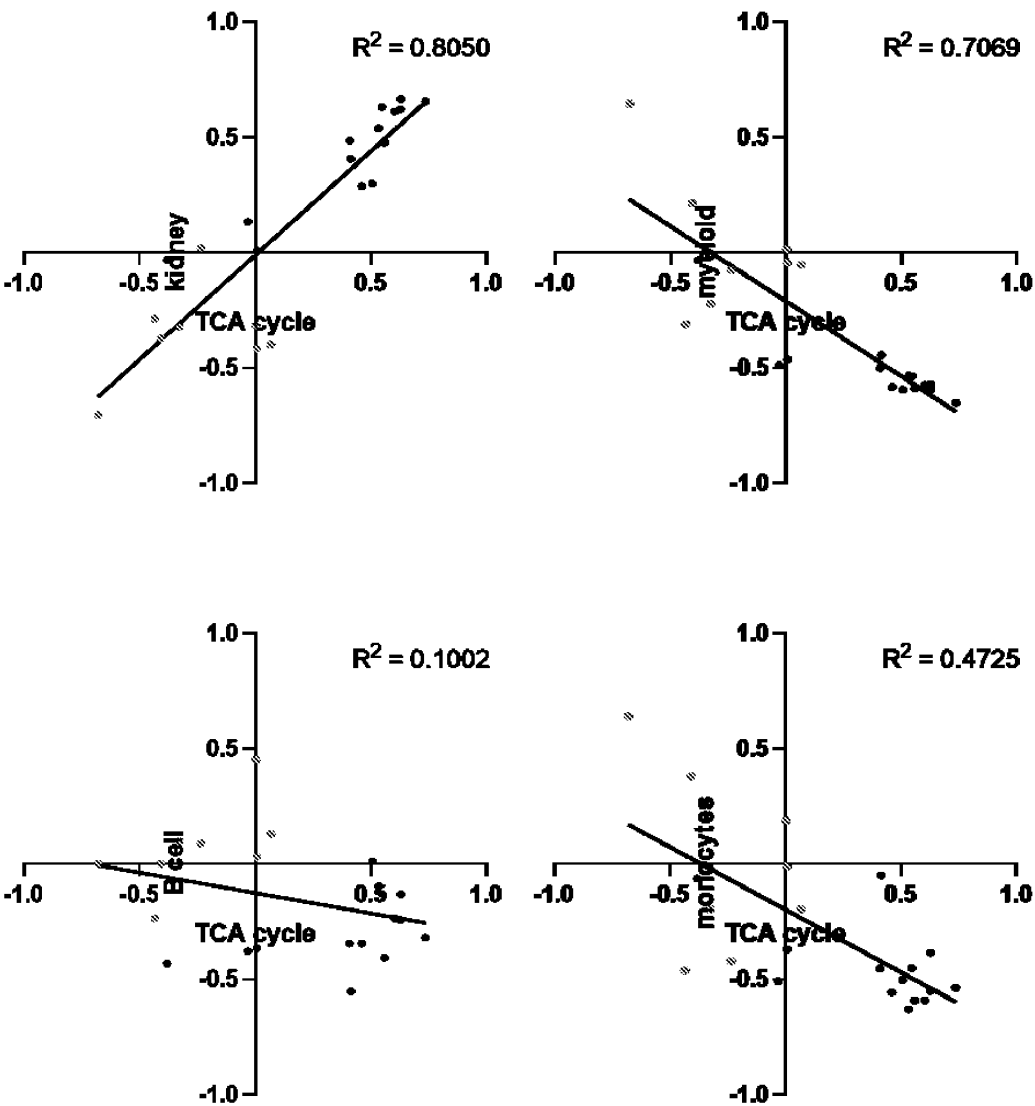


FIG. 38N

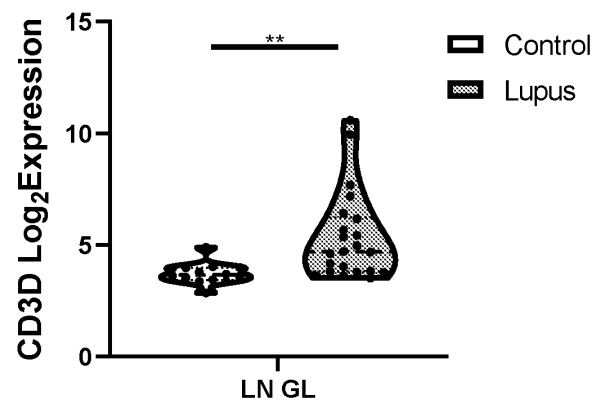


FIG. 38O

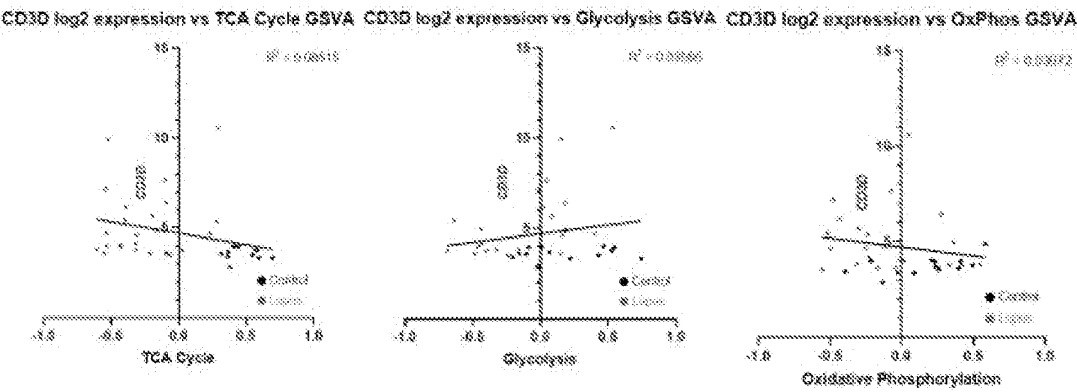


FIG. 38P

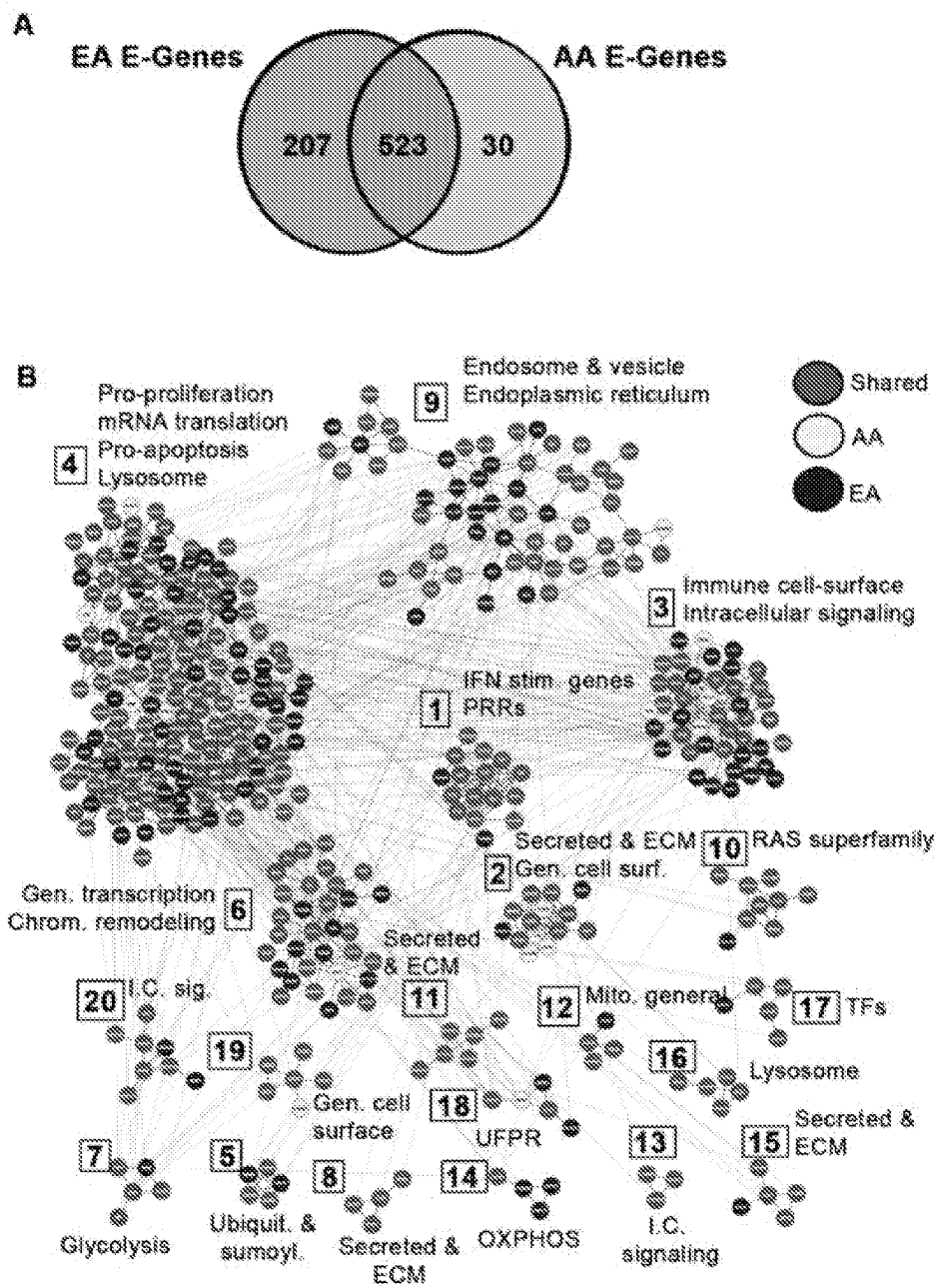


FIG. 39

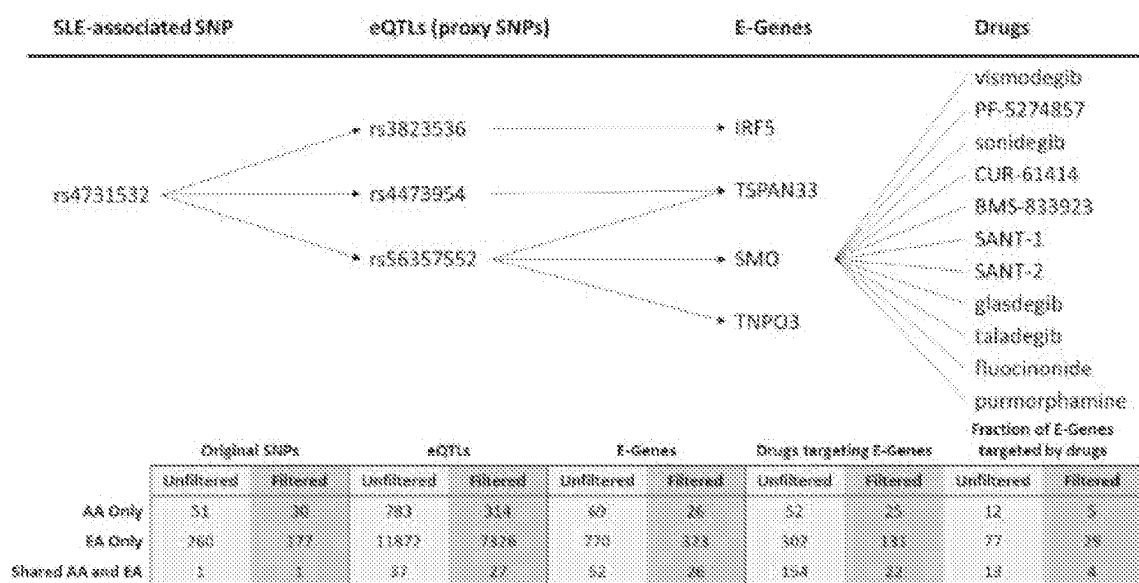


FIG. 40

SNP genomic functional categories

Region		Ancestry			
		EA		AA	
Coding		SNP	%	SNP	%
	Exon	7	2.7	1	1.9
	5' UTR	1	0.4	0	0
	3' UTR	14	5.4	4	7.6
Non-coding					
	miRNA	0	0	0	0
	lncRNA	8	3.0	3	5.7
	TFBS	4	1.5	0	0
	Regulatory	38	14.6	12	23.1
	NT-R	17	6.5	1	1.9
	Other	171	65.8	31	59.6
TOTAL		260	~100	52	~100

NT-R = non-traditional regulatory: intronic or intergenic SNP
with strong regulatory potential

FIG. 41A

Summary of eQTL analysis

Ancestry	Original SNPs	eQTLs	E-Genes
EA	260	11872	770
AA	52	783	69
Shared	1	37	52

FIG. 41B

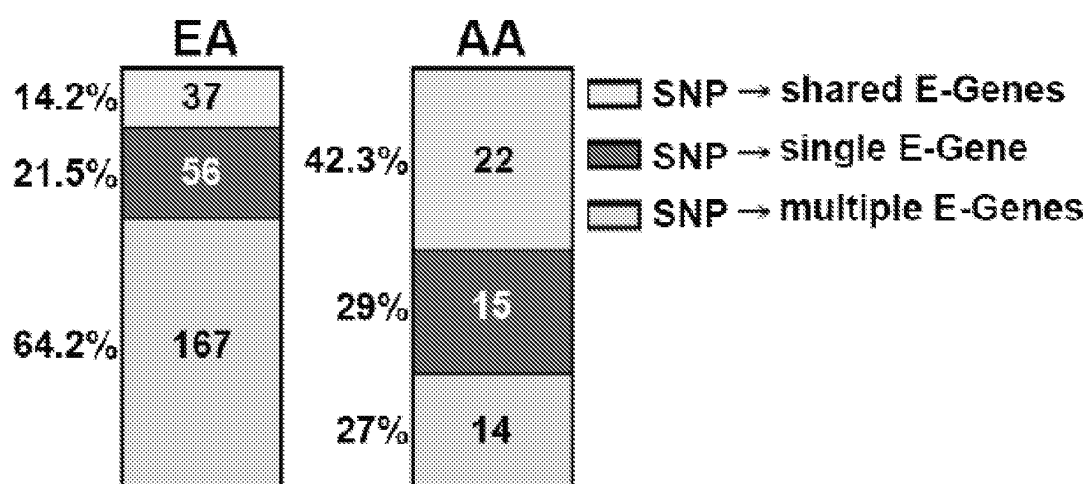


FIG. 41C

EA GO Biological Processes

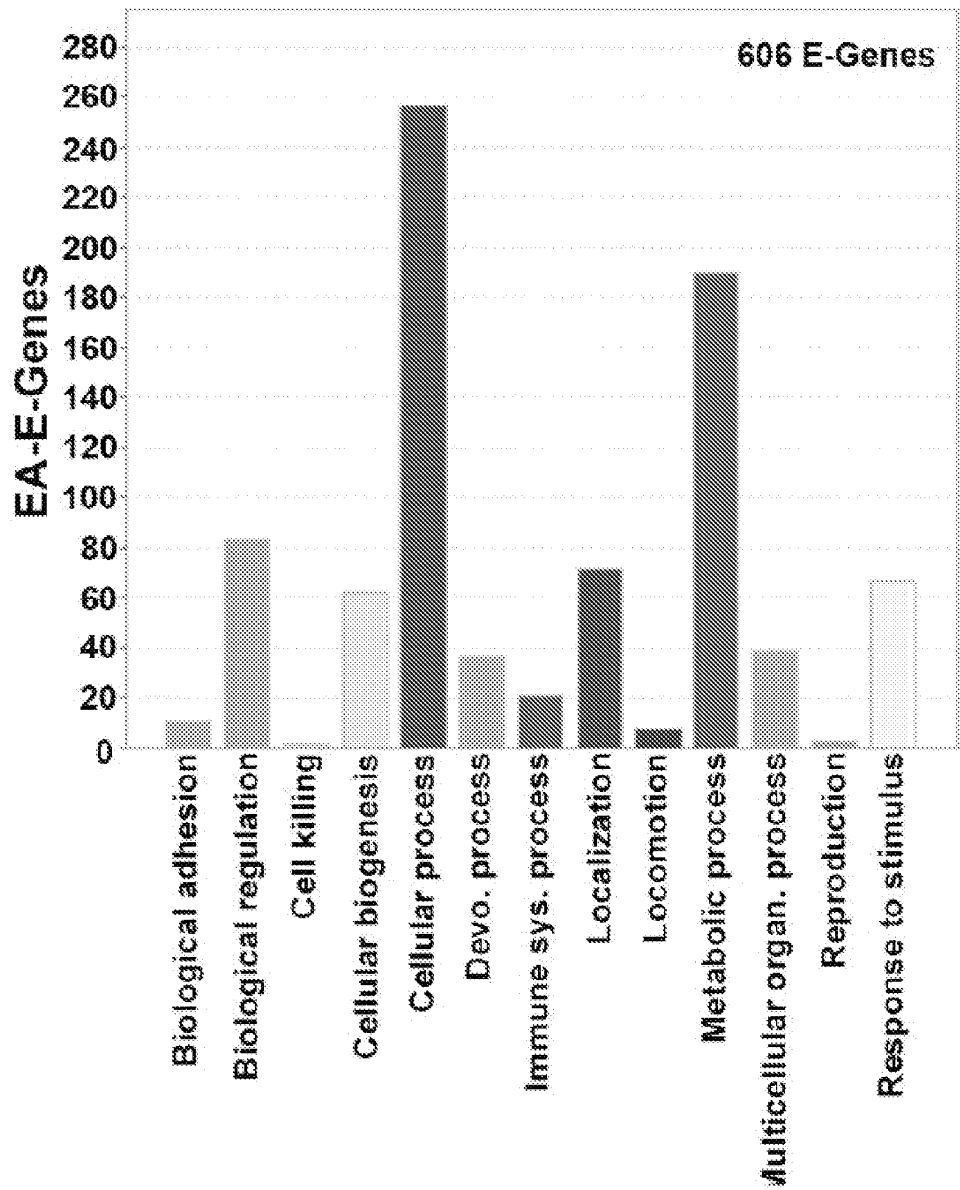


FIG. 42A

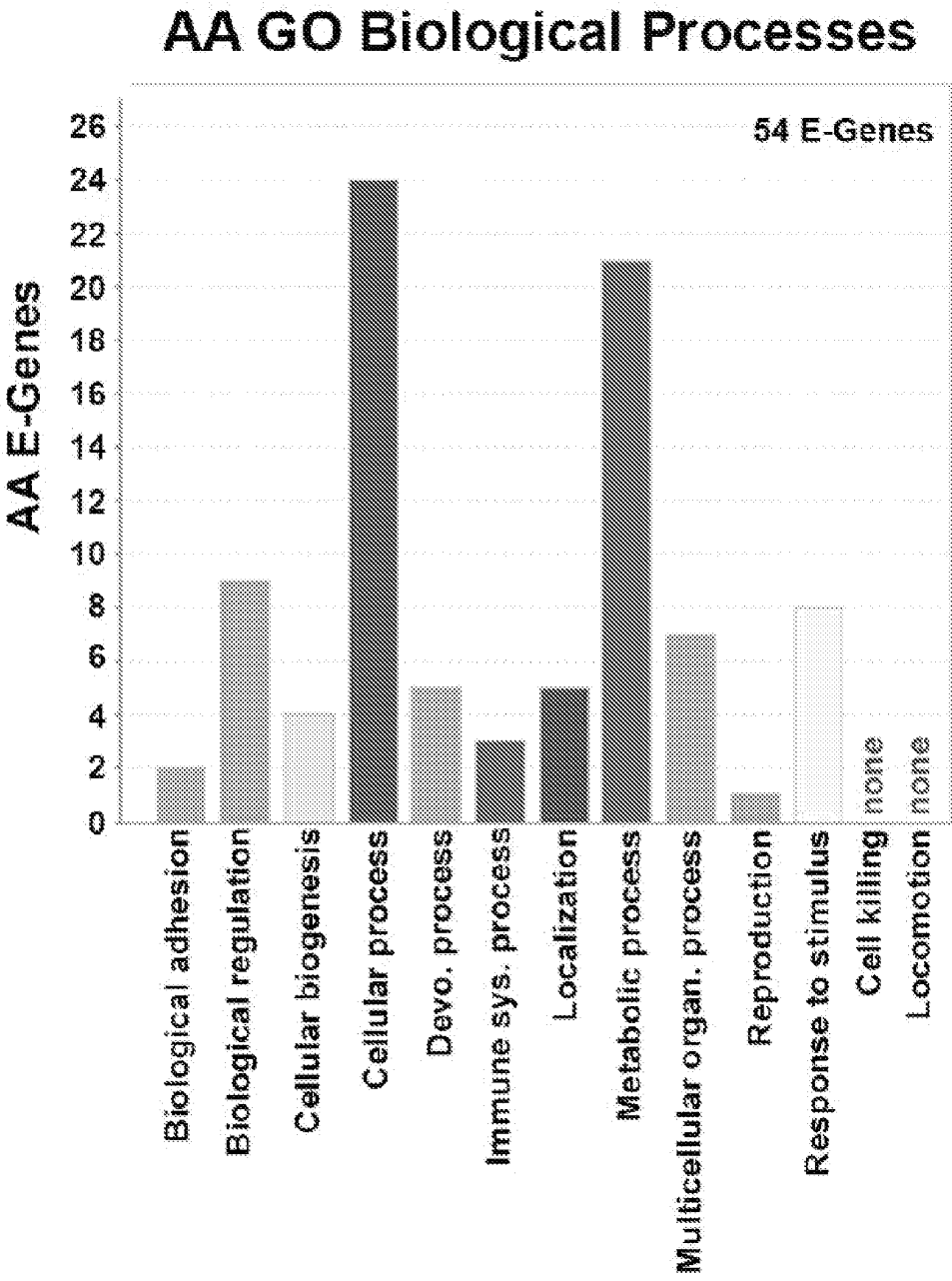


FIG. 42B

EA GO Pathways

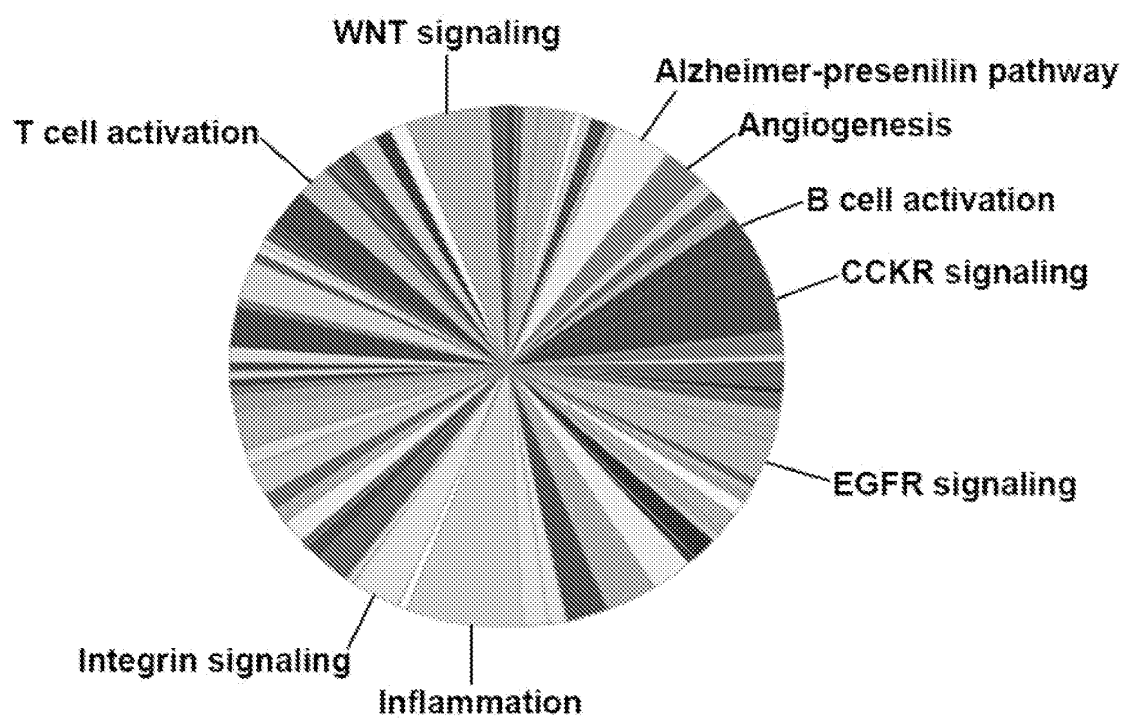


FIG. 42C

AA GO Pathways

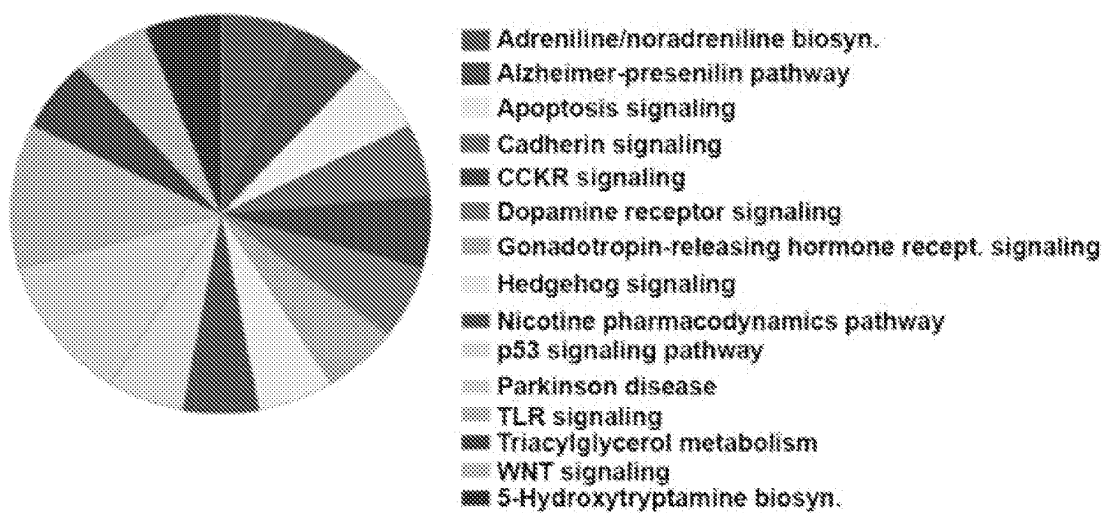


FIG. 42D

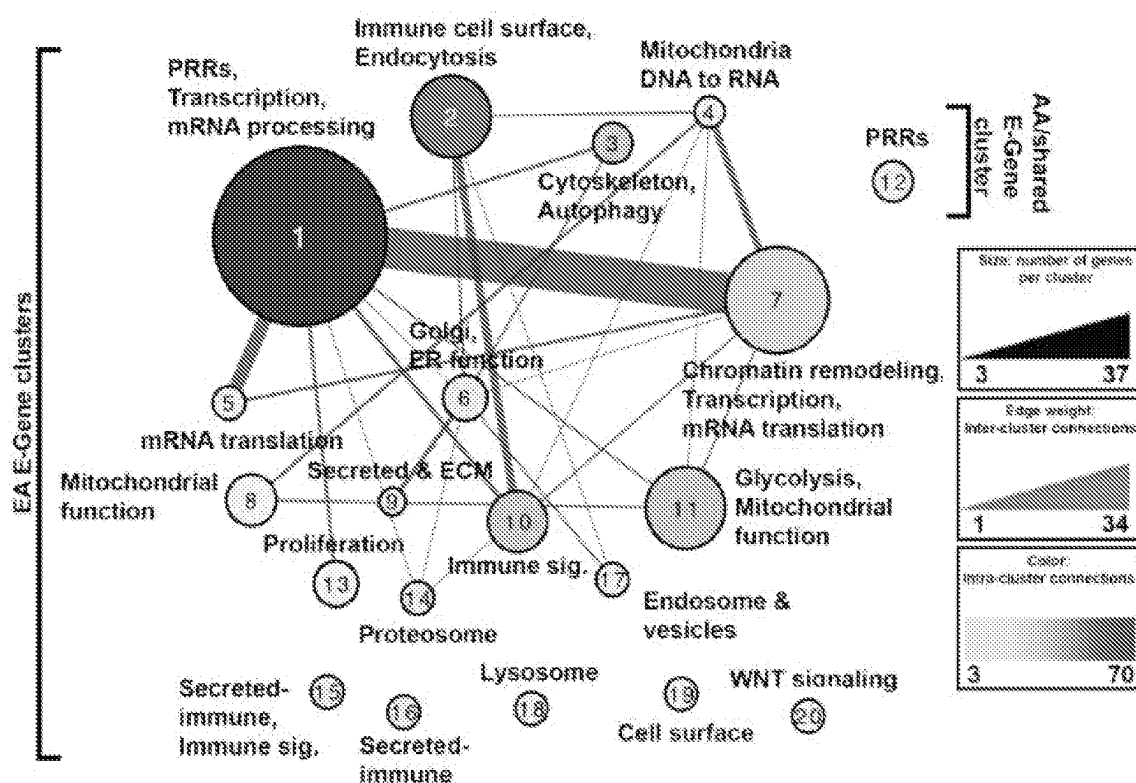


FIG. 43A

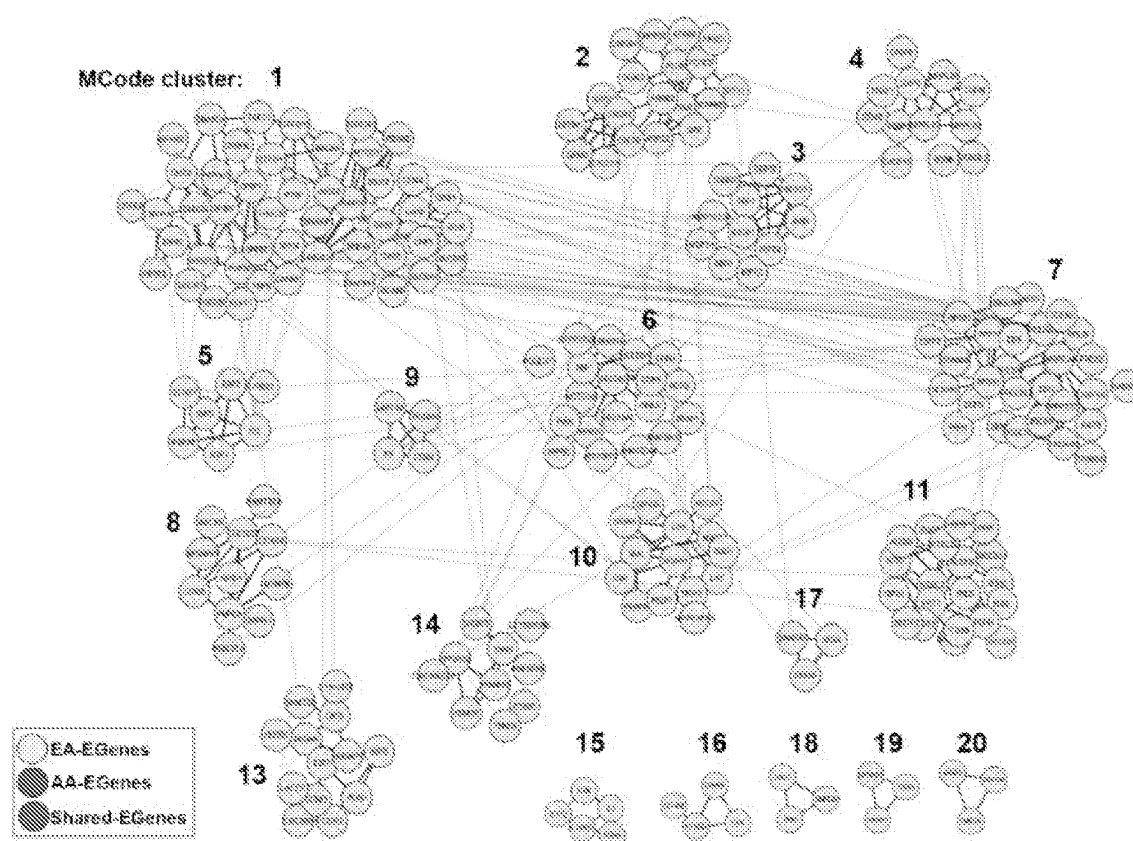


FIG. 43B

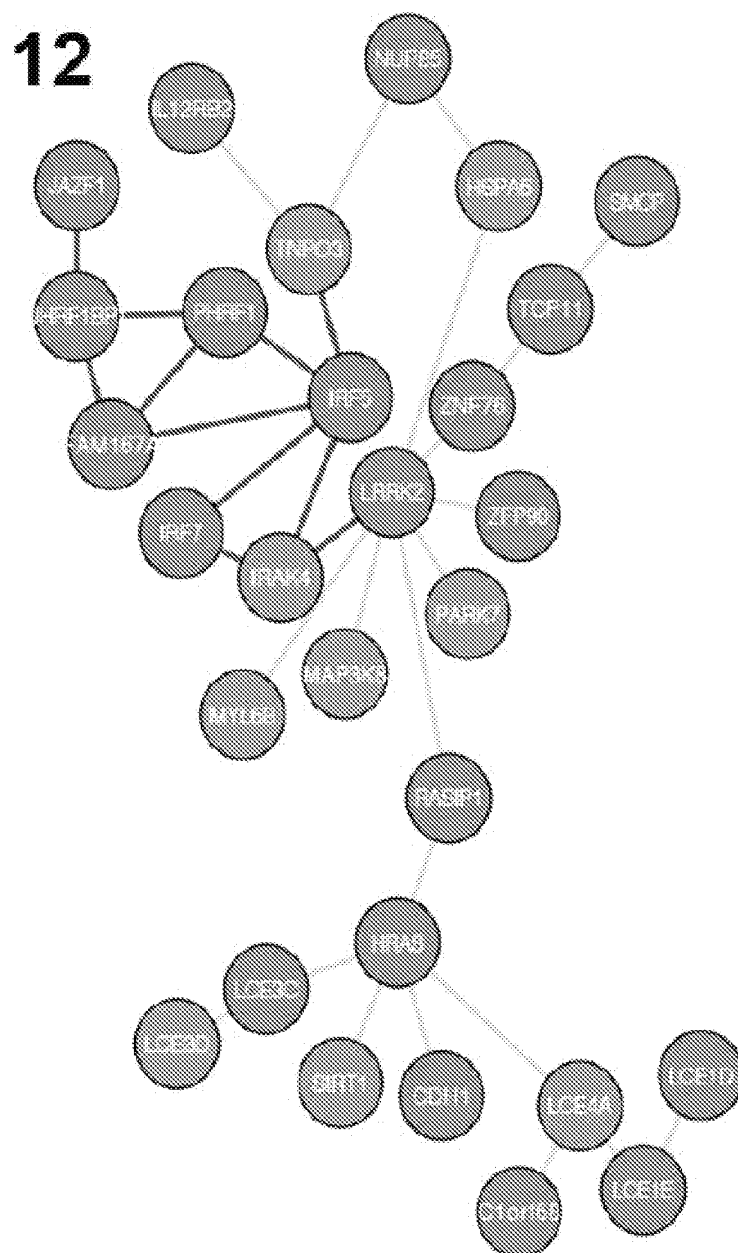


FIG. 43C

EA & AA/shared unclustered

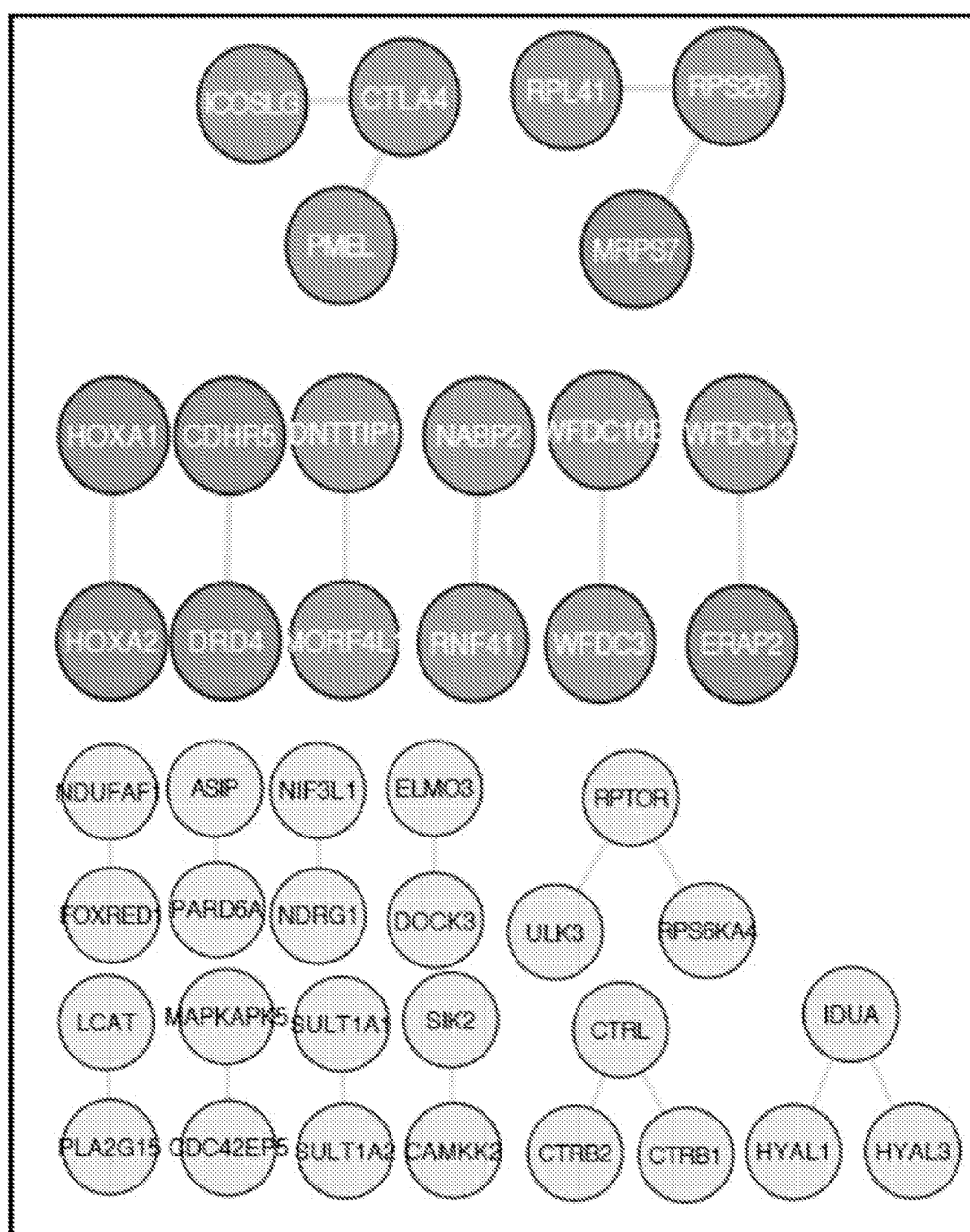


FIG. 43D

DE AA-only

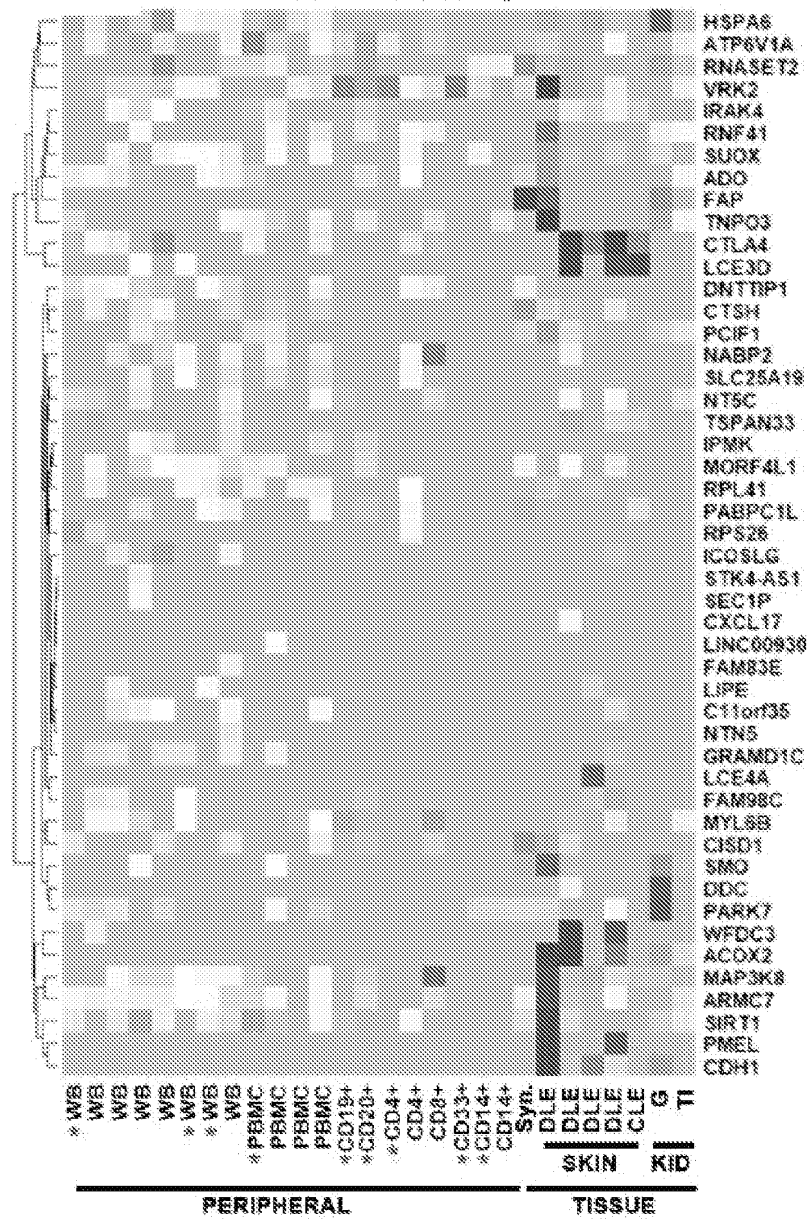


FIG. 44B

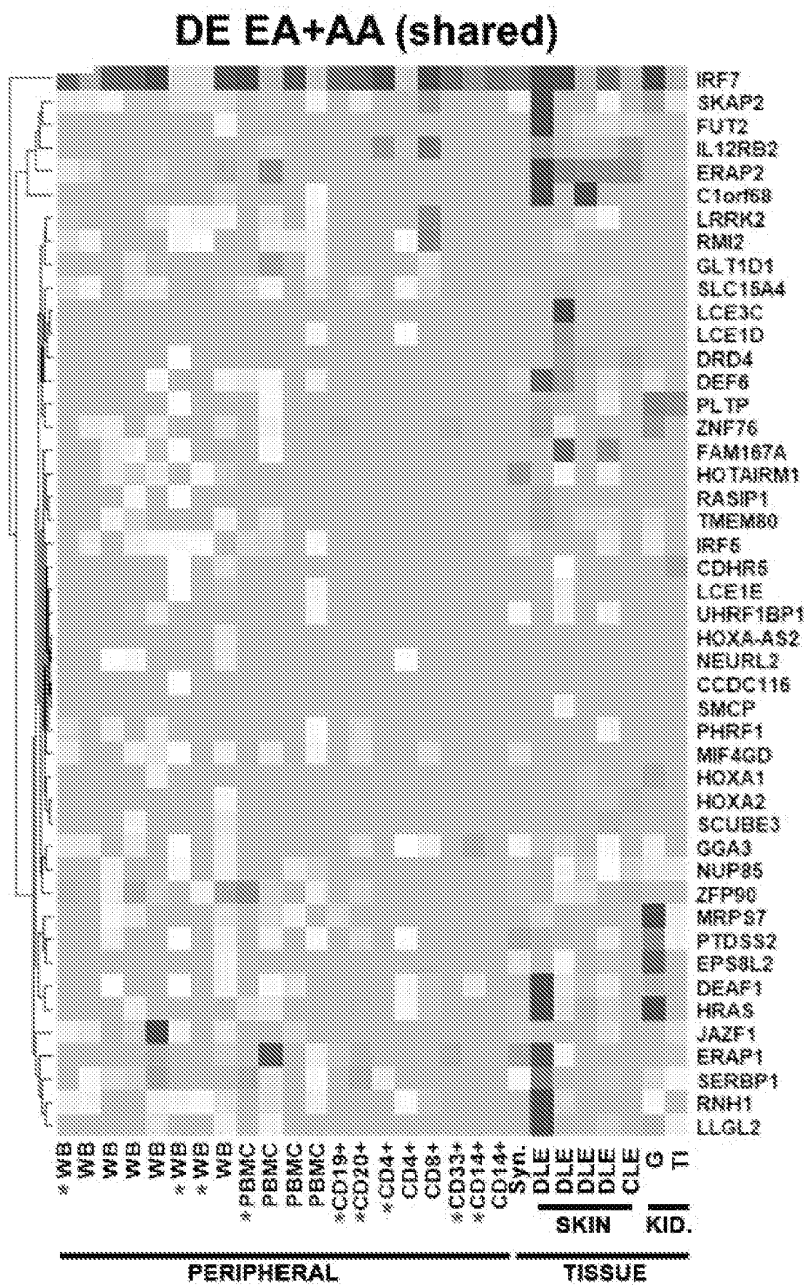


FIG. 44C

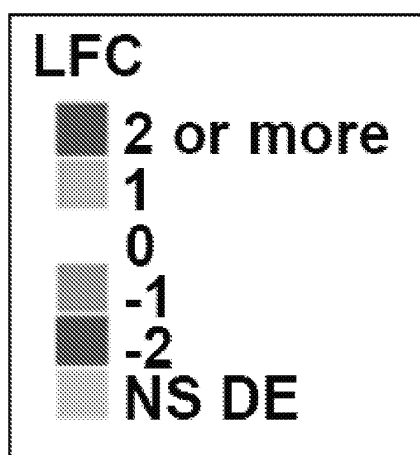


FIG. 44D

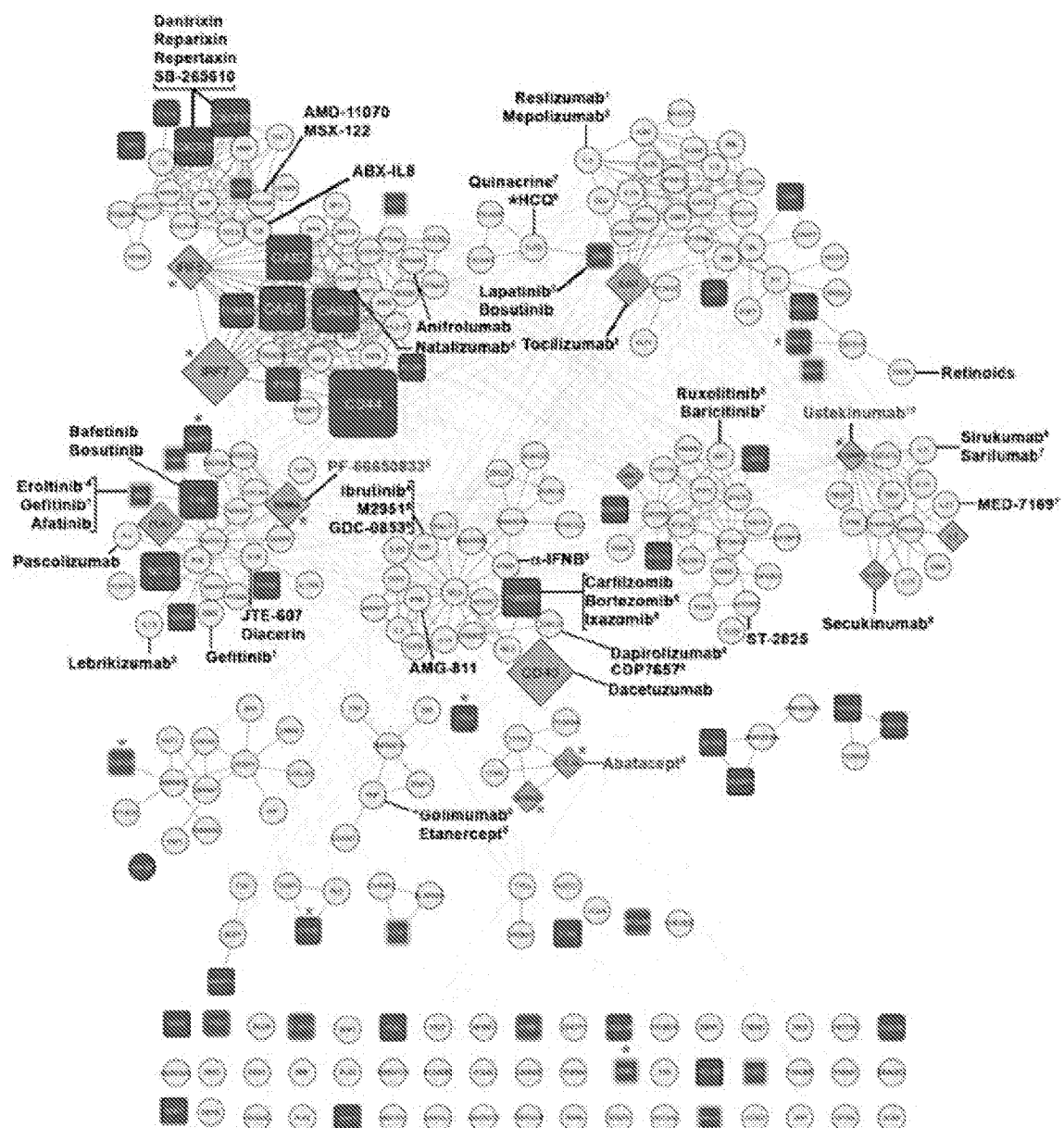


FIG. 45

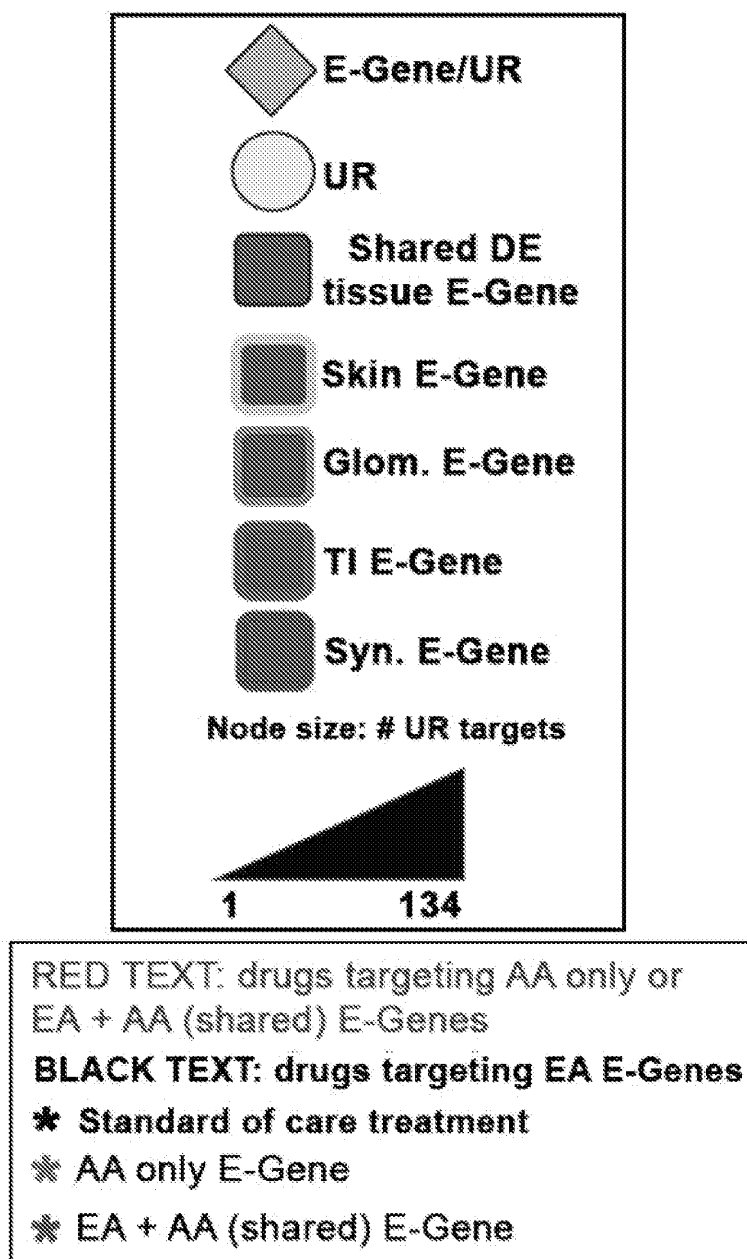


FIG. 46

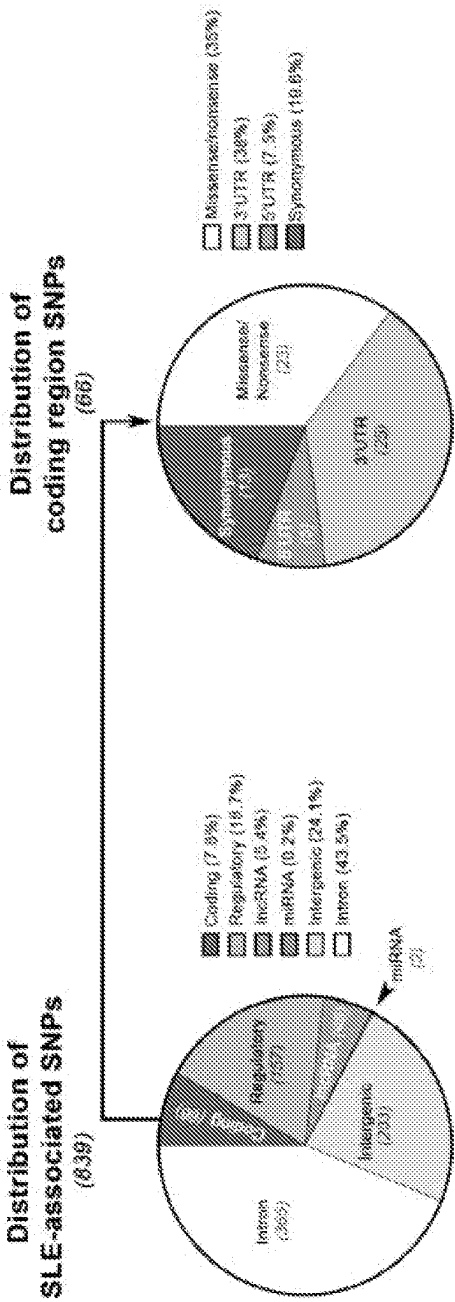


FIG. 47A

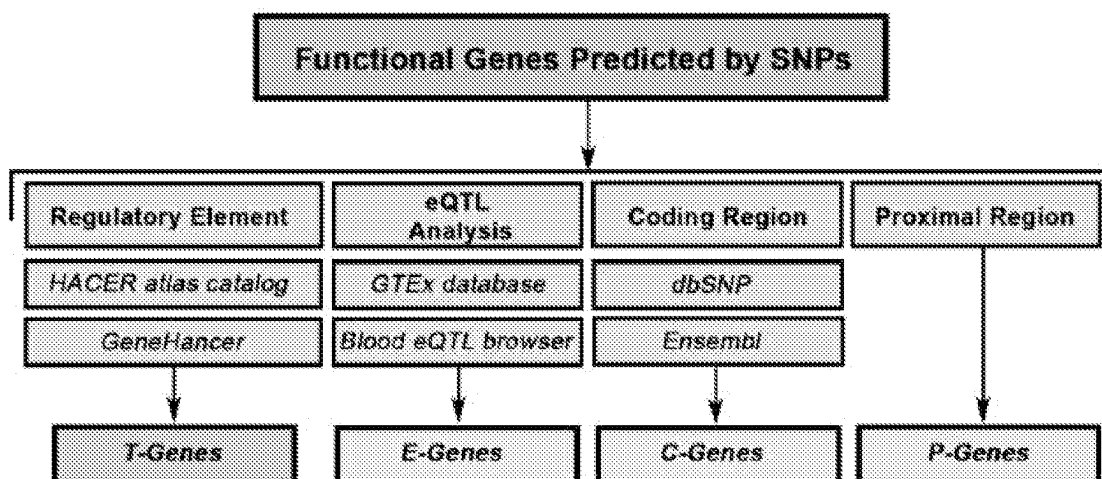


FIG. 47B

SLE-associated SNPs

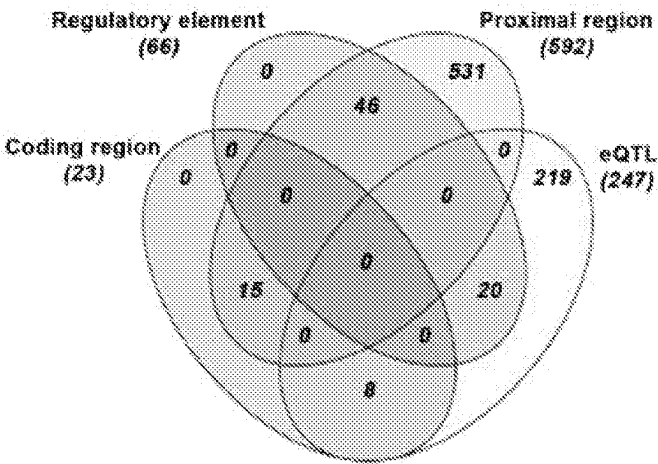


FIG. 47C

Predicted genes

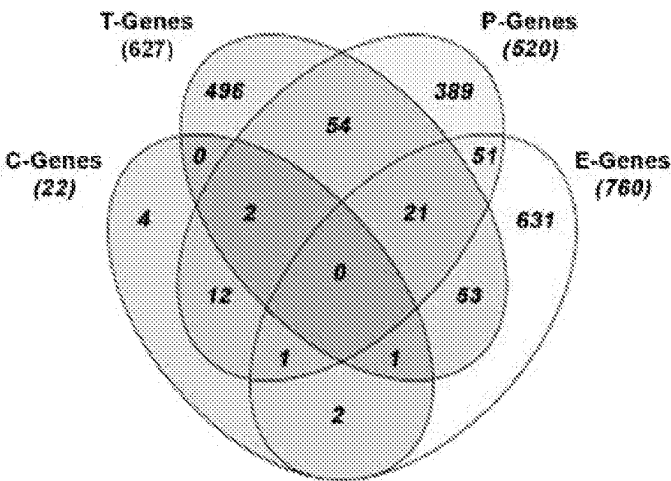


FIG. 47D

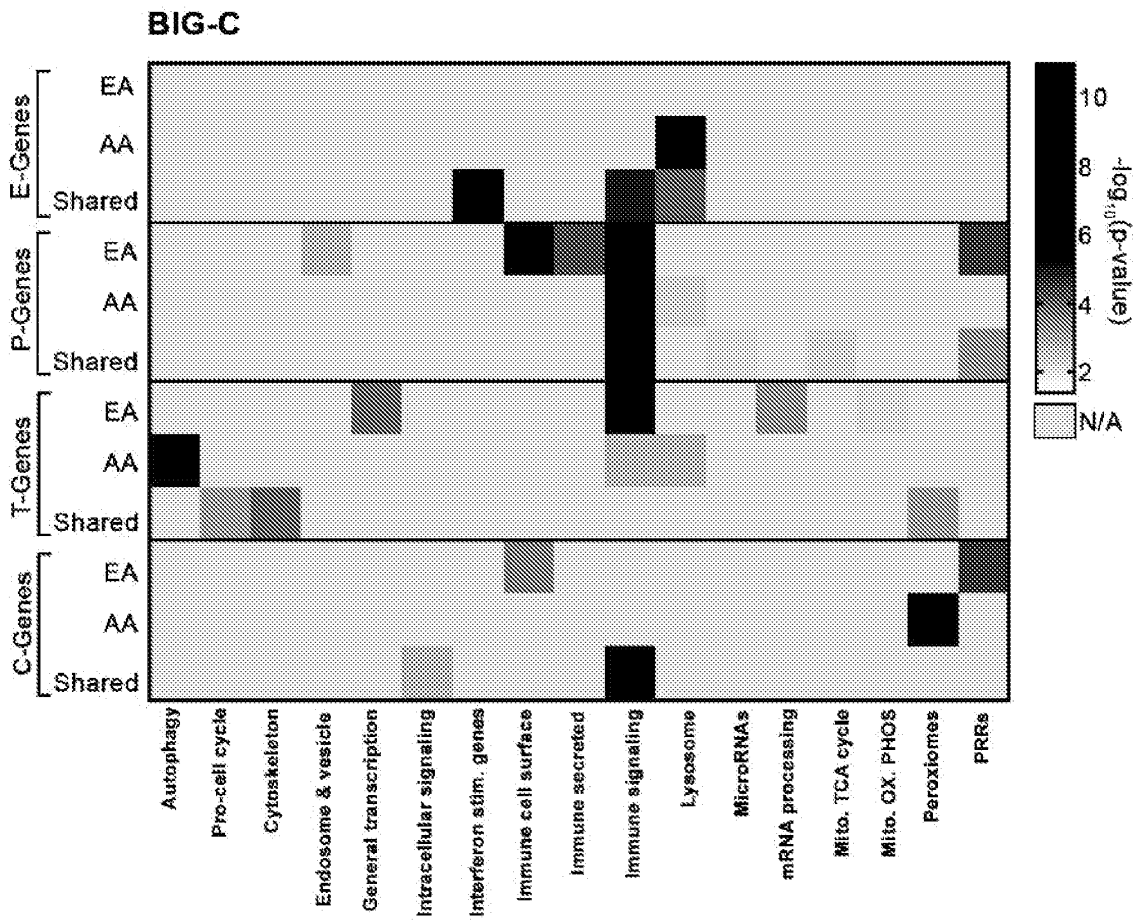


FIG. 48A

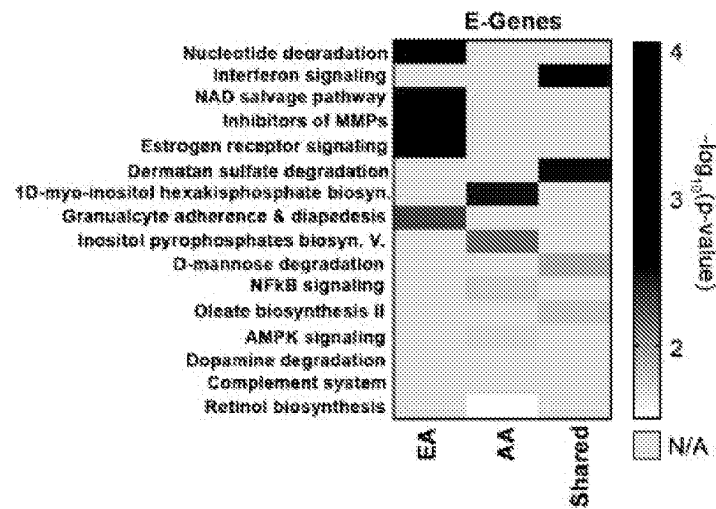


FIG. 48B

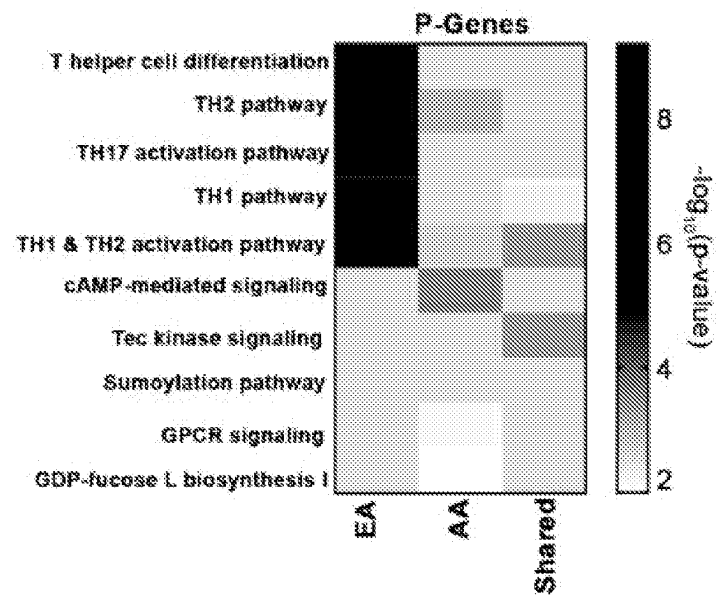


FIG. 48C

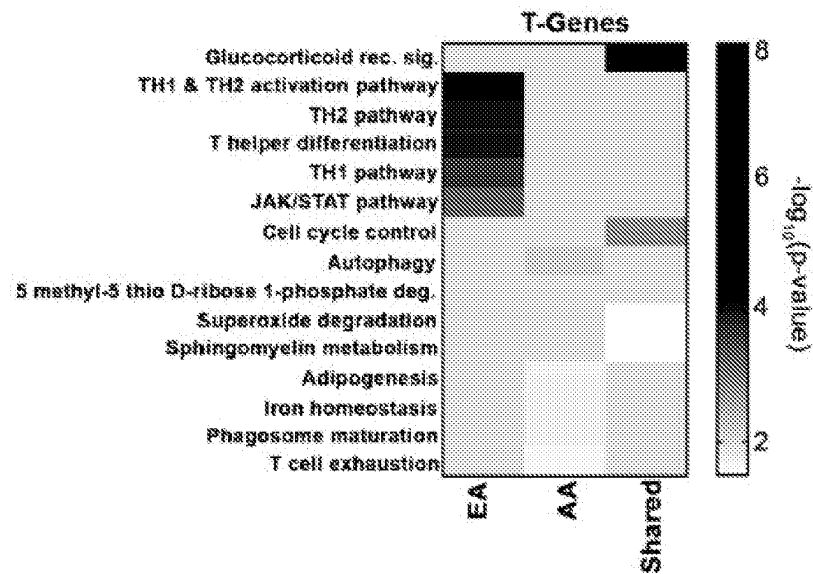


FIG. 48D

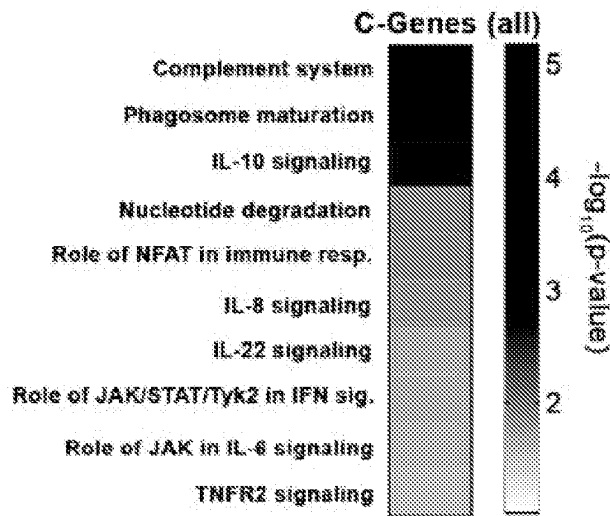


FIG. 48E

E-Genes

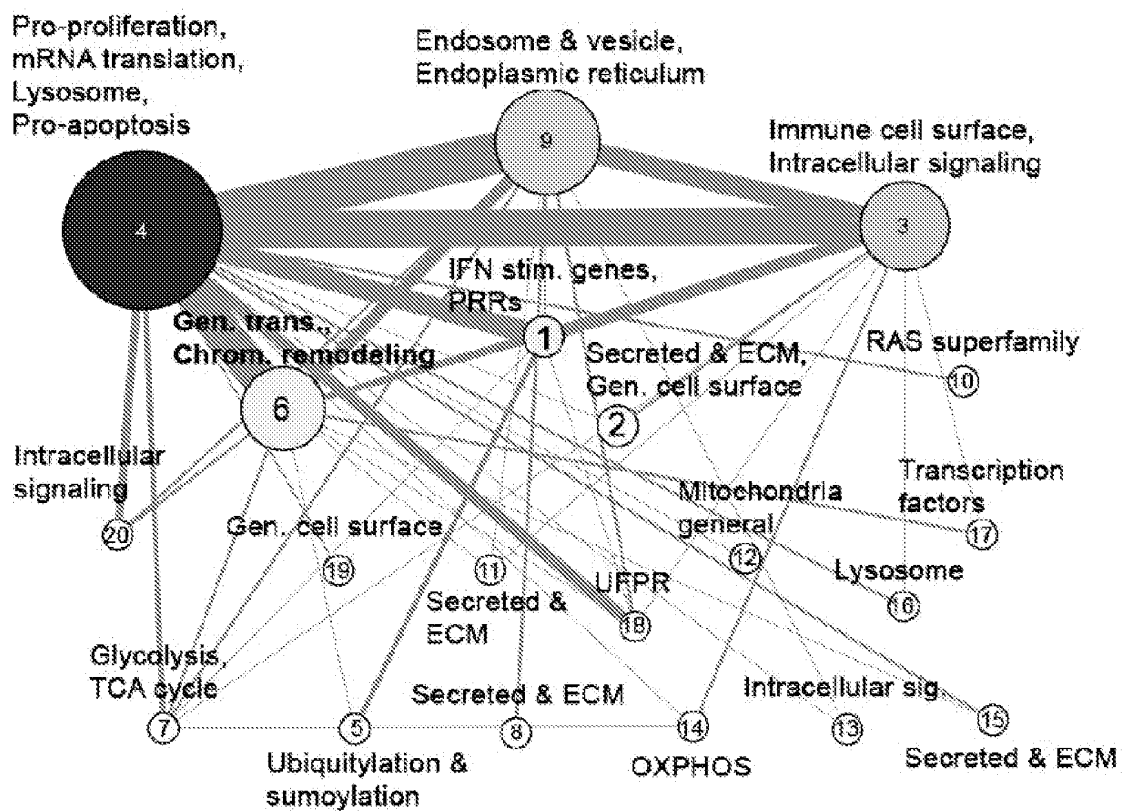


FIG. 49A

P-Genes

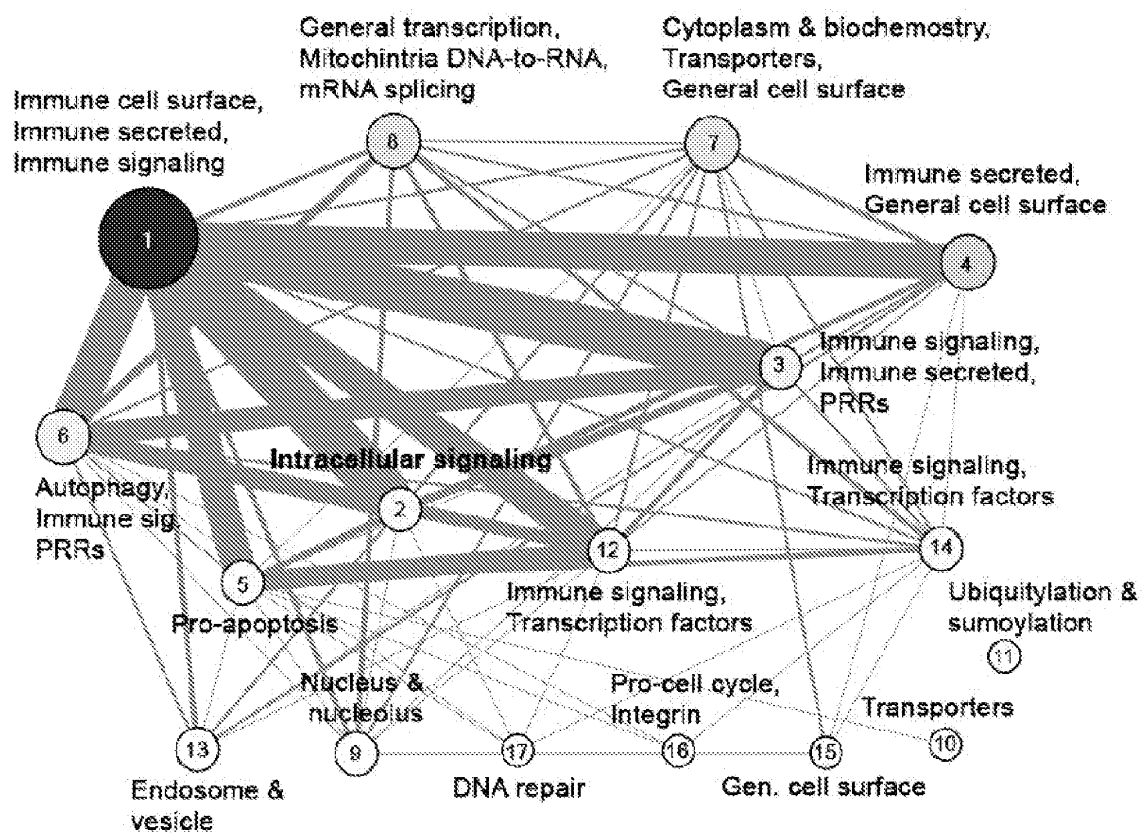


FIG. 49B

T-Genes

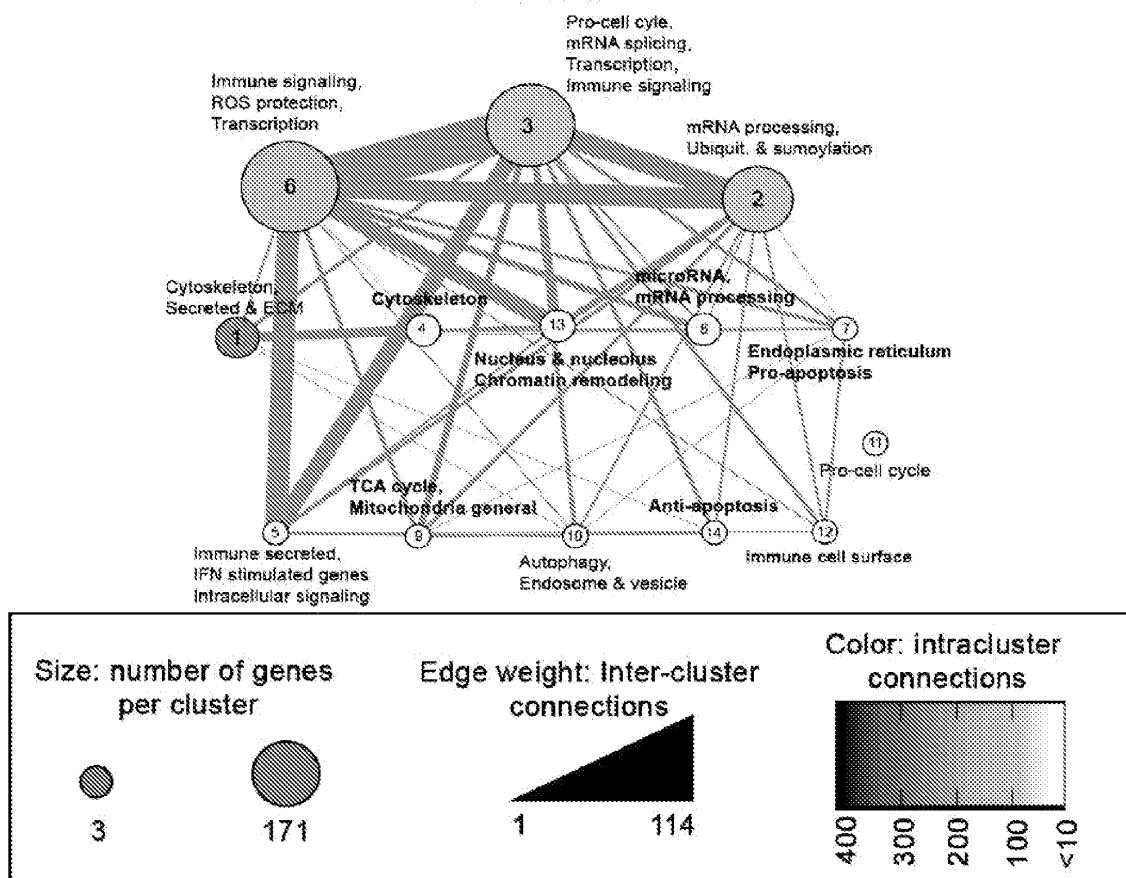


FIG. 49C

Random

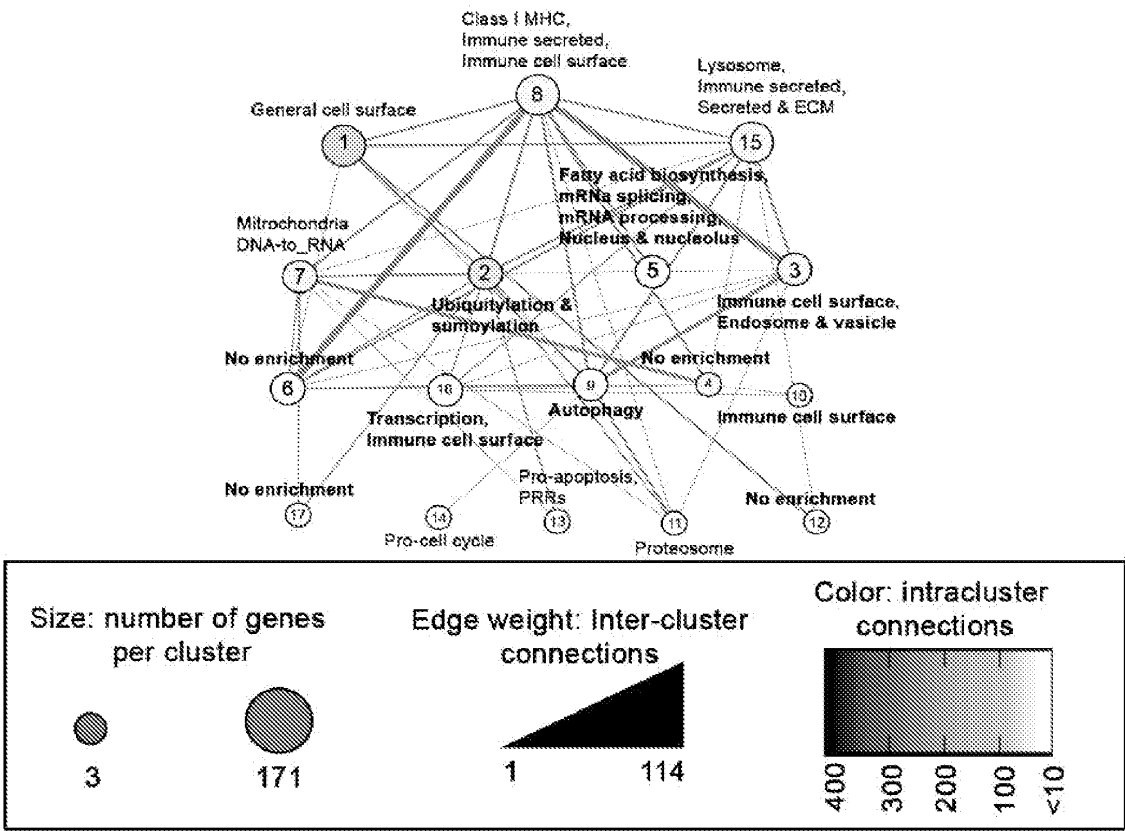


FIG. 49D

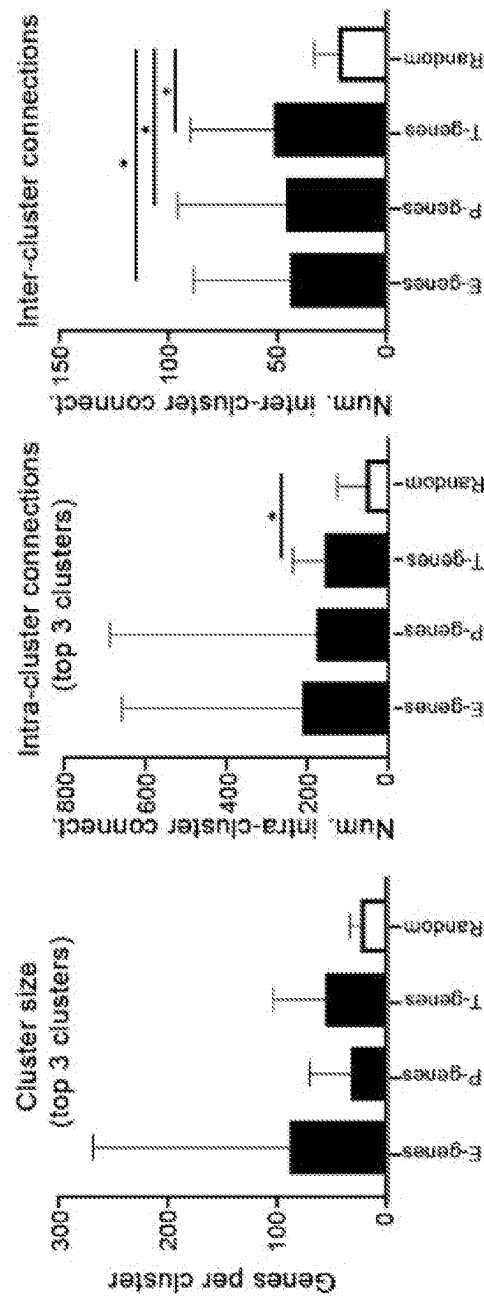


FIG. 49E

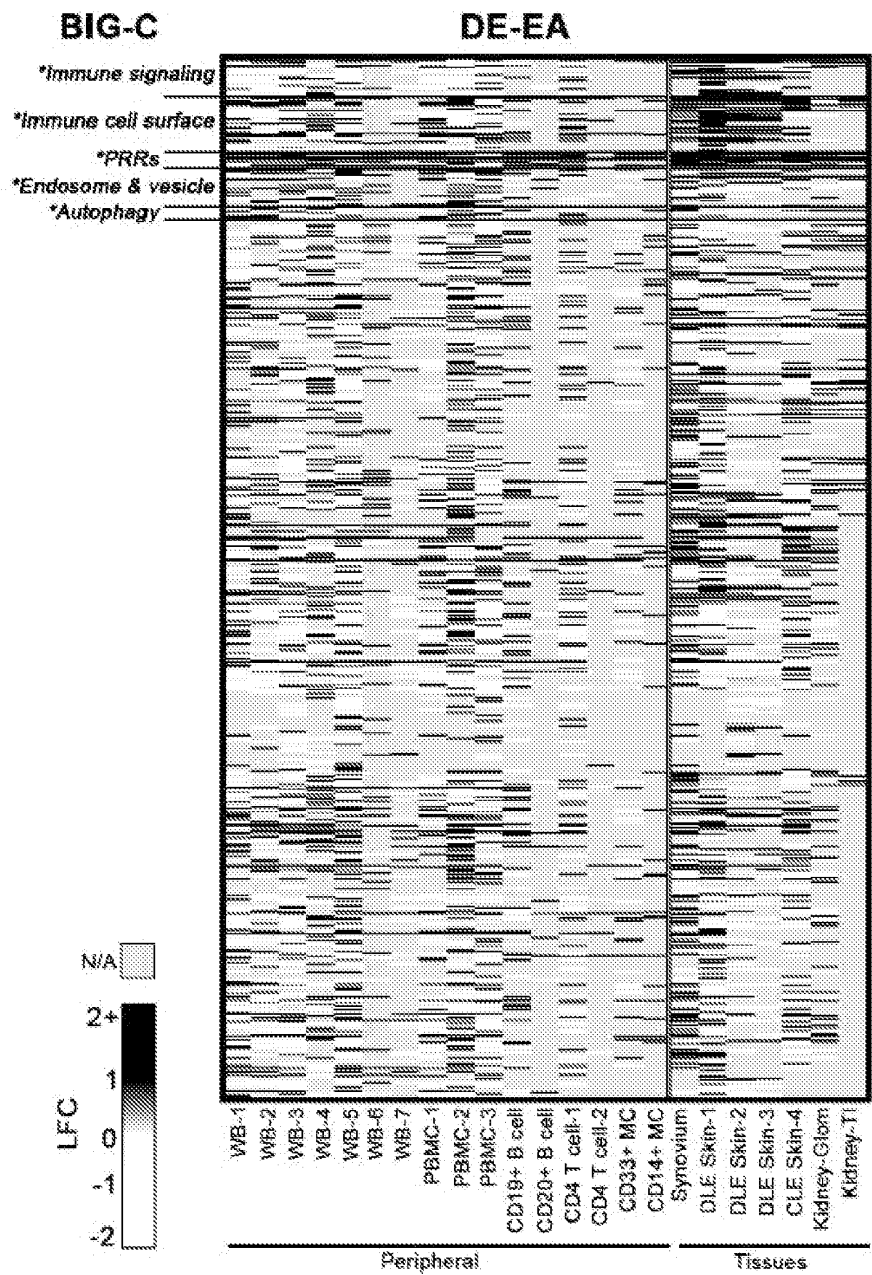


FIG. 50A

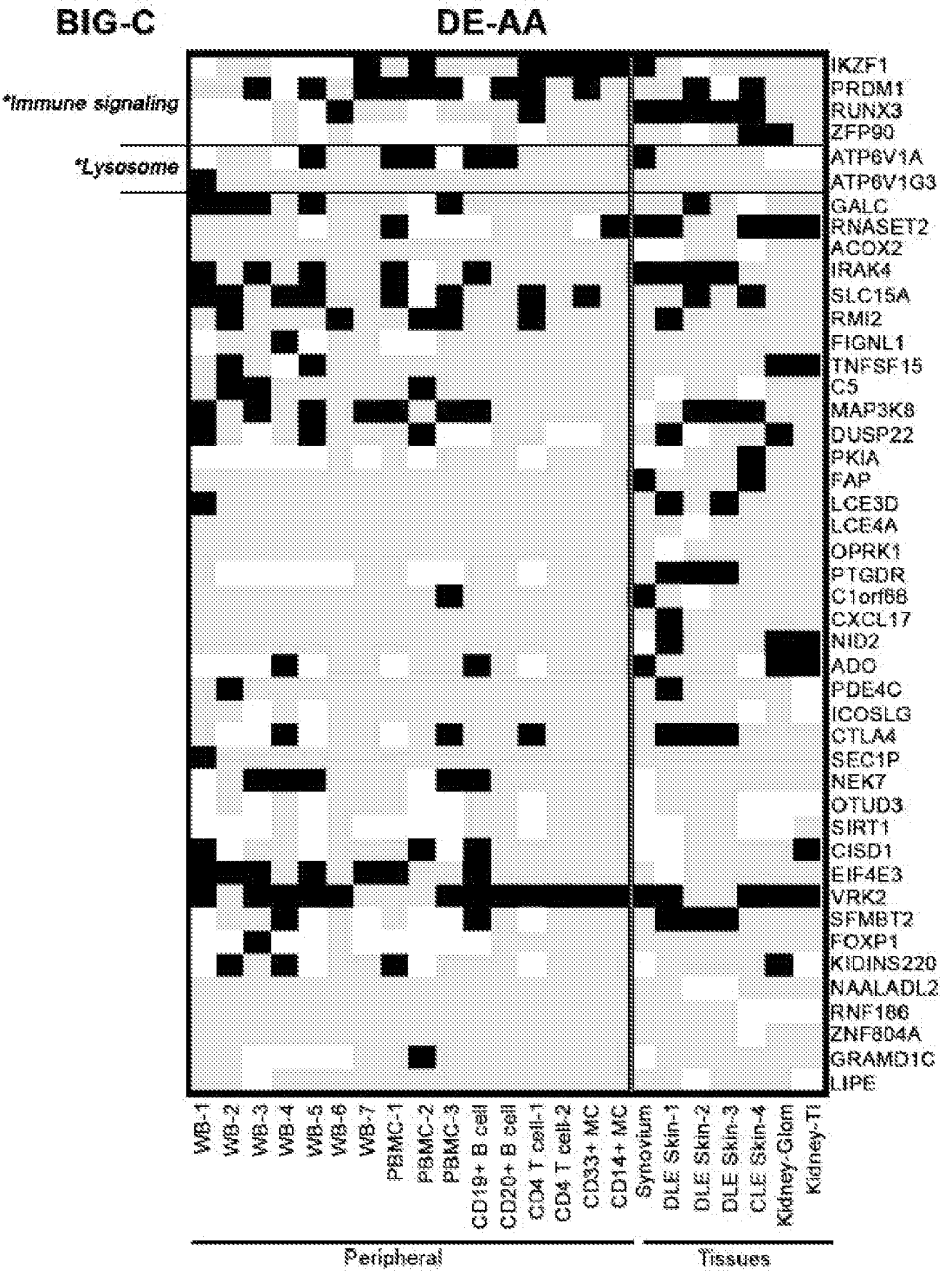


FIG. 50B

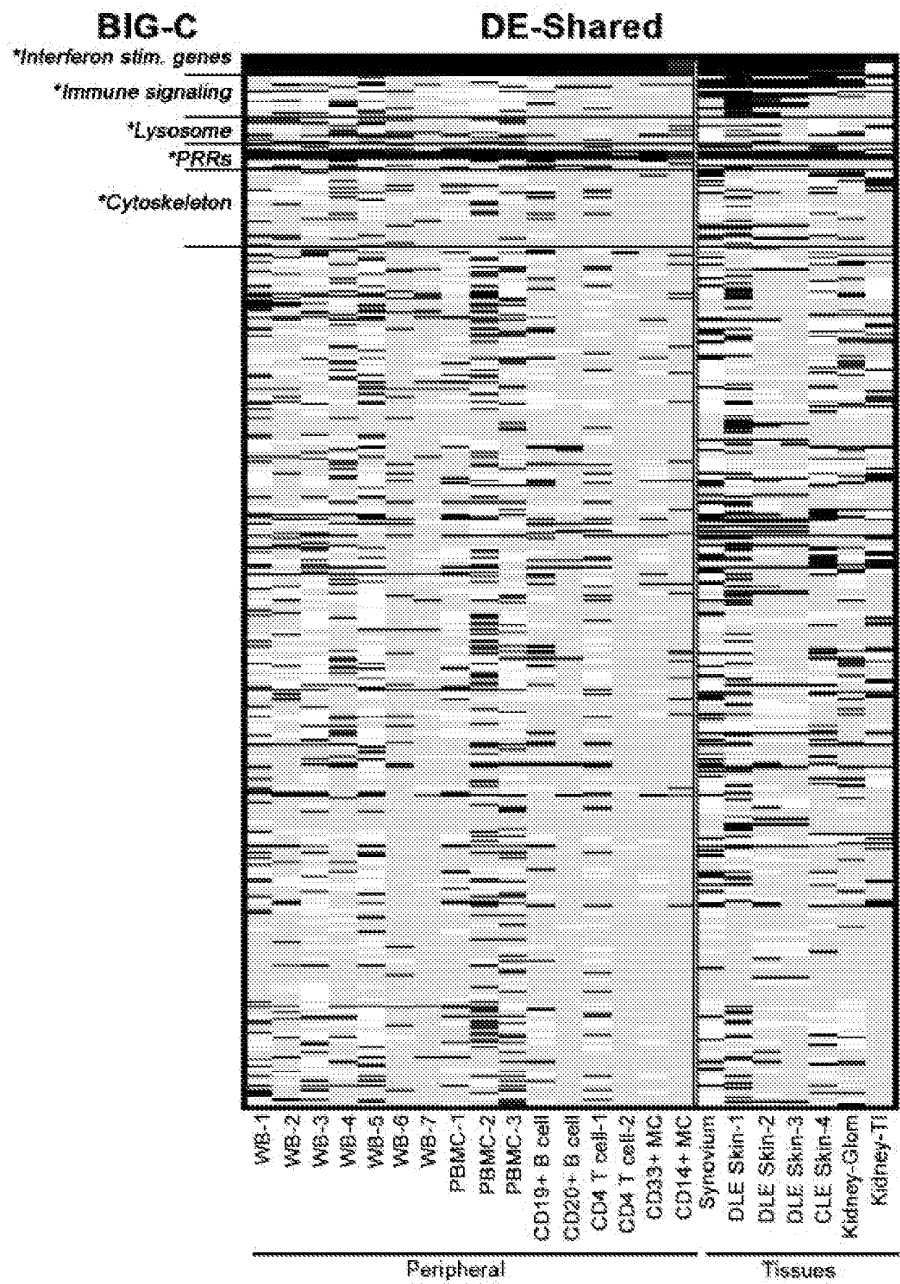


FIG. 50C

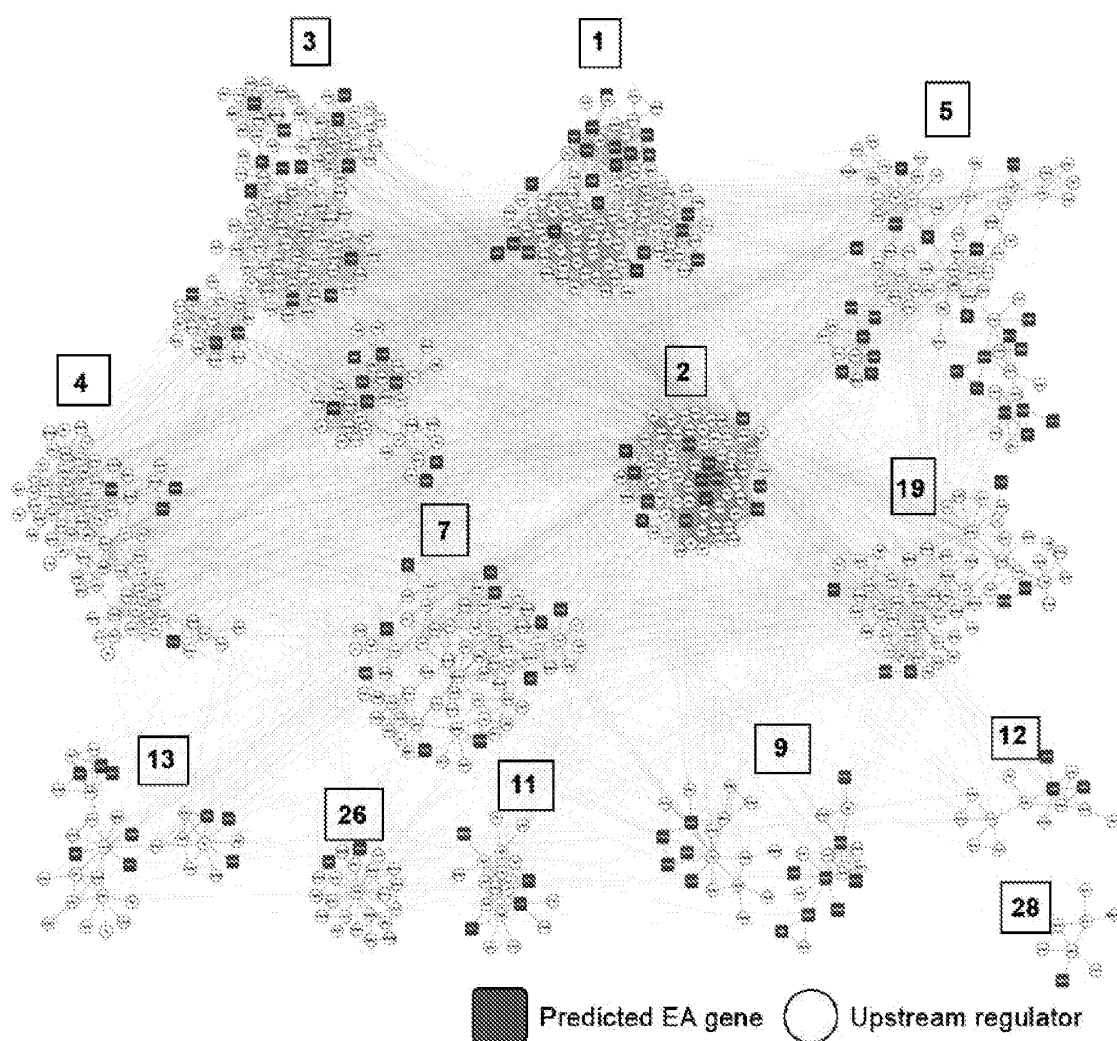


FIG. 51A

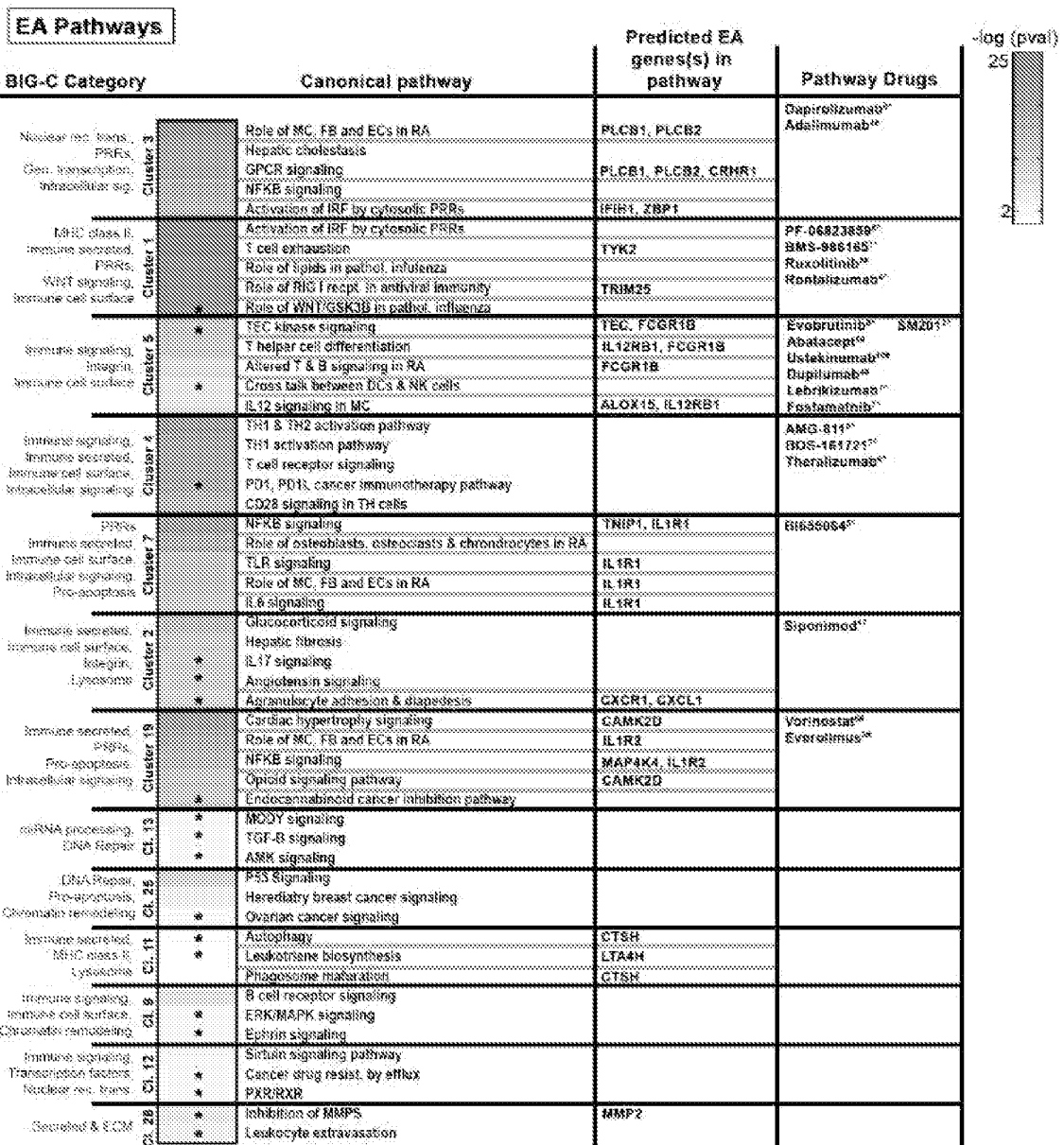


FIG. 51B

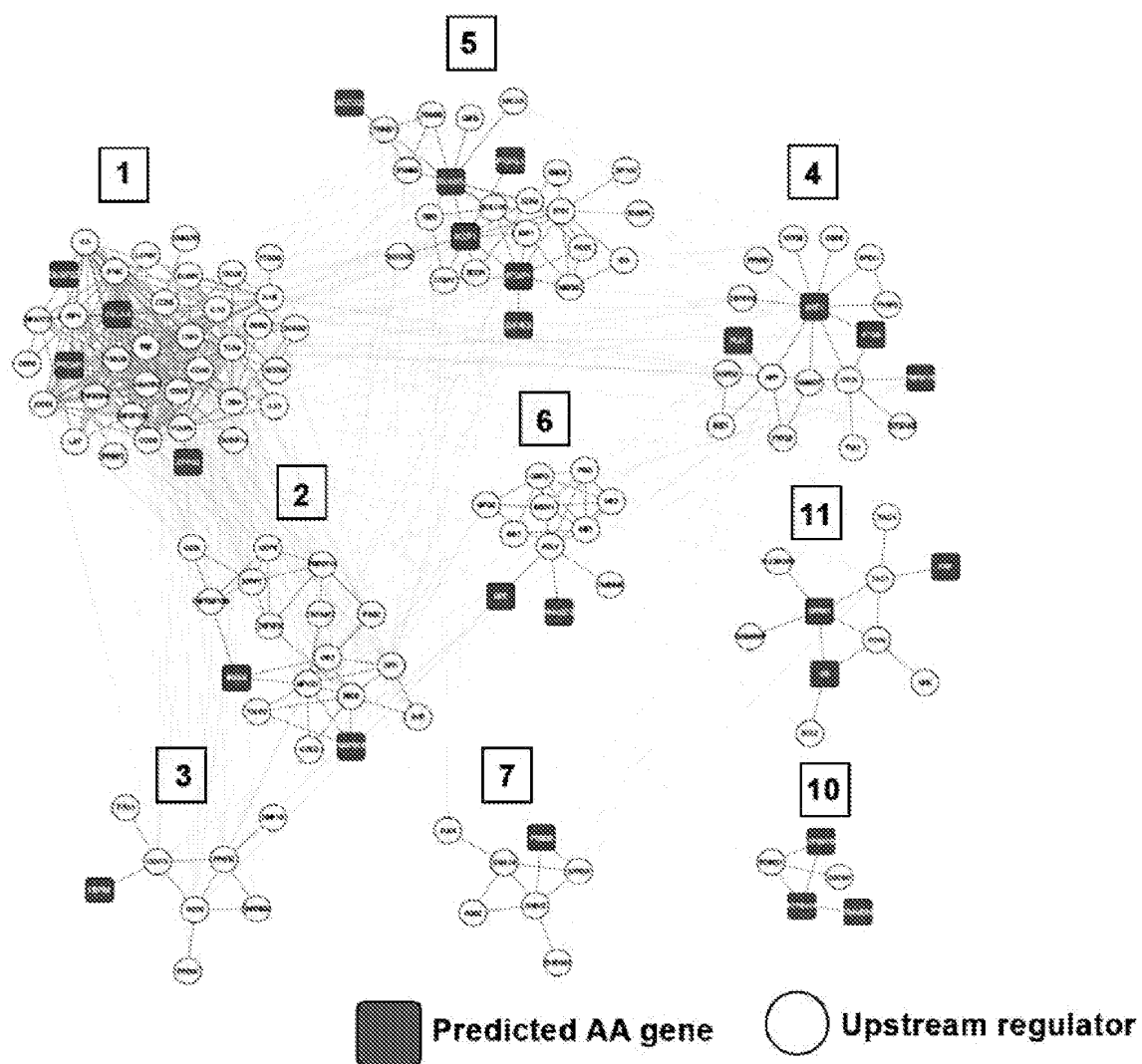


FIG. 52A

BIG-C Category		Canonical Pathway	Predicted AA gene(s) in pathway	Pathway Drugs	-log (pval)
Immune secreted, Immune sig., Immune cell surface	Cluster 1	* Comm. innate & adaptive immune cells TH1 & TH2 activation pathway Altered T & B signaling in RA T helper cell differentiation TH1 pathway		Abatacept [®] Belatacept [®] AMG-811 [®] Selinumab [®] Atacicept [®] Mepolizumab [®] BI655064 [®]	20
Proteasome, Transcription	Cluster 5	* Sumoylation pathway * Adipogenesis * B cell receptor signaling * Ubiquitylation signaling TH2 pathway		Bortezomib [®] Carfilzomib [®] KZR-616 [®]	2
Nuclear receptor trans., DNA repair	Cluster 4	* Death receptor signaling * Sirtuin signaling pathway * DHA pathway * OA pathway * Retinoic acid mediated apoptosis	TNFSF15 ATG5, SIRT1 SIRT1	Curcumin [®] Resveratrol [®]	
PRRs, Immune cell surface, Intracellular sig.	Cluster 2	* PRRs in recognition of bacteria & virus * Role of RIG I reept. in antiviral immunity * CD27 signaling in lymphocytes * NFκB signaling * Hepatic cholestasis	IRAK4, MAP3K8 IRAK4	PF-06659633 [®] PF-06822899 [®]	
Glycolysis, Fatty acid biosynthesis, Mito. general	Cluster 6	* Gluconeogenesis I * Pentose phosphate pathway * Acetyl CoA biosynthesis * Glycerol-3-phosphate shuttle * Insulin receptor signaling	LIPE		
Autophagy	Cluster 11	* THOP1 in Alzheimer's disease * Type I diabetes * Opioid signaling pathway * CTL-mediated target cell apoptosis * Complement system	FAP OPRK1 C5	Eculizumab [®]	
Unfolded protein & stress	Cluster 3	* Unfolded protein response * PEDF signaling * Adipogenesis * OA pathway * ER stress pathway	HSPA6		
General cell surface	Cl. 7	GPCR signaling	PTGDR		
Lysosome	Cl. 10	Phagosome maturation	ATP6V1G3, ATP6V1A		

FIG. 52B

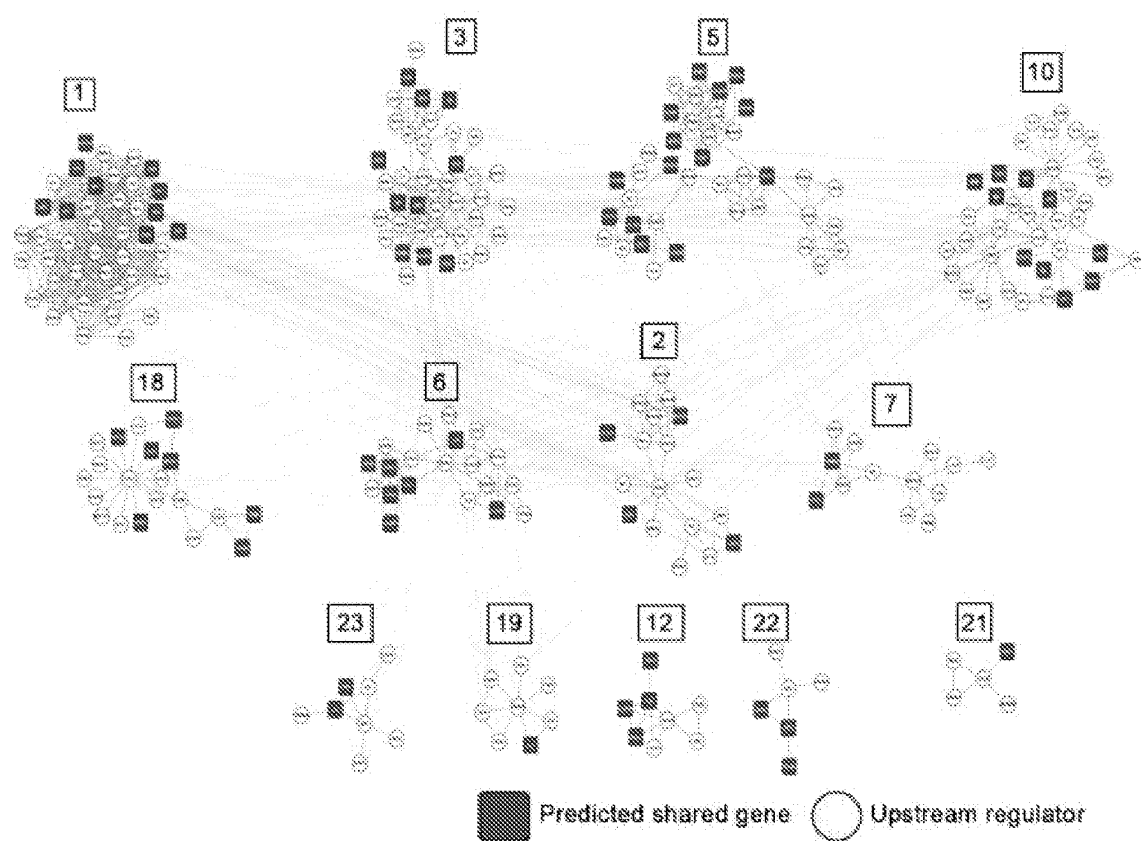


FIG. 53A

BIG-C Category	Canonical pathway	Predicted shared genes(s) in pathway	Pathway Drugs	-log(pval)
IFN stimulated genes, Immune secreted, PRRs, Intracellular signaling	Cluster 1	Activation of IRF by cytosolic PRRs	Rantalizumab ⁴⁹ Ruxolitinib ⁵⁰ PF-06623859 ⁵¹	35
		Interferon signaling		
		Role of lipids in pathol. influenza		
		T cell exhaustion		
		Role of RIG I recept. in antiviral immunity		
Immune secreted, Integrin, Immune signaling, Intracellular signaling	Cluster 3	IL-2 signaling	Sorafenib ⁵² BOS-161721 ⁵³ Dupilumab ⁵⁴	2
		Telomerase signaling		
		Endometrial cancer signaling		
		Role of JAK1 & JAK3 in cytokine signaling		
		GM-CSF signaling		
IFN stimulated genes, PRRs, mRNA splicing, mRNA processing	Cluster 5	Role of RIG I recept. in antiviral immunity	Palbociclib ⁵⁵	
		Activation of IRF by cytosolic PRRs		
		Role of PRRs in recog. bacteria & virus		
		Tight junction signaling		
		CDK5 signaling		
Immune secreted, Immune signaling, Transcription factors, Intracellular signaling	Cluster 10	Role of cytokines in comm. immune cells	Vorinostat ⁵⁶ Tocilizumab ⁵⁷ AMG 811 ⁵⁸	
		TH1 & TH2 activation pathway		
		T helper cell differentiation		
		Role of MC, FB and ECs in RA		
		Cardiac hypertrophy signaling		
mRNA processing, Pro-cell cycle, Gen. transcription, DNA repair	Cluster 18	GADD45 Signaling	Palbociclib ⁵⁵	
		DNA damage induced 14-3-3 signaling		
		Sirtuin signaling pathway		
		Hereditary breast cancer signaling		
		Cell cycle DNA damage G2/S chk. point		
Immune secreted, Immune cell surface, Intracellular signaling	Cluster 6	TREM1 signaling	BI 655064 ⁵⁹ Ustekinumab ⁶⁰	
		TH1 & TH2 activation pathway		
		TH1 activation pathway		
		IL12 signaling in MFC		
		TH2 pathway		
IFN stimulated genes, Nuclear rec. trans., Chromatin remodeling, Intracellular signaling	Cluster 2	RAR activation	Everolimus ⁶¹	
		Glucocorticoid signaling		
		AMK signaling		
		Hereditary breast cancer signaling		
		Role of BRCA1 in DNA damage resp.		
Proteasomes, PRRs, Nuclear rec. trans., Pro-cell cycle	Cluster 7	NFKB signaling	Hydroxychloroquine ^{62,63}	
		TLR signaling		
		Altered T & B signaling in RA		
		Role of MC, FB and ECs in RA		
		Role of PRRs in recog. bacteria & virus		
Immune signaling, Immune cell surface	Cl. 23	T cell receptor signaling	Therelizumab ⁶⁴	
		Role of NFAT in immune response		
		CD28 signaling in TH cells		
Nuclear rec. trans., Secreted & ECM	Cl. 19	Cardiac hypertrophy signaling		
		FGF signaling		
		Regulation of EMT		
Integrin, ER	Cl. 12	Coagulation system	Natalizumab ⁶⁵	
		Caveolar mediated endocytosis sig.		
		TREM1 signaling		
Endocytosis	22	Caveolar mediated endocytosis sig.	CDPA	
Pro-apoptosis	21	ER signaling		

FIG. 53B

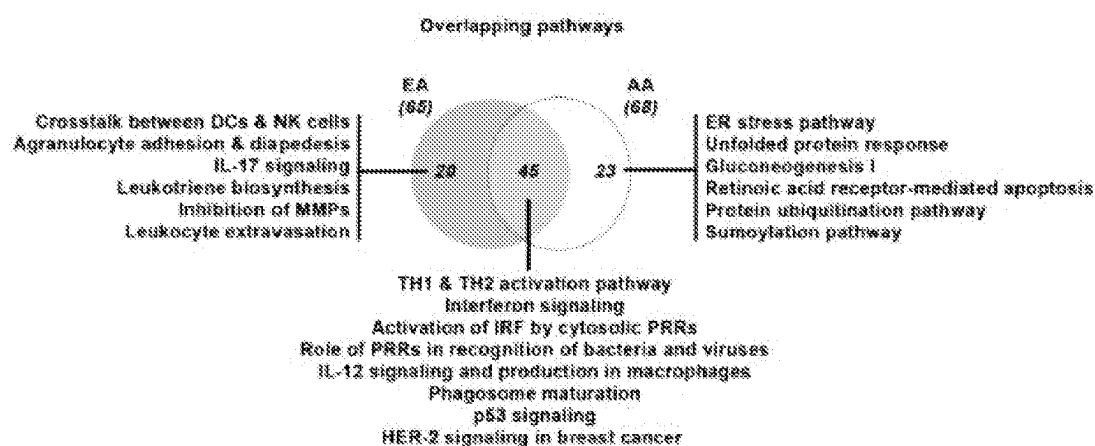


FIG. 54A

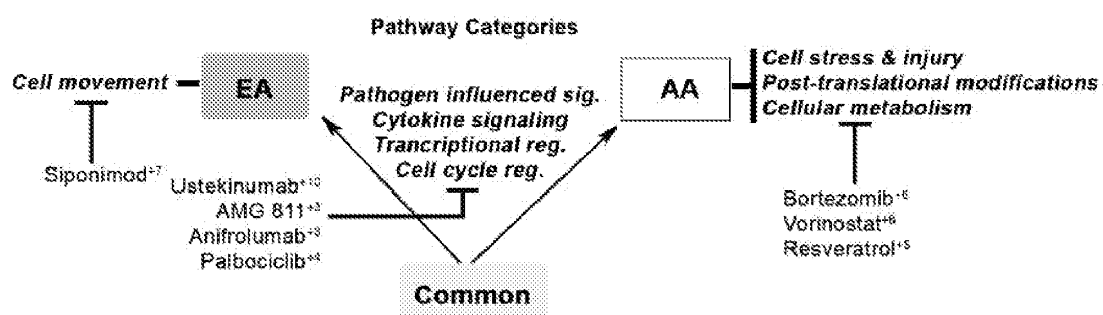


FIG. 54B

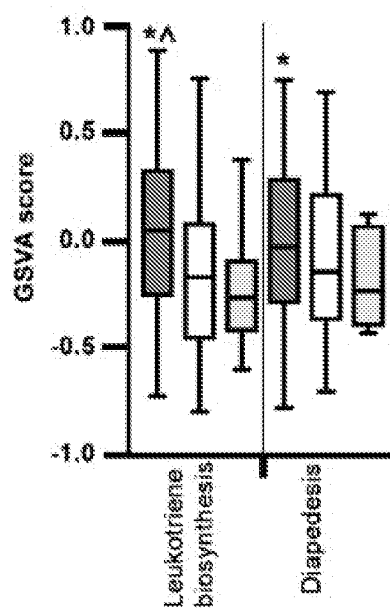


FIG. 54C

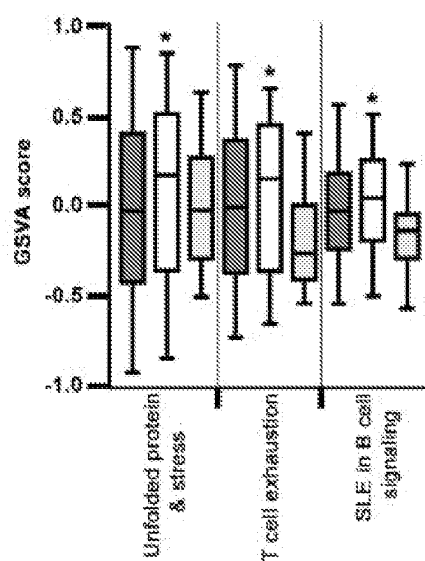


FIG. 54D

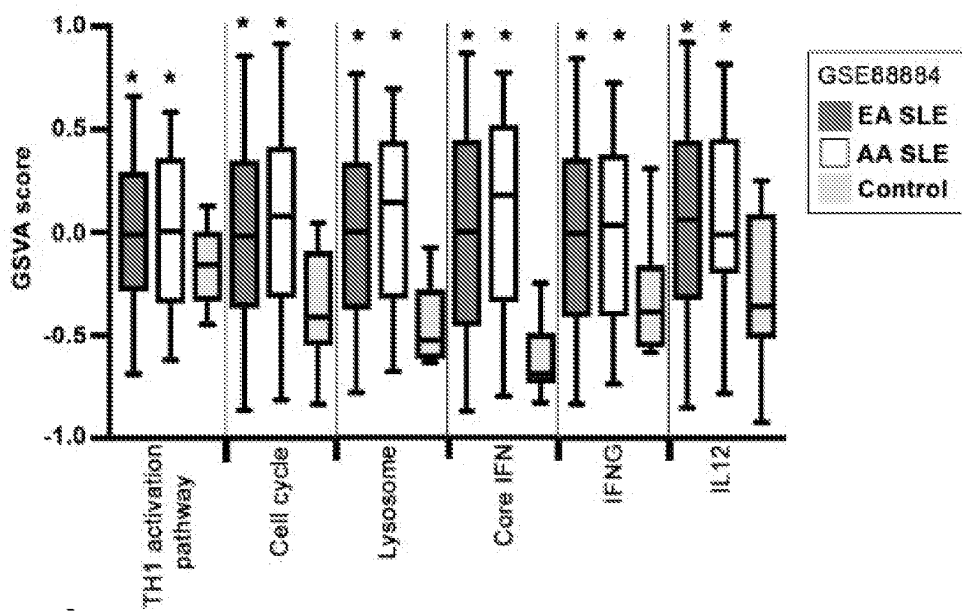


FIG. 54E

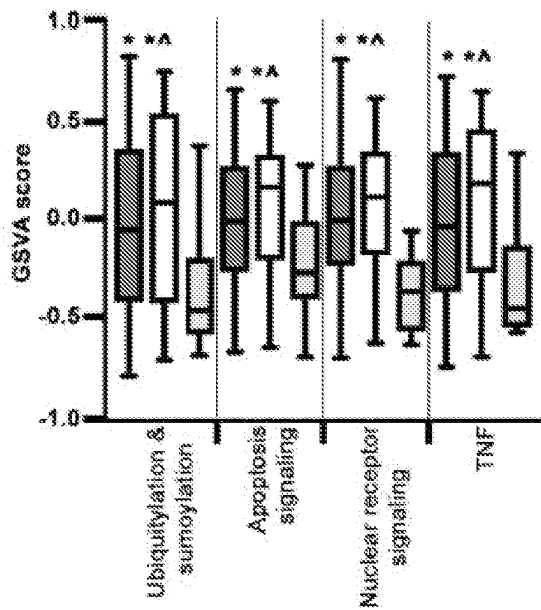


FIG. 54F

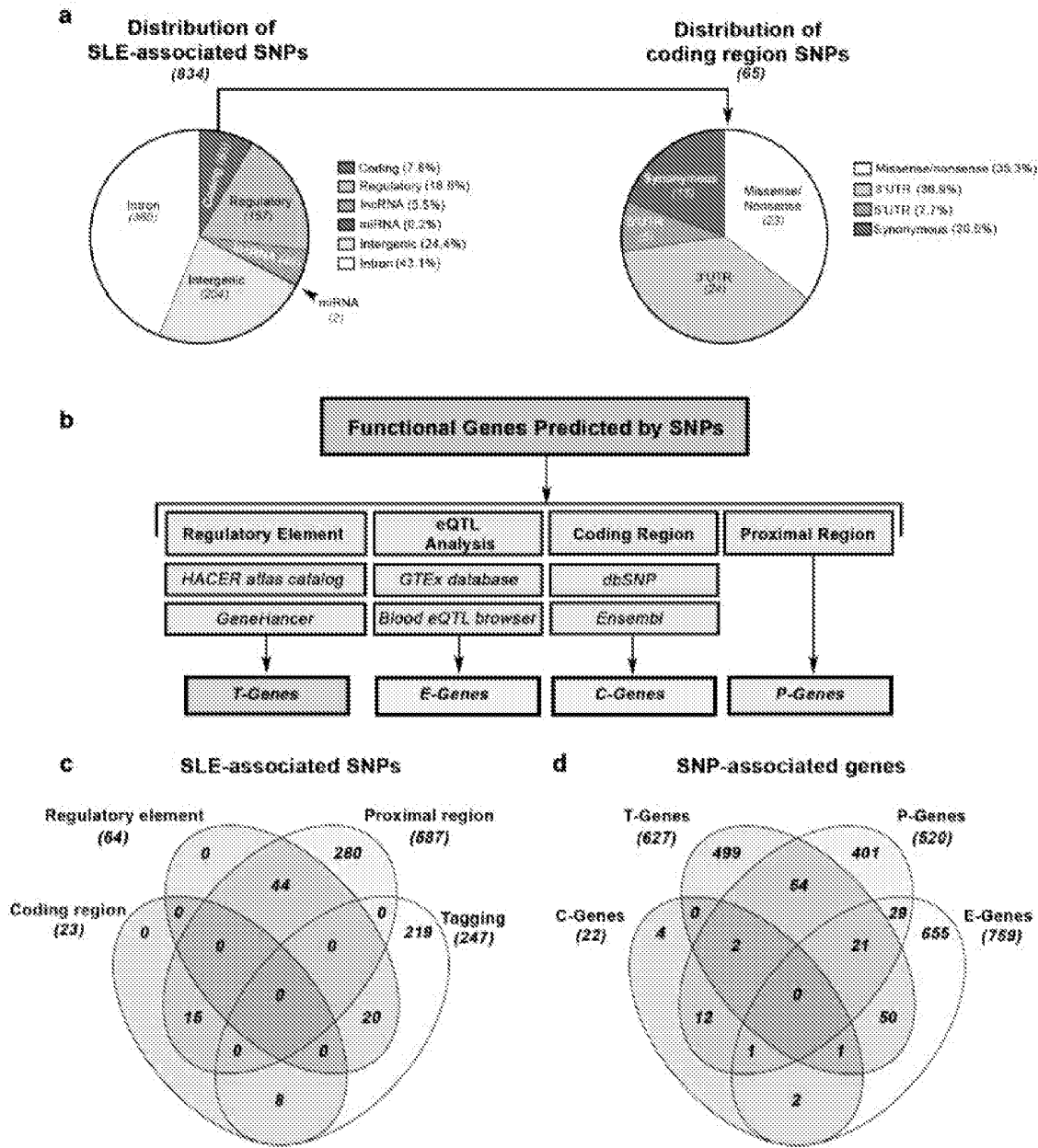


FIG. 55

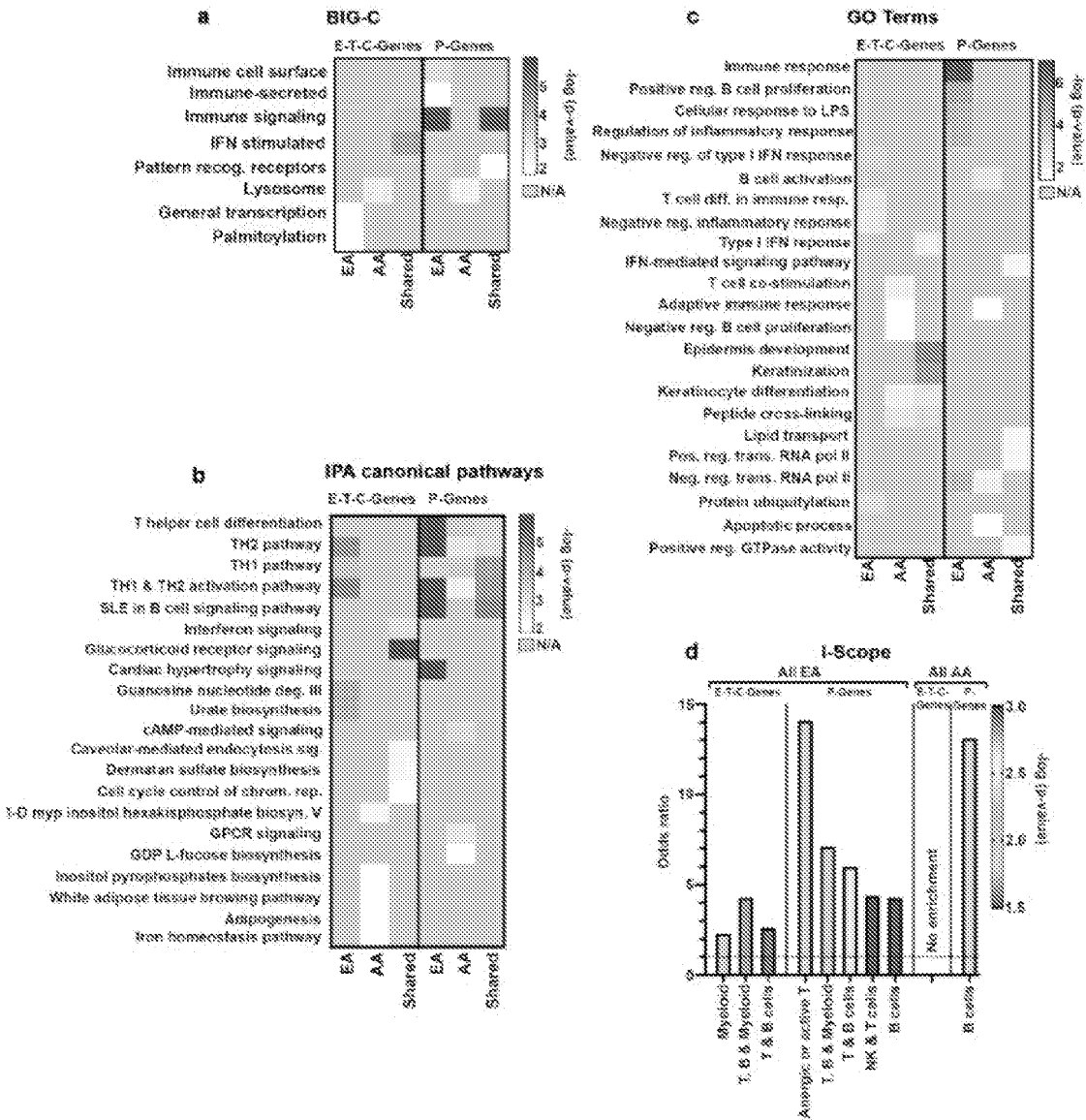


FIG. 56

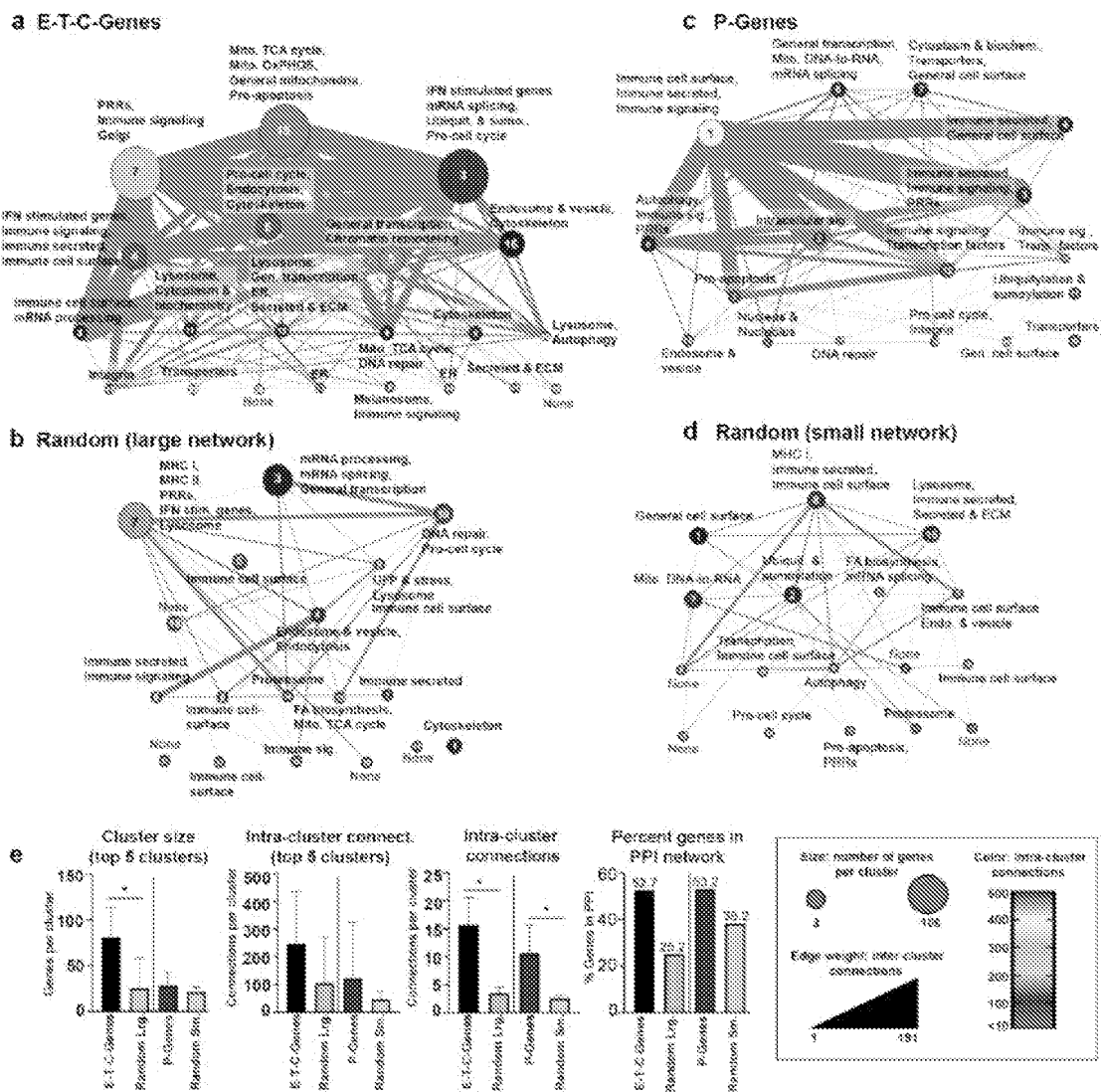


FIG. 57

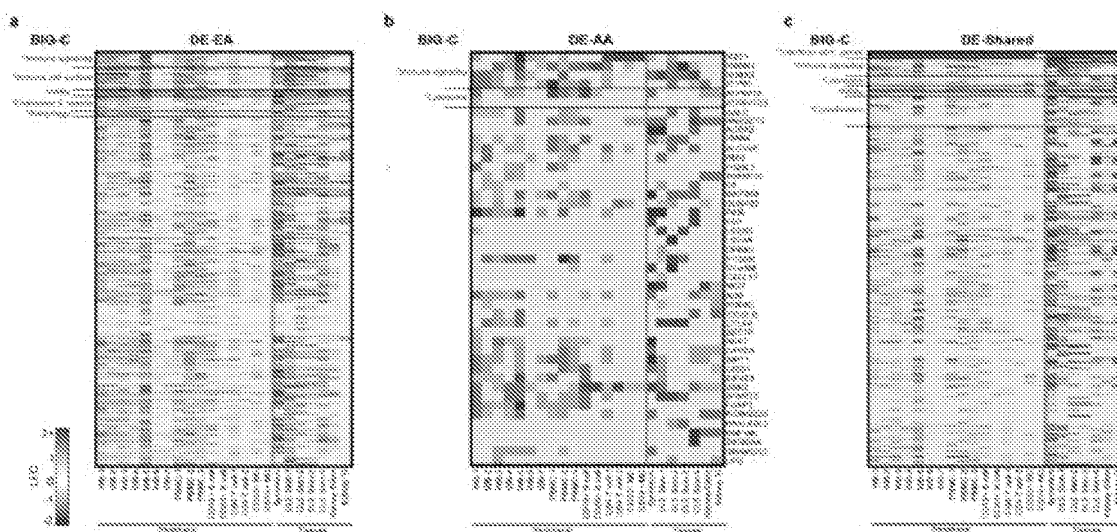


FIG. 58

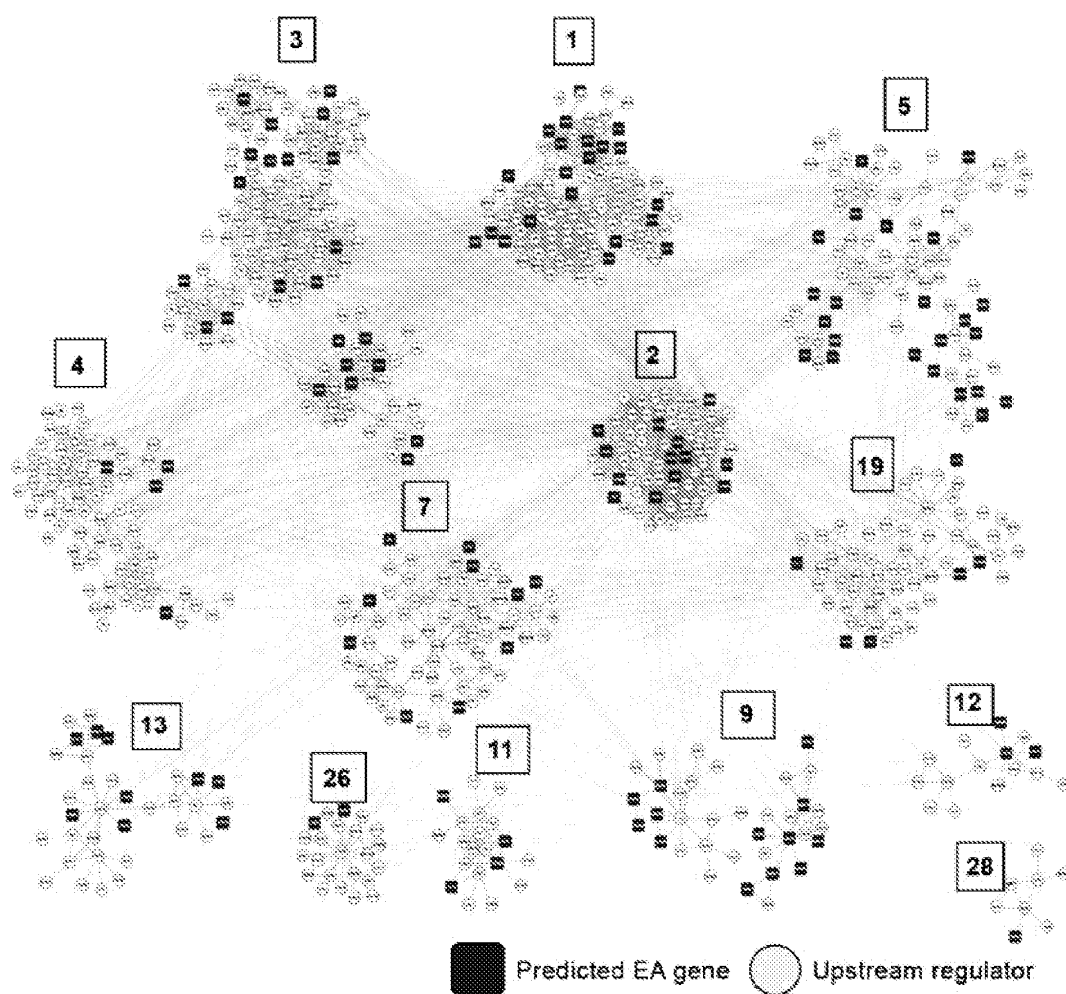


FIG. 59A

EA Pathways		Predicted EA genes(s) in pathway		Pathway Drugs	-log (pval)
BIG-C Category	Canonical pathway				
Nuclear rec. trans., PTORs, Gent. transcription, Interacellular sig.	Cluster 3	Role of MC, PB and ECs in RA	PLCB1, PLCB2	Dapirizumab TM Adalimumab TM	25
		Hepatic cholestasis			
		GPCR signaling	PLCB1, PLCB2, CRHR1		
		NKKB signaling			
		Activation of IRF by cytosolic PRRs	IPRH1, ZBP1		
MHC class II, Immune secreted, PTORs, PANT signaling, Immune cell surface	Cluster 1	Activation of IRF by cytosolic PRRs		PF-06823889 TM BMS-986185 TM Ruxolitinib TM Rontalizumab TM	2
		T cell exhaustion	TYK2		
		Role of lipids in pathol. influenza			
		Role of IRG1 reprot. in antiviral immunity	TRIM25		
		Role of WH1/12K1B in pathol. influenza			
Immune signaling, Integrin, Immune cell surface	Cluster 8	TEC kinase signaling	TEC, FCGR1B	Evobrutinib TM SM201 TM	
		T helper cell differentiation	IL12RB1, FCGR1B	Abatacept TM	
		Altered T & B signaling in RA	FCGR1B	Ustekinumab TM Dupixumab TM Lebrikizumab TM Fostamatinib TM	
		Cross talk between DCs & NK cells			
		IL12 signaling in MC	ALOX15, IL12RB1		
Immune signaling, Immune secreted, Immune cell surface, Interacellular signaling	Cluster 4	TH1 & TH2 activation pathway		AMG-811 TM BOS-161721 TM Theralizumab TM	
		TH1 activation pathway			
		T cell receptor signaling			
		PD1, PD1L cancer immunotherapy pathway			
		CD28 signaling in TH cells			
PTORs, Immune secreted, Immune cell surface, Interacellular signaling, Pro. apoptosis	Cluster 7	NKKB signaling	TRAF1, IL1R1	B-635864 TM	
		Role of osteoblasts, osteoclasts & chondrocytes in RA			
		TLR signaling	IL1R1		
		Role of MC, PB and ECs in RA	IL1R1		
		ILK signaling	IL1R1		
Immune secreted, Immune cell surface, Integrin, Lysosome	Cluster 2	Glucocorticoid signaling		Giprenomed TM	
		Hepatic fibrosis			
		IL17 signaling			
		Angiotensin signaling			
		Granulocyte adhesion & diapedesis	CXCR1, CXCL1		
Immune secreted, PTORs, Pro. apoptosis, Interacellular signaling	Cluster 18	Cardiac hypertrophy signaling	CAMK3D	Vorinostat TM	
		Role of MC, PB and ECs in RA	IL1R2	Everolimus TM	
		NKKB signaling	MAP4K4, IL1R2		
		Opioid signaling pathway	CAMK3D		
		Endoplasmic reticulum cancer inhibition pathway			
mRNA processing, DNA Repair	Cl. 13	MGOY signaling			
		TGF-β signaling			
		AMK signaling			
DNA Repair, Pro. apoptosis, Chromatin remodeling	Cl. 26	P53 Signaling			
		Hereditary breast cancer signaling			
		Ovarian cancer signaling			
Immune secreted, MHC class II, Lysosome	Cl. 11	Autophagy	CTSH		
		Leukotriene biosynthesis	LTA4H		
		Phagosome maturation	CTSH		
Immune signaling, Immune cell surface, Chromatin remodeling	Cl. 8	B cell receptor signaling			
		ERK/MAPK signaling			
		Ephrin signaling			
Immune signaling, Transcription factors, Nuclear rec. trans.	Cl. 12	Sirtuin signaling pathway			
		Cancer drug resist. by efflux			
		PXCRX9			
Secreted & ECM	Cl. 28	Inhibition of MMPs	MMP2		
		Leukocyte extravasation			

FIG. 59B

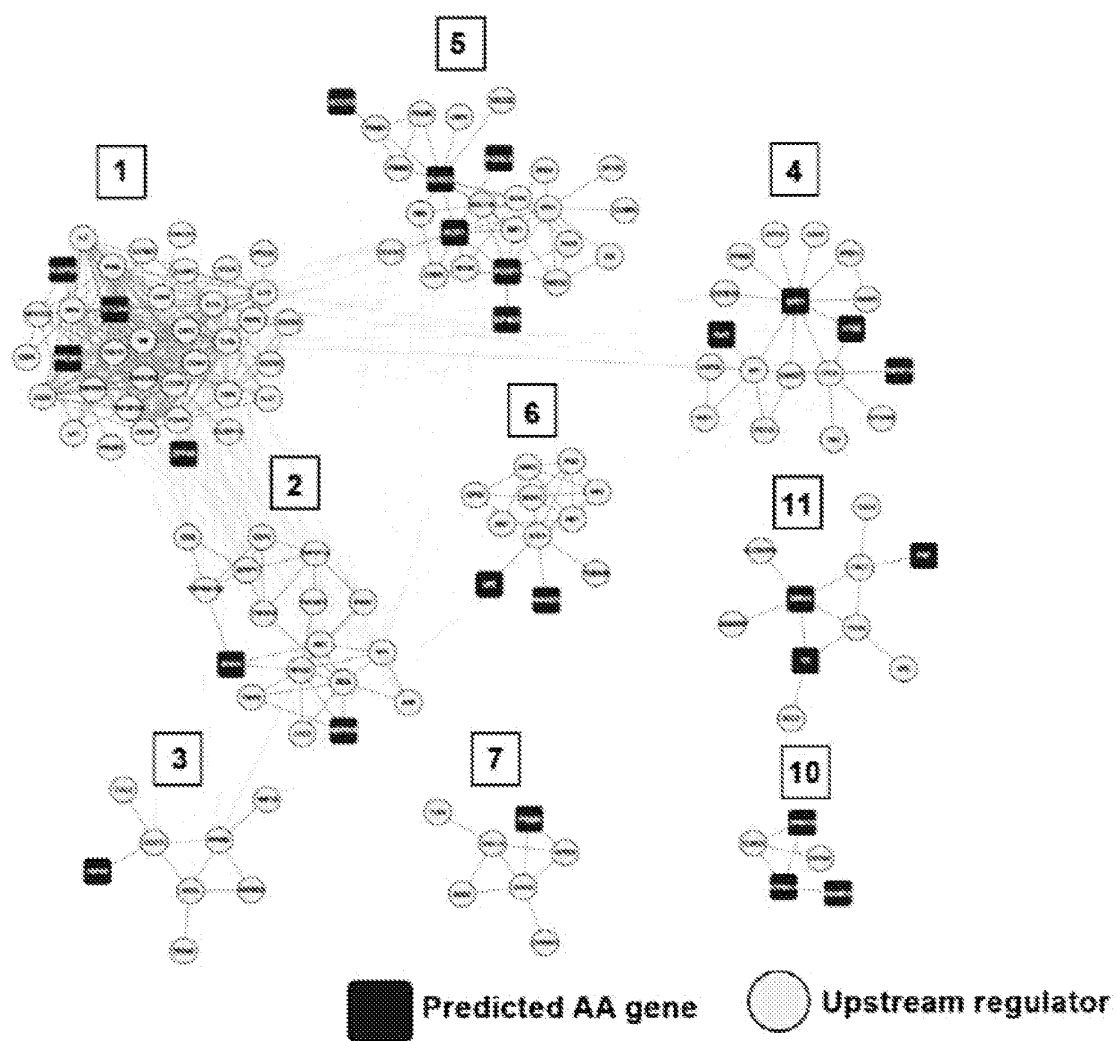


FIG. 60A

AA Pathways

BIG-C Category		Canonical Pathway	Predicted AA gene(s) in pathway	Pathway Drugs	-log (pval)
Immune secreted, Immune sig., Immune cell surface	Cluster 1	Comm. innate & adaptive immune cells		Abatacept [®]	20
		TH1 & TH2 activation pathway		Belatacept [®]	
		Altered T & B signaling in RA		AMG-811 [®]	
		T helper cell differentiation		Belimumab [®]	
		TH1 pathway		Atacicept [®]	
Proteosome, Transcription	Cluster 5	Sumoylation pathway		Mepolizumab [®]	2
		Adipogenesis		Belimumab [®]	
		B cell receptor signaling		Carfilzomib [®]	
		Ubiquitylation signaling		KZR-616 [®]	
		TH2 pathway			
Nuclear receptor trans., DNA repair	Cluster 4	Death receptor signaling	TNFSF15	Curcumin [™]	
		Sirtuin signaling pathway	ATG5, SIRT1	Resveratrol [™]	
		DNA pathway			
		OA pathway	SIRT1		
		Retinoic acid mediated apoptosis			
PRRs, Immune cell surface, Intracellular sig.	Cluster 2	PRRs in recognition of bacteria & virus		PF-06650633 [®]	
		Role of RIG I recept. in antiviral immunity		PF-06623695 [®]	
		CD27 signaling in lymphocytes			
		NFκB signaling	IRAK4, MAP3K8		
		Hepatic cholestasis	IRAK4		
Glycolysis, fatty acid biosynthesis, Mito. general	Cluster 6	Gluconeogenesis I			
		Pentose phosphate pathway			
		Acetyl CoA biosynthesis			
		Glycerol-3-phosphate shuttle			
		Insulin receptor signaling	LIPE		
Autophagy	Cluster 11	THQF I in Alzheimer's disease	FAP	Eculizumab [®]	
		Type I diabetes			
		Opioid signaling pathway	OPRK1		
		CTL-mediated target cell apoptosis			
		Complement system	C5		
Unfolded protein & stress	Cluster 3	Unfolded protein response	HSPA6		
		PEDF signaling			
		Adipogenesis			
		OA pathway			
		ER stress pathway			
General cell surface	Cl. 7	GPCR signaling	PTGDR		
Lysosome	Cl. 10	Phagosome maturation	ATP8V1G3, ATP8V1A		

FIG. 60B

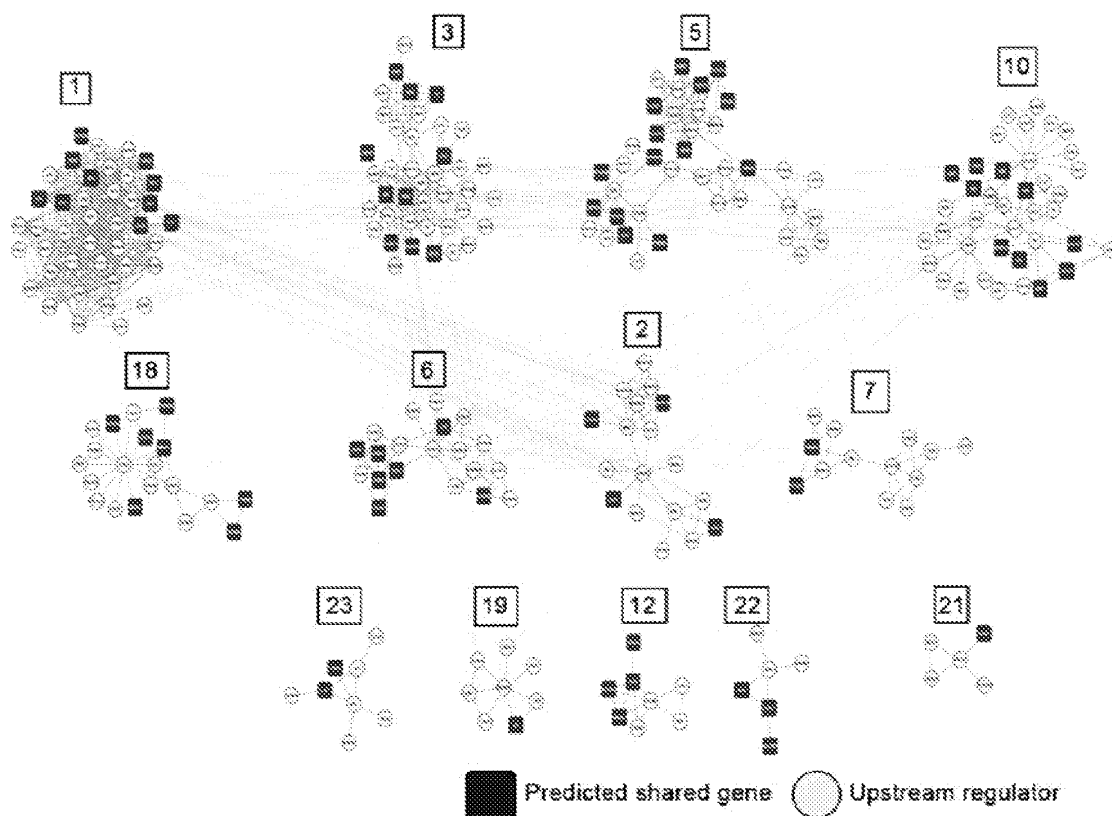
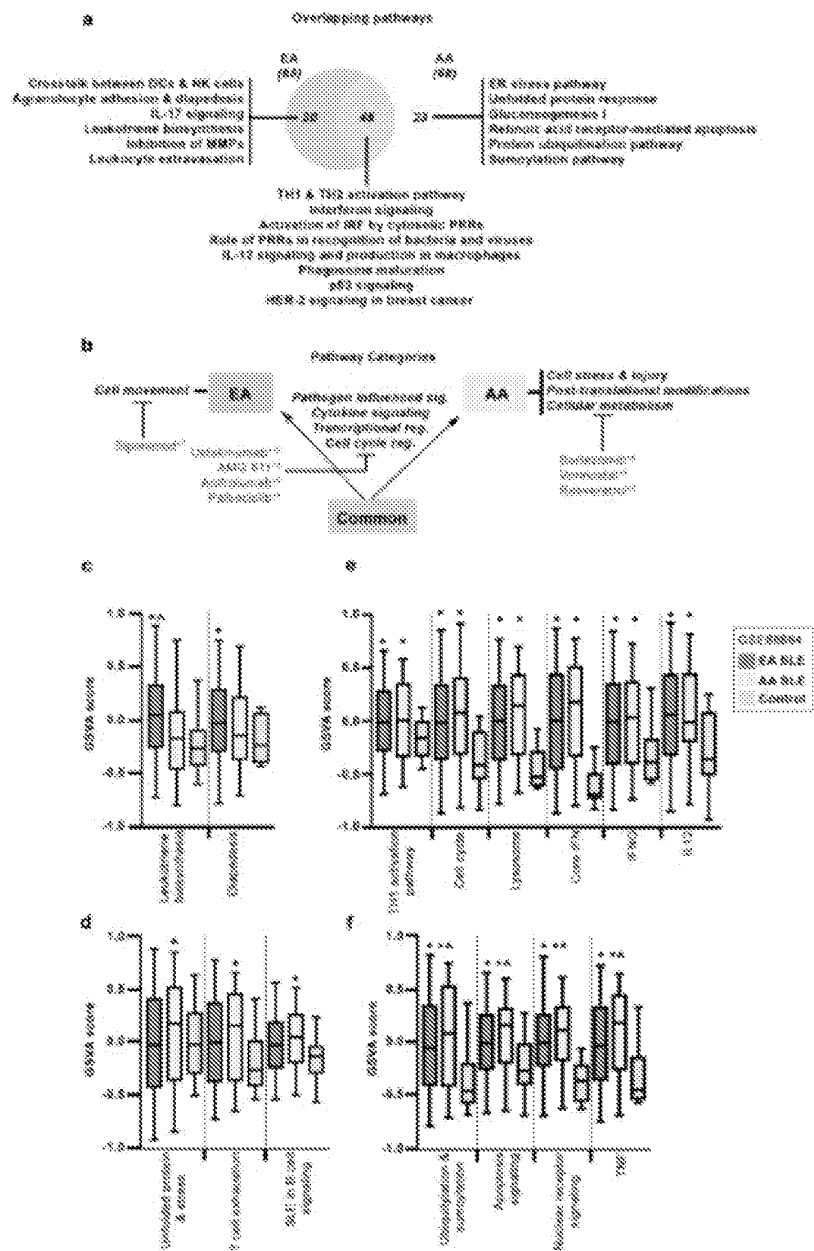


FIG. 61A

Shared Pathways		Predicted shared genes(s) in pathway		Pathway Drugs	-log(pval)
BIG-C Category	Canonical pathway				
IFN stimulated genes, Immune secreted, PRRs, Intracellular signaling	Cluster 1	Activation of IRF by cytosolic PRRs	IRF7	Rentgizumab [®]	35
		Interferon signaling	IFIH, IFI35, MX1, OAS1	Ruxolitinib [®]	
		Role of lipids in pathol. influenza		PF-06823889 [®]	2
		T cell exhaustion	NFATC3		
		Role of RIG I recept. in antiviral immunity	IRF7		
Immune secreted, Integrin, Immune signaling, Intracellular signaling	Cluster 3	IL-2 signaling	HRAS	Sorafenib [™]	35
		Telomerase signaling	HRAS, ETS1	BOS-181721 [™]	
		Endometrial cancer signaling	HRAS	Dupilumab [®]	
		Role of JAK1 & JAK3 in cytokine signaling	HRAS		
		GM-CSF signaling	HRAS		
IFN stimulated genes, PRRs, mRNA splicing, mRNA processing	Cluster 5	Role of RIG I recept. in antiviral immunity		Palbociclib [®]	35
		Activation of IRF by cytosolic PRRs			
		Role of PRRs in recog. bacteria & virus			
		Tight junction signaling	PPP2R1		
		CDK5 signaling	PPP2R1		
Immune secreted, Immune signaling, Transcription factors, Intracellular signaling	Cluster 10	Role of cytokines in comm. immune cells		Varinostat [™]	35
		TH1 & TH2 activation pathway	IL6R	Tocilizumab [™]	
		T helper cell differentiation	IL6R	AMG 811 [™]	
		Role of MC, FB and ECs in RA	IL6R		
		Cardiac hypertrophy signaling	IL6R		
mRNA processing, Pre-cell cycle, Gen. transcription, DNA repair	Cluster 18	GAD65 Signaling	BRCA1	Palbociclib [™]	35
		DNA damage induced 14-3-3 signaling	BRCA1		
		Biruin signaling pathway	BRCA1		
		Hereditary breast cancer signaling	BRCA1		
		Cell cycle DNA damage G2/S chk. point	BRCA1		
Immune secreted, Immune cell surface, Intracellular signaling	Cluster 8	TREM1 signaling		BI 655064 [®]	35
		TH1 & TH2 activation pathway	IL12RB2	Ustekinumab [™]	
		TH1 activation pathway	IL12RB2		
		IL12 signaling in MC	IL12RB2		
		TH2 pathway	IL12RB2		
IFN stimulated genes, Nuclear rec. trans., Chromatin remodeling, Intracellular signaling	Cluster 2	RAR activation	SMARCE1	Everolimus [™]	35
		Glucocorticoid signaling	SMARCE1		
		AMK signaling	SMARCE1, RPTOR		
		Hereditary breast cancer signaling	SMARCE1		
		Role of BRCA1 in DNA damage resp.	SMARCE1		
Proteasome, PRRs, Nuclear rec. trans., Pre-cell cycle	Cluster 7	NFKB signaling		Hydroxychloroquine [™]	35
		TLR signaling			
		Altered T & B signaling in RA			
		Role of MC, FB and ECs in RA			
		Role of PRRs in recog. bacteria & virus			
Immune signaling, Immune cell surface	CL 23	T cell receptor signaling	LAT	Theralizumab [®]	35
		Role of NFAT in immune response	LAT		
		CD28 signaling in TH cells	LAT		
		Cardiac hypertrophy signaling			
		FGF signaling			
Nuclear rec. trans., Secreted & ECM	CL 19	Regulation of EMT			35
		Coagulation system	PLAU	Natalizumab [™]	
		Caveolar mediated endocytosis sig.	ITGAX		
		TREM1 signaling	ITGAX		
		Caveolar mediated endocytosis sig.	COPA		
Endocytosis	22	Caveolar mediated endocytosis sig.	COPA		
Pro-apoptosis	21	ER signaling			

FIG. 61B



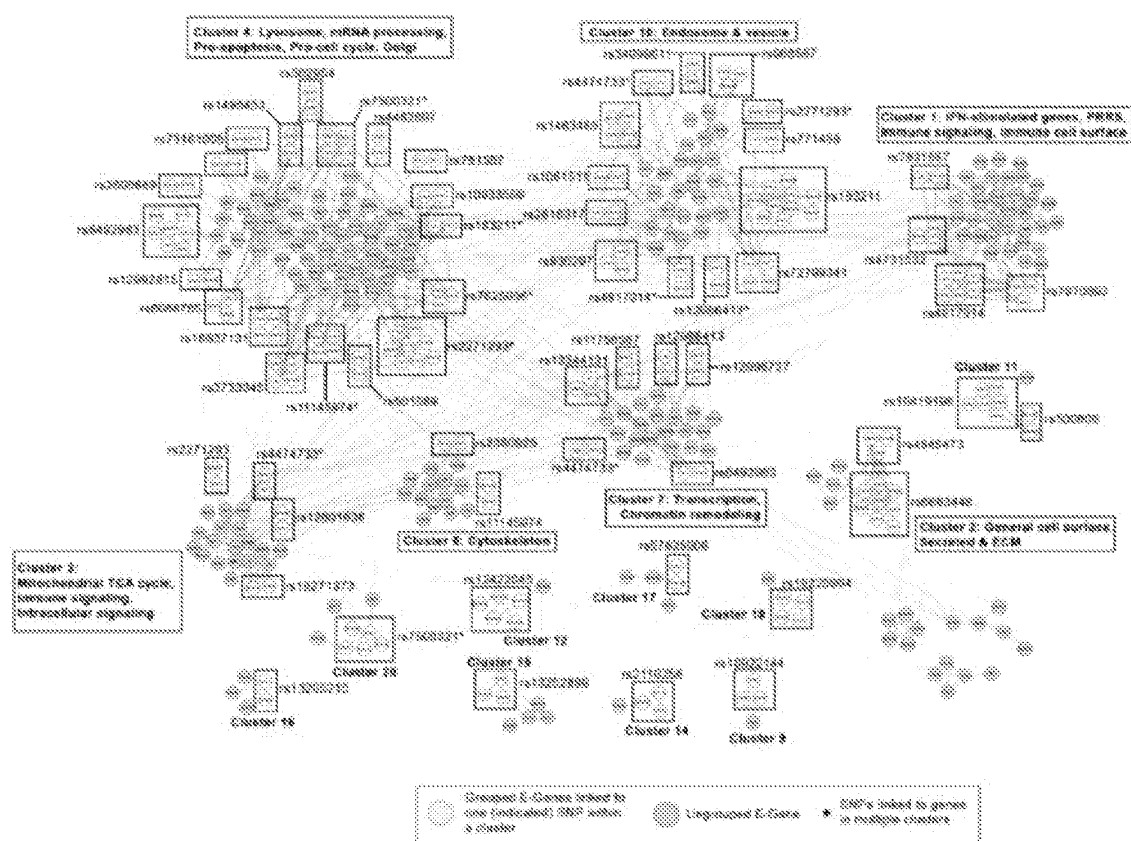


FIG. 63

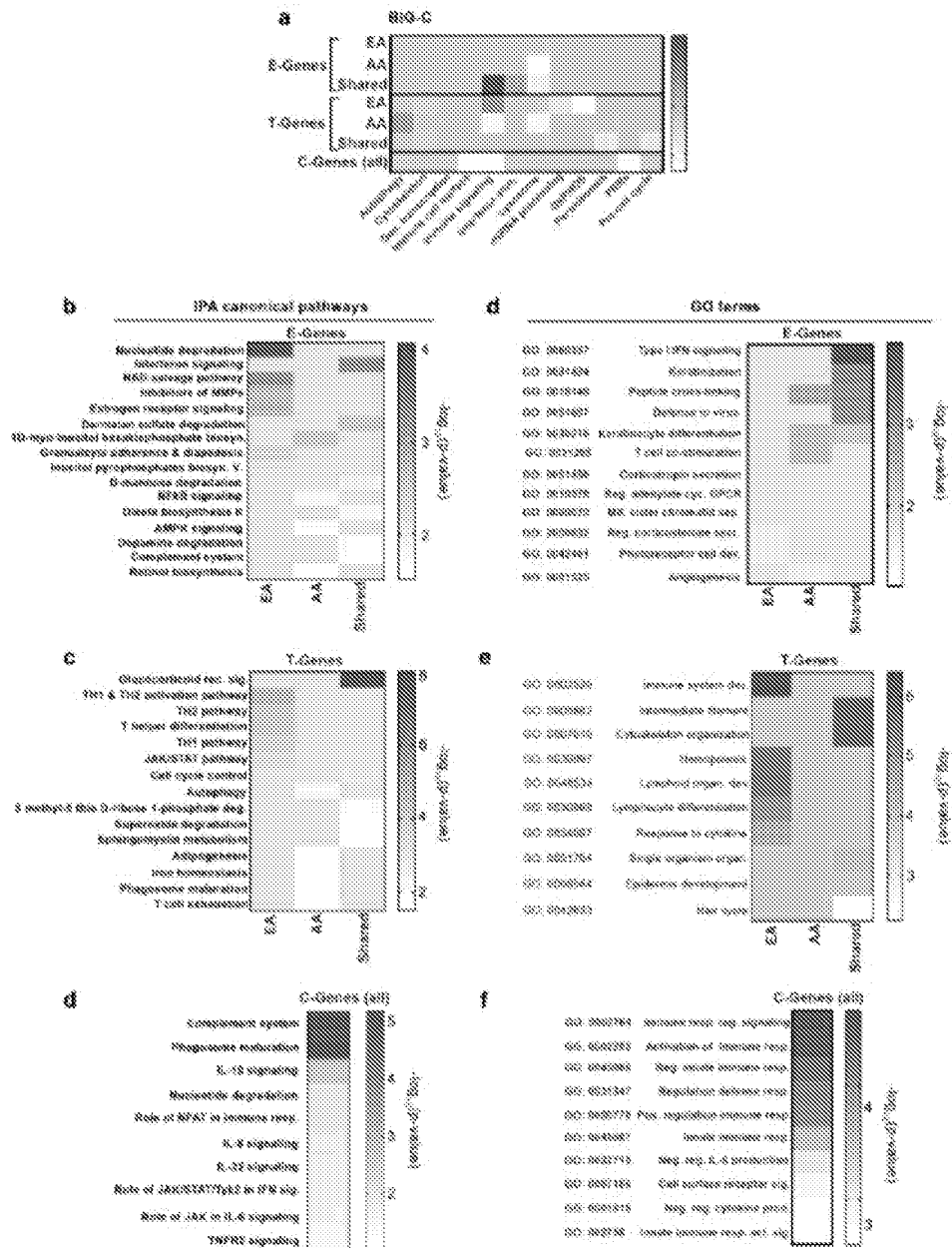
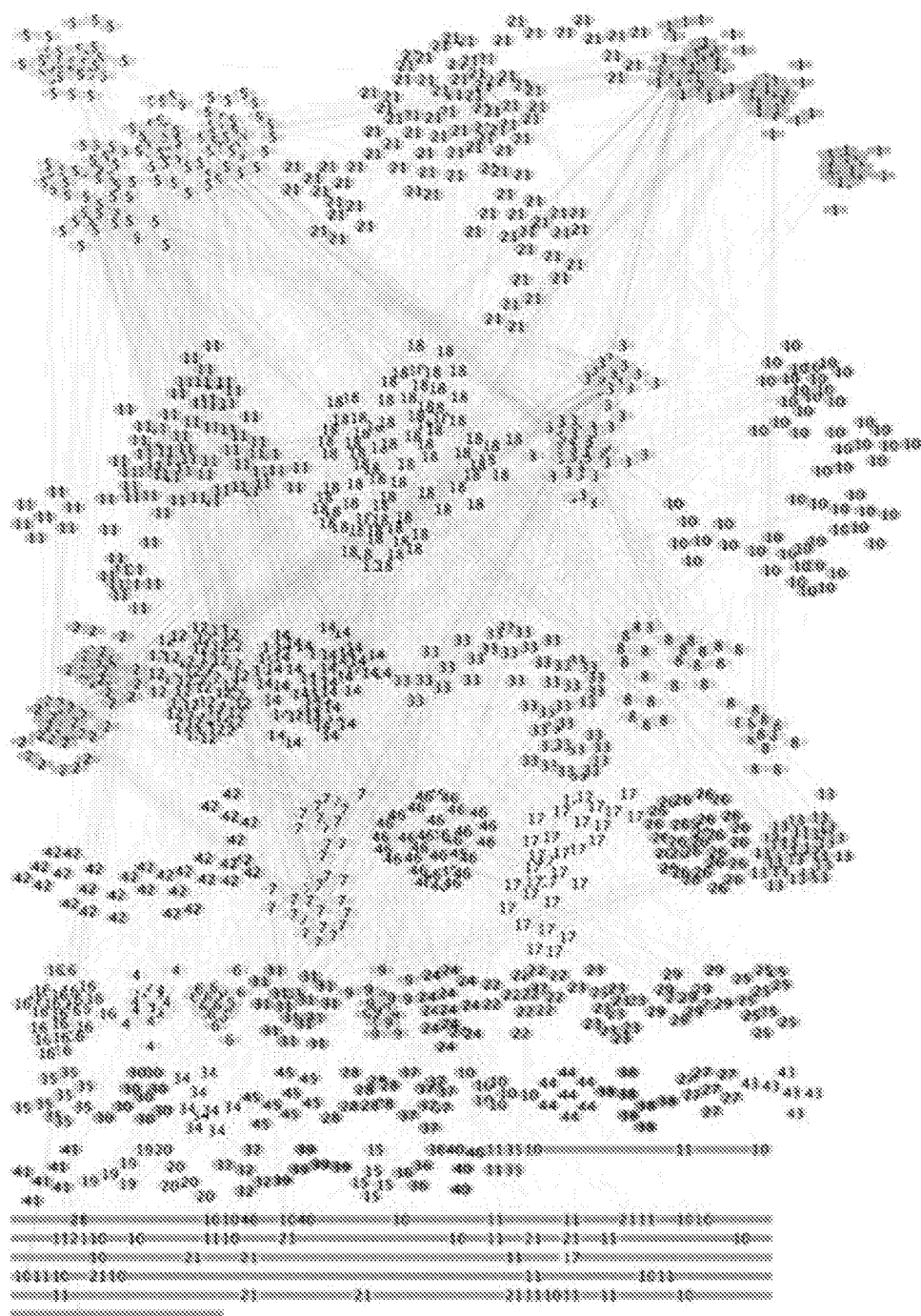


FIG. 64



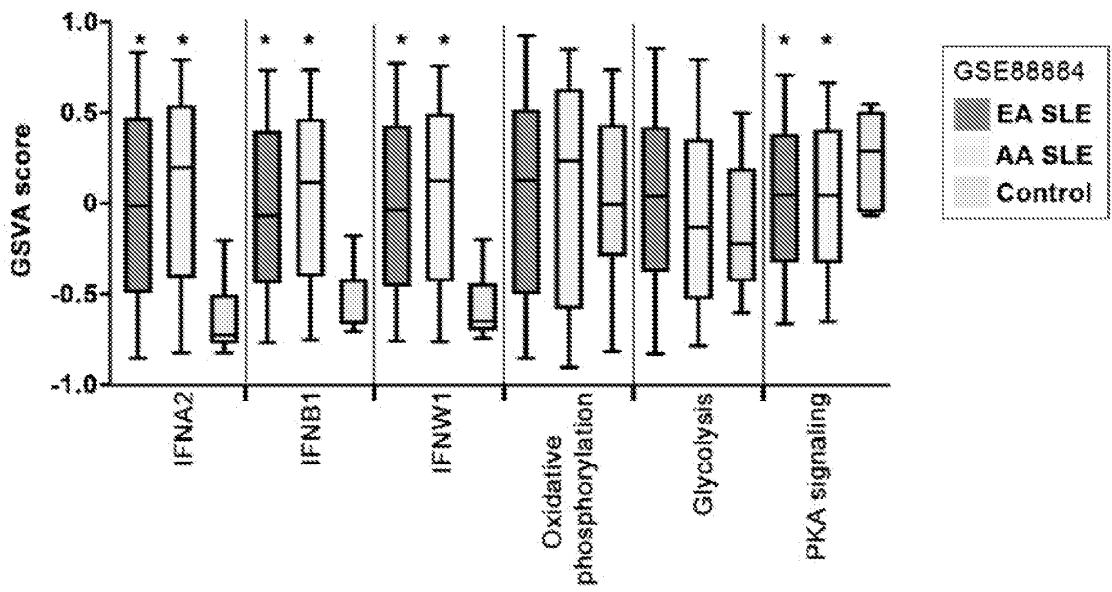


FIG. 66

Ancestral overlap

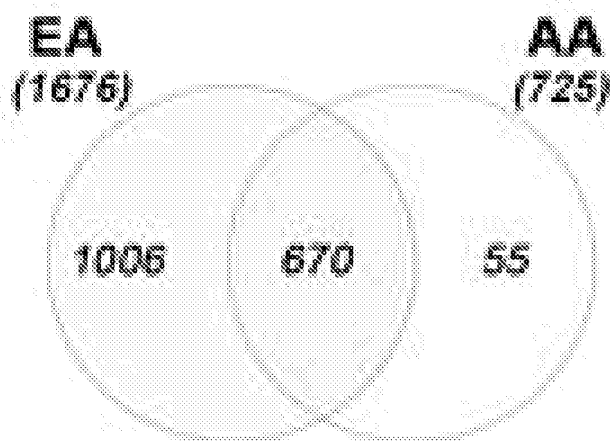


FIG. 67A

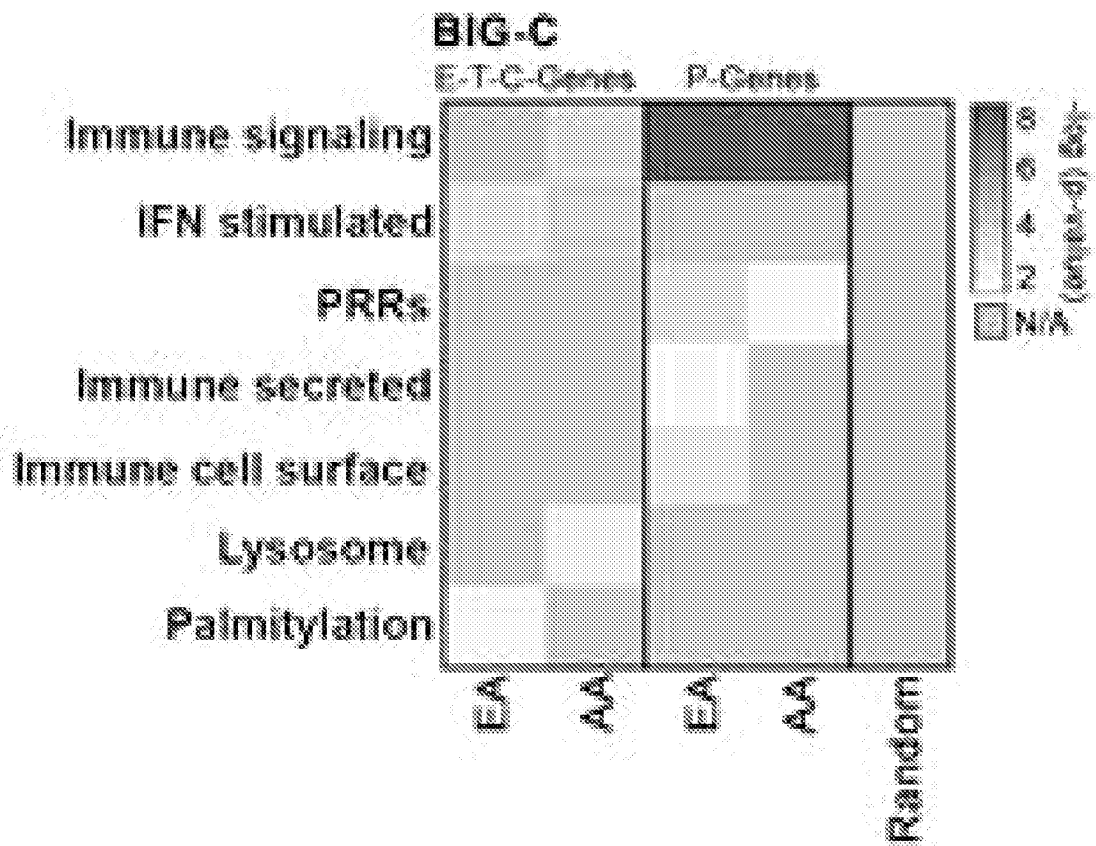


FIG. 67B

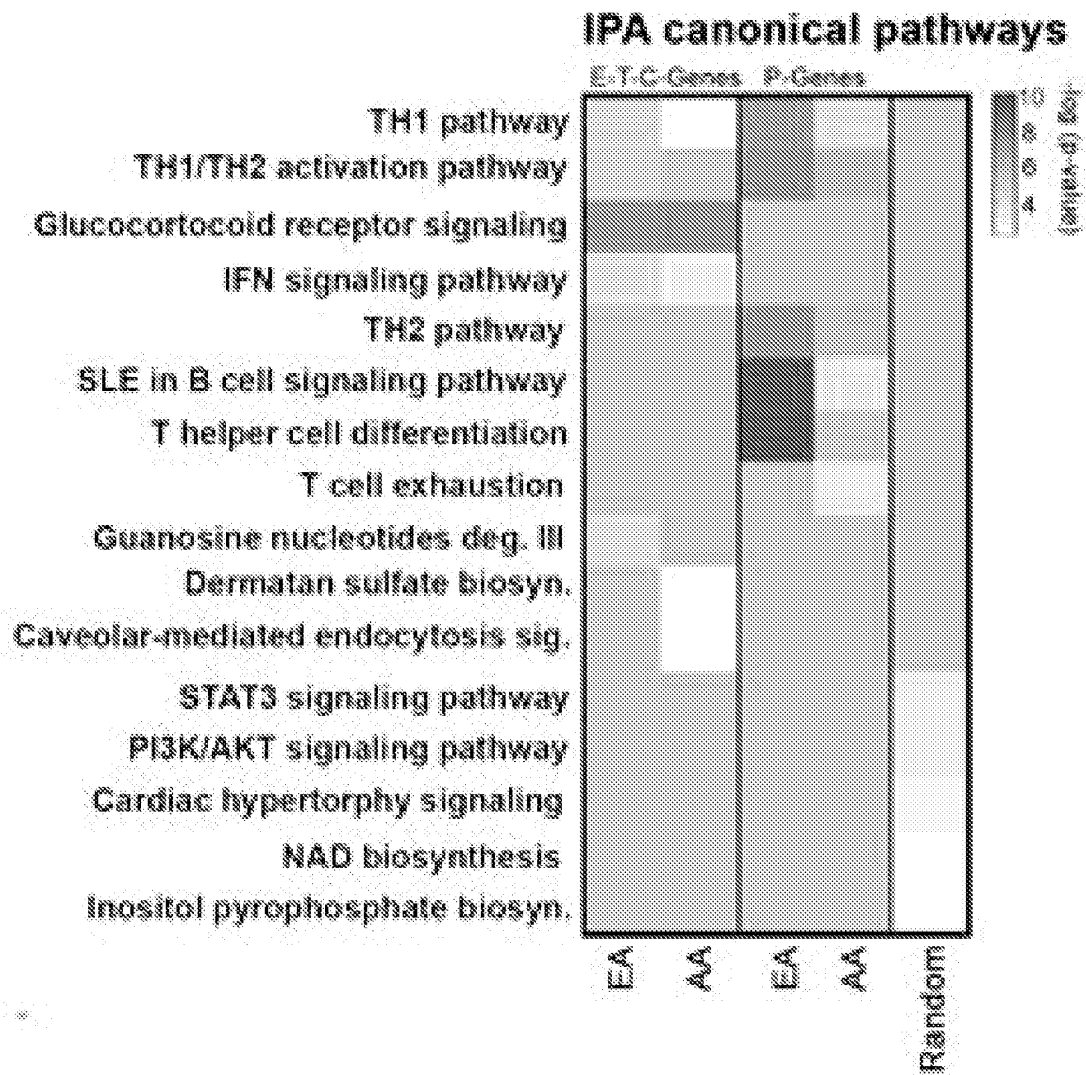


FIG. 67C

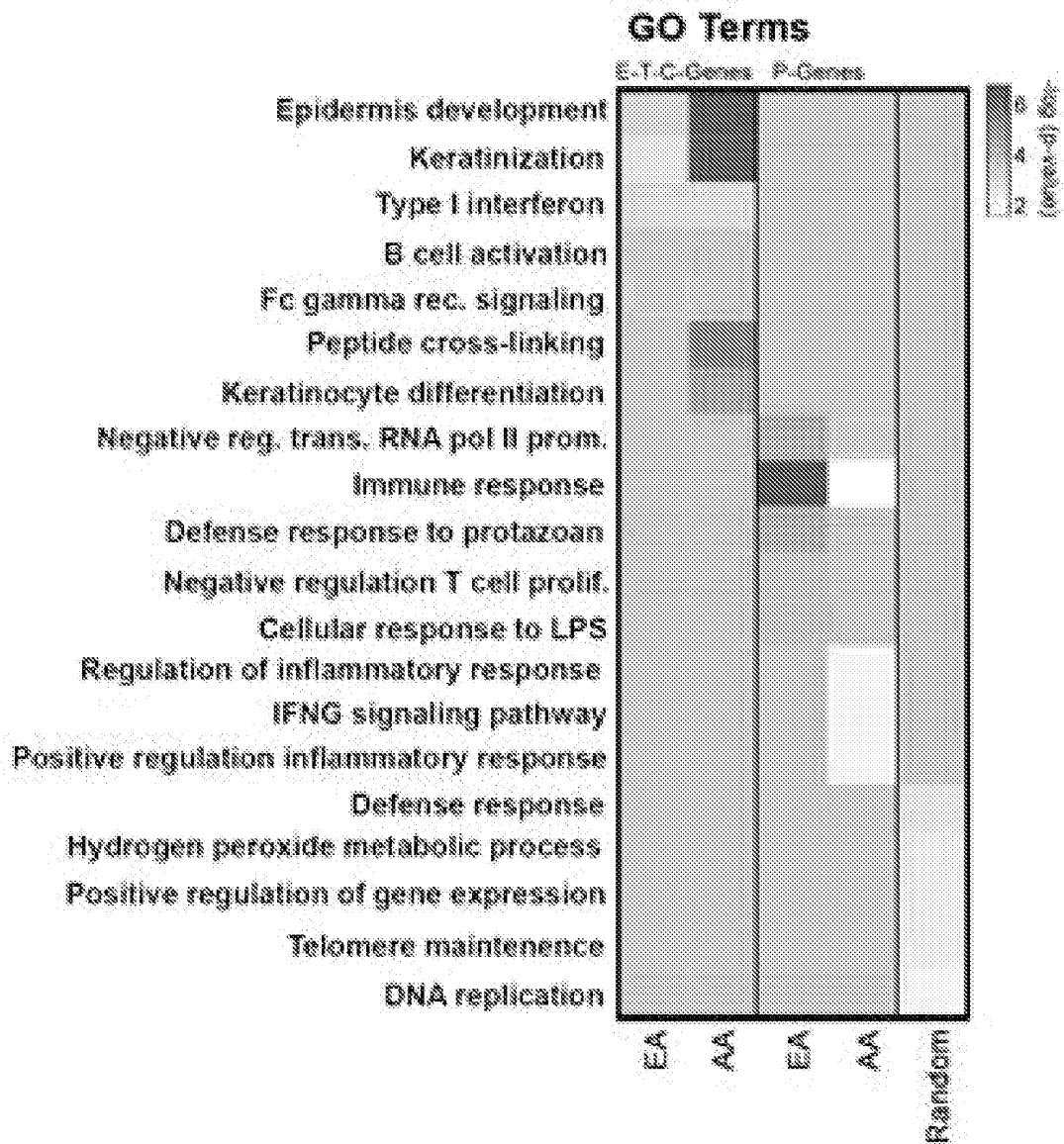


FIG. 67D

SLE-associated SNPs

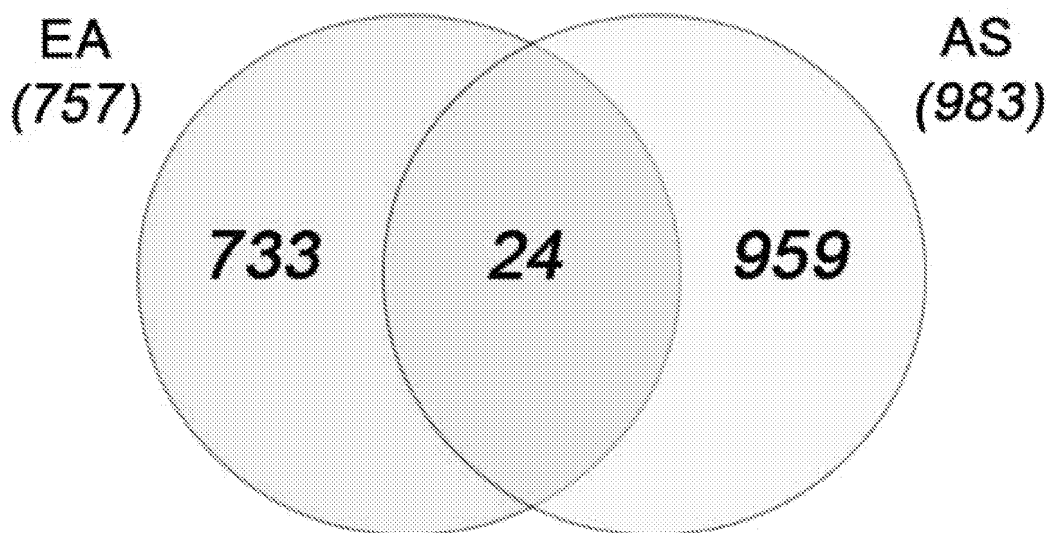


FIG. 68A

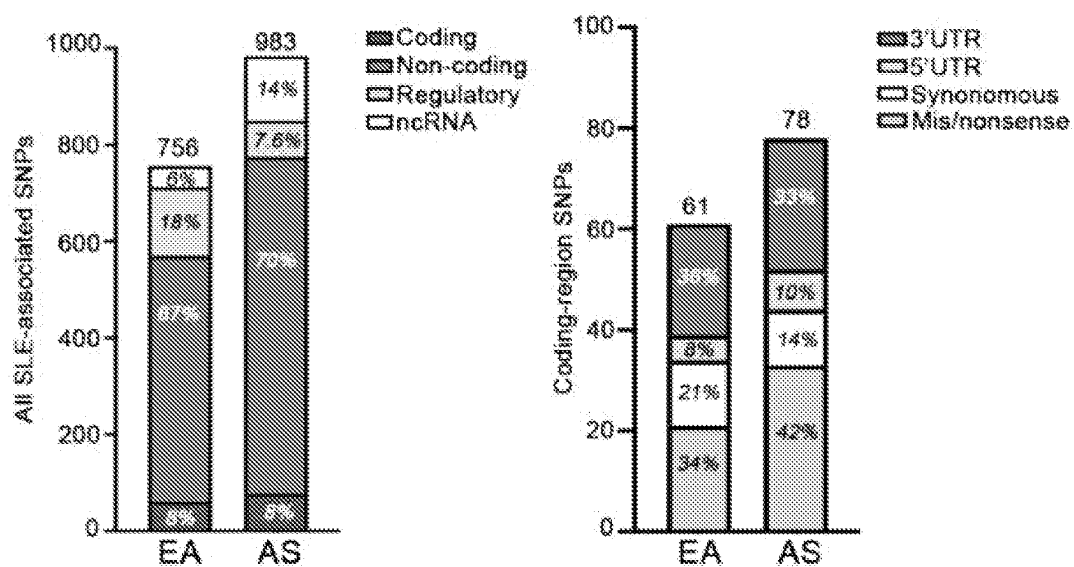


FIG. 68B

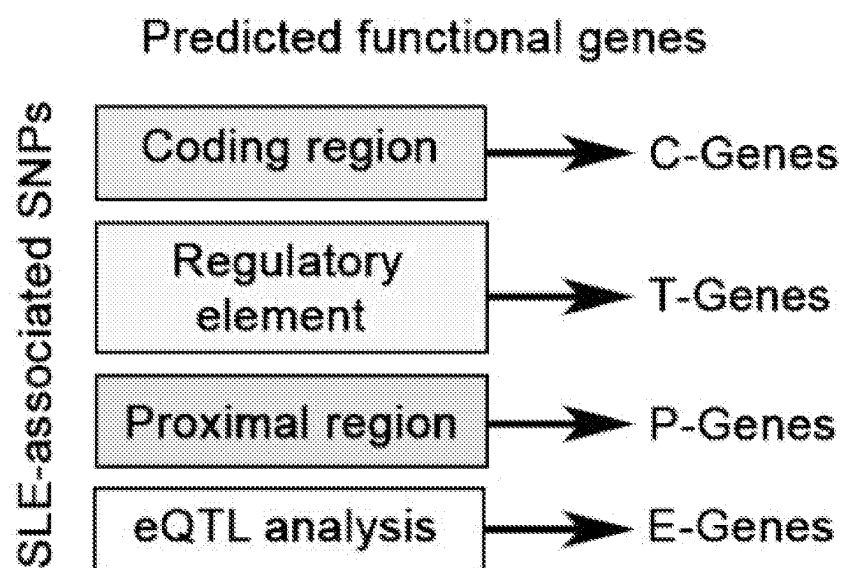


FIG. 68C

EA SNP-associated genes

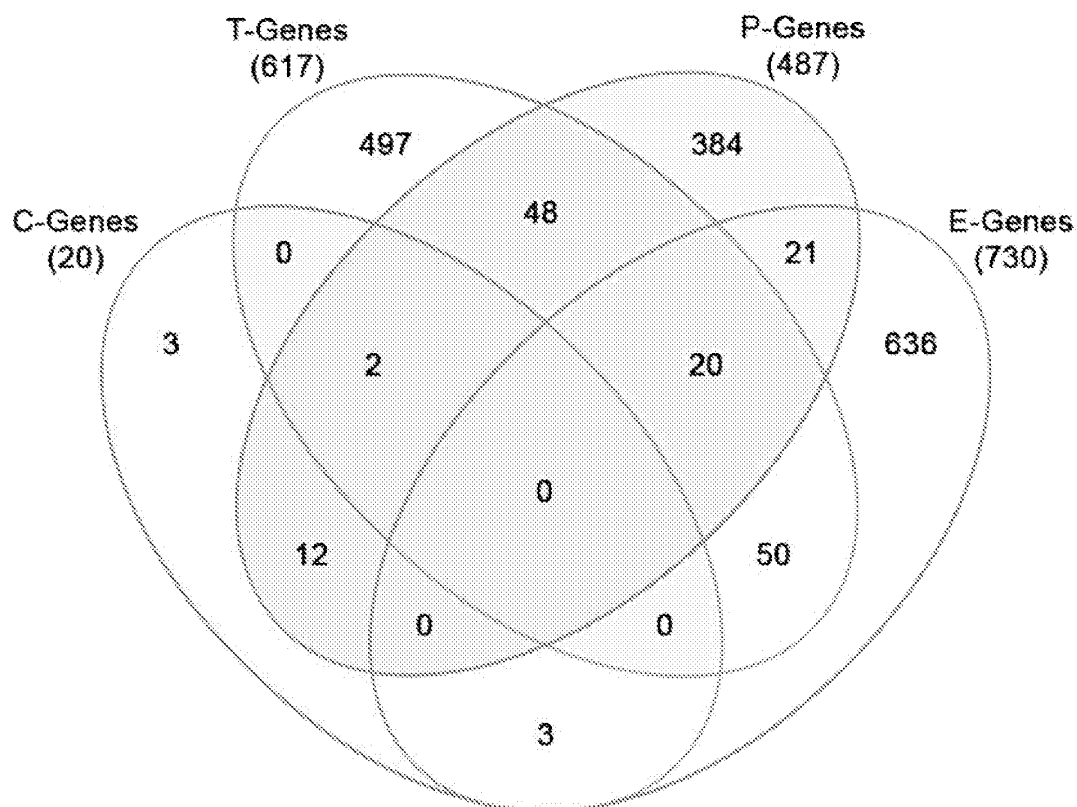


FIG. 68D

AS SNP-associated genes

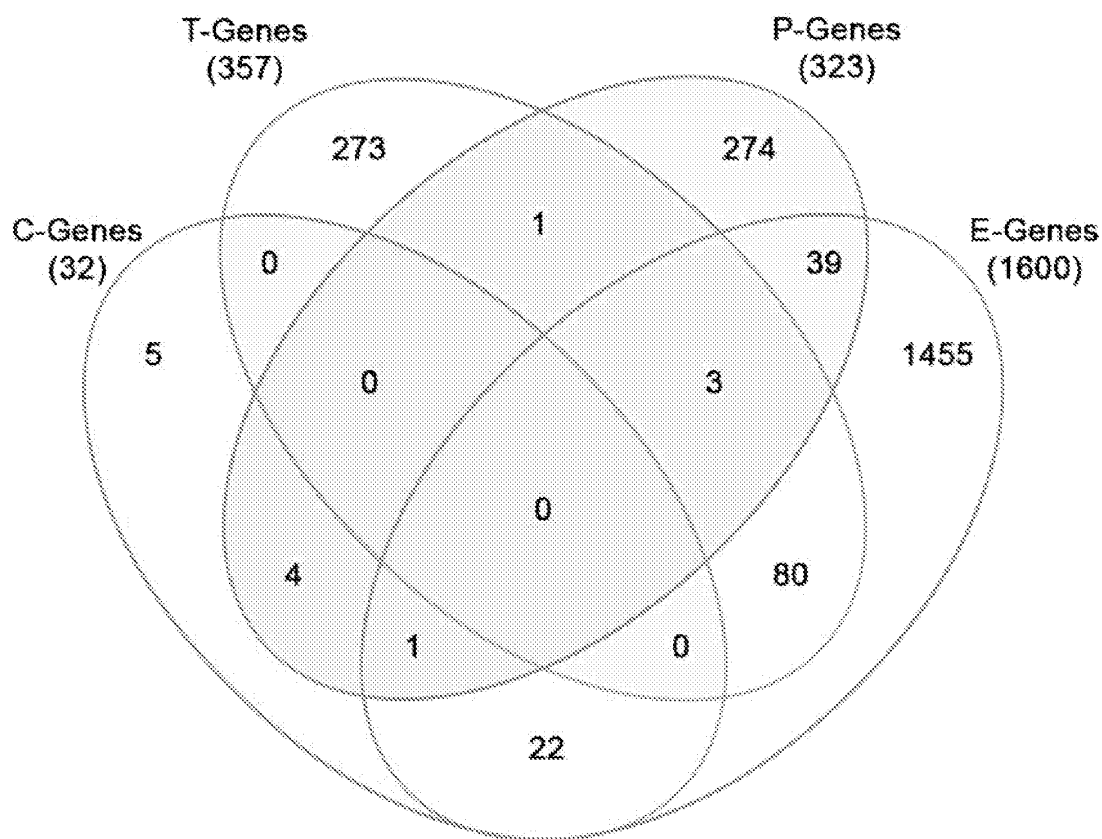


FIG. 68E

SNP-associated genes

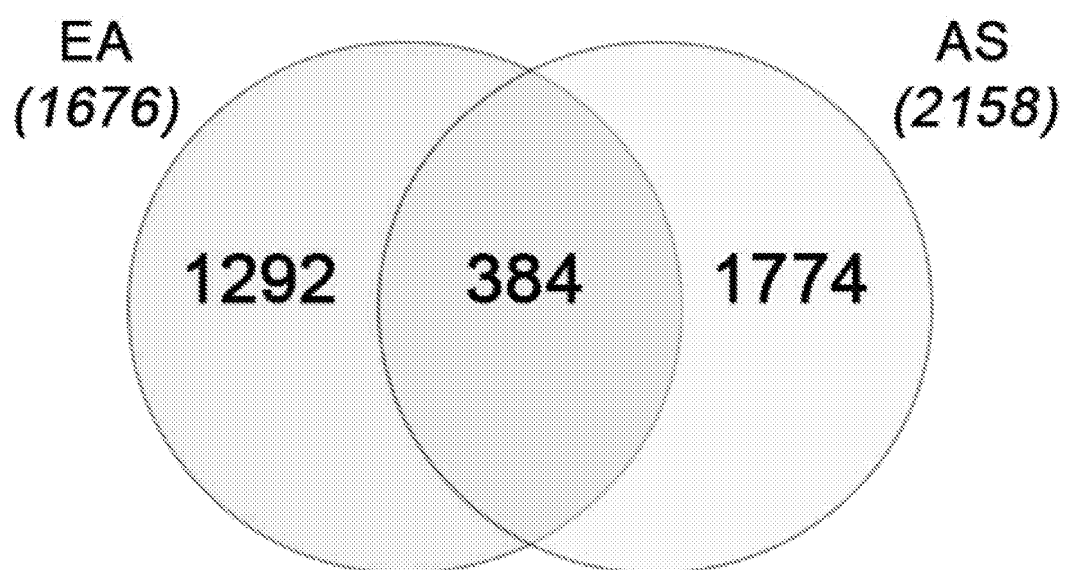


FIG. 69A

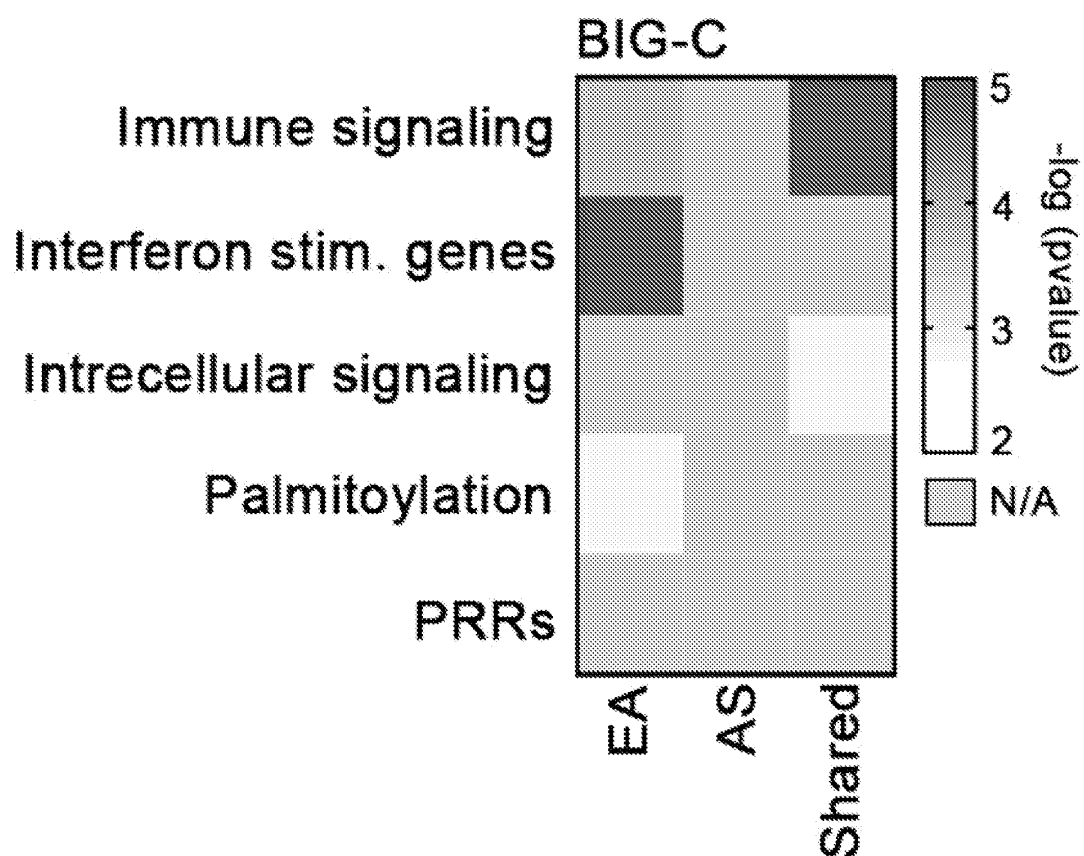


FIG. 69B

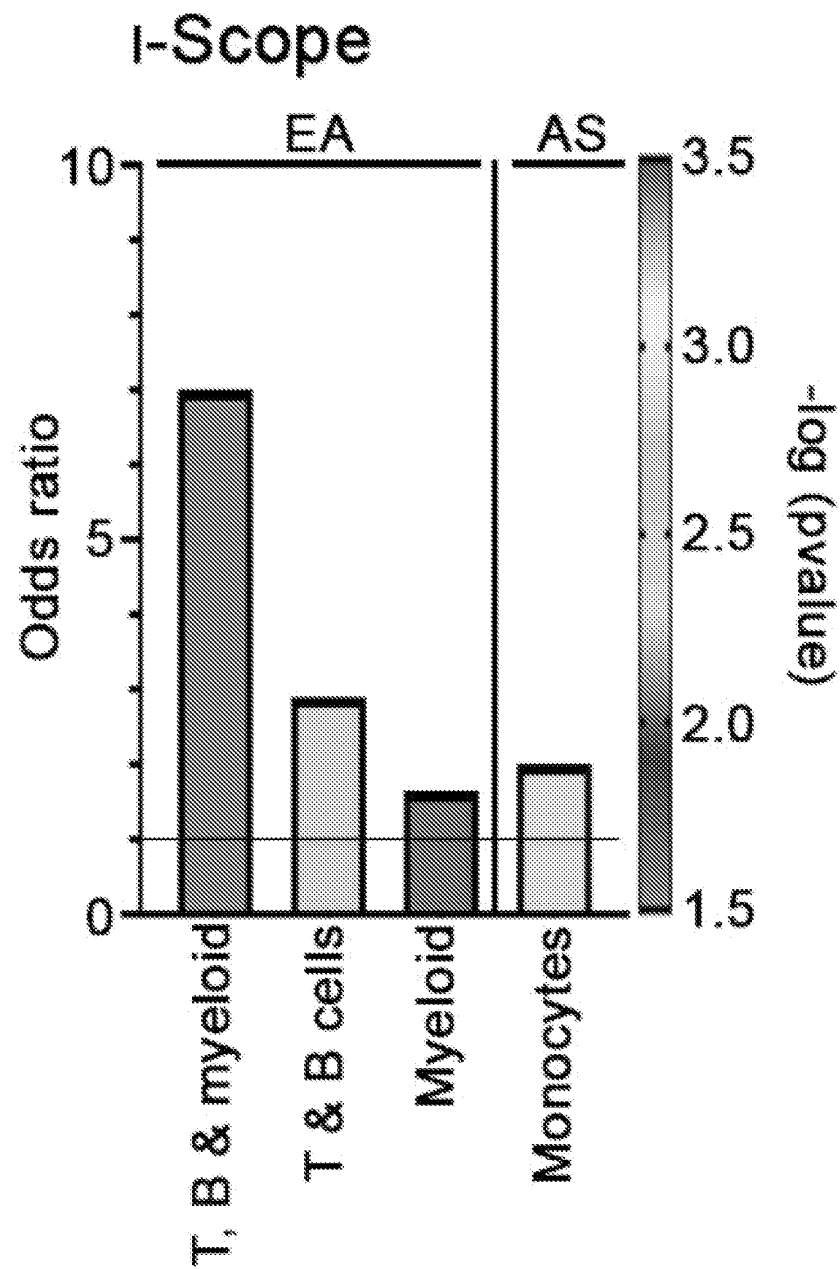


FIG. 69C

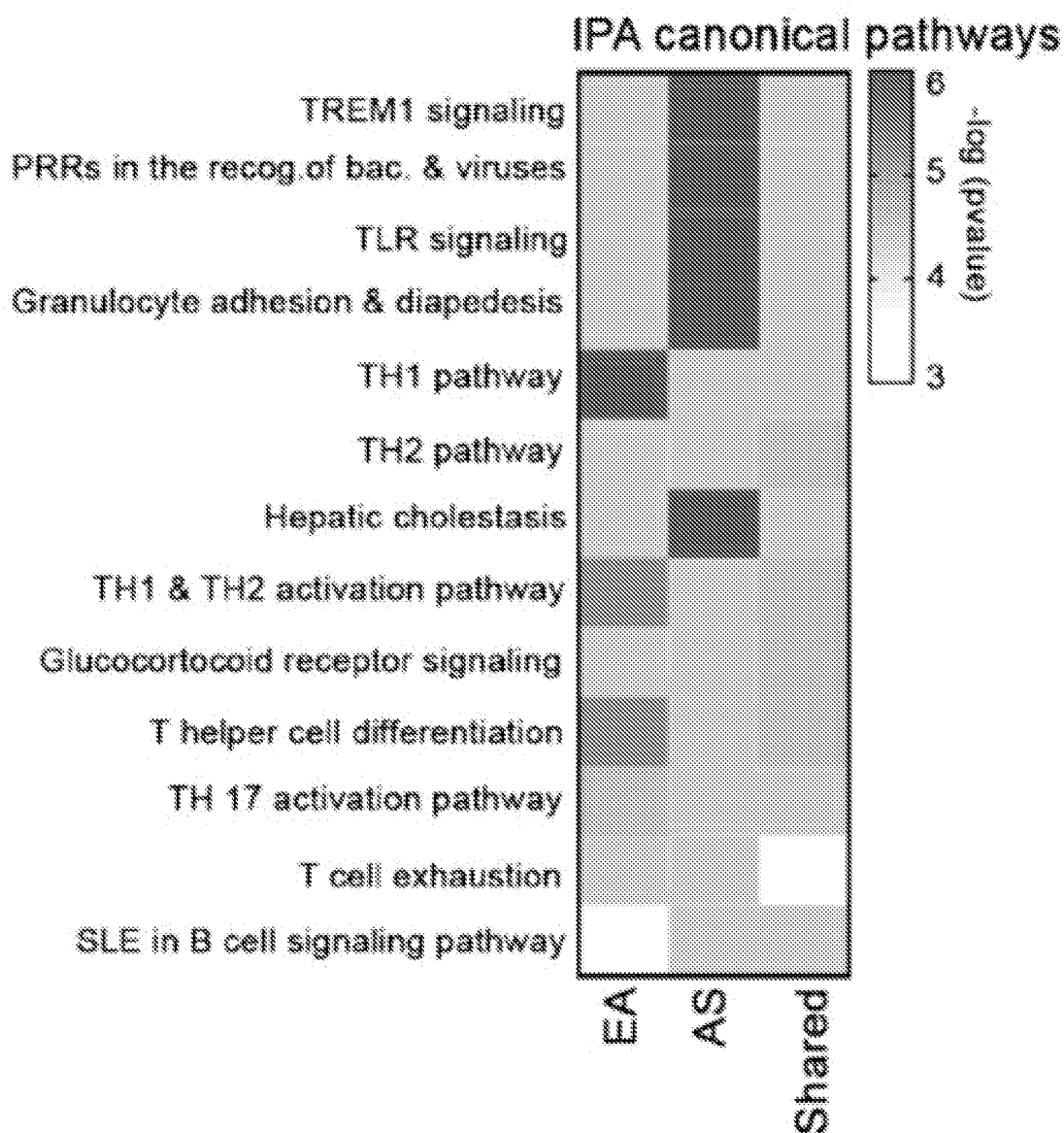


FIG. 69D

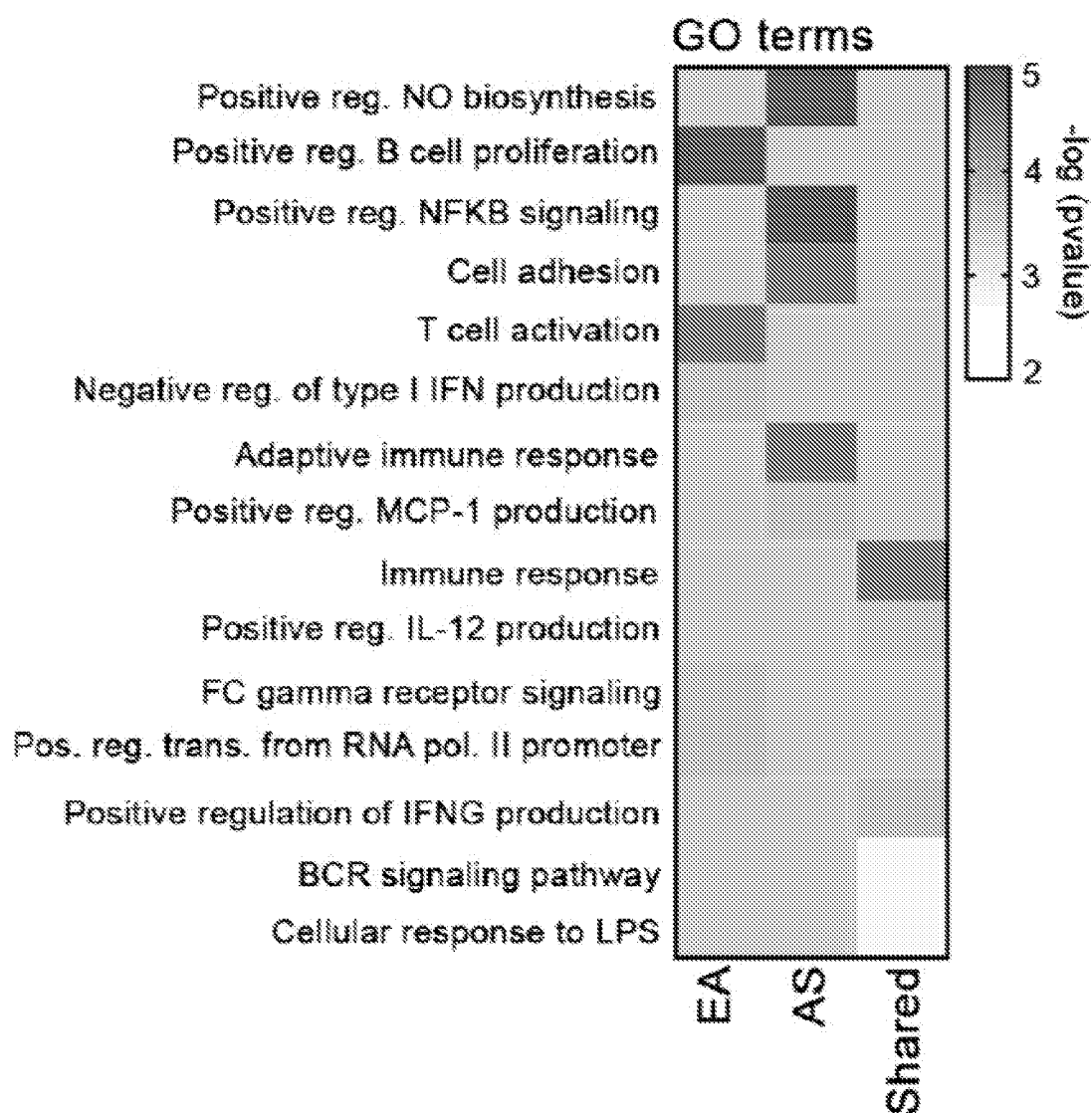


FIG. 69E

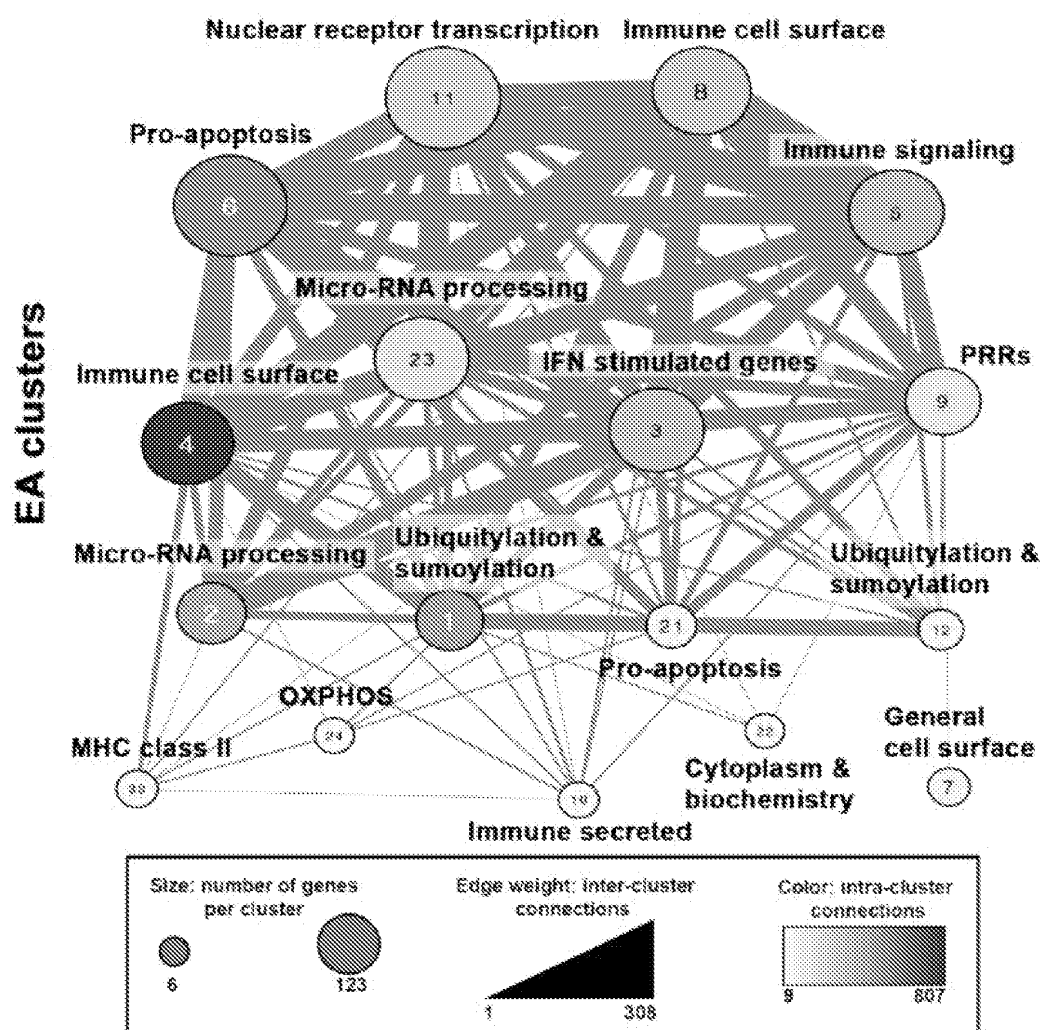


FIG. 70A

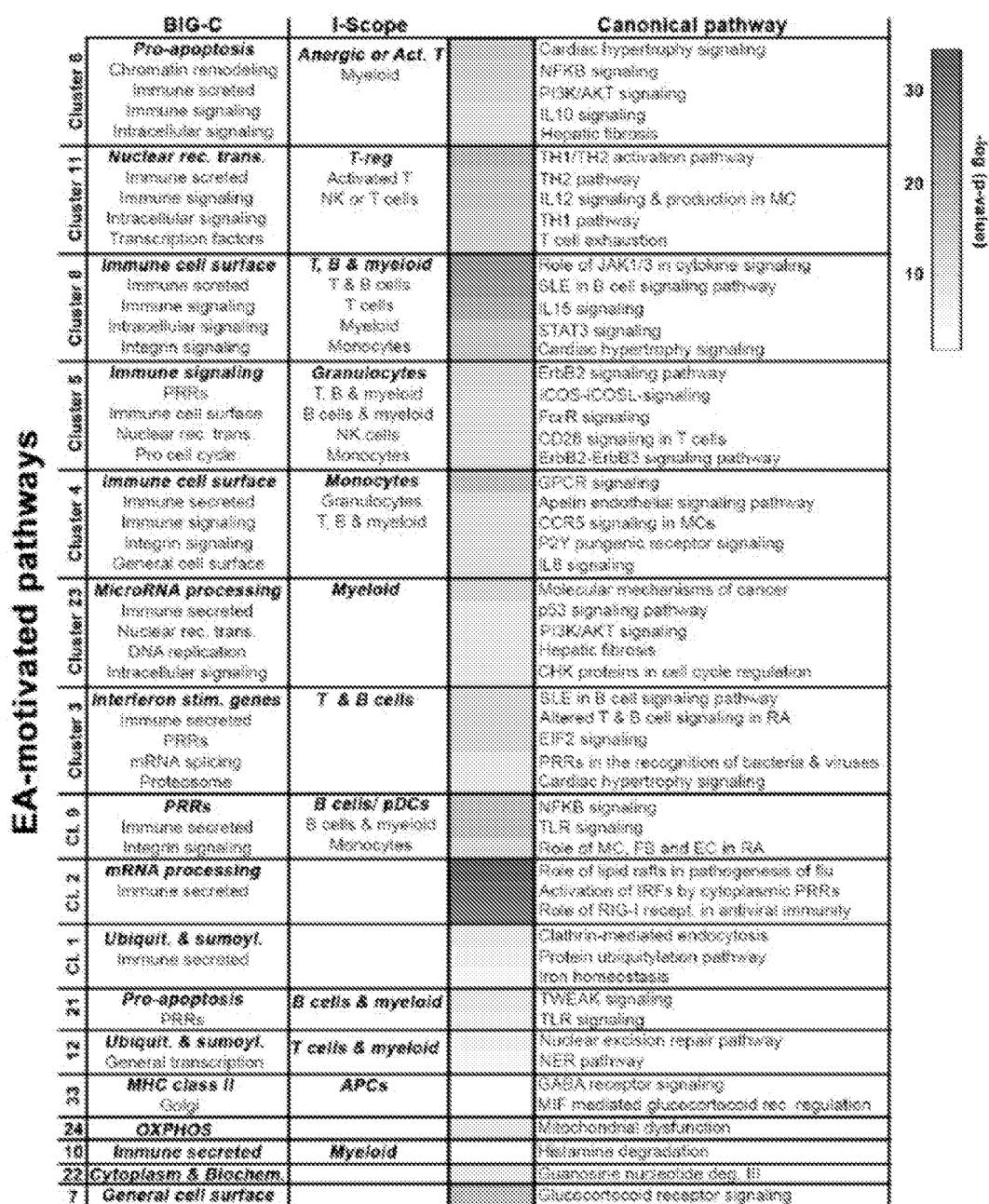


FIG. 70B

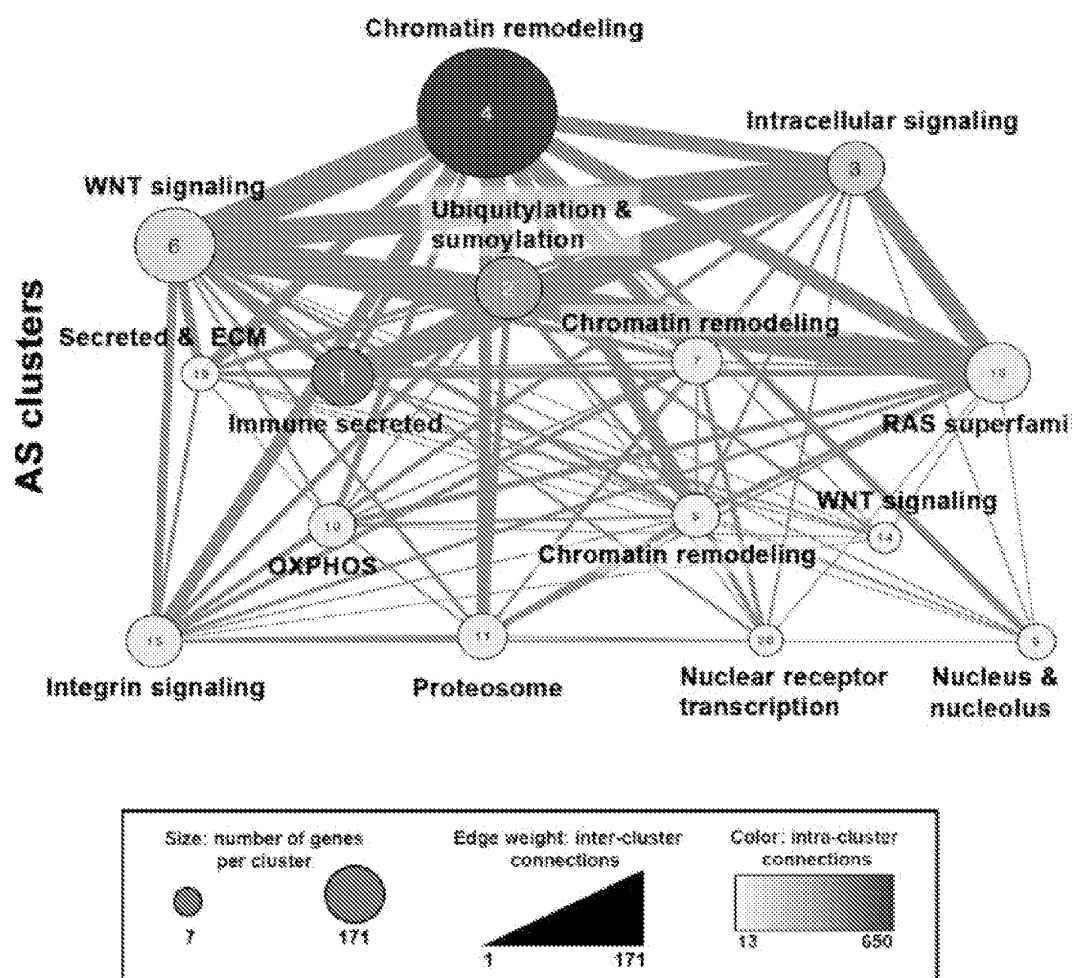


FIG. 70C

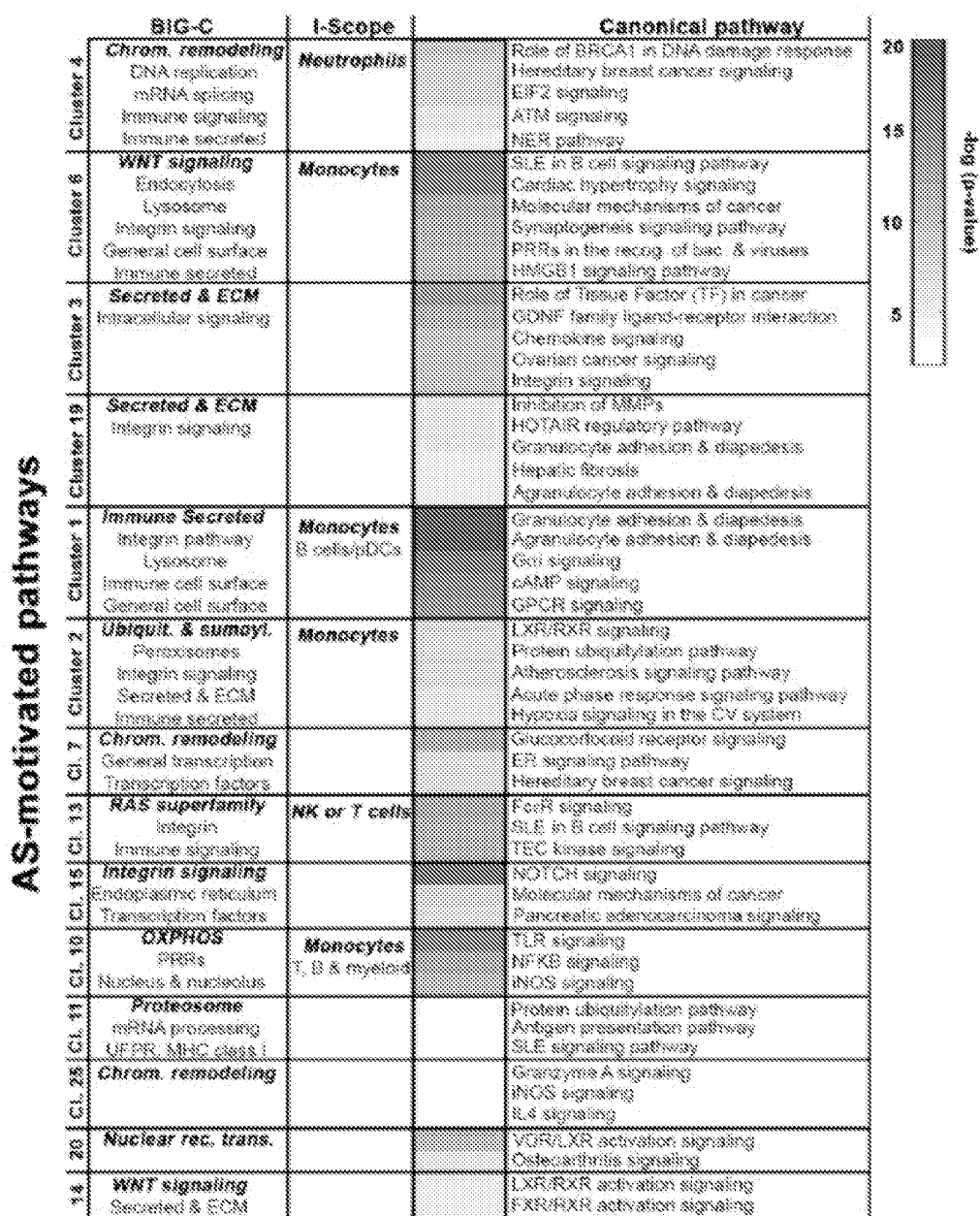


FIG. 70D

Shared clusters

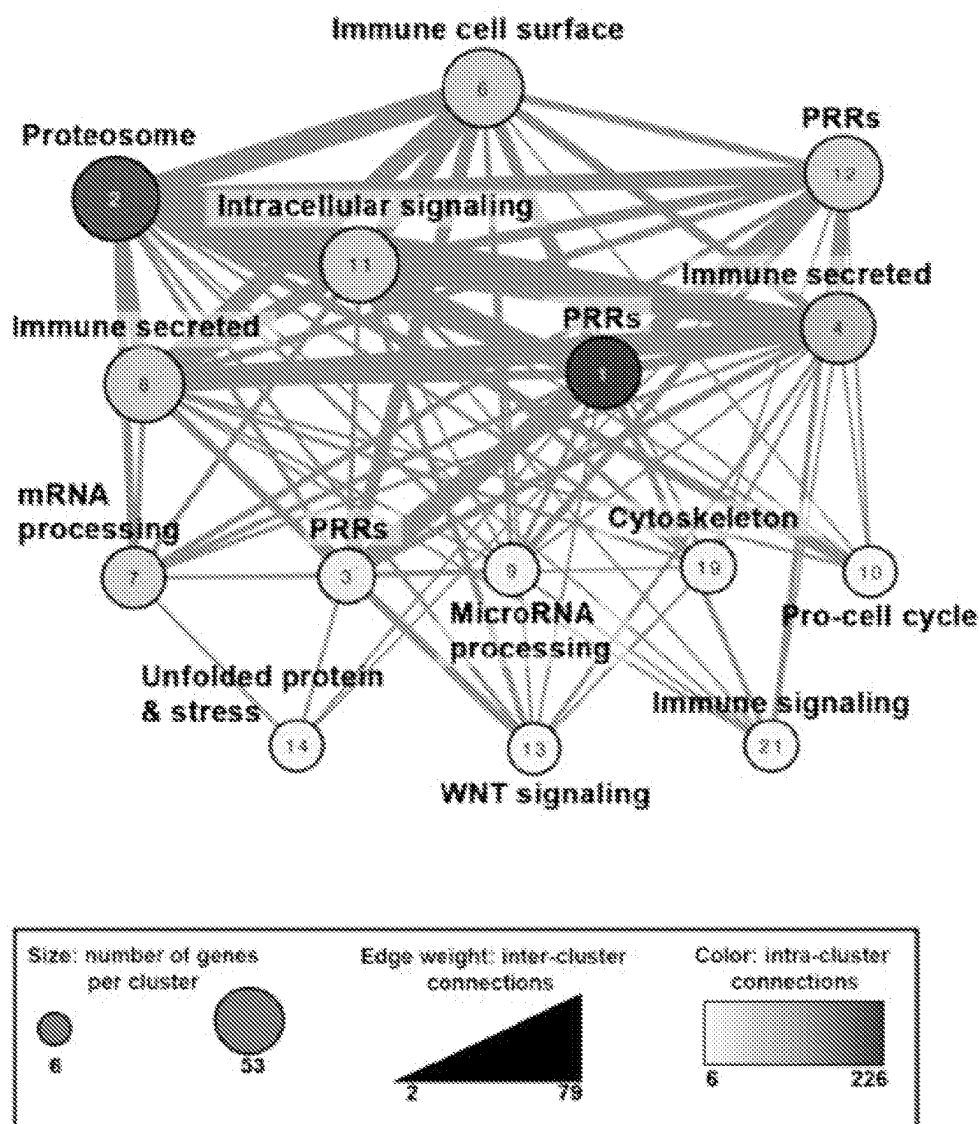


FIG. 71A

Shared pathways

	BIG-C	I-Scope	Canonical pathway
Cluster 2	Proteasome Immune secreted Immune signaling Intracellular signaling		- SLF in B cell signaling pathway - NF-κB signaling - PRRs in recognition of bacteria & viruses - BCR signaling pathway - PI3K signaling in B lymphocytes
Cluster 6	Immune cell surface Immune secreted Nuclear rec. trans. Integrin pathway Peroxisomes	NK or T Treg Anergic or Act. T T cells & myeloid	- TH2 pathway - TH1 & TH2 activation pathway - TH1 pathway - IL12 signaling & production in Mϕ - T helper cell differentiation
Cluster 12	PRRs Intracellular signaling Anti-proliferation	B cells/pDCs Myeloid	- Neuroinflammation signaling pathway - TLR signaling - NF-κB signaling - p38 MAPK signaling - Role of Mϕ, FB and ECs in RA
Cluster 8	Immune secreted Immune secreted Immune signaling Nuclear rec. trans. Pro-apoptosis	B cells & myeloid NK or T cells Myeloid	- T helper cell differentiation - Role of cytokines in communication b/w immune cells - Role of JAK 1/3 in cytokine signaling - TH1 & TH2 activation pathway - Hepatic cholestasis
Cluster 11	Intracellular signaling Immune secreted Immune signaling Immune cell surface	T cells Anergic or Act. T Neutrophils Myeloid	- SCN signaling pathway - SLF in B cell signaling pathway - IL15 signaling - T cell exhaustion - Sperm motility
Cluster 1	PRRs Immune secreted Immune cell surface Chromatin remodeling	T, B & myeloid T & B cells	- Glucocorticoid receptor signaling - Activation of IRFs by cytosolic PRRs - Neuroinflammation signaling pathway - Role of RIG-I recept. in antiviral immunity - RAR activation
Cluster 4	Immune secreted Immune cell surface Intracellular signaling	NK or T cells T, B & myeloid B cells & myeloid Monocytes	- TH1 & TH2 activation pathway - JAK/STAT signaling pathway - Role JAK 1/3 in cytokine signaling - STAT3 signaling - Role of cytokines in communication b/w immune cells
Cl. 7	mRNA processing Intracellular signaling mRNA splicing	B cells & myeloid	- Assembly of RNA pol II complex - ERF2 signaling - SLF signaling pathway
Cl. 5	PRRs Interferon stim. genes Integrin pathway		- Interferon signaling - Tumor function of hepatic NK cells - Leukocyte extravasation
Cl. 9	MicroRNA processing Immune signaling Golgi	T cells	- NOTCH1 signaling - Regulation of EMT - Inhibition of ARE mediated mRNA degradation
Cl. 13	Cytoskeleton		- Caveolar mediated endocytosis signaling - GDNF family ligand-receptor signaling - Insulin receptor signaling pathway
10	Pro-cell cycle	T cells & myeloid	DNA damage induced 14-3-3 signaling
21	Immune signaling	NK or T cell	TH2 pathway
14	UPF response & stress		Unfolded protein response
12	WNT signaling		EGFR receptor signaling
8	General cell surface		Glucocorticoid receptor signaling

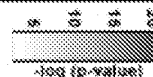


FIG. 71B

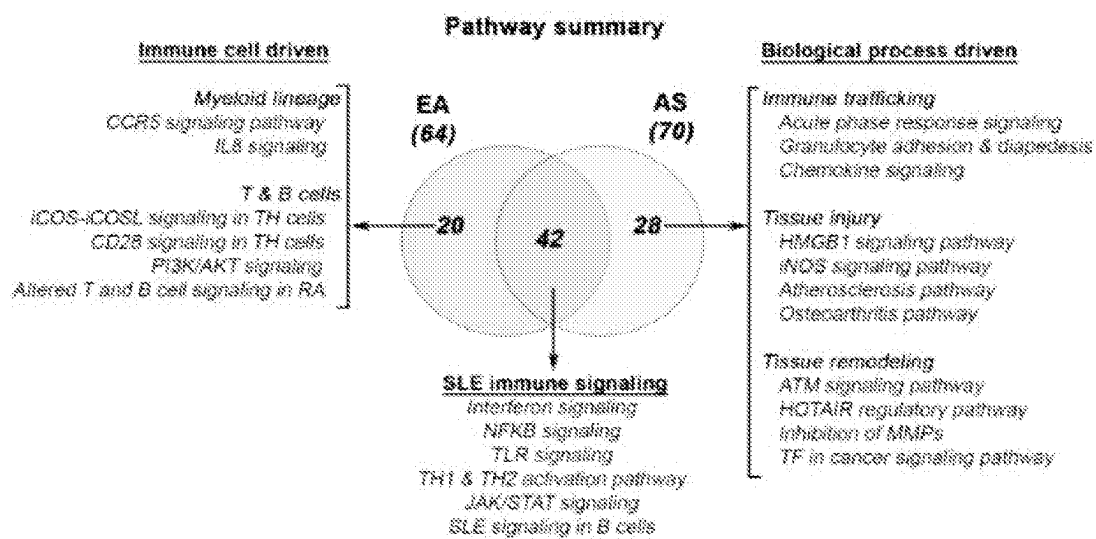


FIG. 71C

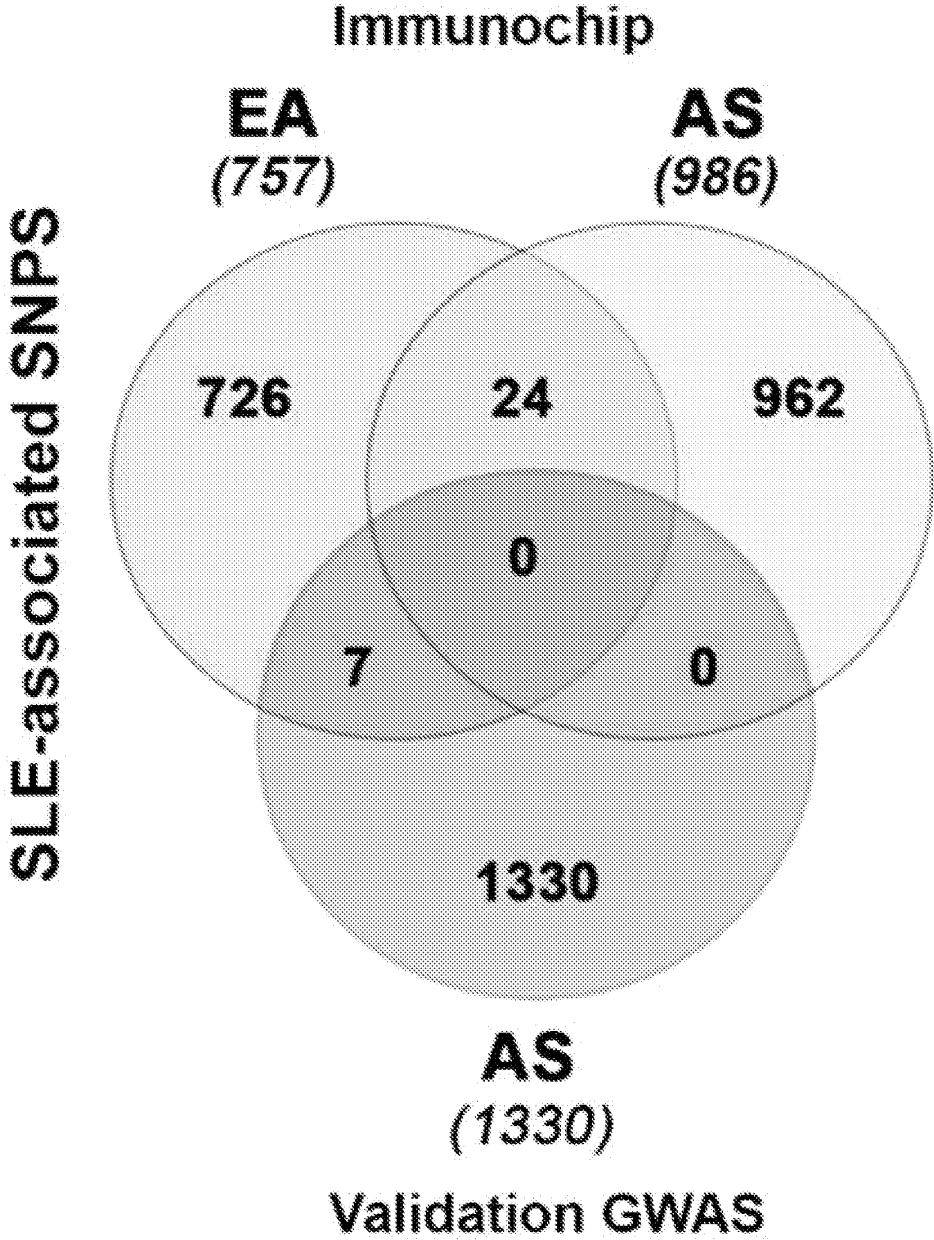


FIG. 72A

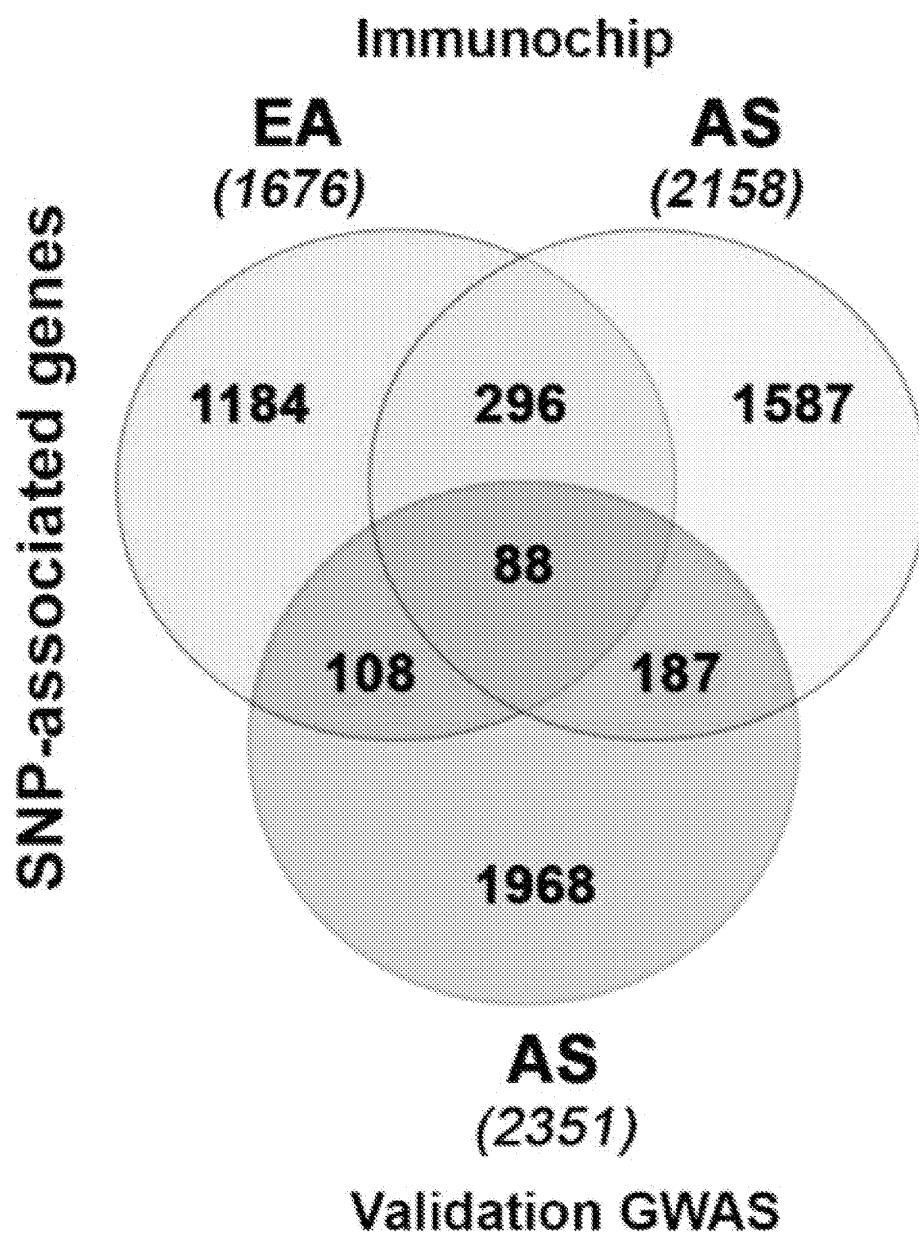


FIG. 72B

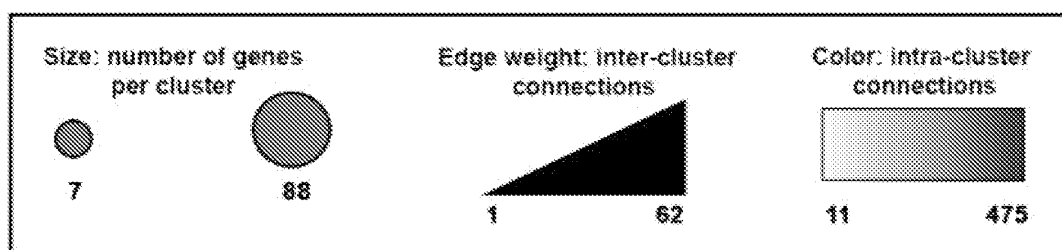
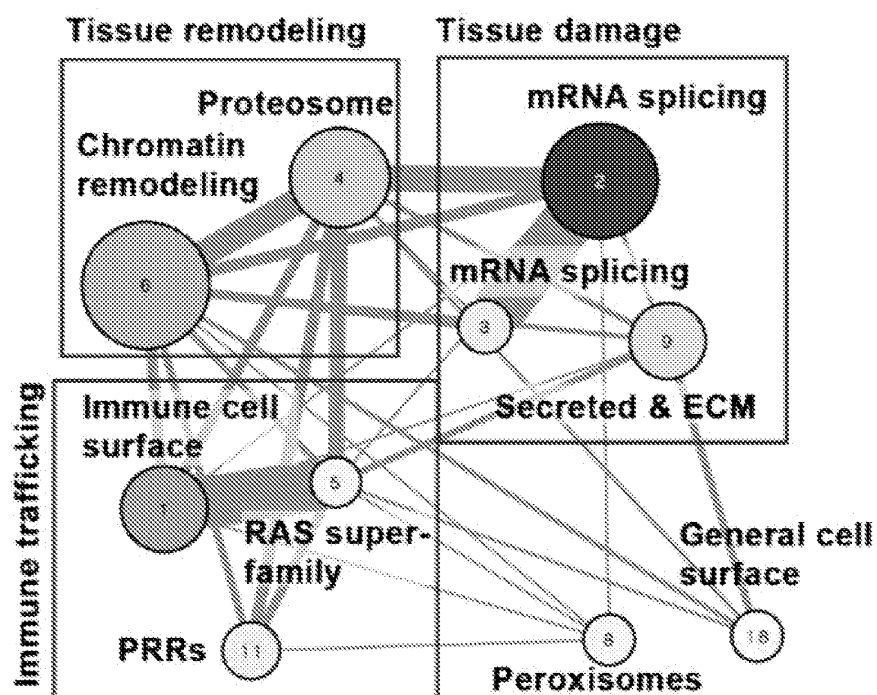


FIG. 72C

	BIG-C	I-Scope	Canonical pathway
Cluster 6	Chromatin remodeling Pro-cell cycle microRNA processing UPF response Intracellular signaling		Inhibition of ARE-mediated mRNA degradation ERK/MAPK signaling HIFPO signaling PKA signaling CDK5 signaling
Cluster 4	Proteosome Endosome Lysosome	T & B cells	Inhibition of ARE-mediated mRNA degradation PRRs in the recognition of bacteria & viruses ErbB2 signaling pathway Neuregulin signaling SLE in B cell signaling
Cluster 2	mRNA splicing mRNA processing Ubiquit. & sumoyl.		EIF2 signaling Regulation of eIF4 & p70S6K signaling mTOR signaling pathway SLE signaling pathway Cleavage & polyaden. of pre-mRNA
Cl. 3	mRNA splicing Nucleus & nucleolus		N/A RNA post-transcriptional modification* Cellular function and maintenance* Cell death and survival*
Cluster 9	Secreted & ECM	Monocytes	Extrinsic prothrombotic activation pathway LXR/RXR signaling pathway FXR/RXR signaling pathway Reelin signaling in neurons Coagulation systems
Cluster 1	Immune cell surface General cell surface		Gn1 signaling pathway Cardiac β -adrenergic signaling pathway Relaxin signaling cAMP signaling G protein signaling mediated by Tubby
Cluster 11	PRRs Interferon stim. genes MHC class I MHC class II Lysosome	B cells/pDCs APCs NK cells	Neuroinflammation signaling pathway Role of RIG-I recept. in antiviral immunity Activation of IRFs by cytosolic PRRs Role of cytokines in communication b/w immune cells Role of lipids/lipid rafts in pathogenesis of influenza
Cl. 8/Cl. 5	RAS superfamily		Gnq signaling pathway CXCR4 signaling
Cl. 8	Peroxisomes		Fatty acid β -oxidation II Glutaryl-CoA degradation
18	General cell surface		Axonal guidance Synaptogenesis

FIG. 72D

GWAS SNPs

SLE

CAD

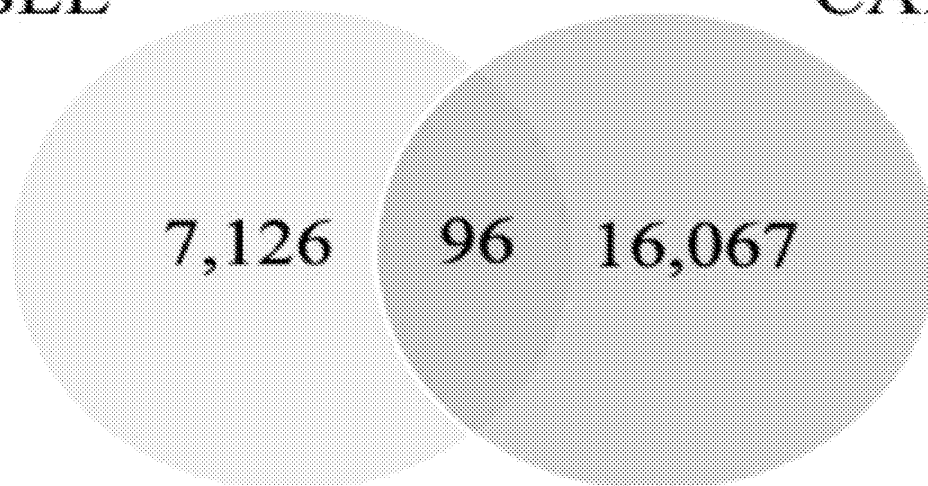
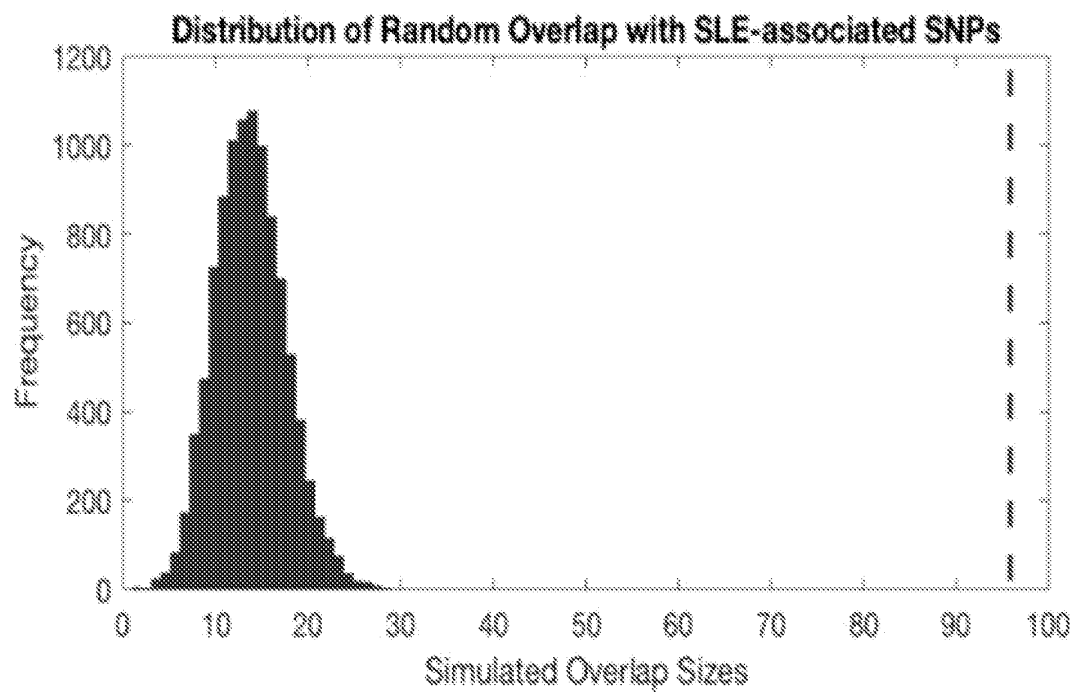
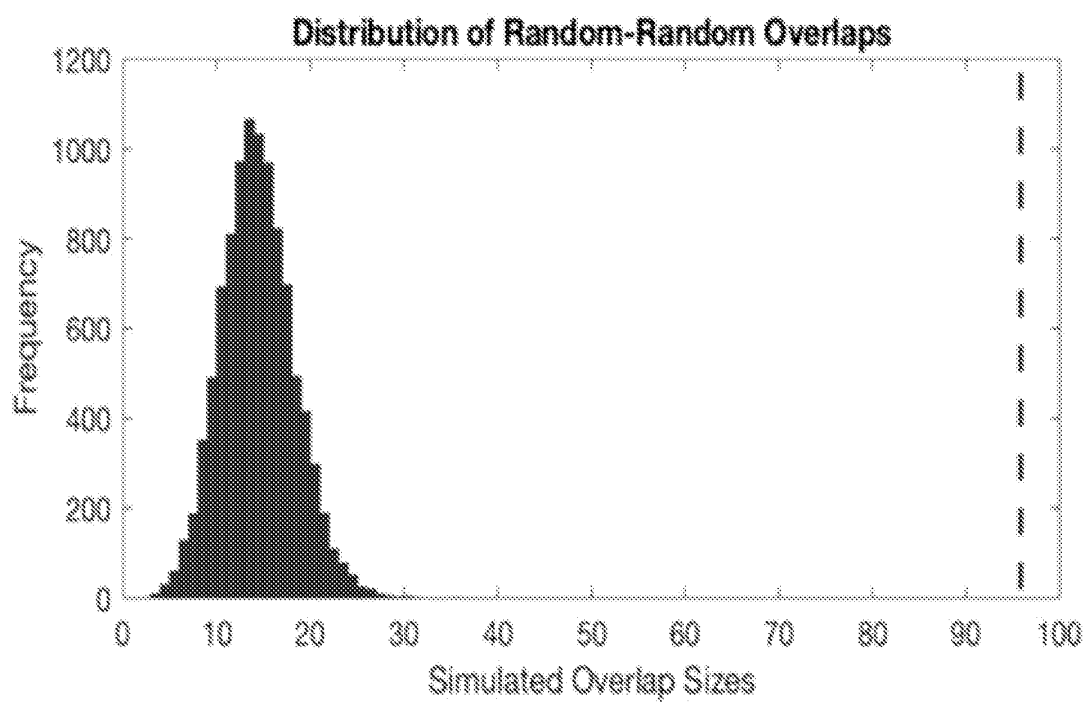


FIG. 73A

Random vs SLE

**FIG. 73B**

Random vs Random

**FIG. 73C**

Random vs CAD

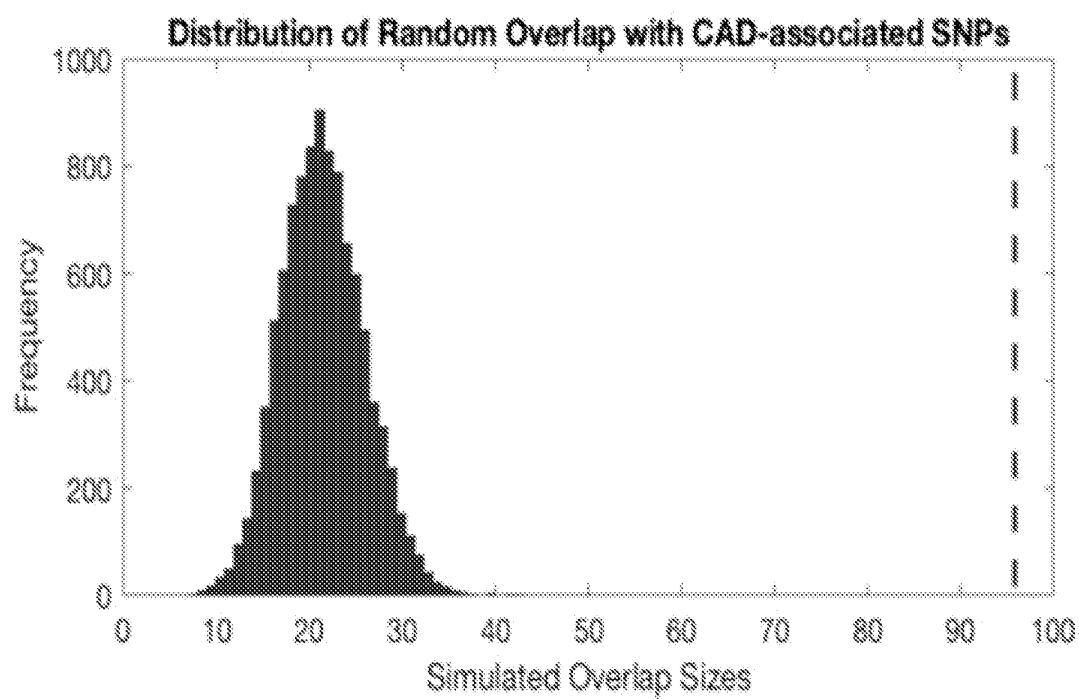
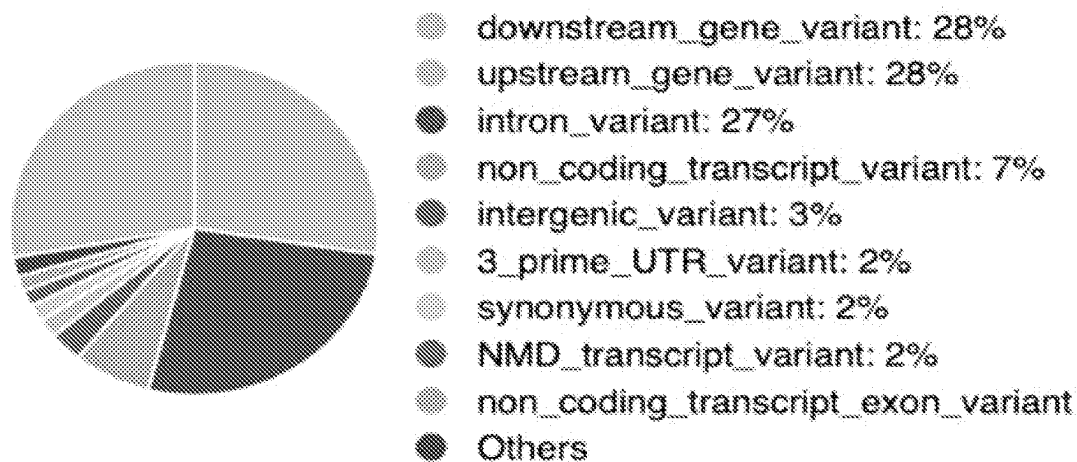
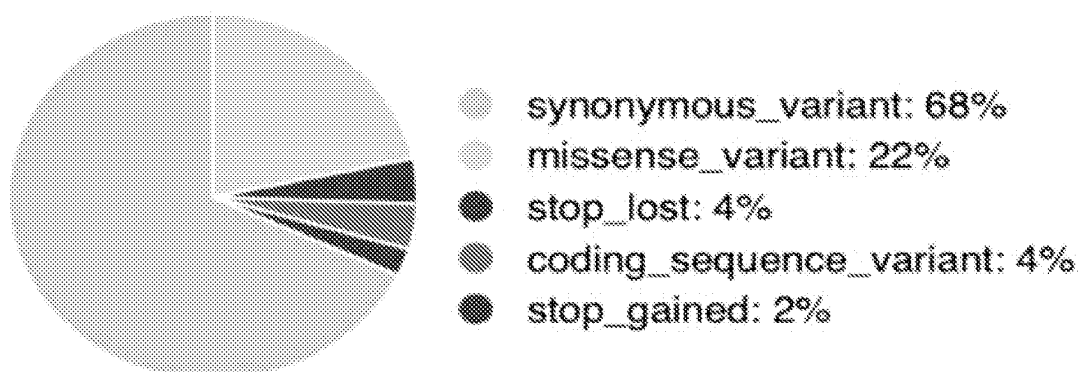


FIG. 73D

Consequences (all)**FIG. 74A****Coding consequences****FIG. 74B**

SLE/CAD-predicted genes

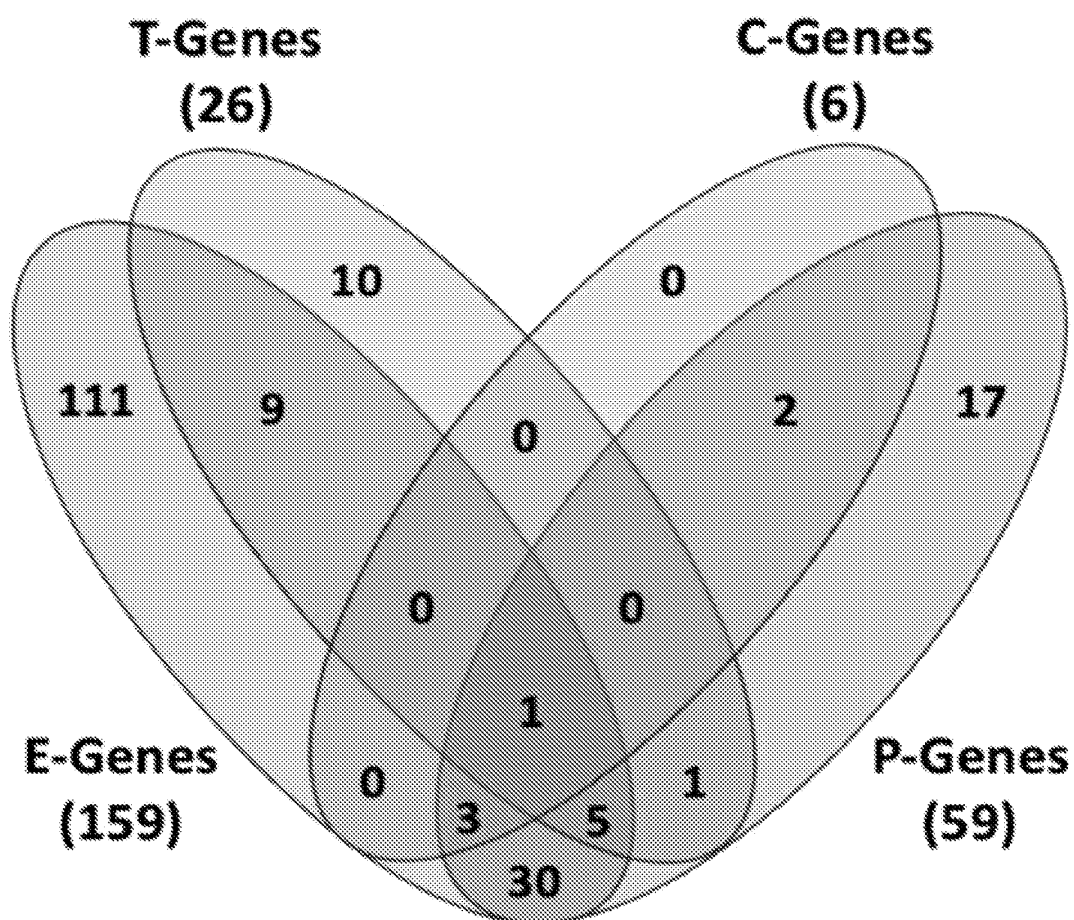


FIG. 75

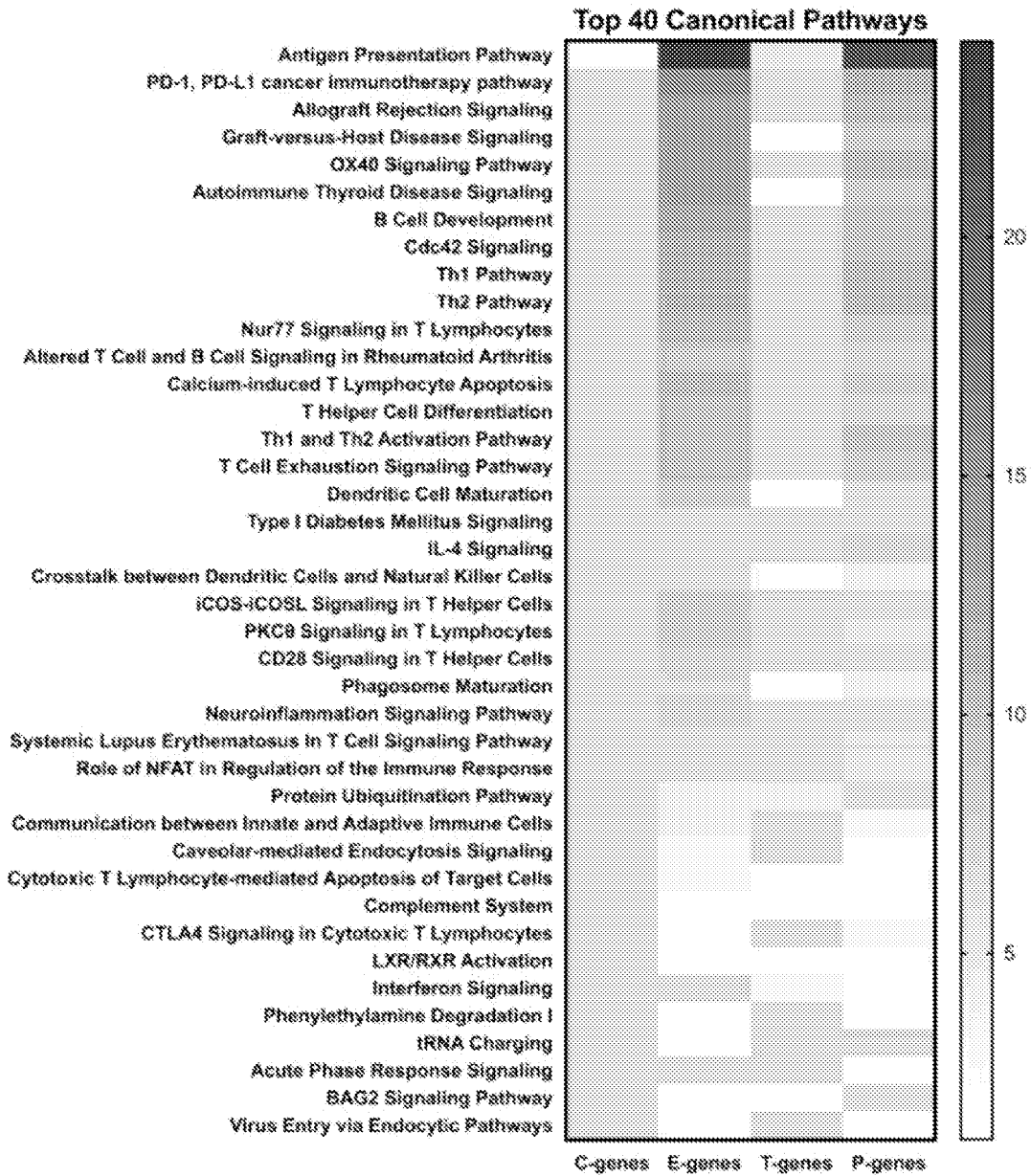


FIG. 76A

ErichR

positive regulation of interferon- α production (GO:0032727)
positive regulation of interferon- β production (GO:0032728)
negative regulation of natural killer cell proliferation (GO:0032818)
negative regulation of type III interferon production (GO:0034345)
cellular response to muramyl dipeptide (GO:0071225)
negative regulation of gamma- δ T cell activation (GO:0046644)
positive regulation of natural killer cell proliferation (GO:0032819)
negative regulation of establishment of T cell polarity (GO:1903904)
negative regulation of alpha-beta T cell activation (GO:0046636)
positive regulation of δ cell receptor signaling pathway (GO:0050861)

FIG. 76B

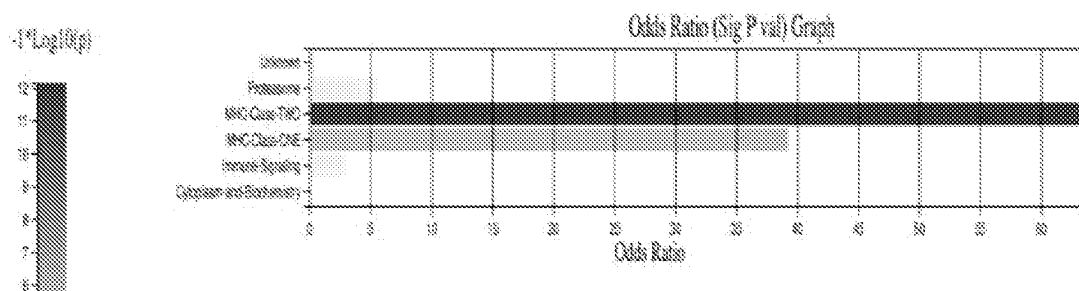
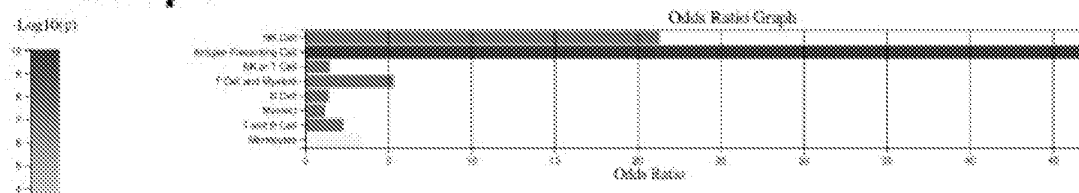
BIG-C**FIG. 76C****I-Scope****FIG. 76D**



FIG. 77

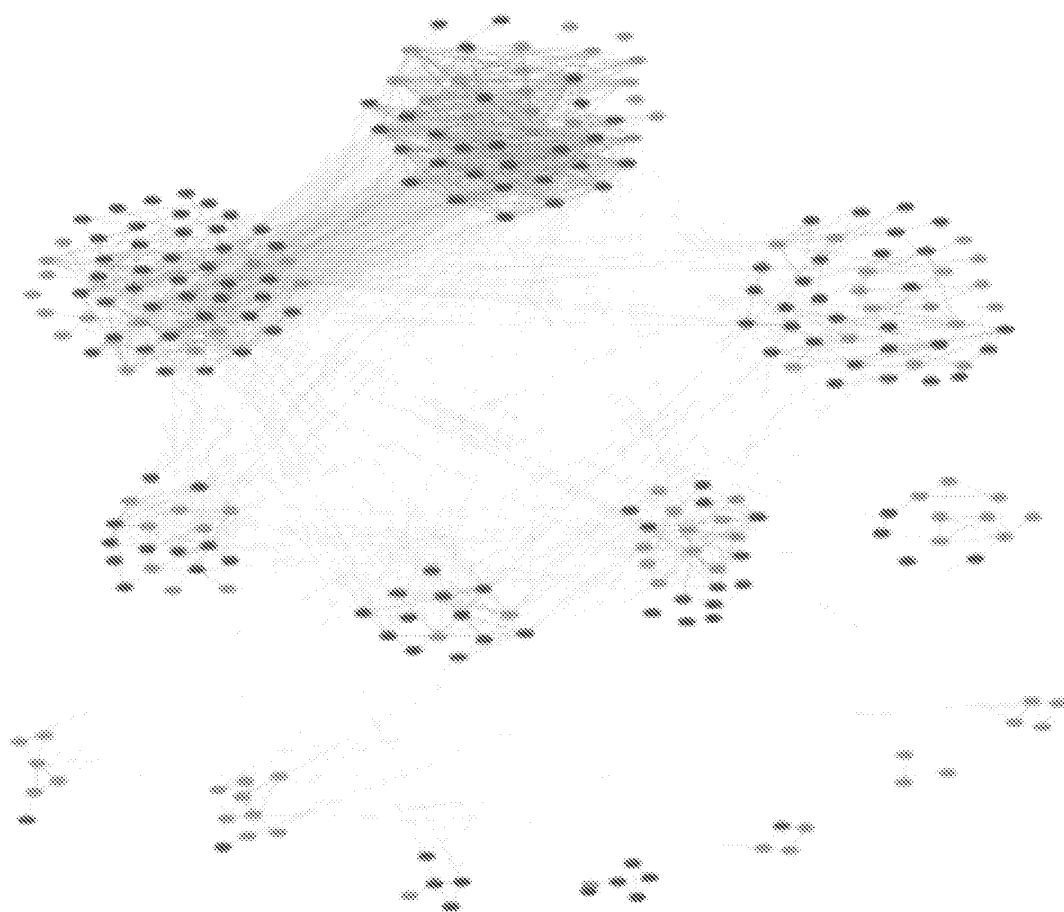


FIG. 78A

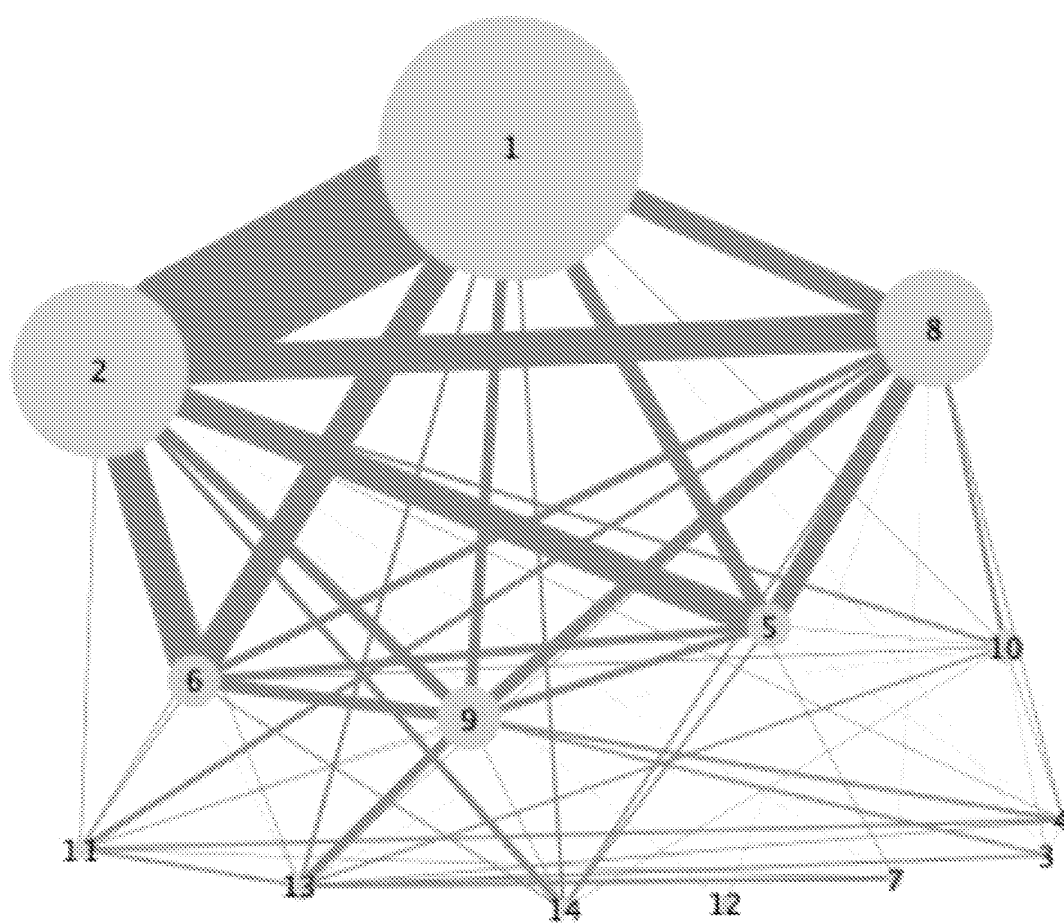


FIG. 78B

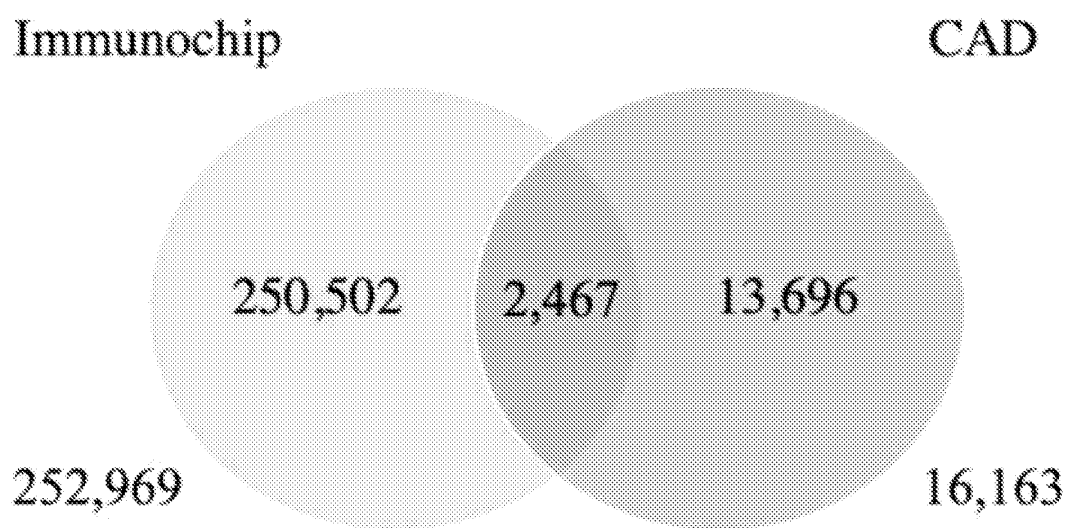


FIG. 79A

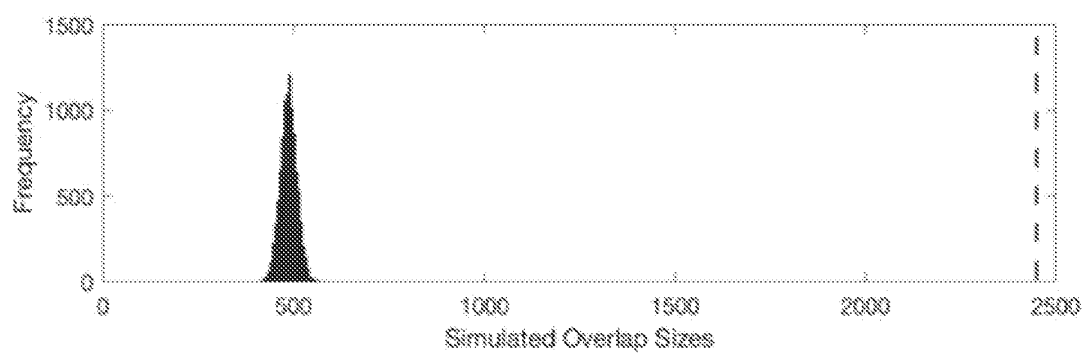


FIG. 79B

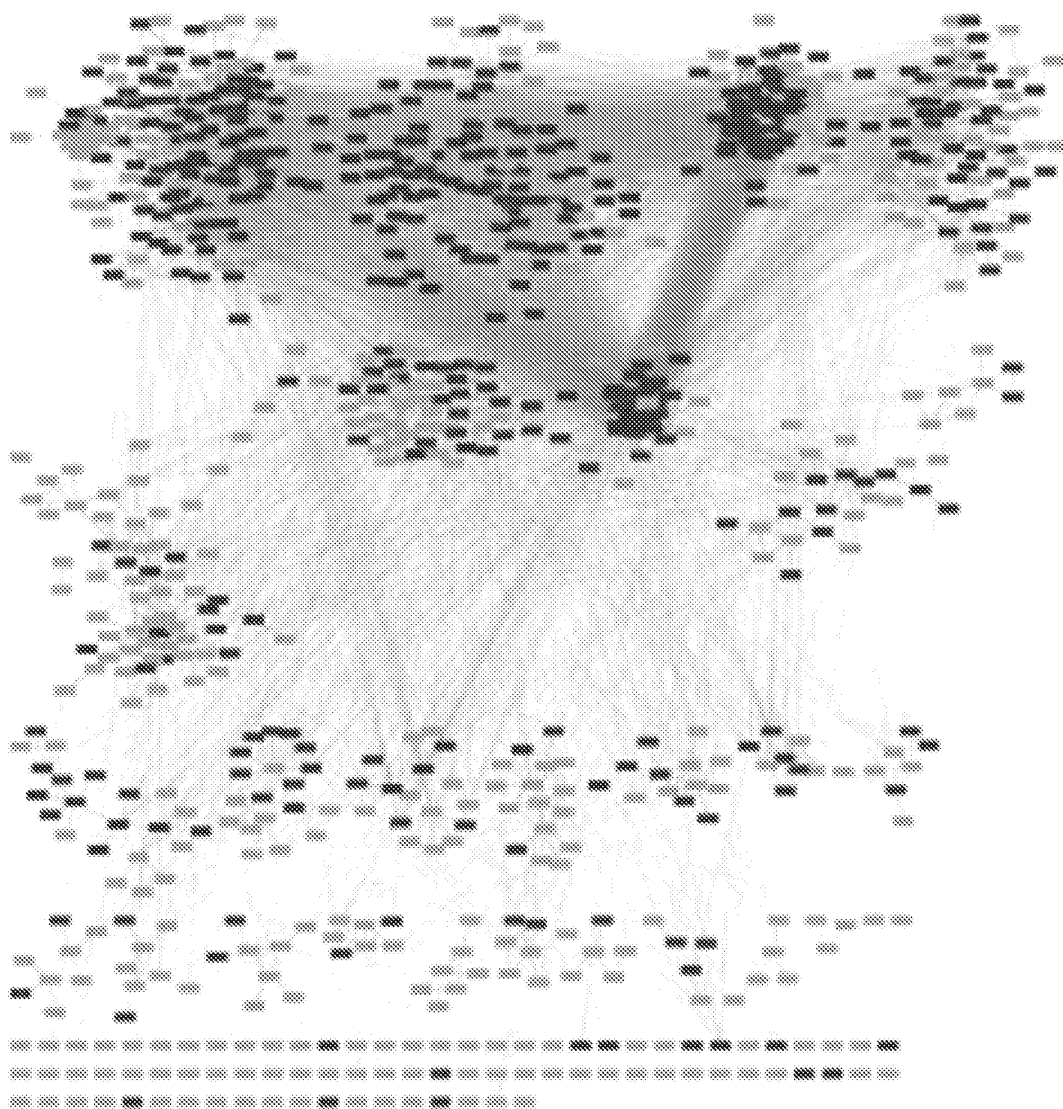


FIG. 80A

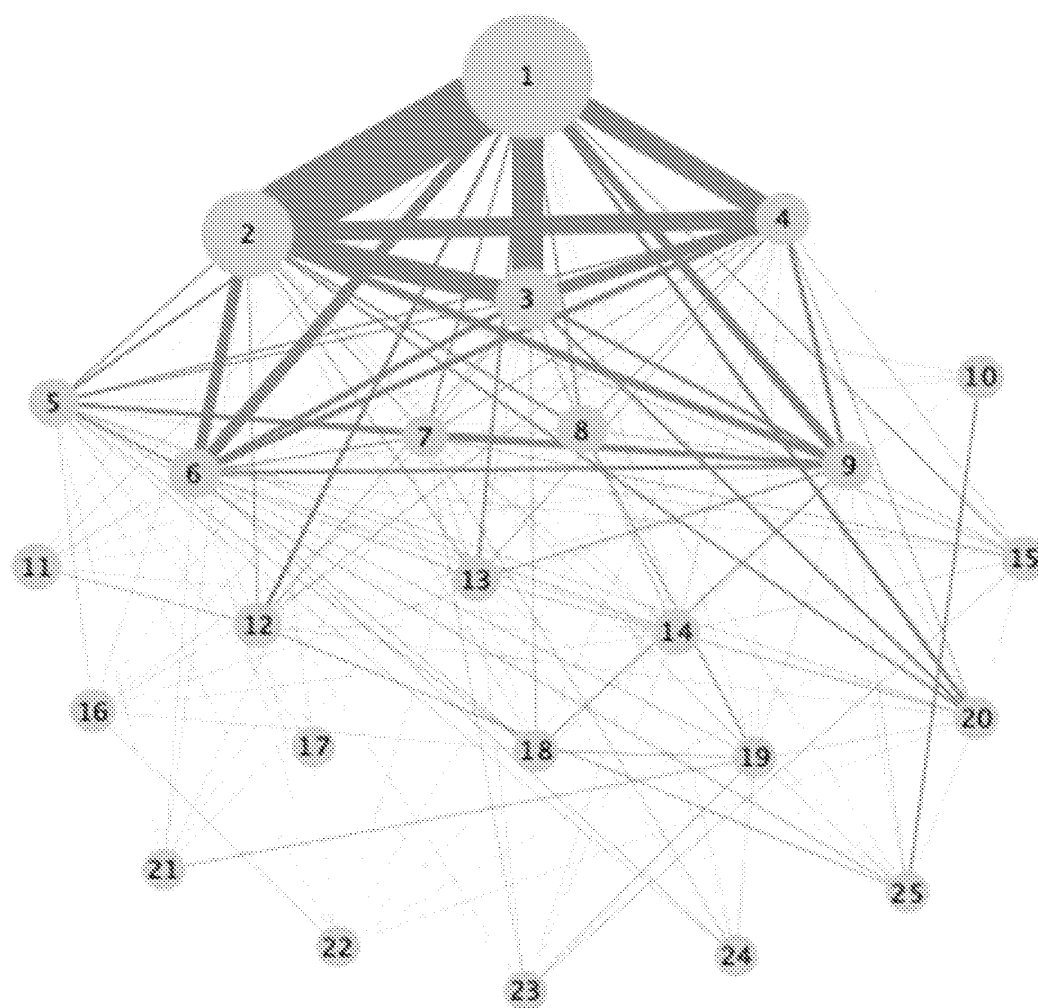


FIG. 80B

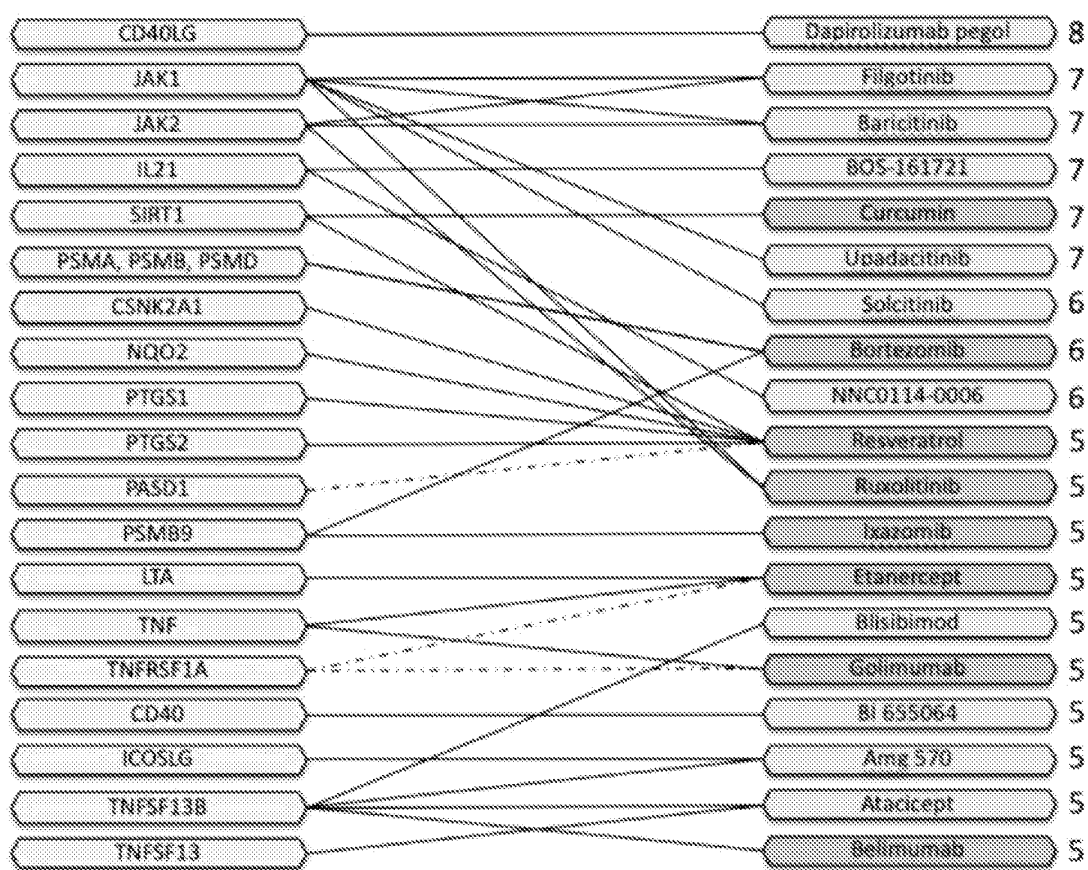


FIG. 81

SLE-associated SNPs

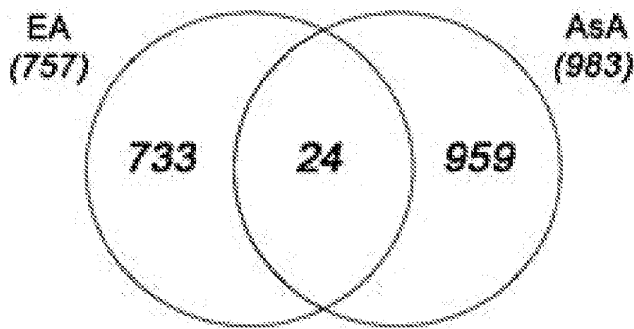


FIG. 82A

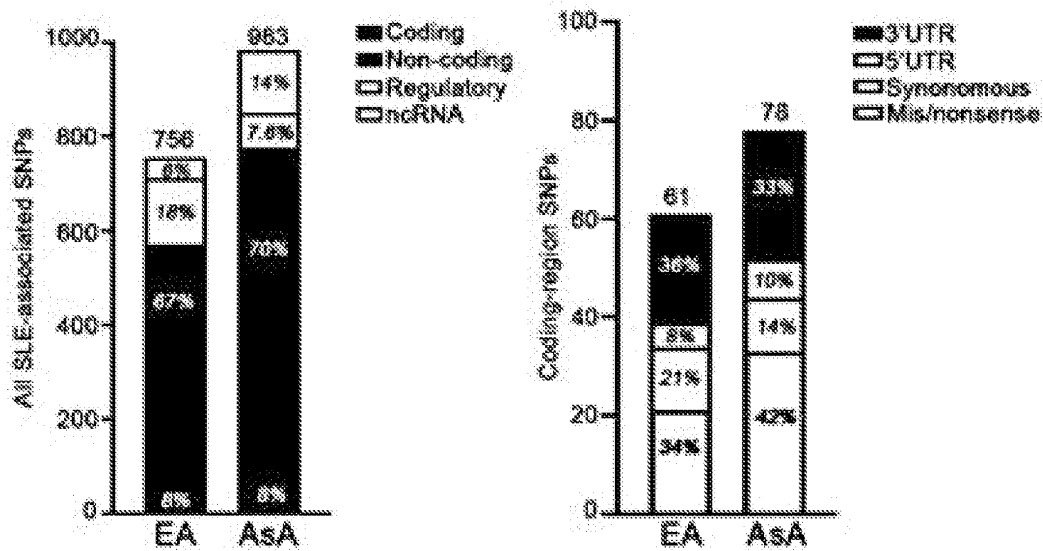


FIG. 82B

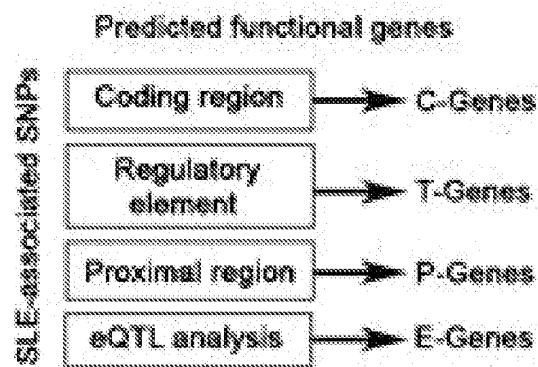


FIG. 82C

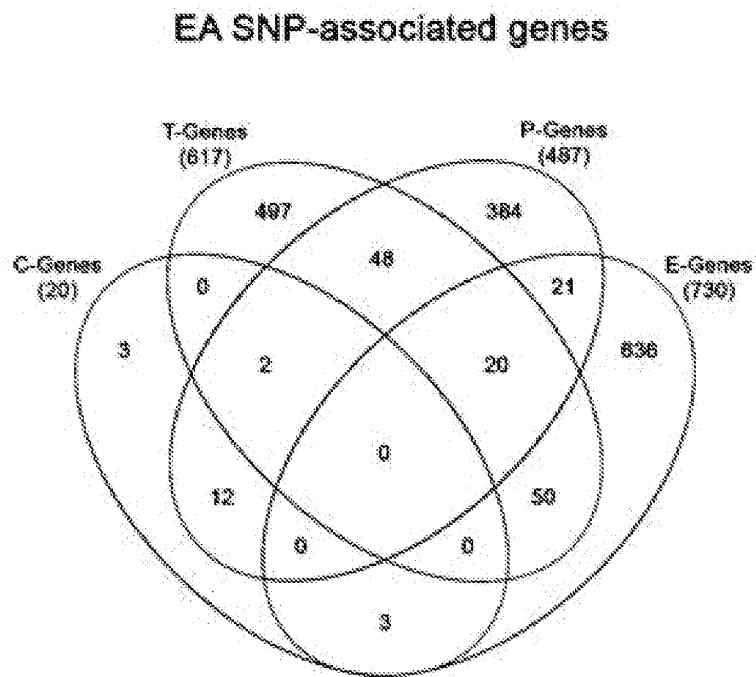
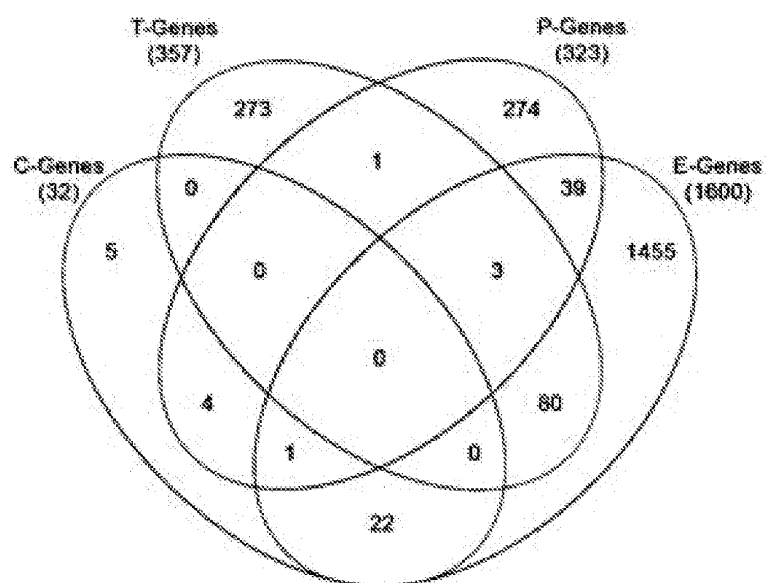


FIG. 82D

AsA SNP-associated genes**FIG. 82E**

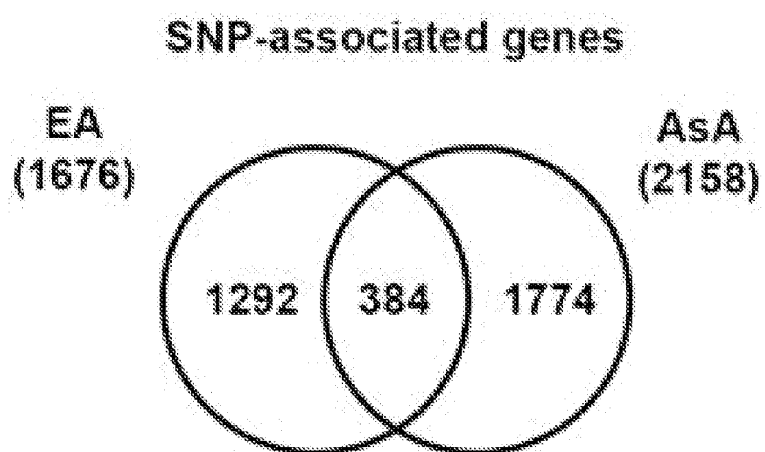


FIG. 83A

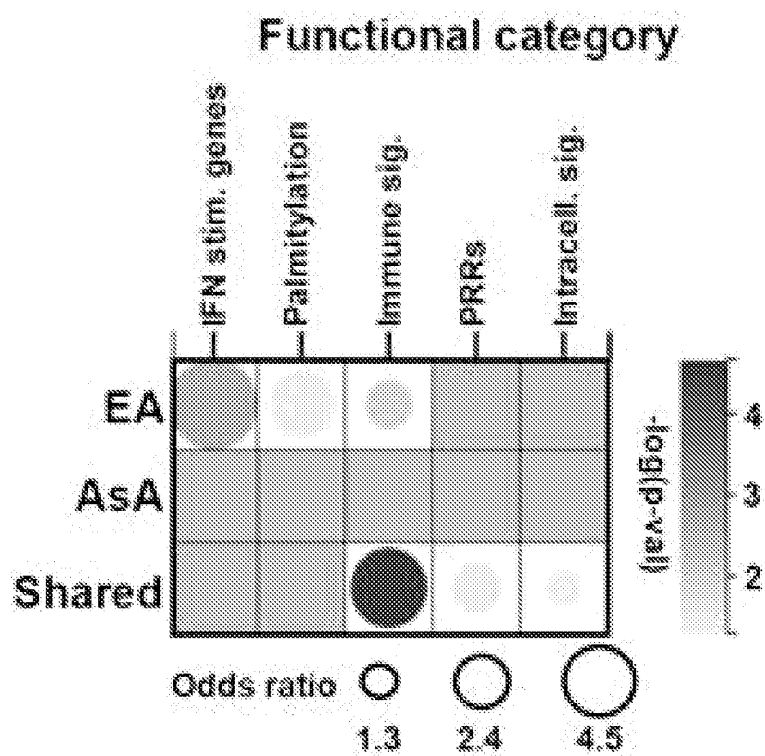


FIG. 83B

Cellular category

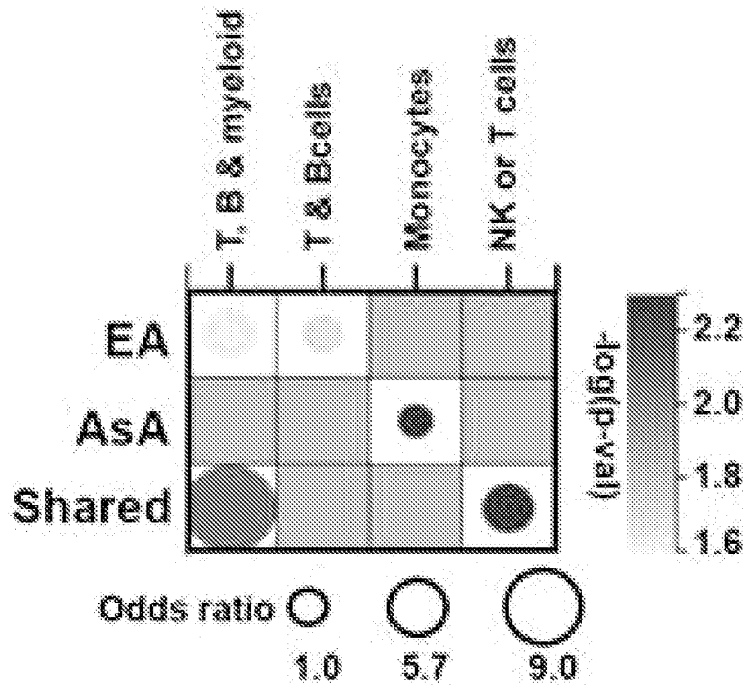


FIG. 83C

Canonical pathways

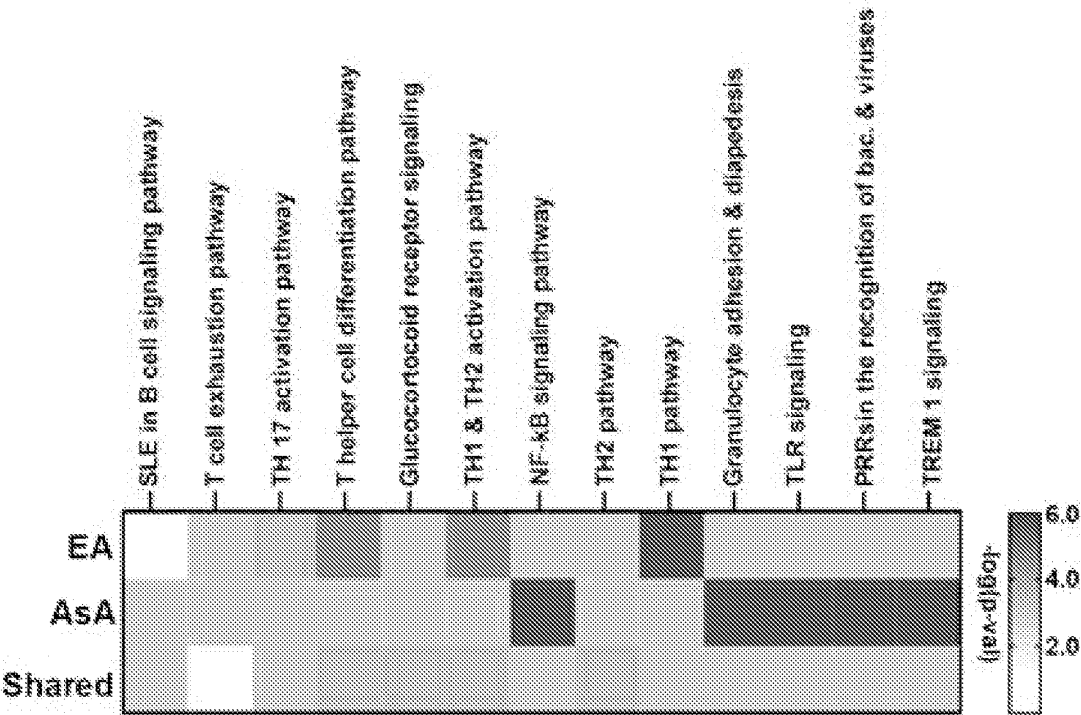


FIG. 83D

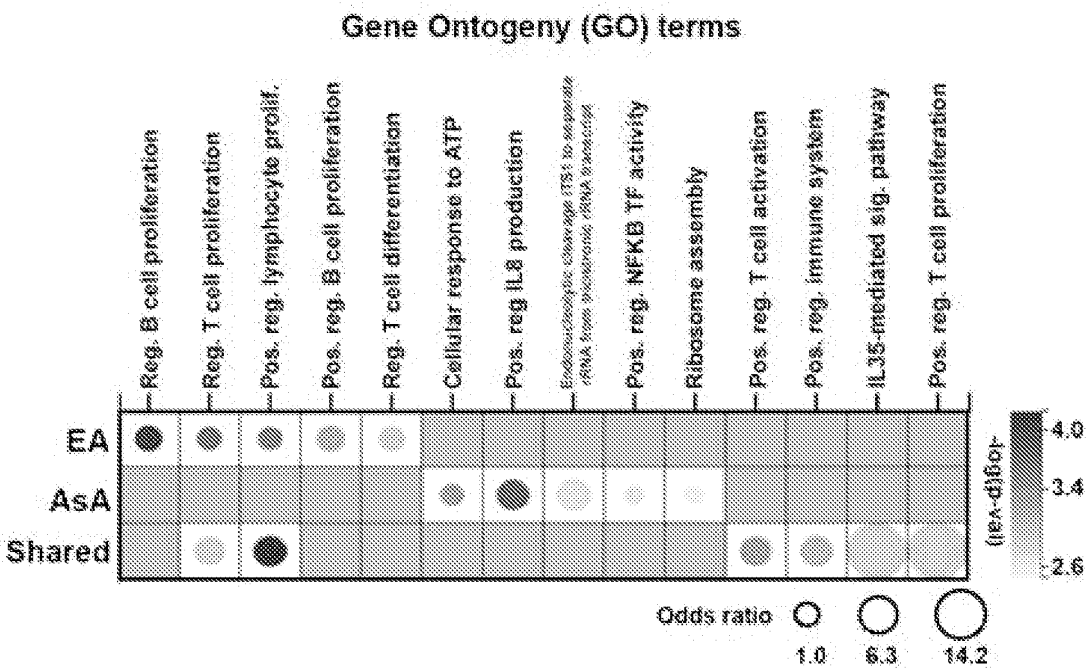


FIG. 83E

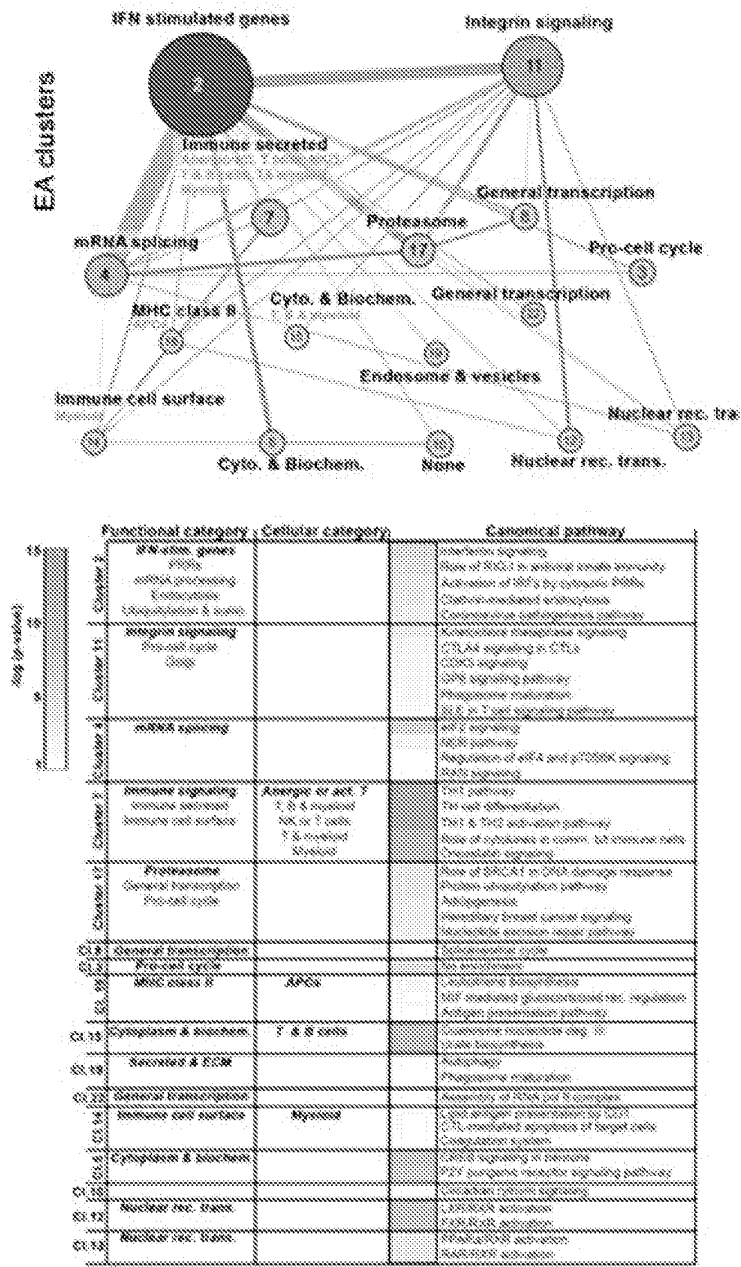


FIG. 84A

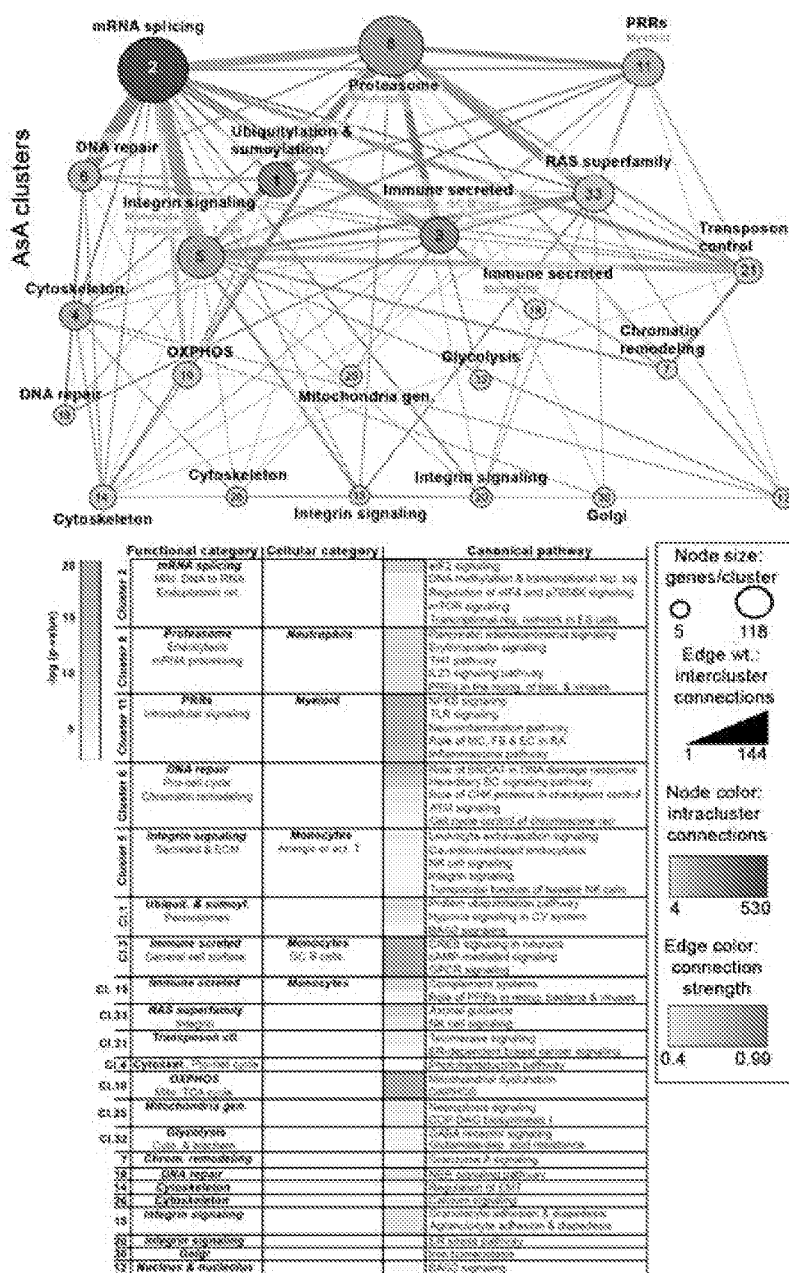


FIG. 84B

Shared clusters

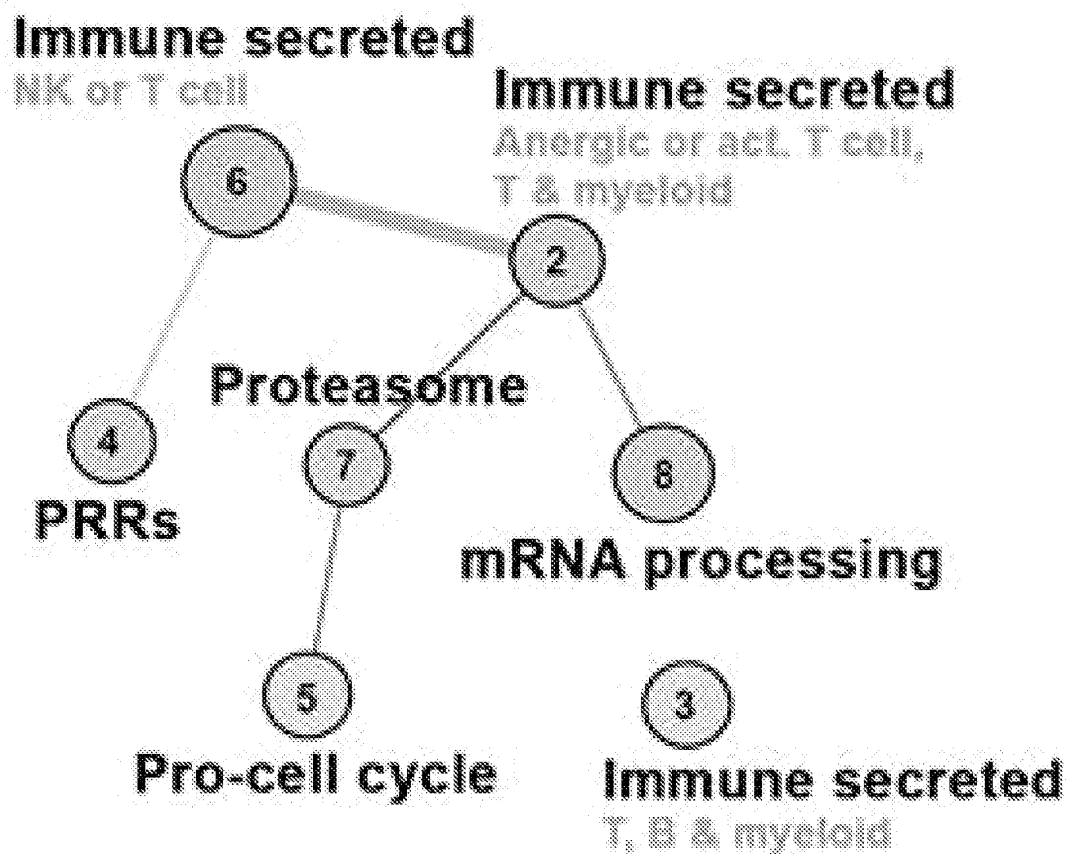


FIG. 85A

Shared pathways

	Functional category	Cellular category	Canonical pathway
Cluster 6	Immune signaling Intracellular signaling	NK or T	STAT3 signaling TH2 pathway TH1 & TH2 activation pathway Glucocorticoid receptor signaling T cell exhaustion pathway
Cluster 2	Immune secreted	Anergic or act. T T & myeloid	Leukocyte extravasation CTLA signaling in CTLs FcγR-mediated phagocytosis in MC & monocytes TLR signaling IL15 production
Cluster 9	mRNA processing mRNA splicing General transcription		Spliceosomal cycle Coronavirus pathogenesis pathway Regulation of eIF4 and p70S6K signaling mTOR signaling eIF2 signaling
Cl. 5	Pro-cell cycle		Mitotic roles of polo-like kinases Kinetochores metaphase signaling
Cl. 4	PRRs		Role of PRRs in recog. of bacteria & virus IFN signaling
Cl. 3	Immune secreted	T, B & myeloid	Granulocyte adhesion & diapedesis Agranulocyte adhesion & diapedesis
Cl. 7	Proteasome Anti-proliferation Ubiquitylation & sumo.		Protein ubiquitylation pathway Antiproliferative role of TQB in T cell signaling Cell cycle: G2/M DNA damage checkpoint control reg.

FIG. 85B

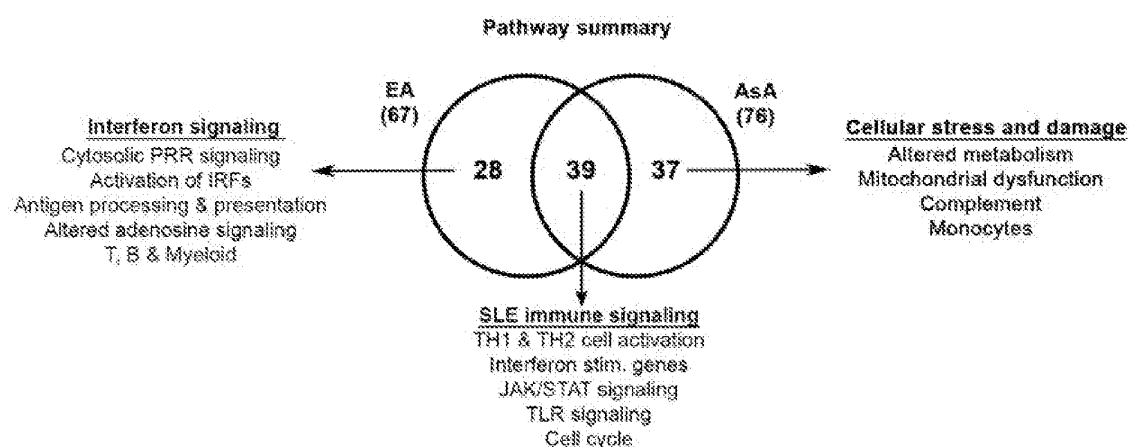


FIG. 85C

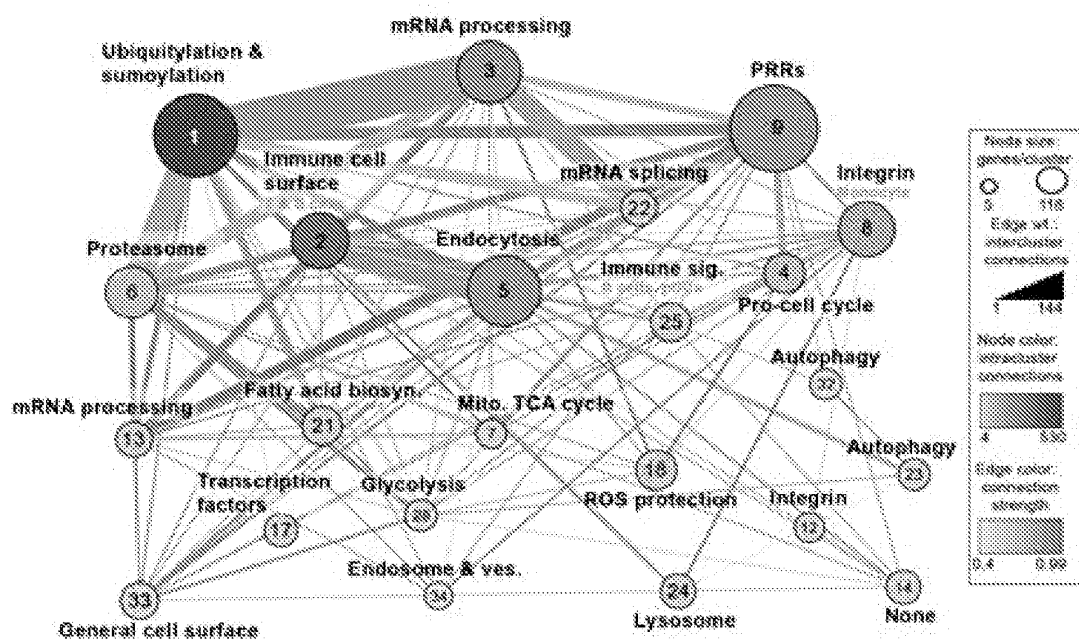


FIG. 86

	Functional category	Cellular category	Canonical pathway
Cluster 1	Ubiquit. & sumo. mRNA splicing		eIF2 signaling Regulation of eIF2 and pTOSK signaling mTOR signaling Coronavirus pathogenesis pathway Protein ubiquitination pathway
Cluster 2	mRNA processing mRNA splicing		SLC signaling pathway Spliceosomal cycle Assembly of RNA pol. II complex Cleavage & polyadenylation of pre-mRNA NER pathway
Cluster 9	PRRs IFN-stimulated genes Pro-cell cycle Intracellular signaling		Kinetochore metaphase signaling HSP70 signaling Cell cycle control of chromosome replication ATM signaling Inflammasome pathway
Cluster 18	Proteasome MHC class I Pro-cell cycle		Antigen presentation pathway Protein ubiquitination pathway Interferon pathway
Cluster 12	Immune cell surface General cell surface	T & B cells	CREB signaling in neurons Breast cancer regulation by stratinin I cAMP-mediated signaling
Cluster 15	Endocytosis Immune secreted		Gastrin-mediated signaling CREB signaling in neurons Cardiac hypertrophy pathway
Cluster 22	mRNA processing Immune signaling		
Cluster 25	Pro-cell cycle Intracellular signaling	B cells pDCs	Neuroinflammation signaling pathway SLC signaling pathway Inflammasome pathway
Cluster 14	Integrin signaling Secreted & ECM	Monocytes	HSP70 signaling 14-3-3 mediated signaling
Cluster 13	mRNA processing		Caveolin-mediated endocytosis signaling Reg. of cellular mech. by calpain proteases Inhibition of ARE-mediated mRNA degradation NOTAIR reg. pathway
Cluster 21	Fatty acid biosyn. Peroxisomes		PCOS signaling NFKB signaling
Cluster 27	Mito. TCA cycle, Mito. general, Peroxisomes		Glutamine degradation I Glycine cleavage complex
Cluster 18	ROS protection		Chondroitin sulfate degradation
Cluster 22	Autophagy		GABA receptor signaling
Cluster 33	General cell surface		Ca12/13 signaling Signaling by RHO family GTPases
Cluster 17	Trans. factors		
Cluster 28	Glycolysis		Fatty acid alpha-oxidation
Cluster 12	Integrin signaling		GPR signaling pathway
Cluster 23	Autophagy		Superpathway of amino acid phosphate compounds
Cluster 34	Endosome & ves.		Role of MAPK sig. in pathogenesis of flu.
Cluster 24	Lysosome		CXPROR
Cluster 14	Mitochondrial dysfunction Synaptogenesis		

FIG. 86 (continued)

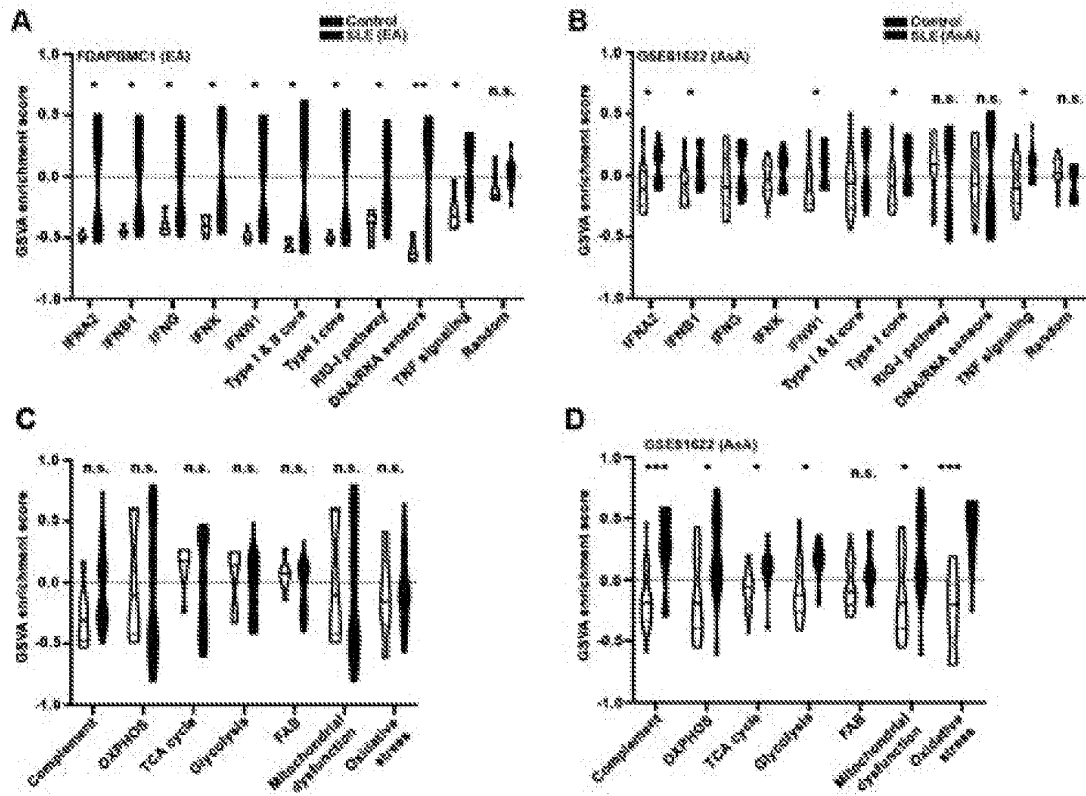


FIG. 87

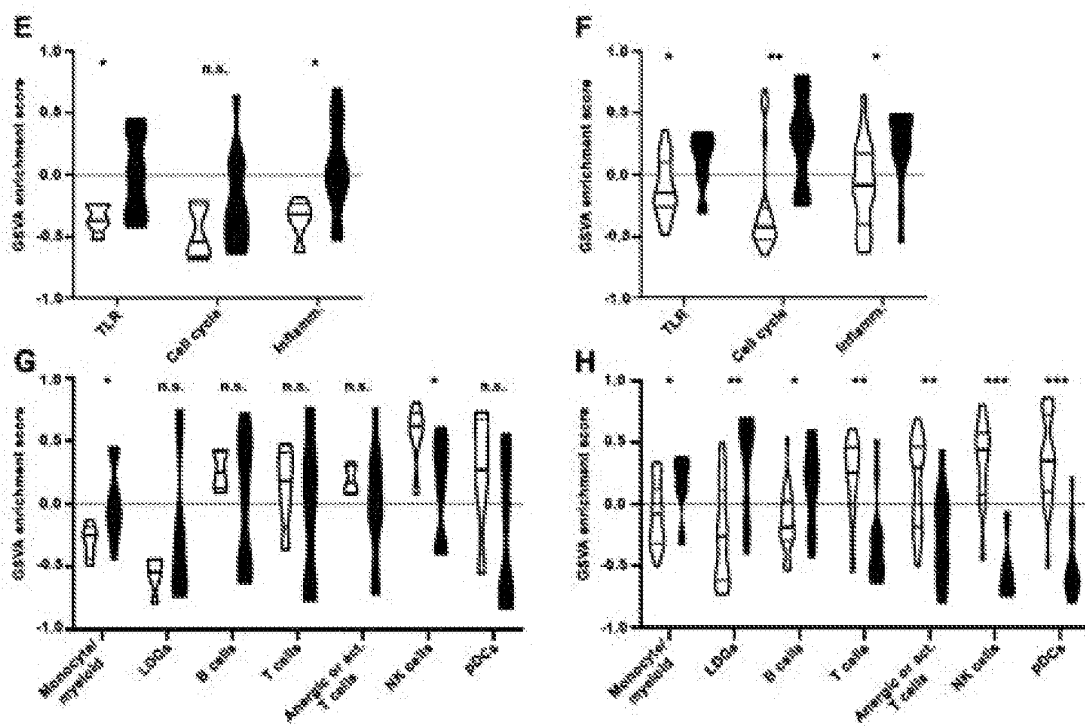


FIG. 87 (continued)

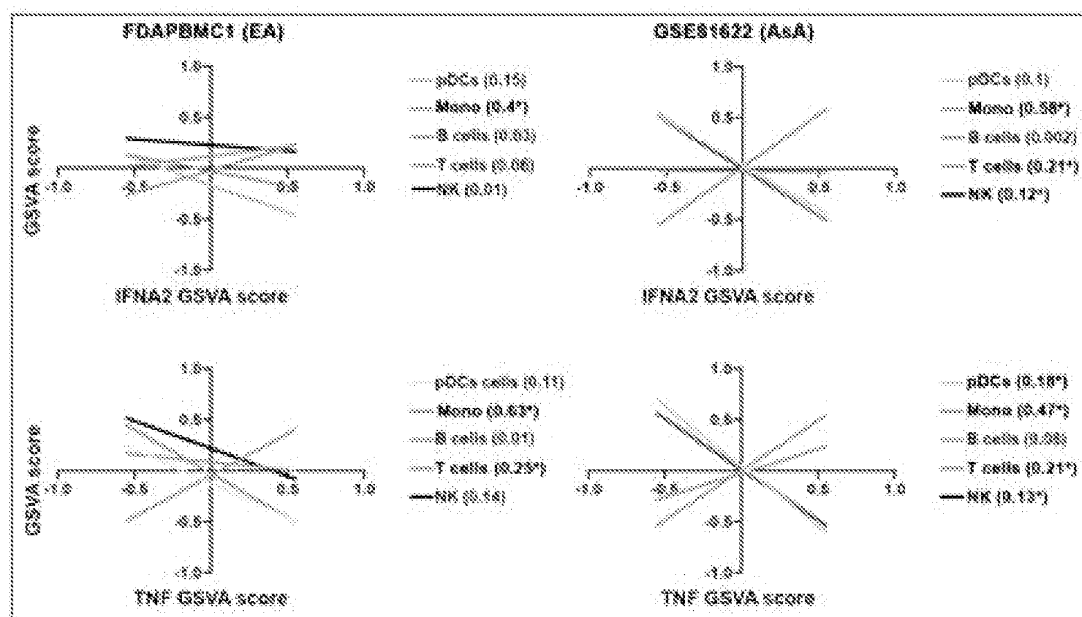


FIG. 88A

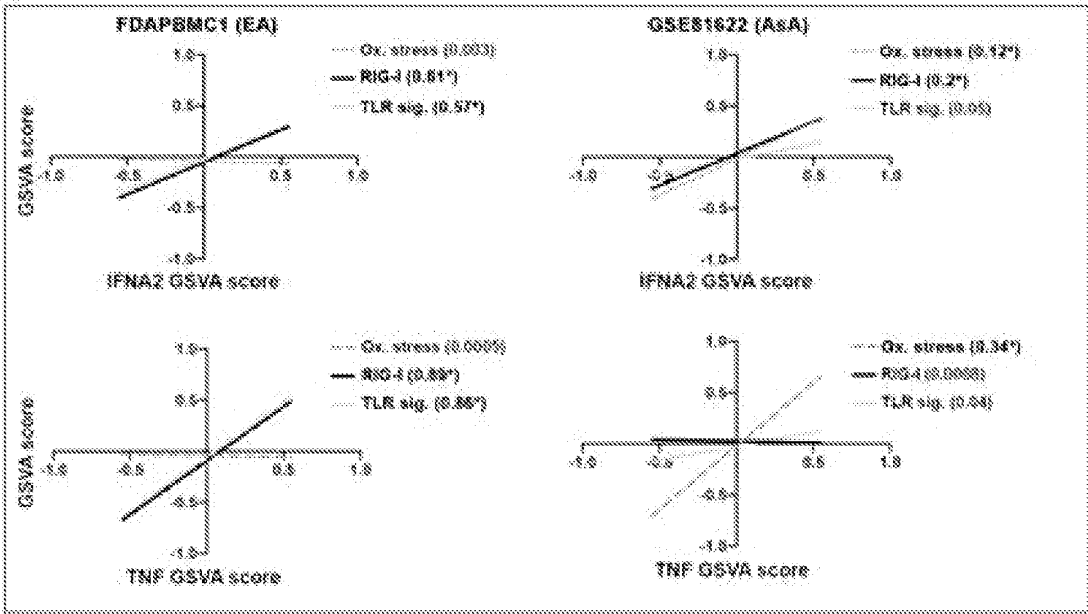


FIG. 88B

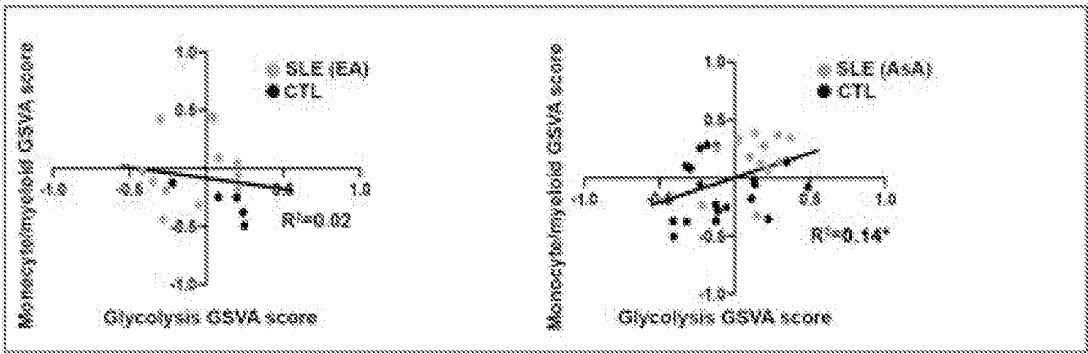


FIG. 88C

Exposure: SLE GWAS (Bentham)

Outcome: CAD GWAS (UKBB)

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	685	1.5E-02	5.9E-03	1.0E-02
Weighted median	685	5.6E-03	4.6E-03	2.2E-01
Inverse variance weighted	685	1.5E-02	4.1E-03	1.8E-04
Robust adjusted profile score (RAPS)	685	9.2E-03	4.3E-03	3.0E-02
MR-PRESSO (raw)	685	1.5E-02	4.1E-03	2.0E-04
MR-PRESSO (outlier-corrected)	26 outliers	5.6E-03	3.4E-03	1.0E-01

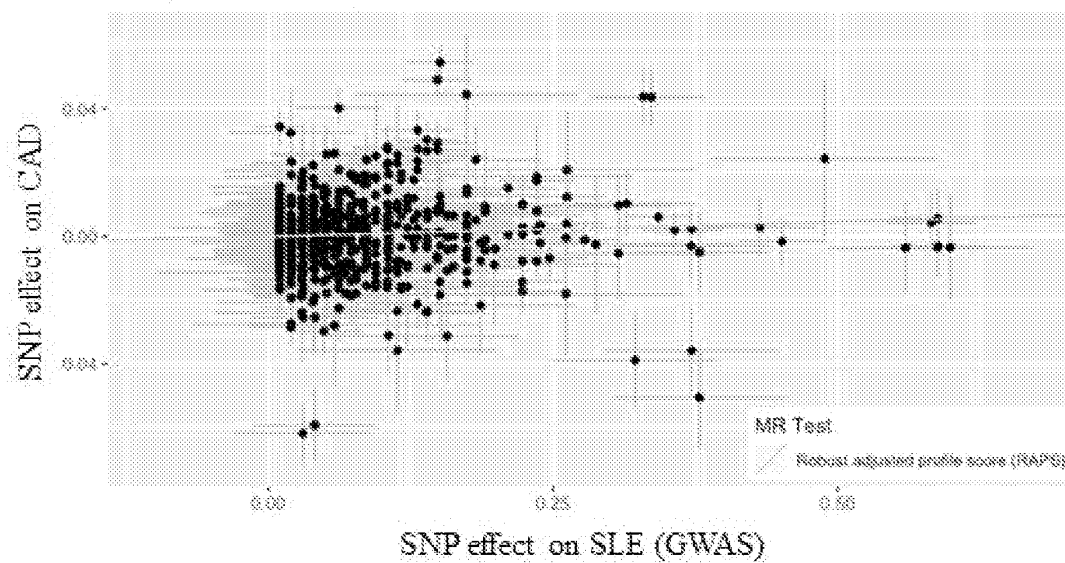


FIG. 89A

Exposure: SLE Immunochip (Langefeld)

Outcome: CAD GWAS (UKBB)

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	613	1.7E-02	8.0E-03	3.9E-02
Weighted median	613	9.1E-03	4.2E-03	3.1E-02
Inverse variance weighted	613	1.6E-02	3.6E-03	1.2E-05
Robust adjusted profile score (RAPS)	613	1.2E-02	3.9E-03	2.0E-03
MR-PRESSO (raw)	613	1.6E-02	3.6E-03	1.5E-05
MR-PRESSO (outlier-corrected)	24 outliers	9.2E-03	3.0E-03	2.0E-03

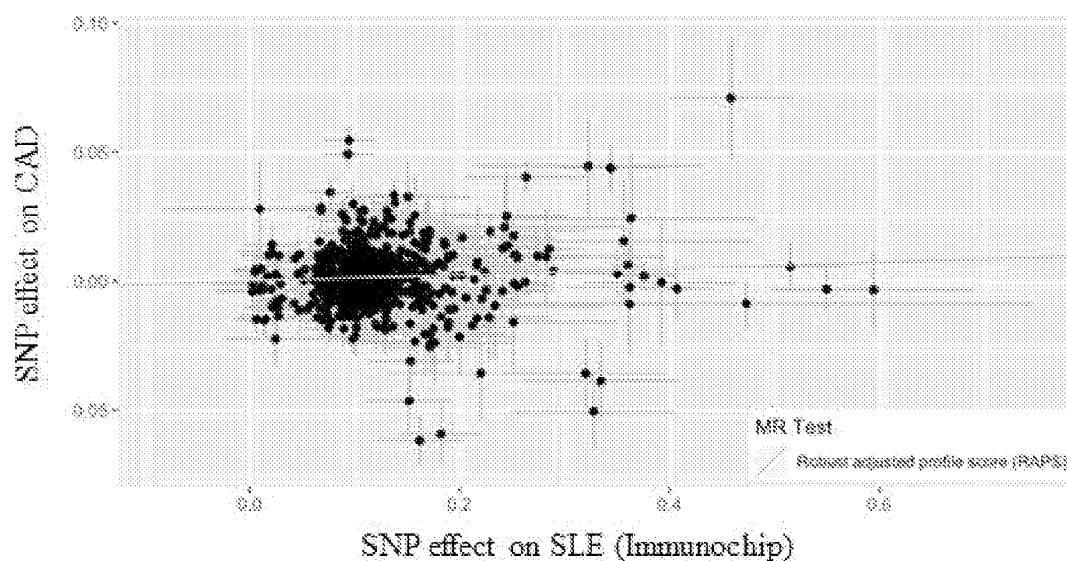


FIG. 89B

Exposure: SLE GWAS (Bentham)

Outcome: CAD GWAS (UKBB)

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	829	-2.5E-02	3.6E-03	1.5E-11
Weighted median	829	-9.1E-03	1.6E-03	4.0E-08
Inverse variance weighted	829	-1.4E-02	1.6E-03	1.9E-20
MR-RAPS	829	-1.1E-02	1.4E-03	6.4E-14

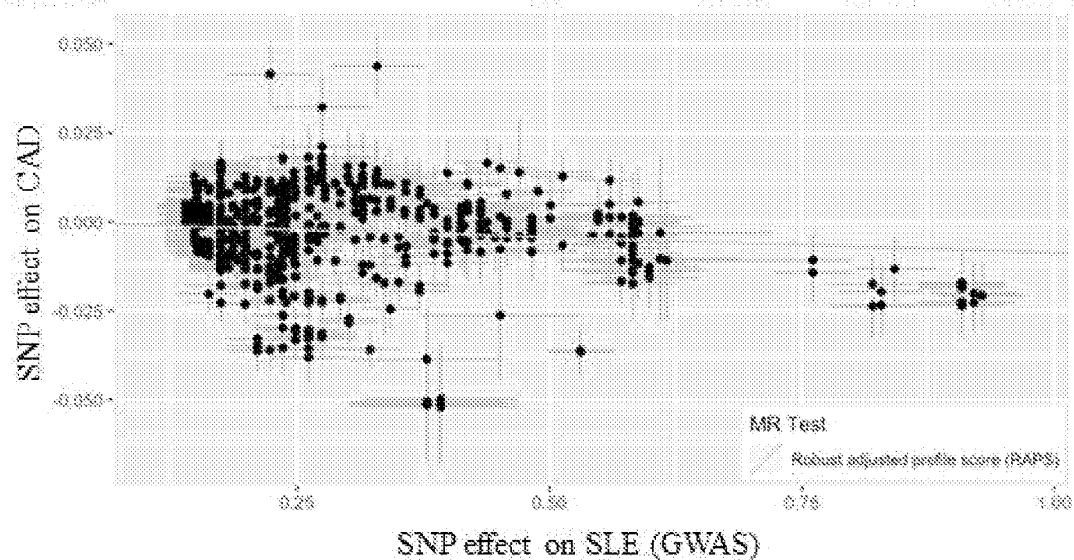


FIG. 90A

Exposure: SLE ImmunoChip (Langefeld)

Outcome: CAD GWAS (UKBB)

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	829	-1.6E-02	3.1E-03	3.5E-07
Weighted median	829	-7.8E-03	1.5E-03	8.8E-08
Inverse variance weighted	829	-1.2E-02	1.4E-03	1.4E-17
MR-RAPS	829	-8.8E-03	1.3E-03	5.7E-11

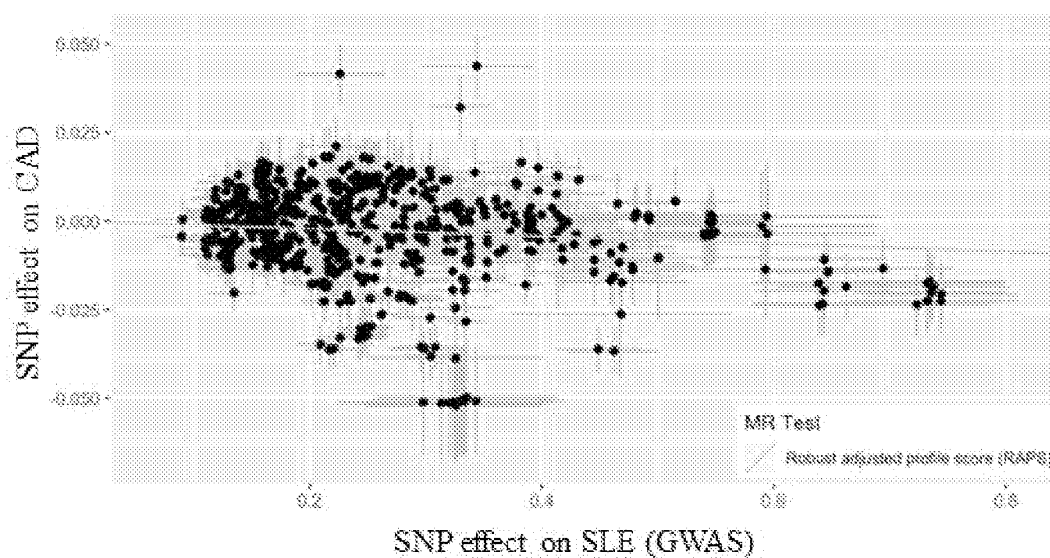


FIG. 90B

Exposure: SLE GWAS (Bentham)

Outcome: CAD GWAS (UKBB)

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	526	-2.5E-03	4.1E-03	5.4E-01
Weighted median	526	3.7E-03	2.0E-03	6.6E-02
Inverse variance weighted	526	4.6E-03	1.6E-03	3.2E-03
MR-RAPS	526	5.4E-03	1.7E-03	1.1E-03
MR-PRESSO (raw)	526	4.6E-03	1.6E-03	3.3E-03
MR-PRESSO (outlier-corrected)	10 outliers	4.9E-03	1.5E-03	9.3E-04

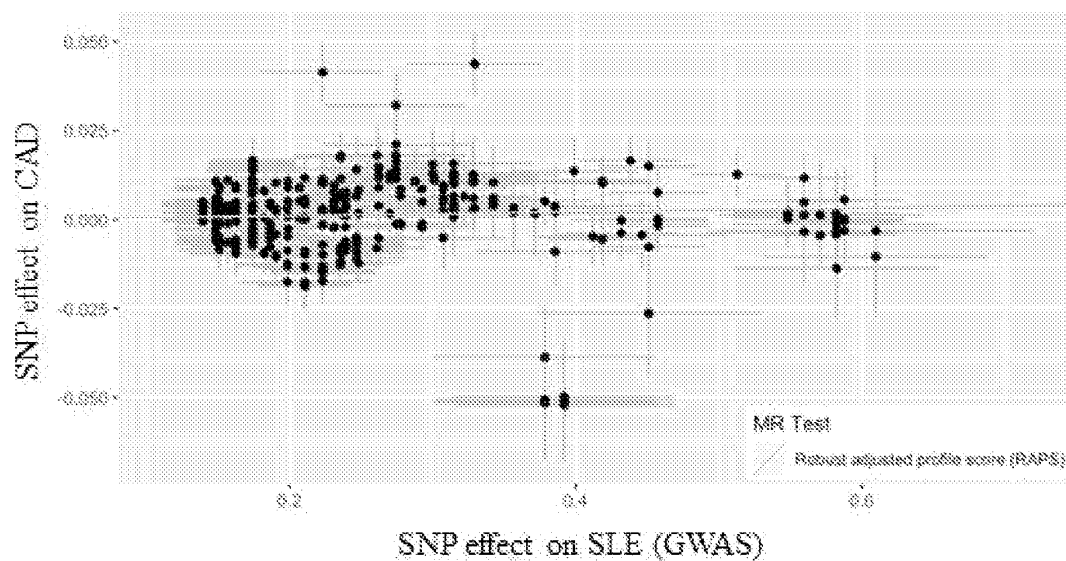


FIG. 91A

Exposure: SLE Immunochip (Langefeld)

Outcome: CAD GWAS (UKBB)

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	526	-4.0E-03	4.3E-03	3.5E-01
Weighted median	526	3.5E-03	2.2E-03	1.1E-01
Inverse variance weighted	526	4.8E-03	1.7E-03	5.5E-03
MR-RAPS	526	5.6E-03	1.8E-03	1.9E-03
MR-PRESSO (raw)	526	4.8E-03	1.7E-03	5.7E-03
MR-PRESSO (outlier-corrected)	11 outliers	5.1E-03	1.6E-03	1.7E-03

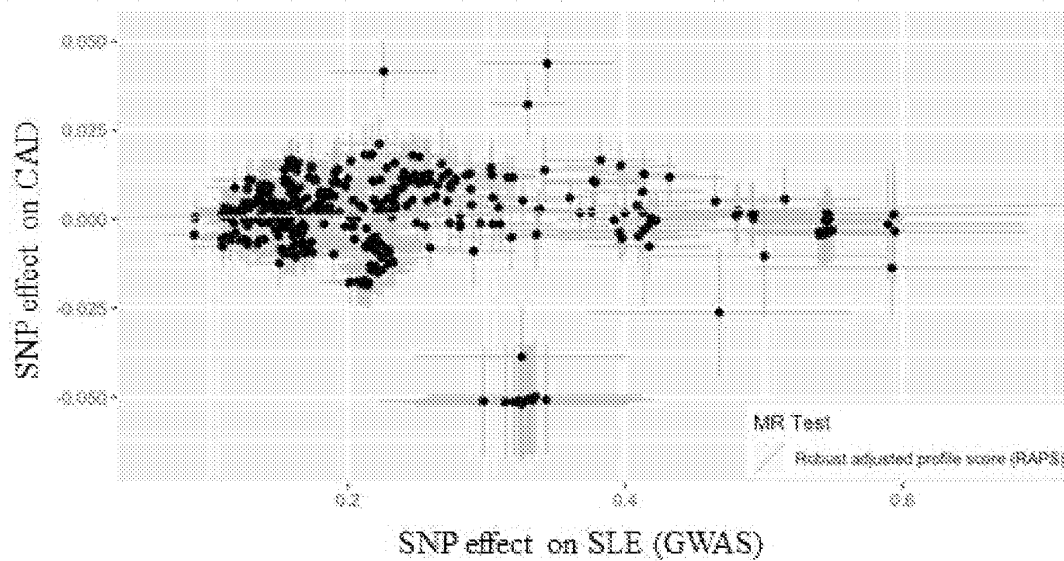
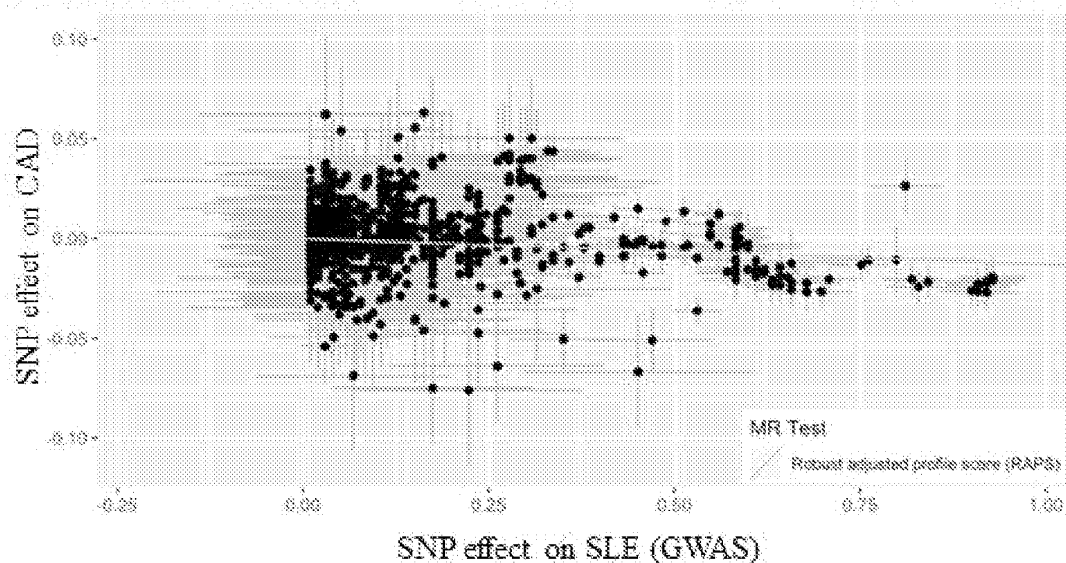


FIG. 91B

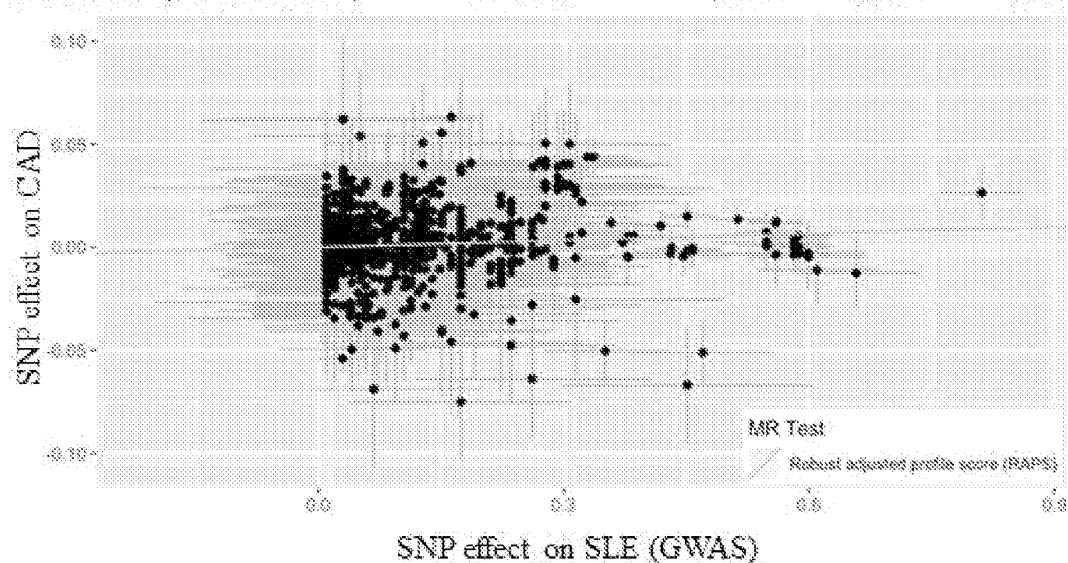
Instrumental Variables: PhenoScanner SNPs associated with SLE**Exposure: SLE GWAS (Bentham)****Outcome: CAD GWAS (UKBB)**

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	911	-1.9E-02	2.3E-03	4.0E-16
Weighted median	911	-2.1E-02	2.0E-03	4.7E-26
Inverse variance weighted	911	-1.1E-02	1.7E-03	6.3E-10
MR-RAPS	911	-1.3E-02	1.7E-03	9.5E-15
MR-PRESSO (raw)	911	-1.1E-02	1.7E-03	9.5E-10
MR-PRESSO (outlier-corrected)	22 outliers	-1.2E-02	1.4E-03	2.8E-16

**FIG. 92A**

Instrumental Variables: PhenoScanner non-HLA SNPs associated with SLE**Exposure: SLE GWAS (Bentham)****Outcome: CAD GWAS (UKBB)**

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	791	1.1E-02	3.6E-03	3.1E-03
Weighted median	791	3.0E-03	3.3E-03	3.7E-01
Inverse variance weighted	791	1.2E-02	2.5E-03	2.3E-06
MR-RAPS	791	1.1E-02	2.6E-03	3.0E-05
MR-PRESSO (raw)	791	1.2E-02	2.5E-03	2.7E-06
MR-PRESSO (outlier-corrected)	13 outliers	7.5E-03	2.1E-03	3.6E-04

**FIG. 92B**

Exposure: SLE GWAS (Bentham)**Outcome: CAD GWAS (UKBB)**

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	317	-6.0E-03	4.4E-03	1.7E-01
Weighted median	317	-1.9E-02	1.9E-03	7.9E-23
Inverse variance weighted	317	-2.6E-02	2.1E-03	1.8E-35

Exposure: SLE Immunochip (Langefeld)**Outcome: CAD GWAS (UKBB)**

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	317	-2.0E-02	5.5E-03	3.2E-04
Weighted median	317	-2.5E-02	2.3E-03	6.9E-29
Inverse variance weighted	317	-3.3E-02	2.3E-03	1.3E-45

FIG. 93A**Exposure: SLE GWAS (Bentham)****Outcome: CAD GWAS (UKBB)**

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	33	-2.4E-01	4.4E-02	6.8E-06
Weighted median	33	-6.4E-02	8.1E-03	3.7E-15
Inverse variance weighted	33	-5.6E-02	5.7E-03	1.6E-22

Exposure: SLE Immunochip (Langefeld)**Outcome: CAD GWAS (UKBB)**

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	33	-1.3E-01	2.5E-02	9.2E-06
Weighted median	33	-6.5E-02	8.0E-03	4.3E-16
Inverse variance weighted	33	-6.2E-02	6.1E-03	3.2E-24

FIG. 93B

Exposure: SLE GWAS (Bentham)					
Outcome: CAD GWAS (UKBB)					
MR method	# of SNPs	Causal Estimate	Std. Error	P-value	
MR Egger	103	8.1E-02	1.3E-02	2.9E-08	
Weighted median	103	1.0E-02	4.1E-03	1.4E-02	
Inverse variance weighted	103	1.7E-02	3.1E-03	7.1E-08	
Exposure: SLE Immunochip (Langefeld)					
Outcome: CAD GWAS (UKBB)					
MR method	# of SNPs	Causal Estimate	Std. Error	P-value	
MR Egger	103	1.1E-01	1.8E-02	9.5E-09	
Weighted median	103	1.1E-02	4.8E-03	2.5E-02	
Inverse variance weighted	103	1.9E-02	3.7E-03	1.2E-07	

FIG. 94A

Exposure: SLE GWAS (Bentham)					
Outcome: CAD GWAS (UKBB)					
MR method	# of SNPs	Causal Estimate	Std. Error	P-value	
MR Egger	25	2.4E-02	1.4E-02	9.1E-02	
Weighted median	25	2.4E-02	5.8E-03	2.4E-05	
Inverse variance weighted	25	2.1E-02	4.3E-03	5.0E-07	
Exposure: SLE Immunochip (Langefeld)					
Outcome: CAD GWAS (UKBB)					
MR method	# of SNPs	Causal Estimate	Std. Error	P-value	
MR Egger	25	2.9E-02	1.6E-02	8.9E-02	
Weighted median	25	2.7E-02	6.6E-03	3.3E-05	
Inverse variance weighted	25	2.5E-02	5.0E-03	4.9E-07	

FIG. 94B

Exposure: SLE GWAS (Bentham)				
Outcome: CAD GWAS (UKBB)				
MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	60	6.2E-02	6.8E-02	3.7E-01
Weighted median	60	5.5E-02	6.8E-03	5.8E-16
Inverse variance weighted	60	4.5E-02	4.6E-03	2.3E-22

Exposure: SLE Immunochip (Langefeld)				
Outcome: CAD GWAS (UKBB)				
MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	60	1.1E-01	7.3E-02	1.3E-01
Weighted median	60	6.1E-02	7.8E-03	4.7E-15
Inverse variance weighted	60	5.0E-02	5.1E-03	1.5E-22

FIG. 94C

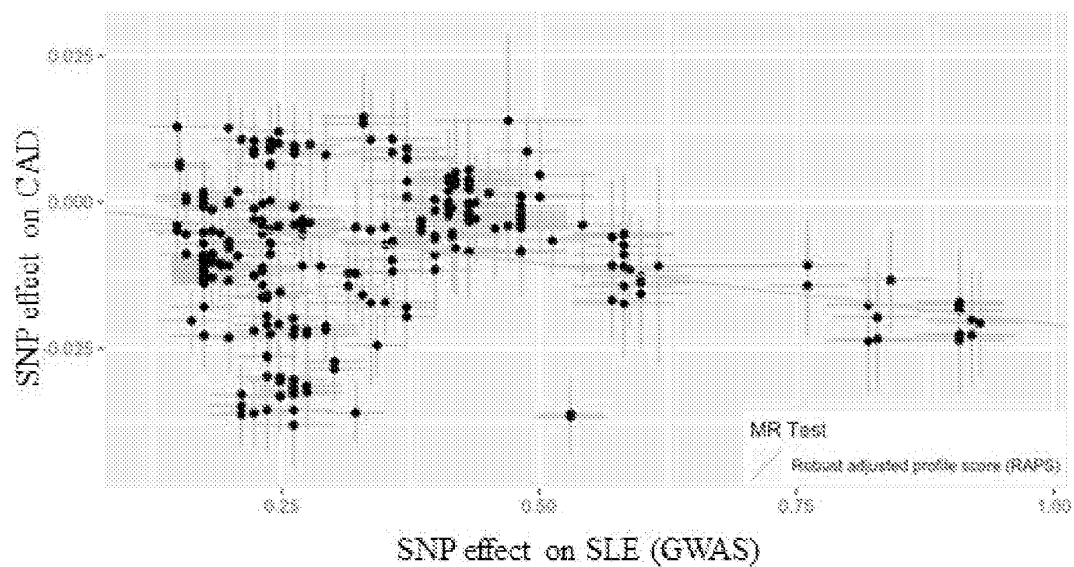
Exposure: SLE GWAS (Bentham)				
Outcome: CAD GWAS (UKBB)				
MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	86	6.5E-02	2.1E-02	3.1E-03
Weighted median	86	1.6E-02	5.3E-03	2.6E-03
Inverse variance weighted	86	1.9E-02	3.8E-03	6.7E-07

Exposure: SLE Immunochip (Langefeld)				
Outcome: CAD GWAS (UKBB)				
MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	86	4.3E-02	1.3E-02	1.9E-03
Weighted median	86	2.3E-02	5.6E-03	3.1E-05
Inverse variance weighted	86	2.1E-02	4.0E-03	1.5E-07

FIG. 94D

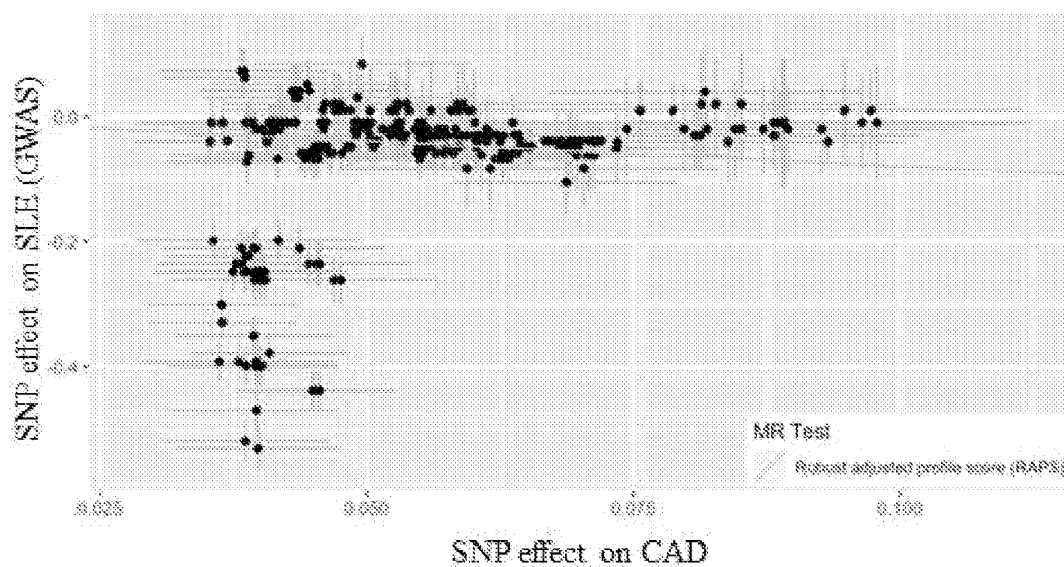
Instrumental Variables: SLE-associated HLA SNPs**Exposure: SLE GWAS (Bentham)****Outcome: CAD GWAS (UKBB)**

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	303	-4.4E-03	4.5E-03	3.2E-01
Weighted median	303	-1.9E-02	2.0E-03	4.1E-22
Inverse variance weighted	303	-2.7E-02	2.1E-03	1.8E-35
MR-RAPS	303	-2.1E-02	1.8E-03	1.5E-30

**FIG. 95A**

Instrumental Variables: CAD-associated HLA SNPs**Exposure: CAD GWAS (UKBB)****Outcome: SLE GWAS (Bentham)**

MR method	# of SNPs	Causal Estimate	Std. Error	P-value
MR Egger	509	3.5E+00	4.0E-01	1.1E-16
Weighted median	509	-5.7E-01	4.4E-02	3.8E-37
Inverse variance weighted	509	-1.3E+00	9.8E-02	4.0E-40
MR-RAPS	509	-7.9E-01	6.3E-02	5.0E-36

**FIG. 95B**

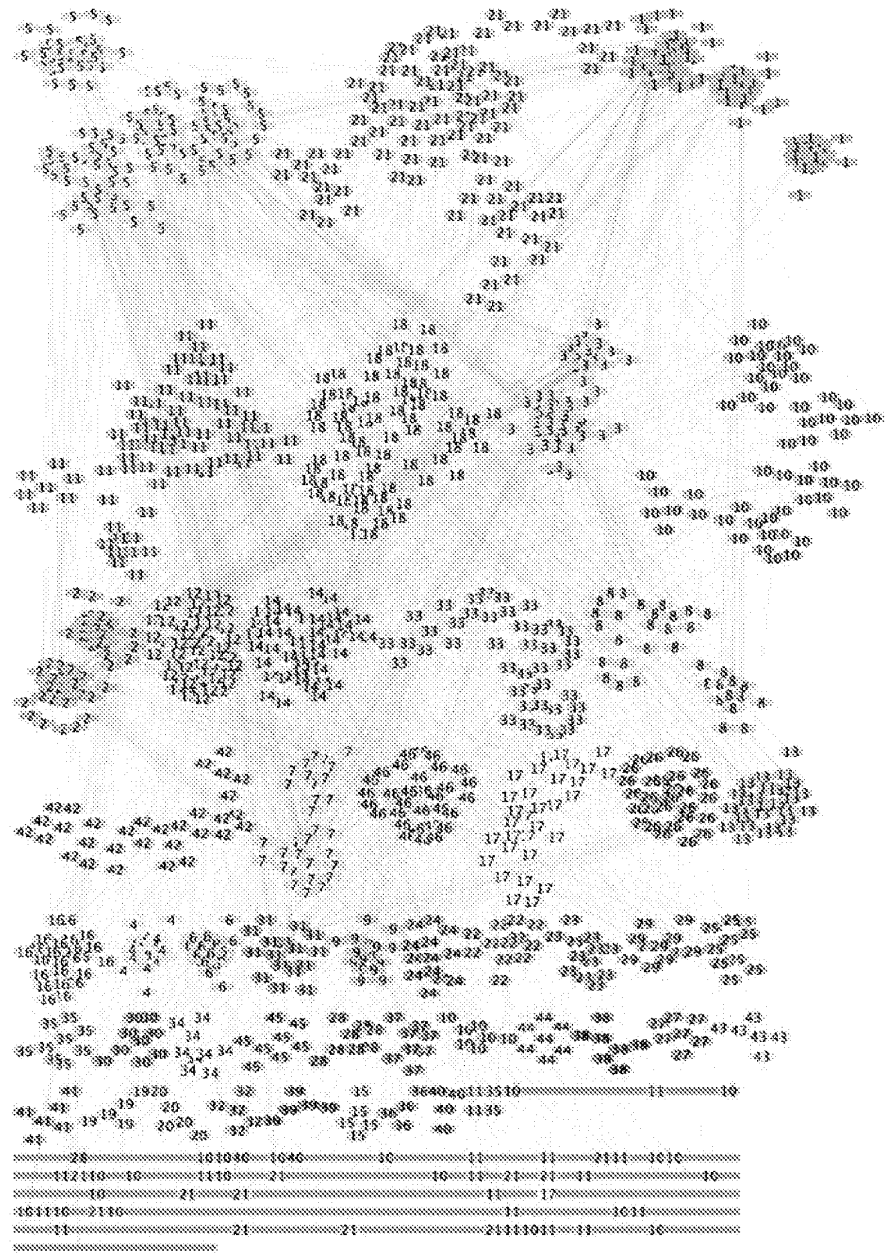


FIG. 96

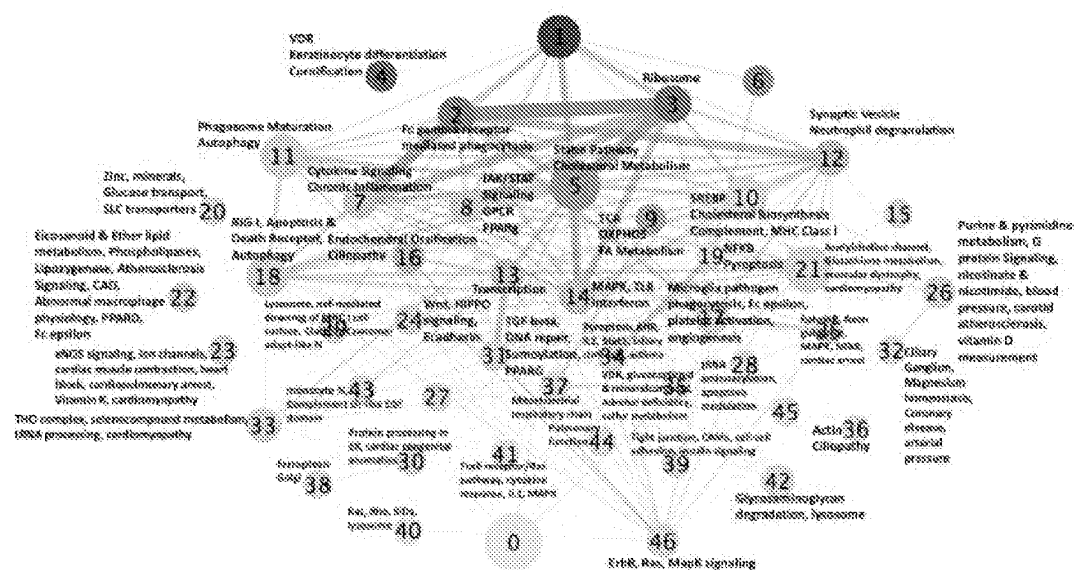


FIG. 97



FIG. 98A

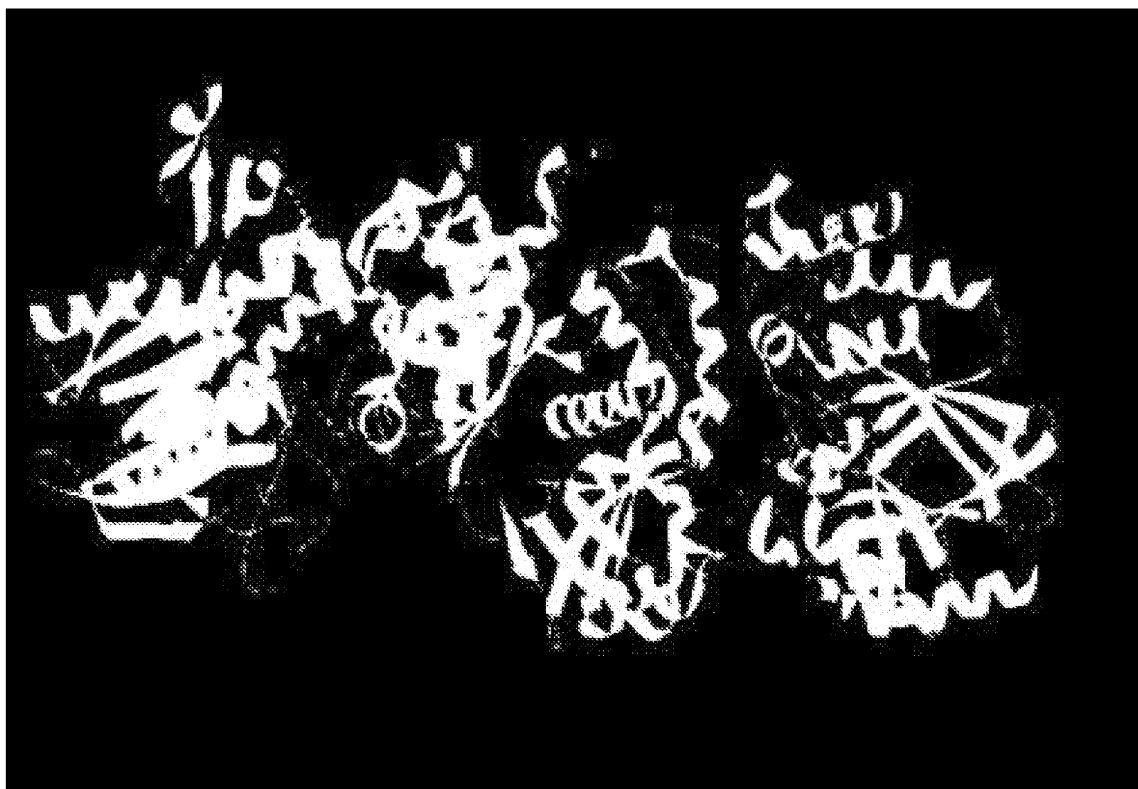


FIG. 98B

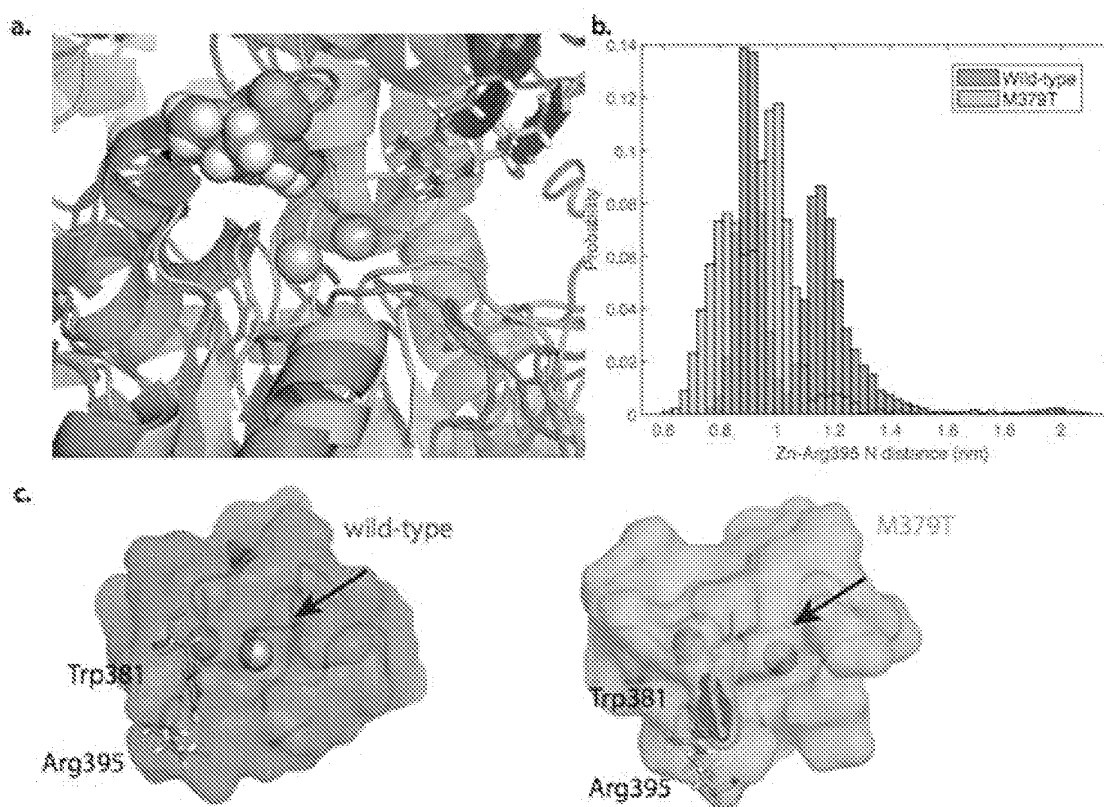


FIG. 99

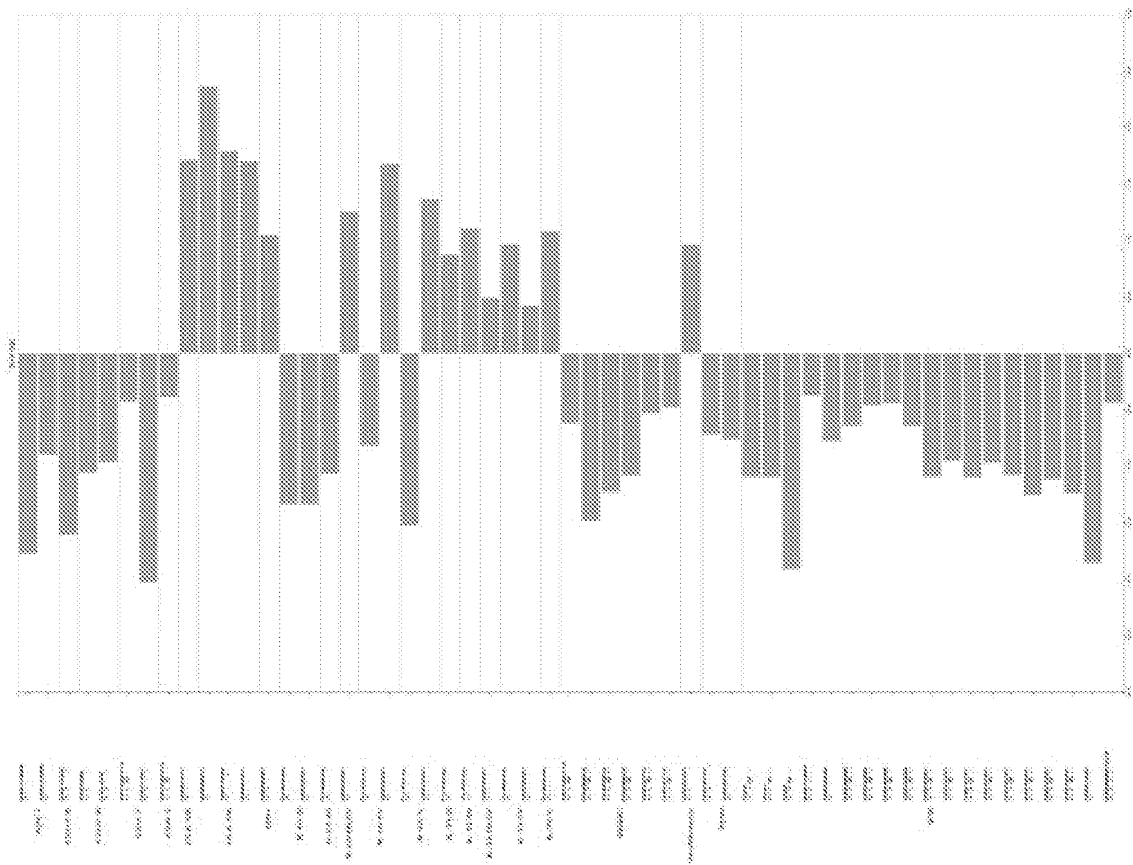


FIG. 100

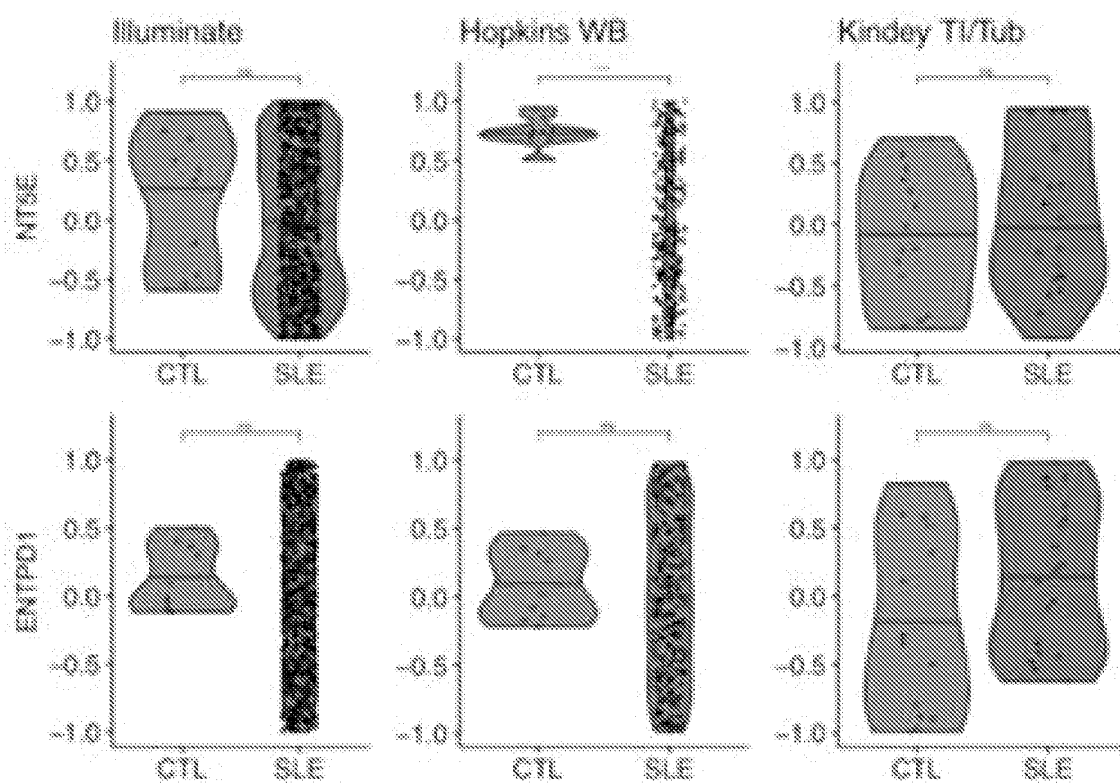


FIG. 101A

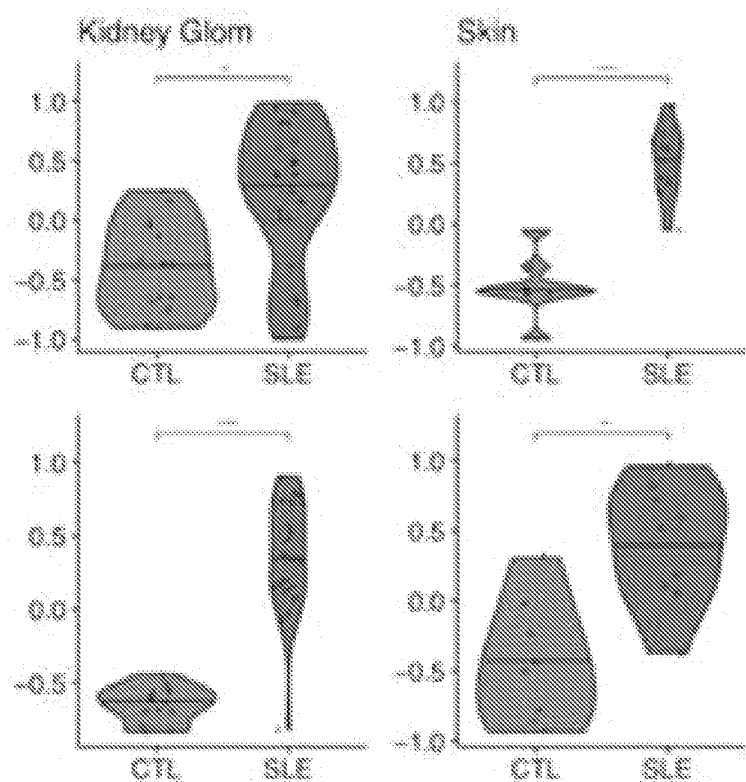


FIG. 101A (continued)

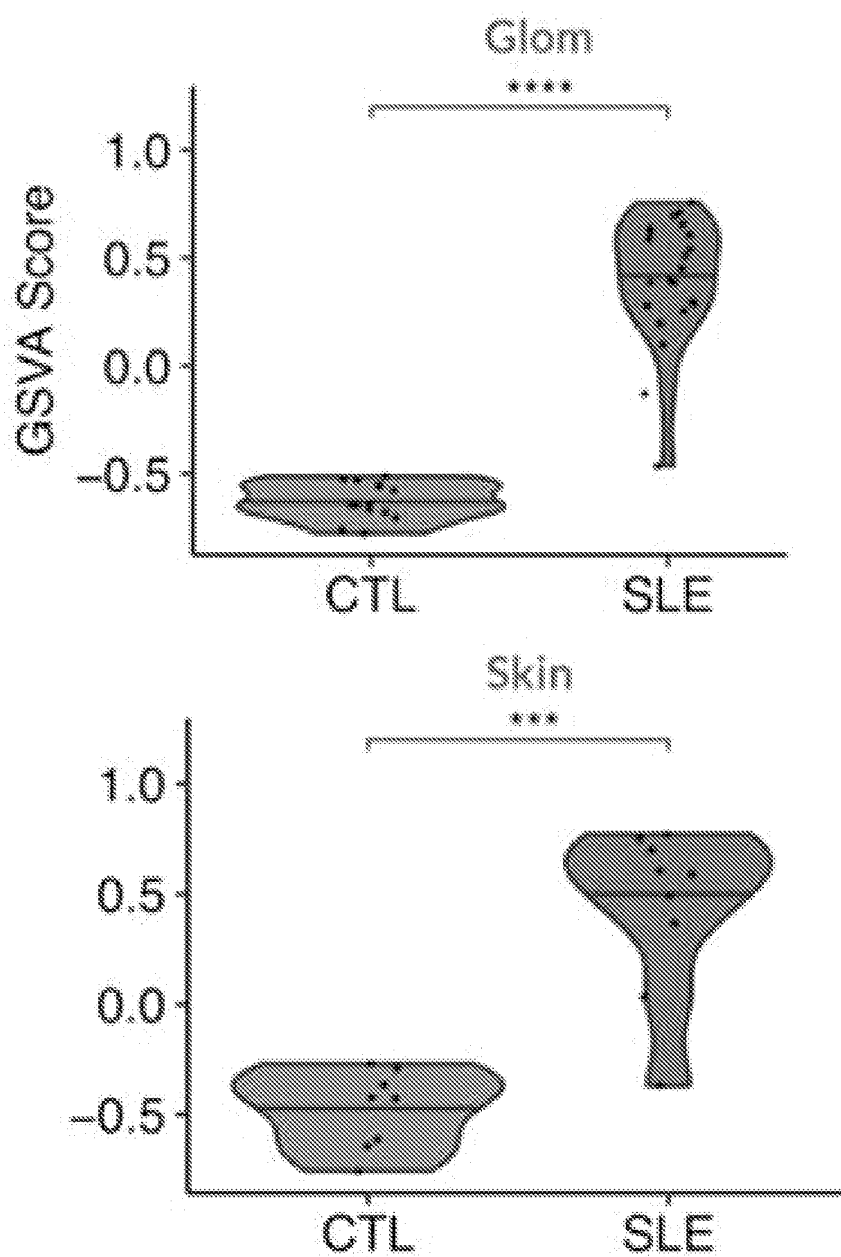


FIG. 101B

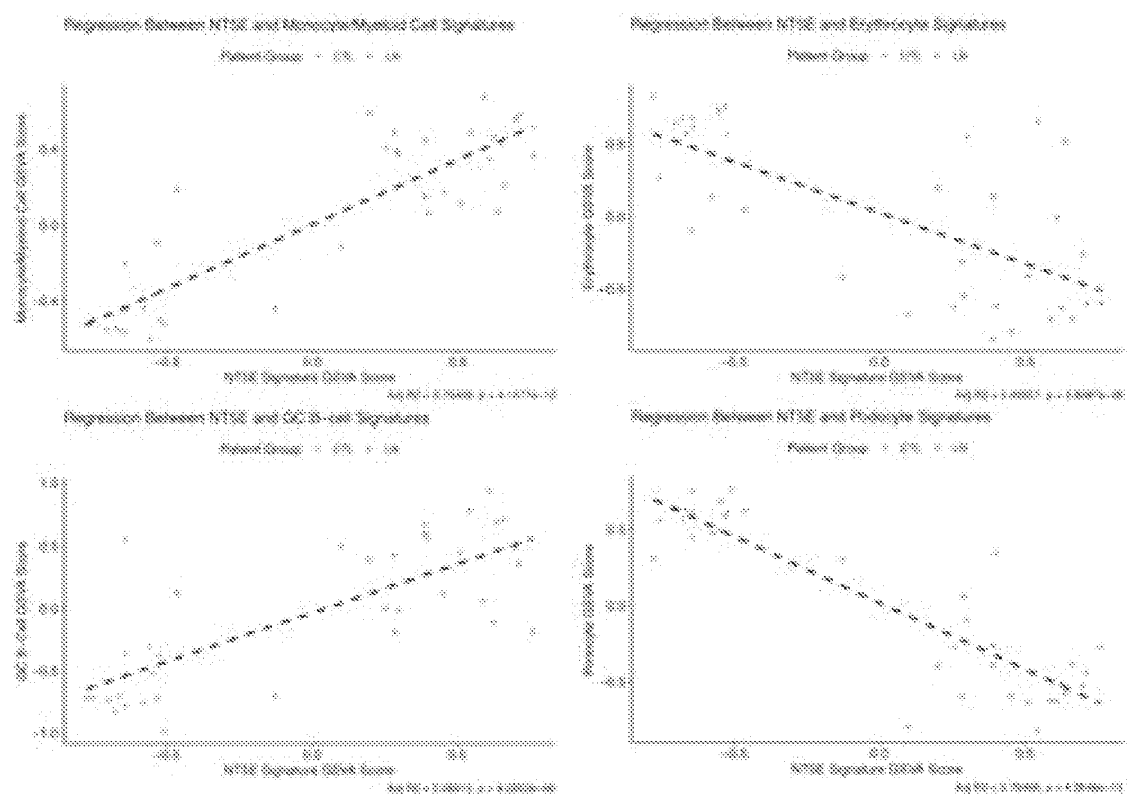


FIG. 102A

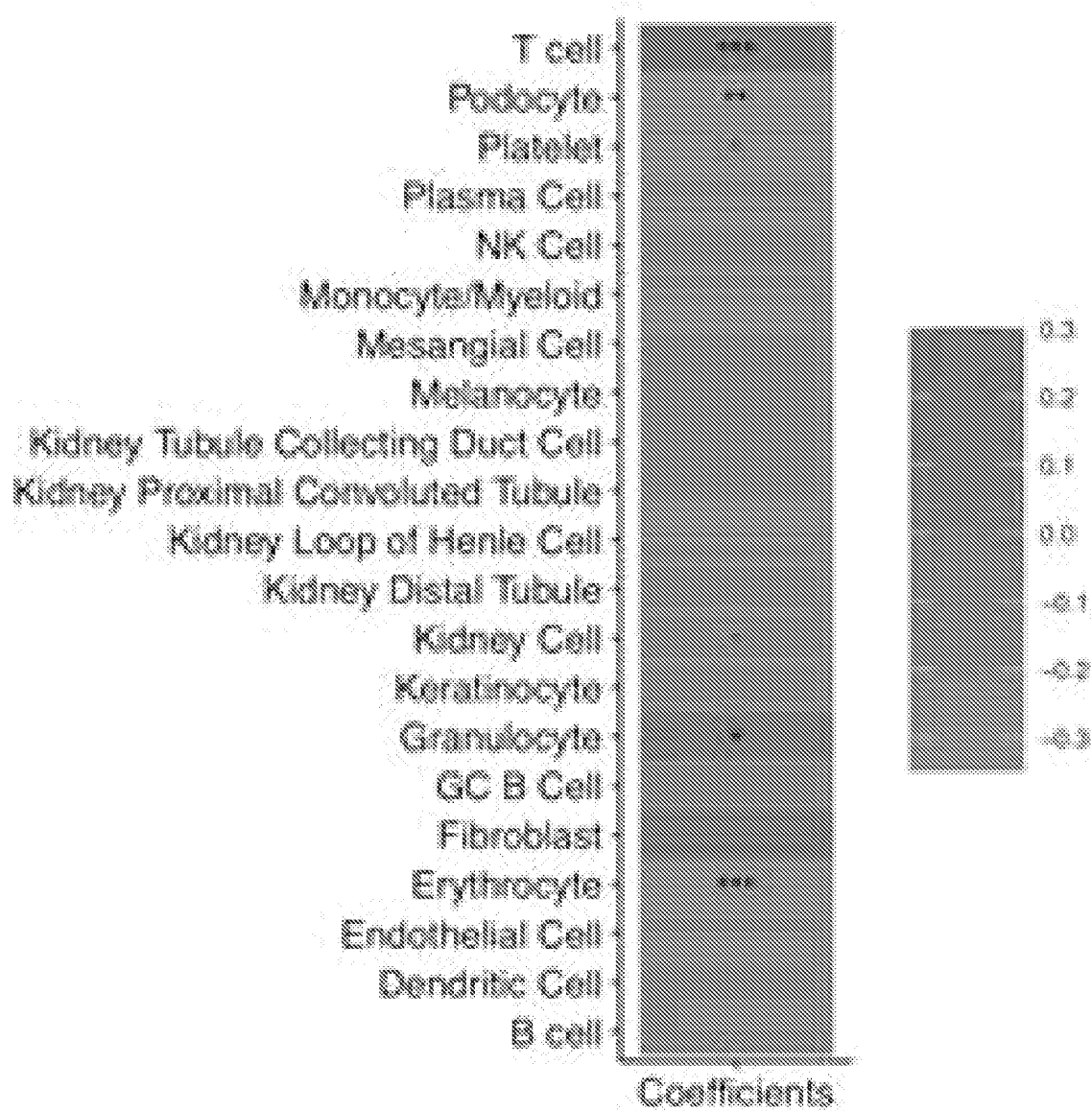


FIG. 102B

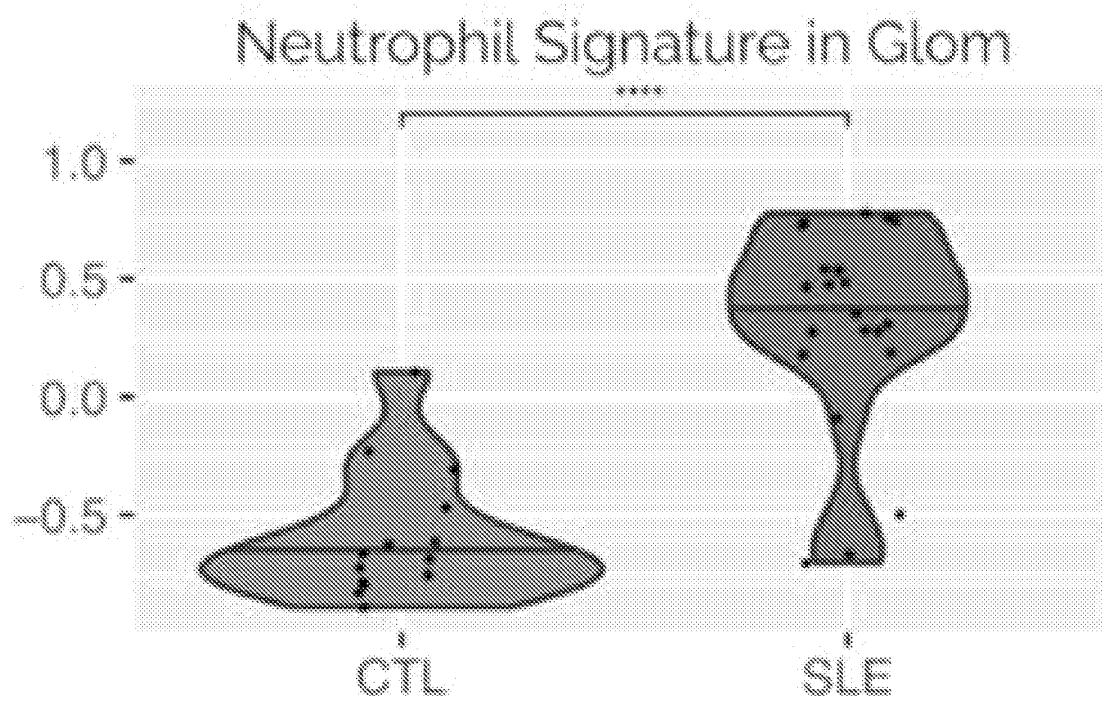


FIG. 103A

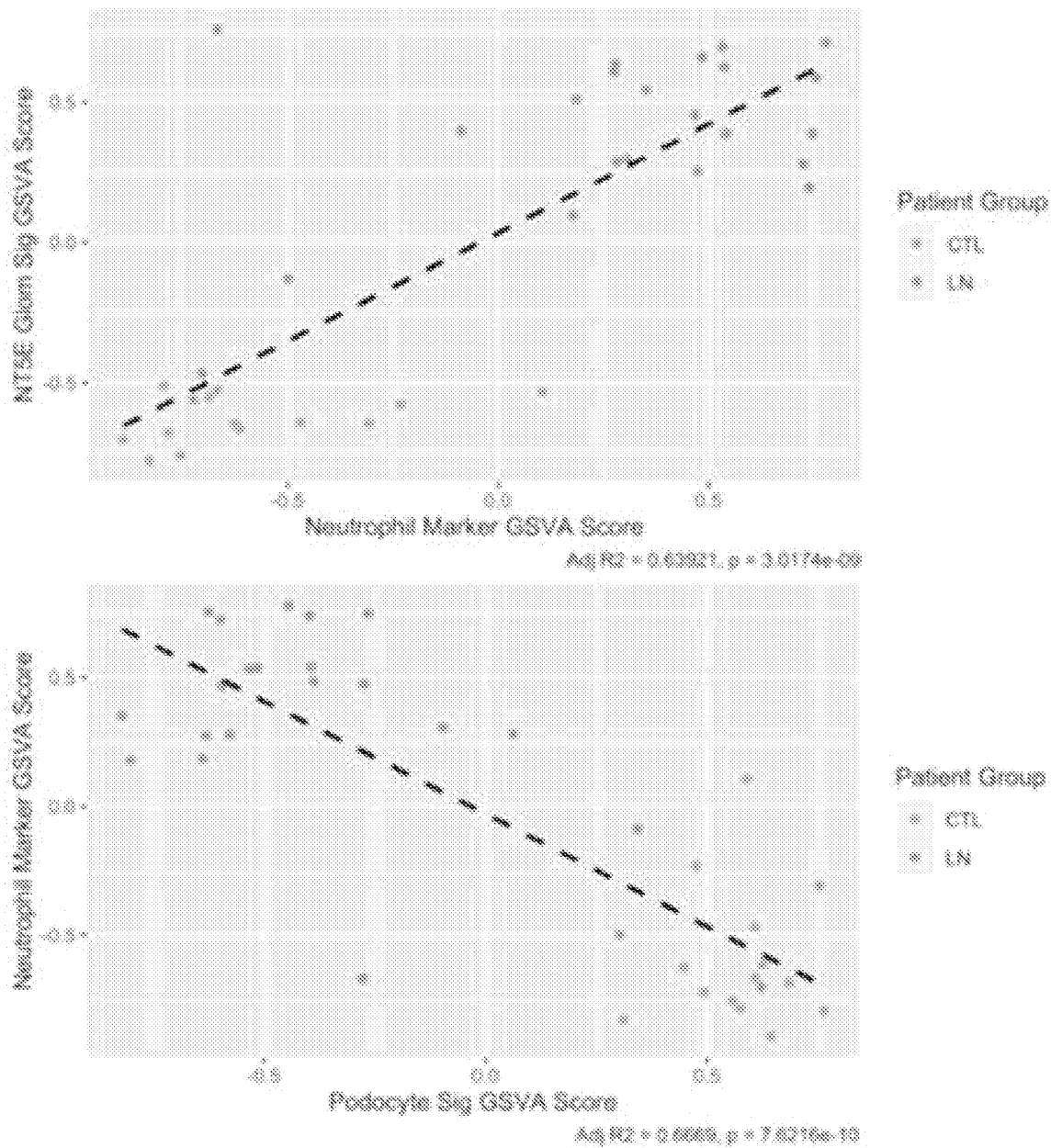


FIG. 103B

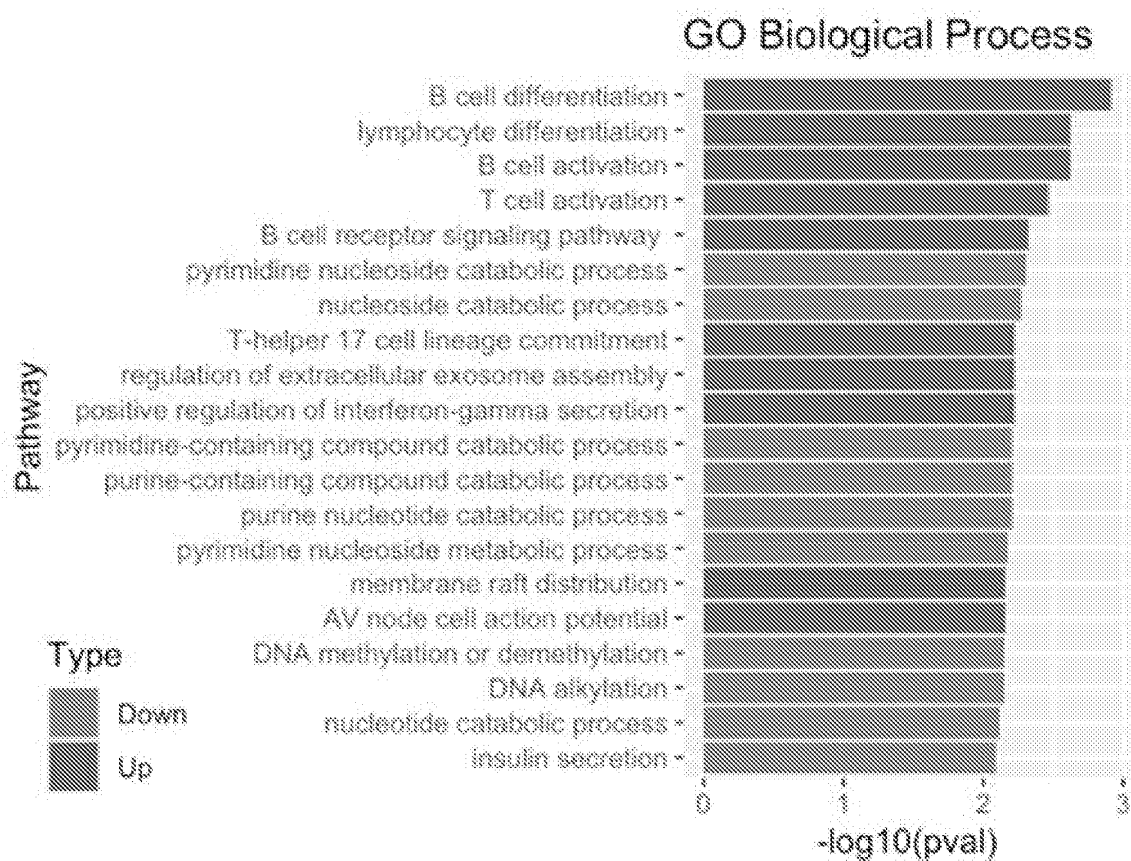


FIG. 104

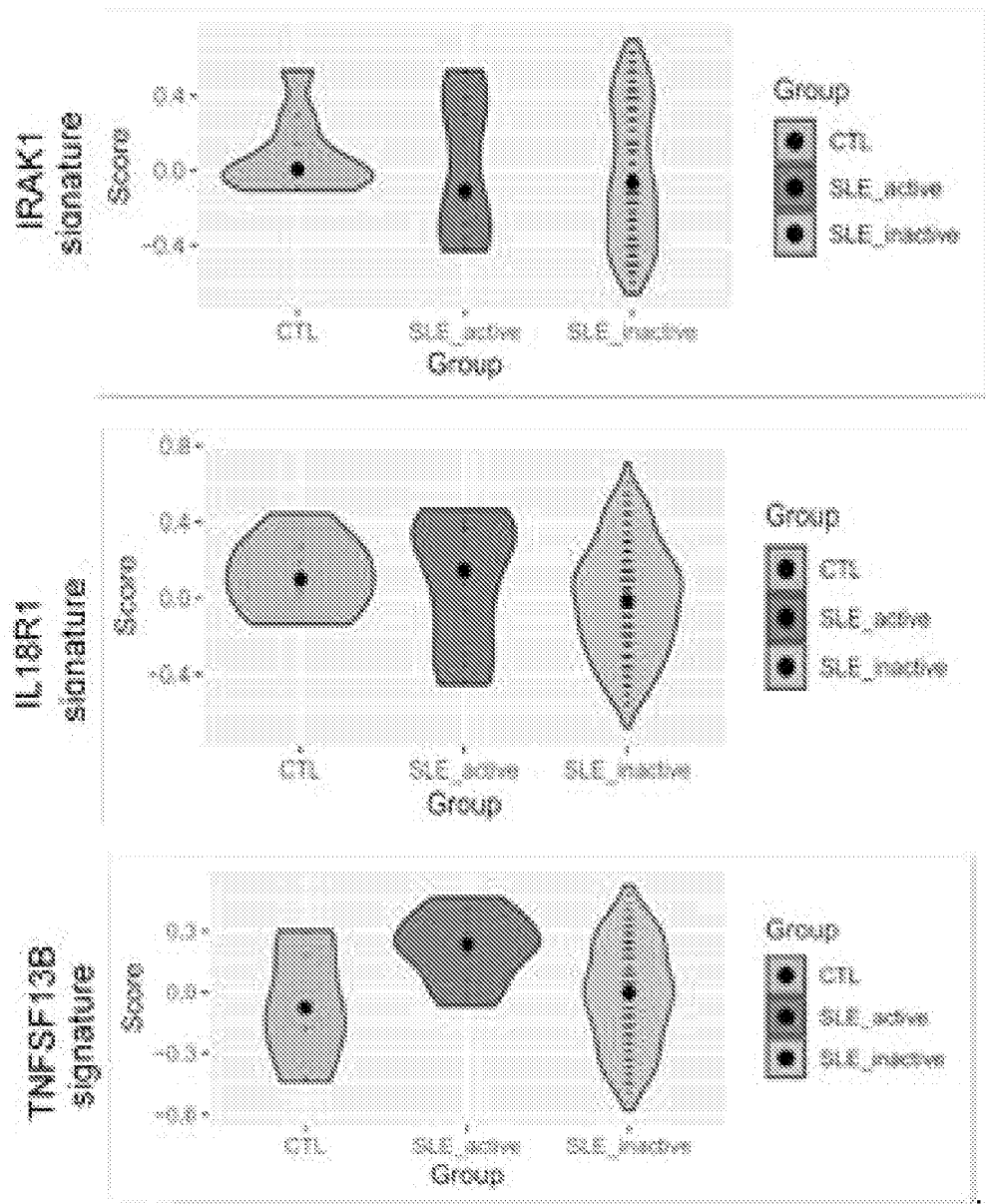


FIG. 105

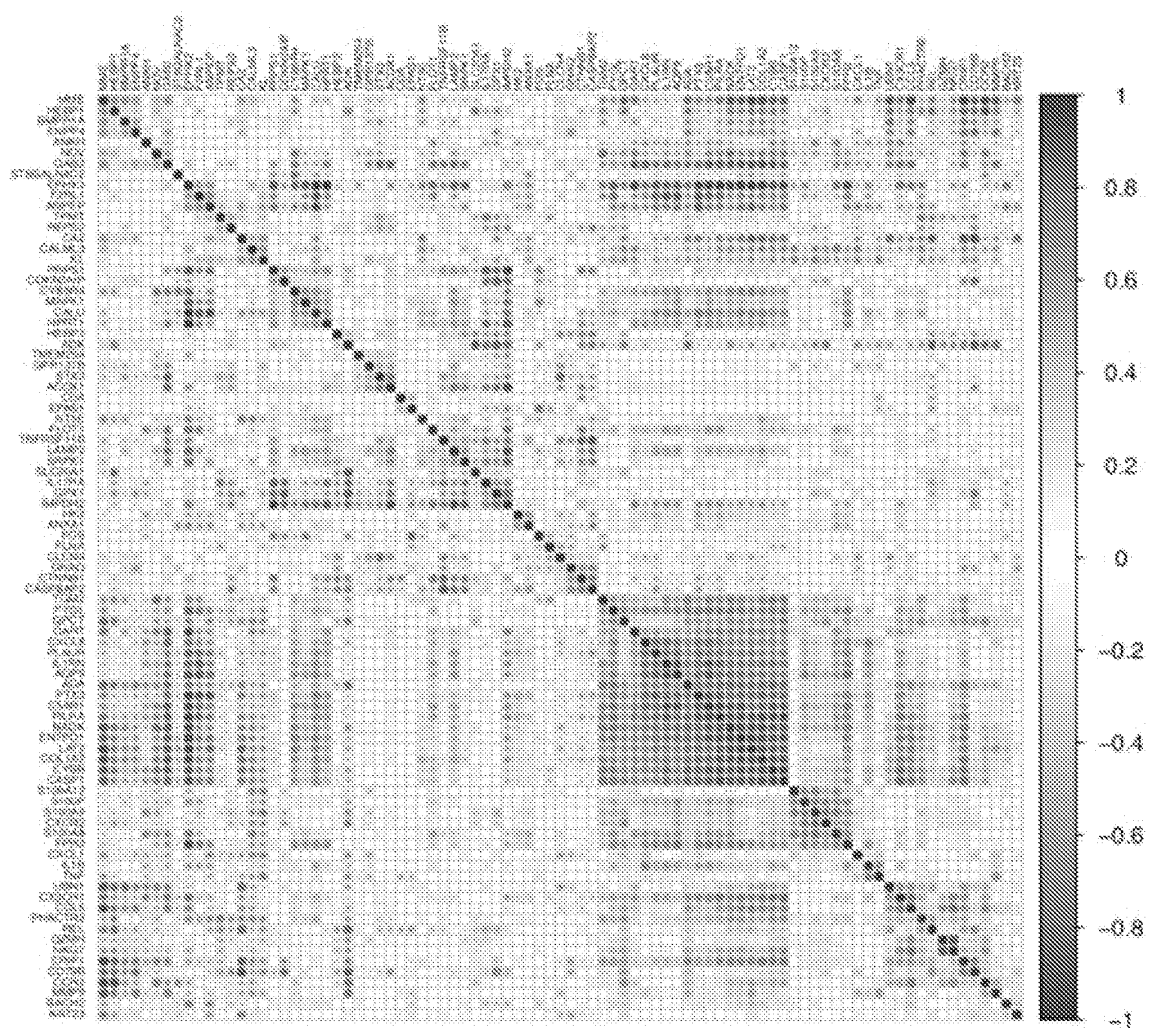


FIG. 106