

Fig 3. Clinical characteristics of four MS subgroups classified by T cell gene expression profiling. MS patients were classified into four distinct subgroups named A, B, C, and D by hierarchical clustering analysis of 286 genes differentially expressed in peripheral blood T cells between 72 untreated MS patients and 22 control (CN) subjects, as shown in Fig 1. The bar represents clinical data derived from individual patients. The number of relapse, the day of IVMP treatment, the day of hospitalization, and the number of lesions on T2-weighted MRI are derived from the data during 2 years before enrollment. Abbreviations: EDSS, Expanded Disability Status Scale; IVMP, intravenous methylprednisolone pulse; R/NR, responder/nonresponder.

Fig 4. Induction of IFN-responsive genes in IFN β -treated MS patients. Seventy-two MS patients were divided into IFN β -treated group (IFN β +, n = 46) and untreated group (IFN β -, n = 26) by the patient's own determination upon enrollment (See Supplementary Table 2 online). A cluster of the genes significantly upregulated exclusively in IFN β -treated patients at 6 months after starting the treatment is shown. A set of known IFN-responsive genes (IRGs) are indicated by star. The results are expressed as a matrix format as described in the footnote of Fig 1.

Fig 5. The temporal profile of induction of IFN-responsive genes in IFN β responders and nonresponders during IFN β treatment. Among 72 MS patients enrolled, 46 patients had received a two year-treatment of IFN β (see Supplementary Table 2 online). Blood samples were collected three times: before starting IFN β treatment (Pre), and at 3 months (3M) and 6 months (6M) after the treatment. Based on the IFN β responder/nonresponder score (Table 1), IFN β -treated patients were separated into 19 IFN β responders (R: the left), 7 nonresponders (L: the right), and 13 patients categorized into the undermined group with 7 dropouts (see Table 3). The temporal profile of expression of IFN-responsive genes (IRGs), including IFN-stimulated protein

15 (ISG15), small inducible cytokine A2 (SCYA2), TNF receptor subfamily member 1B (TNFRSF1B), and IFN α -inducible protein 27 (IFI27), is shown. The vertical axis represents the gene expression level (GEL), while the horizontal axis indicates the time course.

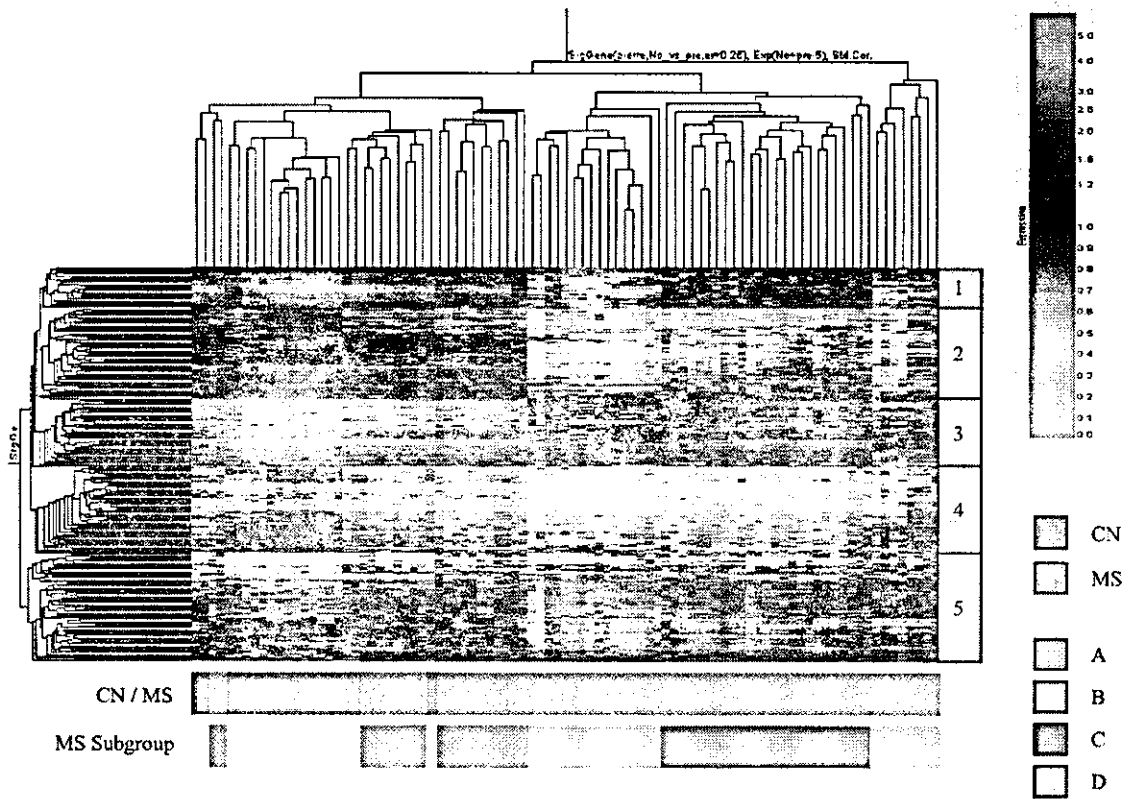


Fig 1. Hierarchical clustering analysis of 286 genes differentially expressed between 72 untreated MS patients and 22 control subjects.

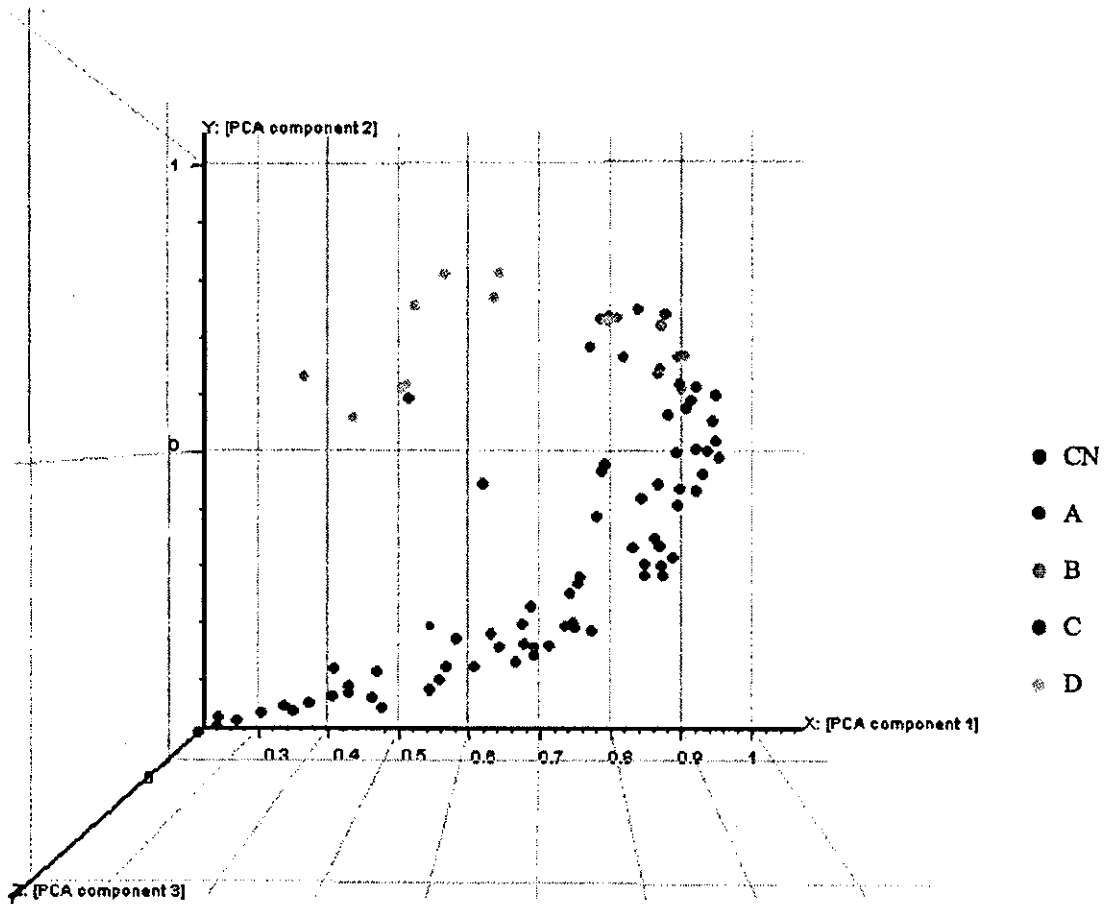


Fig 2. Principal component analysis (PCA) of 286 genes differentially expressed between 72 untreated MS patients and 22 control subjects.

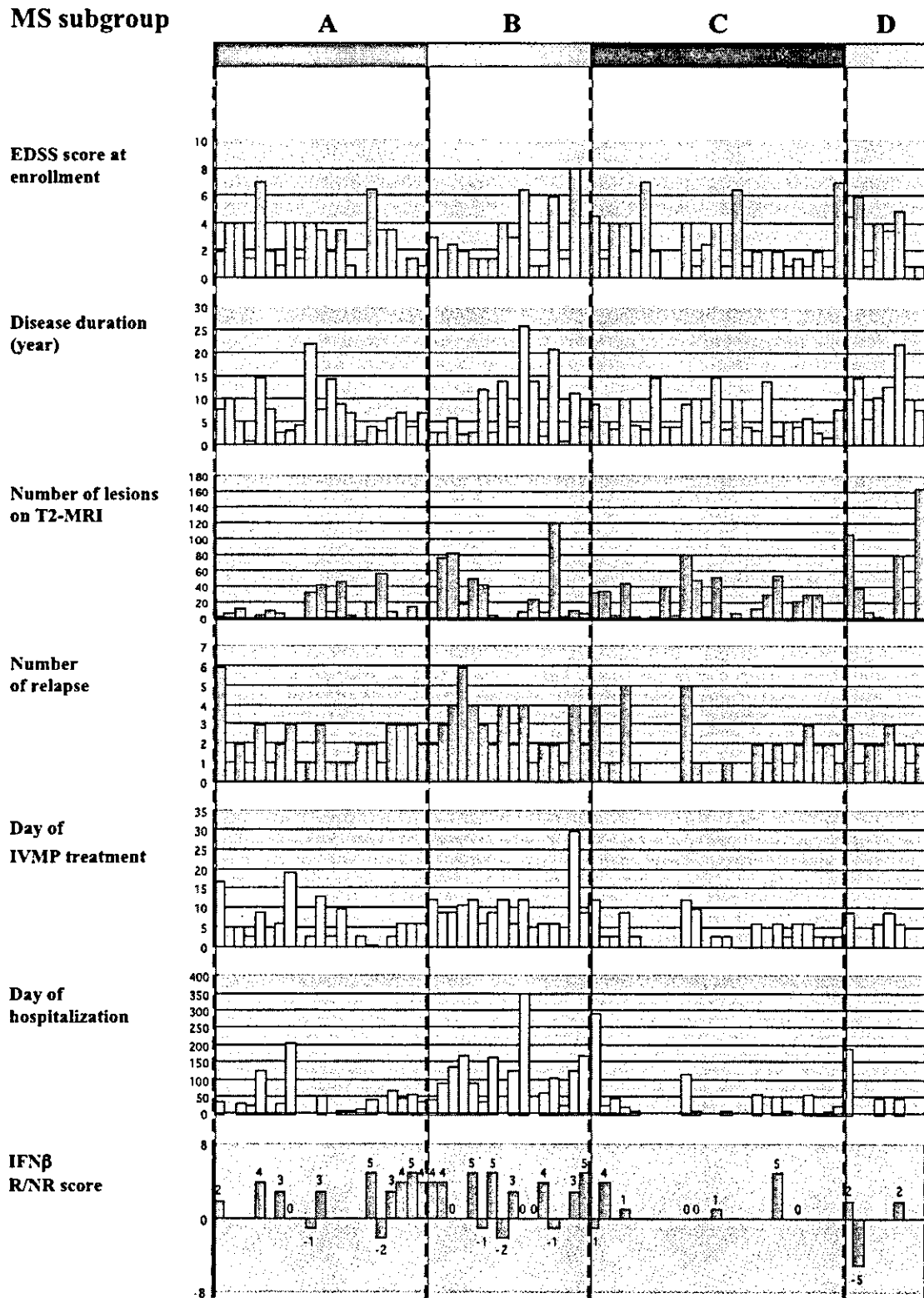


Fig 3. Clinical characteristics of four MS subgroups classified by T cell gene expression profiling.

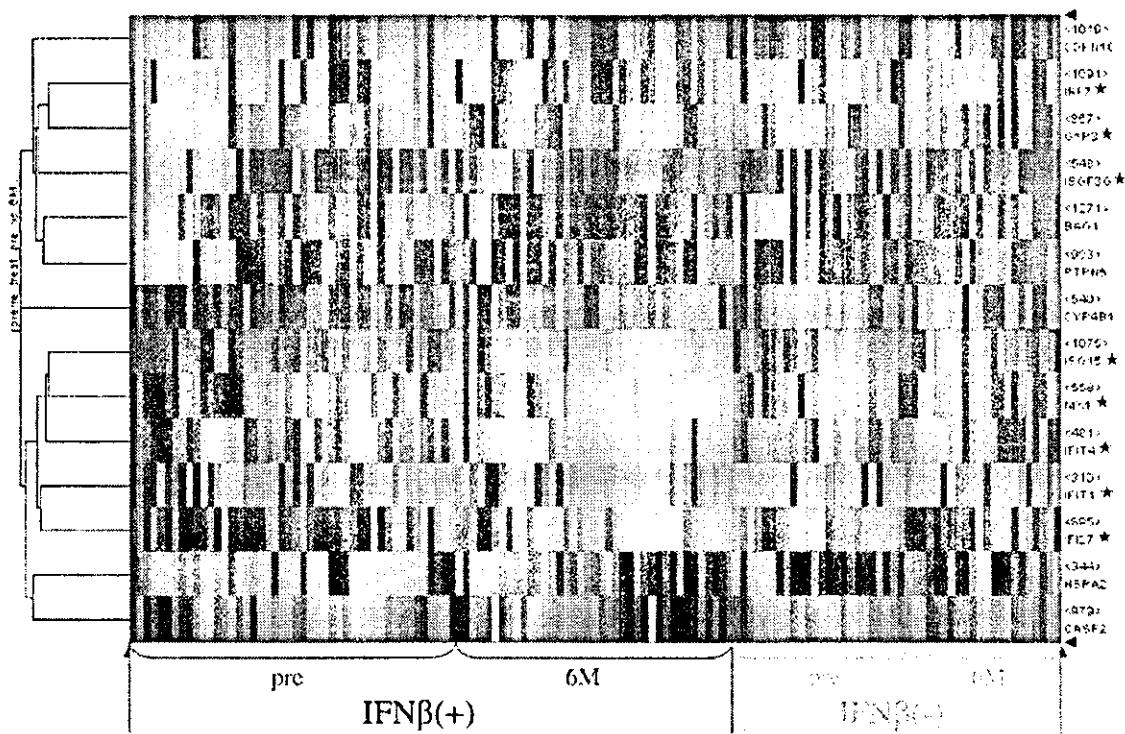


Fig 4. Induction of IFN-responsive genes in IFNβ-treated MS patients.

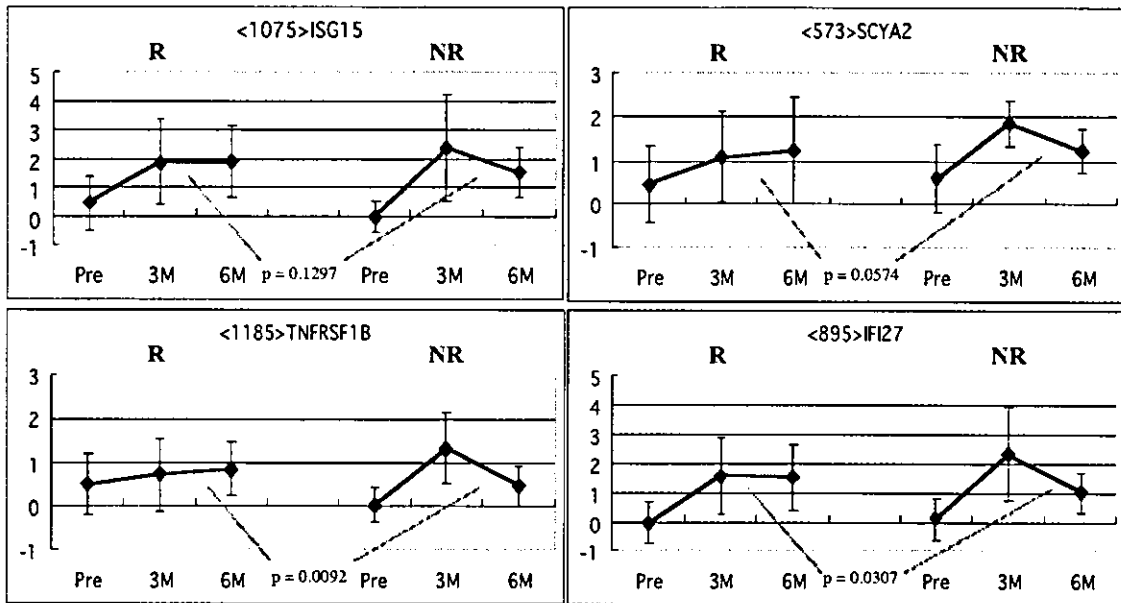


Fig 5. The temporal profile of induction of IFN-responsive genes in IFN β responders and nonresponders during IFN β treatment.

Table 1. IFN β Responder/Nonresponder Score

Category	The parameter related to IFN β treatment in MS	Rank and score of the therapeutic response		
		poor	intermediate	good
#1	Number of relapse after 2 years/number of relapse before 2 years score	≥ 1.5 (-1)	1.5-0.5 0	≤ 0.5 (+1)
#2	Number of IVMP treatment after 2 years/number of IVMP treatment before 2 years score	≥ 1.5 (-1)	1.5-0.5 0	≤ 0.5 (+1)
#3	Day of hospitalization after 2 years/day of hospitalization before 2 years score	≥ 1.5 (-1)	1.5-0.5 0	≤ 0.5 (+1)
#4	EDSS score before treatment- EDSS score in 2 years after treatment score	≤ -0.5 (-1)	0.5-(-0.5) 0	≥ 0.5 (+1)
#5	Number of lesions on T2-weighted MRI in 2 years after treatment/number of lesions on T2-weighted MRI before treatment score	≥ 1.2 (-1)	1.2-0.8 0	≤ 0.8 (+1)
#6	Patient's satisfaction score	unsatisfied (-1)	neither satisfied nor unsatisfied 0	satisfied (+1)

The total responder/nonresponder score of six categories ranges from the maximum value of +6 to the minimum value of -6. The patients with the score equal to +3 or greater than +3 were classified as responder (R), the score ranging from 0 to +2 as undetermined (UD), and the score equal to -1 or smaller than -1 as nonresponder (NR). Abbreviations: IVMP, intravenous methylprednisolone pulse.

Table 2. Clinical Characteristics of Four MS Subgroups Classified by T Cell Gene Expression Profiling

	Total	A	B	C	D	UC
The patients enrolled (n)	72	21	16	25	8	2
Age of the patients (average, SD)	36.1±10.3	33.5±8.7	36.7±9.9	36.2±10.2	39.8±15.5	41.5
Male to female ratio of the patients	17 to 55	4 to 17	4 to 12	8 to 17	0 to 8	1 to 1
RRMS to SPMS ratio of the patients	65 to 7	19 to 2	13 to 3	24 to 1	7 to 1	2 to 0
CMS to non-CMS ratio of the patients	57 to 15	16 to 5	13 to 3	21 to 4	6 to 2	1 to 1
The patients with CBR-restricted lesion distribution (n, %)	6 (8.3%)	1 (4.8%)	0 (0%)	5 (20%)	0 (0%)	0 (0%)
The patients with SC involvement (n, %)	51 (70.8%)	16 (76.1%)	12 (75.0%)	15 (60.0%)	6 (75.0%)	2 (100%)
Disease duration (year; average, SD)	7.7±5.4	7.2±5.0	8.1±7.5	6.5±4.0	11.8±5.0	10.5
EDSS score at enrollment (average, SD)	2.8±2.0	2.7±1.9	2.9±2.2	2.5±2.1	3.3±2.0	4.3
Number of relapse (average, SD)	1.9±1.5	1.9±1.4	2.8±1.4*	1.4±1.5*	1.8±1.2	2
Day of IVMP treatment (average, SD)	5.9±5.8	5.4±5.5	9.6±6.4**	3.8±3.8**	3.8±4.2	18
Day of hospitalization (average, SD)	49.7±70.0	37.9±49.1	105.9±86.9***	29.9±61.3***	32.3±66.2	31
Number of lesions on T2-weighted MRI (average, SD)	24.7±31.9	14.5±16.7	29.7±36.2	22.6±22.4	51.4±61.1	9.5

MS patients were classified into four distinct subgroups named A, B, C, and D by hierarchical clustering analysis of 286 genes differentially expressed in T cells between 72 untreated MS patients and 22 control (CN) subjects, as shown in Fig 1. Clinically, they were separated into the conventional form of MS (CMS) and non-CMS composed of the opticospinal form and multifocal recurrent myelitis. The number of relapse, the day of IVMP treatment, the day of hospitalization, and the number of lesions on T2-weighted MRI are derived from the data during 2 years before enrollment. The data derived from individual patients are illustrated in Fig. 3. The differences between the pairs (*, **, and ***) are statistically significant ($p = 0.0128$, 0.0183 , and 0.0329). Abbreviations: UC, unclassifiable; RRMS, relapsing-remitting MS; SPMS, secondary progressive MS; CMS, conventional form of MS; CBR, cerebrum; SC, spinal cord; EDSS, Expanded Disability Status Scale; IVMP, intravenous methylprednisolone pulse.

Table 3. IFN β Treatment Effects in Four MS Subgroups Classified by T Cell Gene Expression Profiling

	Total	A	B	C	D	UC
IFNβ-treated patients (n)	46	14	14	11	5	2
Age of IFNβ-treated patients (average, SD)	34.9 \pm 9.2	33.2 \pm 7.6	36.5 \pm 10.4	33.1 \pm 8.3	36.2 \pm 13.3	41.5
Male to female ratio of IFNβ-treated patients	8 to 38	1 to 13	3 to 11	3 to 8	0 to 5	1 to 1
IFNβ responder/nonresponder score (average, SD)	1.9 \pm 2.6	2.5 \pm 2.3	2.1 \pm 2.6	1.3 \pm 2.1	-0.3 \pm 4.0	3
Dropout during a 2 year-treatment (n)	7	2	0	3	2	0
IFNβ responder (n, %)	19 (41.3%)	8 (57.1%)	8 (57.1%)	2 (18.2%)	0 (0%)	1 (50%)
IFNβ nonresponder (n)	7	2	3	1	1	0
Undetermined group (n)	13	2	3	5	2	1
The patients with adverse effects after treatment (n, %)	29 (63.0%)	8 (57.1%)	9 (64.3%)	7 (63.6%)	4 (80%)	1 (50%)
Increase in the number of lesions on T2-weighted MRI during a 2 year-treatment (average, SD)	1.7 \pm 9.7	-2.0 \pm 7.1	2.8 \pm 6.6	7.6 \pm 15.8	-0.7 \pm 8.1	-3.5
The patients satisfied with IFNβ treatment (n, %)	17 (37.0%)	8 (57.1%)	6 (42.9%)	2 (18.2%)	0 (0%)	1 (50%)
The patients neither satisfied nor unsatisfied with IFNβ treatment (n)	21	4	7	7	2	1
The patients unsatisfied with IFNβ treatment (n)	8	2	1	2	3	0

MS patients were classified into four distinct subgroups named A, B, C, and D by hierarchical clustering analysis of 286 genes differentially expressed in T cells between 72 untreated MS patients and 22 control (CN) subjects. Among 72 MS patients, 46 patients were treated with IFN β for two years (see Supplementary Table 2) and the therapeutic effects were evaluated by IFN β responder/nonresponder score shown in Table 1. Abbreviations: UC, unclassifiable.

Supplementary Table 1 Online.

A Set of 286 Genes Differentially Expressed in T Cells between 72 Untreated MS Patients and 22 Control Subjects

<Gene No.> Symbol	Gene class	Name	Keyword	Category	GenBank
<68>RGS14	Class 1	Homo sapiens regulator of G protein signaling RGS14 mRNA, complete cds.	Human regulator of G protein signaling 14 (RGS14)	Signal	AF037195
<903>PTPN6	Class 1	H. sapiens PTP1C mRNA for protein-tyrosine phosphatase 1C.; Protein tyrosine phosphatase, non-receptor type 6; SHP-1	protein tyrosine phosphatase 1C; PTP1C gene; SH2 domain	Signal	X62055
<949>E2F4	Class 1	Homo sapiens E2F transcription factor 4, p107/p130-binding (E2F4)	E2F-4, a new member of the E2F transcription factor family, interacts with p107	TF	NM_001950
<1296>COX15	Class 1	Homo sapiens COX15 (yeast) homolog, cytochrome c oxidase assembly protein (COX15)	Identification and characterization of human cDNAs specific to BCS1, PET112, SCO1, COX15, and COX11, five genes involved in the formation and function of the mitochondrial respiratory chain	mitochondria & stress	NM_004376
<1020>TCFL1	Class 1	Human YL-1 mRNA for YL-1 protein (nuclear protein with DNA-binding ability), complete cds	Molecular cloning of a novel human cDNA on chromosome 1q21 and its mouse homolog encoding a nuclear protein with DNA-binding ability	Signal, TF	D43642
<461>NHP2L1	Class 1	Non-histone chromosome protein 2 (S. cerevisiae)-like 1	Cloning and mapping of a human novel cDNA (NHP2L1) that encodes a protein highly homologous to yeast nuclear protein NHP2	Signal	D50420
<507>HDGF	Class 1	Human mRNA for hepatoma-derived growth factor, complete cds	hepatoma-derived GF; hepatoma-derived growth factor	GF	D16431
<36>CSF1R	Class 1	Human macrophage colony stimulating factor I receptor precursor (CSF1R); fms proto-oncogene (c-fms)	c-fms oncogene; fms oncogene; glycoprotein; membrane protein; proto-oncogene; signal peptide	oncogene	X03663
<1203>IL6R	Class 1	Human mRNA for interleukin-6 (IL-6) receptor	BSF-2 receptor; glycoprotein; interferon beta II receptor; interleukin 6 receptor; receptor; transmembrane protein	Cytokine, Signal	X12830
<828>IL17R	Class 1	Homo sapiens IL-17 receptor mRNA, complete cds	Molecular characterization of the human interleukin (IL)-17 receptor	Cytokine	U58917
<369>EP300	Class 1	Human p300 protein mRNA, complete cds	p300; transcriptional adaptor protein; E1A-binding protein; cell cycle regulatory protein	Signal, TF	U01877
<142>TCF17	Class 1	Homo sapiens HKL1 mRNA, complete cds	Cloning, expression and mapping of a novel human zinc-finger gene TCF17 homologous to rodent Kid1	Signal, TF	D89928
<104>IFNAR1	Class 1	Human interferon-alpha receptor (HuIFN-alpha-Rec) mRNA, complete cds	interferon-alpha receptor	Cytokine, Signal	J03171

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<457>CFLAR	Class 1	Homo sapiens Casper mRNA; CASP8 and FADD-like apoptosis regulator; I-FLICE	Casper is a FADD- and caspase-related inducer of apoptosis	apoptosis, Signal	AF010127
<307>ITGB1	Class 1	Integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12):	glycoprotein; integrin; integrin beta 1 subunit.	Signal	X07979
<337>RBBP4	Class 1	Human chromatin assembly factor 1 p48 subunit (CAF1 p48 subunit); retinoblastoma-binding protein 4	binding protein; retinoblastoma binding protein	Signal	X74262
<381>CDC10	Class 1	hCDC10=CDC10 homolog [human, fetal lung, mRNA, 2314 nt].	Molecular cloning of a novel human cDNA homologous to CDC10 in Saccharomyces cerevisiae	CellCycle	S72008
<621>RBL2	Class 1	Human retinoblastoma-like protein 2 (RBL2; RB2); 130-kDa retinoblastoma-associated protein (p130)	E1A binding protein; retinoblastoma-associated protein	Signal, TF	X74594
<565>JAK1	Class 1	Human protein-tyrosine kinase (JAK1) mRNA, Janus kinase 1	Two novel protein-tyrosine kinases, each with a second phosphotransferase-related catalytic domain, define a new class of protein kinase	Signal	M64174
<239>CCNC	Class 1	Human cyclin mRNA	Isolation of three novel human cyclins by rescue of G1 cyclin (Cln) function in yeast	CellCycle	M74091
<189>ATP2C1	Class 1	ATPase, Ca ⁺⁺ -sequestering	Hailey-Hailey disease is caused by mutations in ATP2C1 encoding a novel Ca(2+) pump	ATPase	AF225981
<240>PPP3CB	Class 1	Human calcineurin A2 mRNA;	Cloning of human calcineurin A: Evidence for two isozymes identification of a polyproline structural domain	Signal	M29551
<510>NFATC3	Class 1	Homo sapiens NF-AT4c mRNA, complete cds	Isolation of two new members of the NF-AT gene family and functional characterization of the NF-AT proteins	Signal, TF	L41067
<800>PTPN7	Class 1	Human mRNA for protein-tyrosine phosphatase; Protein tyrosine phosphatase, non-receptor type 7, HePTP	protein-tyrosine phosphatase	Signal	D11327
<364>SCYB5	Class 1	H. sapiens ENA-78 mRNA; Small inducible cytokine subfamily B (Cys-X-Cys), member 5 (epithelial-derived neutrophil-activating peptide 78)	Cloning of a full-length cDNA encoding the neutrophil-activating peptide ENA-78 from human platelets	Cytokine, Signal	X78686
<117>ATP1B3P1	Class 1	ATPase, Na ⁺ /K ⁺ transporting, beta 3 pseudogene	ATPase	ATPase	AF005898
<578>TNFRSF11A	Class 1	Homo sapiens receptor activator of nuclear factor-kappa B (RANK) mRNA, complete cds	A homologue of the TNF receptor and its ligand enhance T-cell growth and dendritic-cell function	Cytokine	AF018253
<838>NPR2L	Class 1	Homo sapiens candidate tumor suppressor gene 21 protein mRNA, complete cds	Homologous to yeast nitrogen permease (candidate tumor suppressor)	suppressor	AF040708

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<678>RAB9	Class 1	Human small GTP binding protein Rab9 mRNA, complete cds.	Cloning and mapping of human Rab7 and Rab9 cDNA sequences and identification of a Rab9 pseudogene	oncogene	U44103
<568>TAF2D	Class 1	TATA box binding protein (TBP)-associated factor, RNA polymerase II, D, 100kD	Specific interactions and potential functions of human TAFII100	polymerase, TF	U80191
<740>MAPK1	Class 2	Human extracellular signal-regulated kinase 2 mRNA; ERK2	Extracellular signal-regulated kinases in T cells: characterization of human ERK1 and ERK2 cDNAs	Signal	M84489
<456>RPC62	Class 2	polymerase (RNA) III (DNA directed) (62kD)	Three human RNA polymerase III-specific subunits form a subcomplex with a selective function in specific transcription initiation	polymerase	U93867
<129>ABCD2	Class 2	Homo sapiens mRNA for adrenoleukodystrophy related protein (ALDR).	adrenoleukodystrophy related protein; ALDR gene	ABC transporter	AJ000327
<782>CYP21A2	Class 2	Human cytochrome P450c21 mRNA, 3' end	cytochrome P450 C21; steroid 21-hydroxylase; steroid 21-monooxygenase	glucocorticoids (Cortisol)	M17252
<177>TGFBRI	Class 2	Human activin receptor-like kinase (ALK-5) mRNA, complete cds	activin; activin receptor-like kinase; serine/threonine kinase; transforming growth factor-beta; transmembrane protein.	GF, Signal	L11695
<173>TCFL5	Class 2	Homo sapiens TCFL5 mRNA for transcription factor-like 5, complete cds	Cloning, mapping, and genomic organization of THLH1, a novel human testis-specific gene containing a basic Helix-Loop-Helix motif	Signal, TF	AB012124
<1011>CASP1	Class 2	Human interleukin 1-beta converting enzyme isoform delta (IL1BCE) mRNA, complete cds	cysteine protease; interleukin 1-beta converting enzyme; apoptotic protein	apoptosis, Signal	U13699
<387>ABCE1	Class 2	H.sapiens mRNA for 2'-5' oligoadenylate binding protein	binding protein; endoribonuclease; regulatory subunit	ABC transporter	X74987
<612>TPST2	Class 2	Homo sapiens tyrosylprotein sulfotransferase-2 mRNA	Molecular cloning and expression of human and mouse tyrosylprotein sulfotransferase-2 and a tyrosylprotein sulfotransferase homologue in Caenorhabditis elegans	sulfotransferase	AF049891
<438>GZMA	Class 2	Human Hanukah factor serine protease (HuHF) mRNA (cytotoxic T-lymphocyte-associated serine esterase 3)	Hanukah factor; T-cell-specific serine protease; natural killer cell-specific serine protease; serine protease	esterase	M18737
<203>TNFSF10	Class 2	Human TNF-related apoptosis inducing ligand TRAIL mRNA, complete cds	a new member of the TNF family that induces apoptosis	Cytokine	U37518
<119>P2Y5	Class 2	Homo sapiens purinergic receptor P2Y5 mRNA	The human purinergic receptor P2Y5 is encoded in intron 17 of the retinoblastoma gene	Signal	AF000546
<196>RUNX1	Class 2	Human AML1 mRNA for AML1b protein (alternatively spliced product), complete cds	AML1b protein; AML1; acute myeloid leukemia; alternative splicing	oncogene	D43968
<315>SCYB10	Class 2	Human mRNA for gamma-interferon inducible early	interferon response; signal peptide	Cytokine	X02530

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		response gene (with homology to platelet proteins).			
<736>EPHX2	Class 2	Human cytosolic epoxide hydrolase mRNA	cytosolic epoxide hydrolase; cytosolic protein; epoxide hydrolase:hydrolase	epoxide hydrolase	L05779
<176>ABCG2	Class 2	Homo sapiens placenta-specific ATP-binding cassette transporter (ABCP) mRNA, complete cds	A human placenta-specific ATP-binding cassette gene (ABCP) on chromosome 4q22 that is involved in multidrug resistance	ABC transporter	AF103796
<168>HSP105B	Class 2	Molecular cloning, expression and localization of human 105 kDa heat shock protein, hsp105D	Molecular cloning, expression and localization of human 105 kDa heat shock protein, hsp105	hsp	AB003333
<140>RBL1	Class 2	Human retinoblastoma related protein (p107) mRNA; Retinoblastoma-like 1	cell cycle regulation protein; retinoblastoma protein; tumor suppressor	CellCycle	L14812
<890>MYC	Class 2	Human mRNA encoding the c-myc oncogene	complementary DNA; oncogene	oncogene, Signal, TF	V00568
<576>GNB5	Class 2	Homo sapiens G protein beta 5 subunit mRNA; Guanine nucleotide binding protein (G protein), beta 5	Cloning and tissue distribution of the human G protein beta 5 cDNA	Signal	AF017656
<268>NR3C2	Class 2	Human mineralocorticoid receptor mRNA (hMR), complete cds	Cloning of human mineralocorticoid receptor complementary DNA: structural and functional kinship with the glucocorticoid receptor	NR3	M16801
<878>IL14	Class 2	Homo sapiens clone 24607 mRNA sequence	FLI_CDNA	Cytokine	AF070546
<924>ABCF2	Class 2	Homo sapiens clone 203 ABC transporter mRNA, complete cds	FLI_CDNA	ABC transporter	AF091073
<339>ST13	Class 2	Homo sapiens putative tumor suppressor ST13 (ST13) mRNA, complete cds	Differential expression of HSU17714 gene in colorectal cancer and normal colonic mucosa	suppressor	U17714
<587>TCF21	Class 2	Homo sapiens epicardin mRNA, complete cds.	epicardin: A novel basic helix-loop-helix transcription factor gene expressed in epicardium, branchial arch myoblasts, and mesenchyme of developing lung, gut, kidney, and gonads	Signal, TF	AF047419
<647>ATP6B2	Class 2	ATPase, H ⁺ transporting, lysosomal (vacuolar proton pump), beta polypeptide, 56/58kD, isoform 2	Heterogeneity of vacuolar H ⁺ -ATPase: differential expression of two human subunit B isoform	ATPase	L35249
<1346>CREB1	Class 2	Homo sapiens cAMP responsive element binding protein 1 (CREB1)	Cyclic AMP-responsive DNA-binding protein: Structure based on a cloned placental cDNA	ATF/CREB	NM_004379
<371>IFI16	Class 2	Homo sapiens interferon, gamma-inducible protein 16 (IFI16) mRNA	A novel gene constitutively expressed in human lymphoid cells is inducible with interferon-gamma in myeloid cells	Cytokine	NM_005531
<374>PMS1	Class 2	Human DNA mismatch repair protein PMS1 (PMS1 protein homolog 1)	Mutations of two PMS homologues in hereditary nonpolyposis colon cancer	DNAREpair	U13695

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<475>HSPA1L	Class 2	Homo sapiens HSPA1L mRNA for Heat shock protein 70 testis variant, complete cds; Heat shock 70kD protein-like 1	HSPA1L; Heat shock protein 70 testis variant	hsp	D85730
<506>HSPA10	Class 2	Homo sapiens heat shock 70kD protein 10 (HSC71) (HSPA10). mRNA	Structure and expression of a human gene coding for a 71 kd heat shock 'cognate' protein	hsp	NM_006597
<373>RAP1A	Class 2	Human ras-related protein (Krev-1) mRNA, complete cds	A ras-related gene with transformation suppressor activity	suppressor	M22995
<308>GNB1	Class 2	Human liver mRNA for beta-subunit signal transducing proteins Gs/Gi (beta-G); Guanine nucleotide binding protein (G protein), beta polypeptide 1	G protein; signal transducing protein; unidentified reading frame	Signal	X04526
<356>MAP3K7	Class 2	Homo sapiens mitogen-activated protein kinase kinase 7 (MAP3K7), mRNA, TAK1	Activation of the hematopoietic progenitor kinase-1 (HPK1)-dependent, stress-activated c-Jun N-terminal kinase (JNK) pathway by transforming growth factor beta (TGF-beta)-activated kinase (TAK1), a kinase mediator of TGF beta signal transduction	Signal	NM_003188
<322>PTPRC	Class 2	Human mRNA for T200 leukocyte common antigen (CD45, LC-A).	alternative splicing; cell surface antigen; cell surface glycoprotein; leukocyte common antigen; phosphoprotein; T200 glycoprotein	Signal	Y00062
<1028>POLR2G	Class 2	polymerase (RNA) II (DNA directed) polypeptide G	Human RNA polymerase II subunit hsRPB7 functions in yeast and influences stress survival and cell morphology	polymerase	U20659
<991>AFG3L2	Class 2	AFG3 (ATPase family gene 3, yeast)-like 2	Identification and characterization of AFG3L2, a novel paraplegin-related gene	ATPase	NM_006796
<503>RAB4	Class 2	Homo sapiens GTP-binding protein (RAB4) mRNA, complete cds.	GTP-binding protein; ras oncogene	oncogene	M28211
<413>GNG10	Class 2	Human G protein gamma-10 subunit mRNA; Guanine nucleotide binding protein 10	Isolation of cDNA clones encoding eight different human G protein gamma subunits, including three novel forms designated the gamma 4, gamma 10, and gamma 11 subunits	Signal	U31383
<38>JUN	Class 2	Homo sapiens v-jun avian sarcoma virus 17 oncogene homolog (JUN) mRNA.	Human proto-oncogene c-jun encodes a DNA binding protein with structural and functional properties of transcription factor AP-1	glucocorticoids (Cortisol)	NM_002228
<1271>BAG1	Class 2	Homo sapiens Bcl-2-binding protein (BAG-1) mRNA	glucocorticoid associated; Cloning of cDNAs encoding the human BAG1 protein and localization of the human BAG1 gene to chromosome 9p12	glucocorticoids (Cortisol)	AF022224
<1353>MAPKAPK3	Class 2	Homo sapiens mitogen-activated protein kinase-activated protein kinase 3	3pK, a new mitogen-activated protein kinase-activated protein kinase located in the small cell lung cancer tumor suppressor gene region	Signal	NM_004635

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<290>STAT1	Class 2	Homo sapiens transcription factor ISGF-3 mRNA, complete cds	transcription factor	Signal, TF	M97935
<485>ARHGDIB	Class 2	Human GDP-dissociation inhibitor protein (Ly-GDI) mRNA, D4-GDI	Ly-GDI, a GDP-dissociation inhibitor of the RhoA GTP-binding protein, is expressed preferentially in lymphocytes	Signal	L20688
<556>SELL	Class 2	selectin L (lymphocyte adhesion molecule 1)	Human homologue of mouse lymph node homing receptor: evolutionary conservation at tandem cell interaction domains	Selectin	M25280
<631>CYP3A5P1	Class 2	Human cytochrome P450 pseudogene mRNA	Isolation of CYP3A5P cDNA from human liver: A reflection of a novel cytochrome p450 pseudogene	P450	L26985
<729>CCND3	Class 2	Homo sapiens cyclin D3 (CCND3) mRNA, complete cds	cyclin D3	CellCycle	M92287
<1317>AKAP2	Class 2	Homo sapiens A kinase (PRKA) anchor protein 2 (AKAP2)	Prediction of the coding sequences of unidentified human genes. XIII. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro	Signal	NM_007203
<1338>KIAA0864	Class 2	Homo sapiens mRNA for KIAA0864 protein, partial cds; IRS-1	Prediction of the coding sequences of unidentified human genes. XII. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro	Insulin	AB020671
<1026>VAV2	Class 2	VAV2=VAV oncogene homolog (human, fetal brain, mRNA Partial, 2753bp)	Identification of VAV2 on 9q34 and its exclusion as the tuberous sclerosis gene TSC1	oncogene	S76992
<659>TTF1	Class 2	transcription termination factor, RNA polymerase	Molecular coevolution of mammalian ribosomal gene terminator sequences and the transcription termination factor TTF-I	polymerase, TF	X83973
<355>RBBP1	Class 2	Homo sapiens retinoblastoma-binding protein 1 (RBBP1) mRNA	Characterization of the retinoblastoma binding proteins RBP1 and RBP2	Signal	NM_002892
<1326>GABPB1	Class 2	Homo sapiens GA-binding protein transcription factor, beta subunit 1 (53kD); nuclear respiratory factor-2	Identity of GABP with NRF-2, a multisubunit activator of cytochrome oxidase expression, reveals a cellular role for an ETS domain activator of viral promoters	mitochondria & stress	NM_005254
<206>IL18R1	Class 2	Human putative transmembrane receptor IL-1Rrp mRNA, complete cds	IL-1Rrp is a novel receptor-like molecule similar to the type I interleukin-1 receptor and its homologues T1/ST2 and IL-1R AcP	Cytokine, Signal	U43672
<340>CDC27	Class 2	Human homologue of S. pombe nuc2+ and A. nidulans bimA; Cell division cycle 27	Linking yeast genetics to mammalian genomes: identification and mapping of the human homolog of CDC27 via the expressed sequence tag database	CellCycle	U00001
<159>ATP6D	Class 2	ATPase, H+ transporting, lysosomal (vacuolar proton pump) 42kD; Vacuolar proton-ATPase, subunit C; V-ATPase, subunit C	Molecular cloning of cDNA encoding the C subunit of H+ATPase from bovine chromaffin granules	ATPase	J05682

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<289>TCF12	Class 2	Homo sapiens transcription factor (HTF4) mRNA, complete cds	Interactions of HTF4 with E-box motifs in the long terminal repeat of human immunodeficiency virus type 1	Signal, TF	M83233
<102>TGFB2	Class 2	Homo sapiens mRNA for TGF-beta1R alpha, complete cds	TGF-beta1R alpha; HTR2-3	GF, Signal	D50683
<437>GSTM3	Class 2	Human glutathione transferase M3 (GSTM3) mRNA	GSTM3 gene; glutathione S-transferase; glutathione S-transferase M3; glutathione transferase	GSTM	J05459
<532>CSNK2A1	Class 2	Human casein kinase II alpha subunit mRNA, complete cds.	Isolation and characterization of human cDNA clones encoding the alpha and alpha' subunits of casein kinase II	Signal	M55265
<372>MERTK	Class 2	Human cellular proto-oncogene (c-mer) tyrosine kinase mRNA	proto-oncogene; tyrosine-kinase; receptor	oncogene	U08023
<405>CSNK1A1	Class 2	Homo sapiens casein kinase I alpha isoform (CSNK1A1) mRNA	Isolation and characterization of human casein kinase I epsilon (CKI), a novel member of the CKI gene family	Signal	L37042
<158>TOP1	no class	Human topoisomerase I mRNA, complete cds	cDNA cloning of human DNA topoisomerase I: catalytic activity of a 67.7-kDa carboxyl-terminal fragment	topoisomerase	J03250
<497>CHST4	no class	Homo sapiens carbohydrate (N-acetylglucosamine 6-O) sulfotransferase 4 (CHST4)	Sulfotransferases of two specificities function in the reconstitution of high endothelial cell ligands for L-selectin	sulfotransferase	NM_005769
<98>SLC35A1	no class	solute carrier family 35 (CMP-sialic acid transporter), member 1	Molecular cloning and characterization of a novel isoform of the human UDP-galactose transporter, and of related complementary DNA belonging to the nucleotide-sugar transporter gene family	polymerase	D87969
<134>ST1B2	no class	Homo sapiens mRNA for ST1B2	Molecular cloning and characterization of rat ST1B1 and human ST1B2 cDNAs, encoding thyroid hormone sulfotransferases	sulfotransferase	D89479
<1318>AGTRL2	Class 3	Homo sapiens angiotensin receptor-like 2 (AGTRL2)	Molecular cloning of a novel platelet protein showing homology to the angiotensin II receptor C-terminal domain	angiotensin	NM_005162
<449>PRKCQ	Class 3	Human protein kinase C theta (PKC) mRNA: Protein kinase C, theta	Molecular cloning and characterization of PKC theta, a novel member of the protein kinase C (PKC) gene family expressed predominantly in hematopoietic cells	Signal	L07032
<471>RPA1	Class 3	Replication protein A1 (70kD)	Characterization of a cDNA encoding the 70-kDa single-stranded DNA-binding subunit of human replication protein A and the role of the protein in DNA replication	Signal	M63488
<489>PDCD8	Class 3	Homo sapiens apoptosis-inducing factor AIF mRNA, nuclear gene encoding mitochondrial protein; Programmed cell death 8	Molecular characterization of mitochondrial apoptosis-inducing factor	Signal	AF100928
<408>PRKDC	Class 3	Homo sapiens DNA-dependent protein kinase catalytic subunit (DNA-PKcs)	DNA-dependent protein kinase catalytic subunit: a relative of phosphatidylinositol 3-kinase and the ataxia telangiectasia gene	Signal	U47077

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		mRNA	product		
<205>MADH4	Class 3	Human homozygous deletion target in pancreatic carcinoma (DPC4); mothers against dpp homolog 4 (SMAD4)	Homozygous deletion map at 18q21.1 in pancreatic cancer	Signal, suppressor, TF	U44378
<273>MX2	Class 3	Human interferon-induced cellular resistance mediator protein (MxB) mRNA	interferon-induced cellular resistance mediator protein; interferon-inducible protein	Cytokine	M30818
<447>PECAM1	Class 3	Platelet/endothelial cell adhesion molecule (CD31 antigen), neutrophil: CD31	PECAM-1 (CD31) cloning and relation to adhesion molecules of the immunoglobulin gene superfamily	Signal	M28526
<1288>VCAM1	Class 3	Homo sapiens vascular cell adhesion molecule 1 (VCAM1)	Direct expression cloning of vascular cell adhesion molecule 1, a cytokine-induced endothelial protein that binds to lymphocytes	glucocorticoids (Cortisol)	NM_001078
<1330>GNG2	Class 3	Homo sapiens clone FLB4307 PRO1107 mRNA	Functional prediction of the coding sequences of 75 new genes deduced by analysis of cDNA clones from human fetal liver	Signal	AF130106
<566>RALB	Class 3	Human GTP-binding protein (RALB) mRNA, complete cds.	Chromosomal localization and cDNA sequence of human ralB, a GTP binding protein	oncogene	M35416
<637>GAPCENA	Class 3	rab6 GTPase activating protein (GAP and centrosome-associated)	Characterization of GAPCenA, a GTPase activating protein for Rab6, part of which associates with the centrosome	Gap-junction	AJ011679
<385>CDC16	Class 3	Human CDC16Hs mRNA, complete cds	CDC27Hs colocalizes with CDC16Hs to the centrosome and mitotic spindle and is essential for the metaphase to anaphase transition	CellCycle	U18291
<563>PIM1	Class 3	Human h-pim-1 protein (h-pim-1) mRNA, complete cds	c-myc proto-oncogene	oncogene	M54915
<126>RAB7L1	Class 3	Homo sapiens mRNA for small GTP-binding protein, complete cds	small GTP-binding protein; RAB7L1	oncogene	D84488
<1017>BAK1	Class 3	Human bcl2 homologous antagonist/killer (BAK)	Induction of apoptosis by the Bcl-2 homologue Bak	apoptosis	U23765
<1376>SGK2	Class 3	Homo sapiens serum/glucocorticoid regulated kinase 2	Characterization of the structure and regulation of two novel isoforms of serum- and glucocorticoid-induced protein kinase	hyperosmotic stress	NM_016276
<478>TRA@	Class 3	Human mRNA for T-cell receptor alpha chain (TCR-alpha).	membrane protein; T-cell receptor; T-cell receptor alpha	Signal	X02592
<12>TGFB1	Class 3	Human transforming growth factor-beta (TGF-beta; TGFB)	signal peptide; transforming growth factor-beta	GF, Signal	X02812
<751>PMM1	Class 3	phosphomannomutase 1	Cloning and characterization of human phosphomannomutase, a mammalian homologue of yeast SEC53	polymerase	U86070
<531>CSNK2A2	Class 3	Human casein kinase II alpha' subunit mRNA, complete cds	Isolation and characterization of human cDNA clones encoding the alpha and the alpha' subunits of casein kinase II	Signal	M55268

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<786>PLCB2	Class 3	Homo sapiens phospholipase C-beta-2 mRNA; Phospholipase C, beta 2	Cloning, sequencing, expression, and G-q-independent activation of phospholipase C-beta2	Signal	M95678
<434>ERCC3	Class 3	Human DNA repair helicase (ERCC3) mRNA, complete cds	Cockayne's syndrome; DNA repair protein; excision repair protein; helicase	TF	M31899
<961>NFRKB	Class 3	Human R kappa B mRNA, complete cds	Cloning of R kappa B, a novel DNA-binding protein that recognizes the interleukin-2 receptor alpha chain kappa B site	Signal	U08191
<538>CDK2	Class 3	Human cdc2-related protein kinase mRNA, complete cds	cdc2-related protein kinase	CellCycle, Signal	M68520
<755>ERBB2	Class 3	Human tyrosine kinase-type receptor (HER2) mRNA; ERBB2; neu proto-oncogene	tyrosine kinase	oncogene	M11730
<28>HRAS	Class 3	Homo sapiens v-Ha-ras Harvey rat sarcoma viral oncogene homolog (HRAS)	Complete nucleotide sequences of the T24 human bladder carcinoma oncogene and its normal homologue	oncogene, Signal	NM_005343
<1308>SLC1A1	Class 3	Human glutamate transporter mRNA; HEACC1	Neuron-specific human glutamate transporter: molecular cloning, characterization and expression in human brain	hyperosmotic stress	U08989
<148>NBS1	Class 3	Nijmegen breakage syndrome 1 (nibrin)	The hMre11/hRad50 protein complex and Nijmegen breakage syndrome: linkage of double-strand break repair to the cellular DNA damage response	Signal	AF058696
<847>IL2RG	Class 3	Human mRNA for interleukin 2 receptor gamma chain	interleukin 2 receptor; interleukin 2 receptor gamma chain	Cytokine, Signal	D11086
<201>ATM	Class 3	Human ataxia telangiectasia (ATM) mRNA	The complete sequence of the coding region of the ATM gene reveals similarity to cell cycle regulators in different species	Signal, suppressor	U33841
<237>CDC2L5	Class 3	Human cdc2-related protein kinase (CHED) mRNA; Cell division cycle 2-like 5 (cholinesterase-related cell division controller)	cdc2-related protein kinase	CellCycle	M80629
<1313>STIP1	Class 3	Homo sapiens stress-induced-phosphoprotein 1 (Hsp70/Hsp90-organizing protein)	Molecular cloning and expression of a transformation-sensitive human protein containing the TPR motif and sharing identity to the stress-inducible yeast protein STI1	stress	NM_006819
<814>ABCF1	Class 3	Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA, complete cds	ABC50, a novel human ATP-binding cassette protein found in tumor necrosis factor-alpha-stimulated synoviocytes	ABC transporter	AF027302
<913>SPIB	Class 3	H.sapiens Spi-B mRNA; Spi-B transcription factor (Spi-1/PU.1 related)	ets gene family; Spi-B protein	TF	X66079
<227>ADH2	Class 3	Human class I alcohol dehydrogenase (ADH2) beta-1 subunit mRNA	Genotyping of human alcohol dehydrogenases at the ADH2 and ADH3 loci following DNA sequence amplification	ADH	M21692

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<1341>GNAQ	Class 3	Homo sapiens guanine nucleotide binding protein (G protein), q polypeptide	Molecular cloning of human G alpha q cDNA and chromosomal localization of the G alpha q gene (GNAQ) and a processed pseudogene	Signal	NM_002072
<657>ABCB10	Class 3	Human ATP-binding cassette protein mRNA 06B09 clone, partial cds	Characterization and mapping of three new mammalian ATP-binding transporter genes from an EST database	ABC transporter	U18237
<665>PAK2	Class 3	Human p21-activated protein kinase (PAK-gamma; PAK2); PAK65: S6/H4 kinase	Human p21-activated protein kinases regulate actin organization in mammalian cells	Signal	U24153
<100>STAC	Class 3	Homo sapiens mRNA for stac, (src homology three (SH3) and cysteine rich domain)	Stac, a novel neuron-specific protein with cysteine-rich and SH3 domains	Signal	D86640
<156>ERBB4	Class 3	Homo sapiens receptor tyrosine kinase (ERBB4) gene, complete cds	EGF receptor-related; Her4 tyrosine kinase; receptor	oncogene	L07868
<131>POLE2	Class 3	polymerase (DNA directed), epsilon 2	Purification, cDNA cloning, and gene mapping of the small subunit of human DNA polymerase epsilon	polymerase	AF025840
<718>CD79B	Class 3	Human immunoglobulin superfamily member B cell receptor complex cell surface glycoprotein (IGB) mRNA, CD79B	B cell receptor complex; cell surface glycoprotein	Signal	M89957
<99>ATP7A	Class 3	ATPase, Cu++ transporting, alpha polypeptide (Menkes syndrome)	Isolation of a candidate gene for Menkes disease and evidence that it encodes a copper-transporting ATPase	ATPase	L06133
<1016>ATP6S1	Class 3	ATPase, H+ transporting, lysosomal (vacuolar proton pump), subunit 1	Isolation of expressed sequences encoded by the human Xq terminal portion using microclone probes generated by laser microdissection	ATPase	D16469
<48>EGF	Class 3	Human mRNA for kidney epidermal growth factor (EGF) precursor: urogastrone	epidermal growth factor; glycoprotein; growth factor; membrane protein; signal peptide	GF, Signal	X04571
<1307>AKAP9	Class 3	Homo sapiens A kinase (PRKA) anchor protein (yotiao) 9 (AKAP9)	Yotiao, a novel protein of neuromuscular junction and brain that interacts with specific splice variants of NMDA receptor subunit NR1	Signal	NM_005751
<127>ABCC5	Class 3	Homo sapiens SMRP mRNA, complete cds	cDNA cloning of a short type of multidrug resistance protein homologue, SMRP, from a human lung cancer cell line	ABC transporter	AB005659
<987>TAF2H	no class	TATA box binding protein (TBP)-associated factor, RNA polymerase II, H, 30kD	Human TAFII30 is present in a distinct TFIID complex and is required for transcriptional activation by the estrogen receptor	polymerase, TF	U13991
<642>CHST2	Class 4	Homo sapiens carbohydrate (N-acetylglucosamine-6-O) sulfotransferase 2 (CHST2)	Human N-acetylglucosamine-6-O-sulfotransferase involved in the biosynthesis of 6-sulfo sialyl Lewis X: molecular cloning, chromosomal mapping, and expression in various organs and tumor cells	sulfotransferase	NM_004267