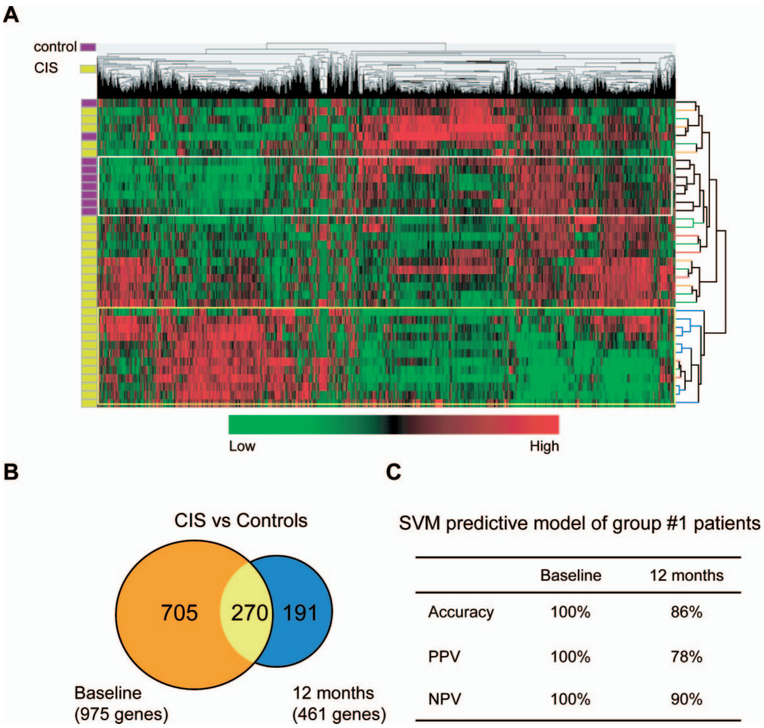
Supporting Information

Corvol *et al.* 10.1073/pnas.0805065105



	Baseline	12 months
Accuracy	100%	86%
PPV	100%	78%
NPV	100%	90%

Fig. S1. Gene expression still differentiates group #1 from other CIS patients 1 year later. (*A*) Hierarchical clustering of the expression of the same 1718 genes as in Fig. 1 but obtained at 12 months. Gene and sample distances were computed as described in Fig. 1. The bars on the left indicate the class of sample: purple = control; yellow = CIS. Group #1 CIS patients are identified by blue lines in the sample's dendrogram and by a yellow box in the heatmap. Control samples are identified by a white box in the heatmap. Other CIS groups (#2, #3, and #4) are no longer identifiable. (*B*) Number of genes differentially expressed in CIS patients compared with controls at baseline (orange circle), at 12 months (blue circle), or on both sets (intersection). (*C*) A support vector machine-based predictive model was built using the expression of 108 genes that distinguished group #1 from other CIS patients. The model classified the samples at baseline (training set) with perfect accuracy. Also the predictive positive (PPV) and negative (PNV) values were 100%. When the same model was used to predict the status of samples taken 1 year later (group #1 or other CIS), the model performed between 80% and 90% in all 3 parameters.

Table S2. Mean predictive accuracy of the top 7 gene pairs

Gene 1	Gene 2	Accuracy, %
RENT1	*TIMP2*	97
ARFGAP1	*FYN*	96
ARSA	*FYN*	95
ARFGAP1	*MAD1L1*	91
ARFGAP1	*CCDC12*	89
IVLBL	*RALGDS*	87
ARFGAP1	*SLC25A28*	86

Table S3. Signature of group 1 patients

Order	Probe set	Symbol	Gene description	Ratio group #1/ other CIS	*P*
1	217800_s_at	NDFIP1	Nedd4 family interacting protein 1	3.8	< 1e-07
2	225247_at	C19orf6	Chromosome 19 open reading frame 6	3.1	1.E-05
3	213915_at	NKG7	Natural killer cell group 7 sequence	2.9	< 1e-07
4	200041_s_at	BAT1	HLA-B associated transcript 1	2.5	< 1e-07
5	211716_x_at	ARHGDIA	Rho GDP dissociation inhibitor (GDI) alpha	2.5	< 1e-07
6	233350_s_at	TEX264	Testis expressed sequence 264	2.4	1.E-06
7	219529_at	CLIC3	Chloride intracellular channel 3	2.4	< 1e-07
8	218607_s_at	SDAD1	SDA1 domain containing 1	2.3	< 1e-07
9	202652_at	APBB1	Amyloid beta (A4) precursor protein-binding, family B, member 1	2.3	9.E-06
10	216520_s_at	TPT1	Tumor protein, translationally-controlled 1	2.3	< 1e-07
11	1554021_a_at	ZNF12	Zinc finger protein 12	2.2	< 1e-07
12	204122_at	TYROBP	TYRO protein tyrosine kinase binding protein	2.2	< 1e-07
13	219878_s_at	KLF13	Kruppel-like factor 13	2.2	< 1e-07
14	216231_s_at	B2M	Beta-2-microglobulin	2.2	2.E-07
15	219571_s_at	ZNF12	Zinc finger protein 12	2.1	< 1e-07
16	214450_at	CTSW	Cathepsin W (lymphopain)	2.1	< 1e-07
17	209050_s_at	RALGDS	Ral guanine nucleotide dissociation stimulator	2.0	< 1e-07
18	207088_s_at	SLC25A11	Solute carrier family 25, member 11	1.9	< 1e-07
19	1558215_s_at	UBTF	Upstream binding transcription factor, RNA polymerase I	1.9	< 1e-07
20	200612_s_at	AP2B1	Adaptor-related protein complex 2, beta 1 subunit	1.9	< 1e-07
21	227266_s_at	FYB	FYN binding protein (FYB-120/130)	1.9	< 1e-07
22	205480_s_at	UGP2	UDP-glucose pyrophosphorylase 2	1.8	< 1e-07
23	201831_s_at	VDP	Vesicle docking protein p115	1.8	2.E-06
24	232535_at		DKFZp434L201	1.8	1.E-07
25	244042_x_at		Transcribed locus	1.8	1.E-05
26	233713_at	SMYD2	SET and MYND domain containing 2	1.8	< 1e-07
27	211947_s_at	BAT2D1	BAT2 domain containing 1	1.8	< 1e-07
28	212368_at	ZNF292	Zinc finger protein 292	1.7	< 1e-07
29	217854_s_at	POLR2E	Polymerase (RNA) II (DNA directed) polypeptide E, 25kDa	1.7	< 1e-07
30	217993_s_at	MAT2B	Methionine adenosyltransferase II, beta	1.7	< 1e-07
31	236562_at	ZNF439	Zinc finger protein 439	1.6	< 1e-07
32	200033_at	DDX5	DEAD (Asp-Glu-Ala-Asp) box polypeptide 5	1.6	1.E-07
33	221895_at	MOSPD2	Motile sperm domain containing 2	1.6	8.E-07
34	201998_at	ST6GAL1	ST6 beta-galactosamide alpha-2,6-sialyltranferase 1	1.6	1.E-07
35	209458_x_at	HBA1 /// HBA2	Hemoglobin, alpha 1/// alpha 2	1.6	< 1e-07
36	241838_at		Transcribed locus	1.5	< 1e-07
37	212540_at	CDC34	Cell division cycle 34	1.5	< 1e-07
38	212926_at	SMC5L1	SMC5 structural maintenance of chromosomes 5-like 1	1.5	< 1e-07
39	202283_at	SERPINF1	Serpin peptidase inhibitor, clade F, member 1	1.5	< 1e-07
40	200735_x_at	NACA	Nascent-polypeptide-associated complex alpha polypeptide	1.5	< 1e-07
41	207460_at	GZMM	Granzyme M (lymphocyte met-ase 1)	1.5	< 1e-07
42	211699_x_at	HBA1 /// HBA2	Hemoglobin, alpha 1 /// alpha 2	1.5	< 1e-07
43	208635_x_at	NACA	Nascent-polypeptide-associated complex alpha polypeptide	1.5	< 1e-07
44	209651_at	TGFB1I1	Transforming growth factor beta 1 induced transcript 1	1.5	< 1e-07
45	213687_s_at	RPL35A	Ribosomal protein L35a	1.5	< 1e-07
46	208325_s_at	AKAP13	A kinase (PRKA) anchor protein 13	1.5	< 1e-07
47	203375_s_at	TPP2	Tripeptidyl peptidase II	1.4	2.E-07
48	212063_at	CD44	CD44 antigen	1.4	3.E-07
49	235213_at	ITPKB	Inositol 1,4,5-trisphosphate 3-kinase B	1.4	< 1e-07
50	242778_at	LPXN	Leupaxin	0.8	< 1e-07
51	226843_s_at	PAPD5	PAP associated domain containing 5	0.7	< 1e-07
52	1569599_at	SAMSN1	SAM domain, SH3 domain and nuclear localisation signals, 1	0.7	4.E-05
53	207111_at	EMR1	EGF-like module containing, mucin-like, hormone receptor-like 1	0.7	< 1e-07
54	242918_at	NASP	Nuclear autoantigenic sperm protein (histone-binding)	0.7	< 1e-07
55	1553861_at	TCP11L2	T-complex 11 (mouse) like 2	0.7	2.E-05
56	1552807_a_at	SIGLEC10	Sialic acid binding Ig-like lectin 10	0.6	< 1e-07
57	238545_at	BRD7	Bromodomain containing 7	0.6	< 1e-07
58	202381_at	ADAM9	ADAM metallopeptidase domain 9 (meltrin gamma)	0.6	1.E-05
59	226982_at	ELL2	Elongation factor, RNA polymerase II, 2	0.6	3.E-04
60	202083_s_at	SEC14L1	SEC14-like 1 (S. cerevisiae)	0.6	< 1e-07
61	228284_at	TLE1	Transducin-like enhancer of split 1	0.6	< 1e-07
62	222670_s_at	MAFB	v-maf musculoaponeurotic fibrosarcoma oncogene homolog B	0.6	< 1e-07
63	243296_at	PBEF1	Pre-B-cell colony enhancing factor 1	0.6	3.E-04

Order	Probe set	Symbol	Gene description	Ratio group #1/ other CIS	*P*
64	212840_at	KIAA0794	KIAA0794 protein	0.6	< 1e-07
65	1564164_at	FLJ20054	Hypothetical protein FLJ20054	0.6	< 1e-07
66	204566_at	PPM1D	Protein phosphatase 1D magnesium-dependent, delta isoform	0.6	4.E-06
67	226643_s_at	LOC134492	NudC domain containing 2	0.6	< 1e-07
68	228049_x_at		Transcribed locus	0.6	< 1e-07
69	217602_at	PPIA	Peptidylprolyl isomerase A (cyclophilin A)	0.5	8.E-06
70	215023_s_at	PEX1	Peroxisome biogenesis factor 1	0.5	6.E-07
71	1567213_at	PNN	Pinin, desmosome associated protein	0.5	< 1e-07
72	209160_at	AKR1C3	Aldo-keto reductase family 1, member C3	0.5	< 1e-07
73	205789_at	CD1D	CD1D antigen, d polypeptide	0.5	5.E-04
74	208750_s_at	ARF1	ADP-ribosylation factor 1	0.5	3.E-05
75	201151_s_at	MBNL1	muscleblind-like (Drosophila)	0.5	< 1e-07
76	212649_at			0.5	< 1e-07
77	229733_s_at	CBX6	Chromobox homolog 6	0.5	2.E-04
78	203603_s_at	ZFHX1B	Zinc finger homeobox 1b	0.5	7.E-05
79	201110_s_at	THBS1	Thrombospondin 1	0.5	1.E-06
80	1555226_s_at	C1orf43	Chromosome 1 open reading frame 43	0.5	3.E-05
81	1559249_at	ATXN1	Ataxin 1	0.5	2.E-06
82	204286_s_at	PMAIP1	Phorbol-12-myristate-13-acetate-induced protein 1	0.5	1.E-07
83	229204_at	HP1-BP74	Heterochromatin protein 1, binding protein 3	0.5	< 1e-07
84	219099_at	C12orf5	Chromosome 12 open reading frame 5	0.5	< 1e-07
85	213183_s_at	CDKN1C	Cyclin-dependent kinase inhibitor 1C (p57, Kip2)	0.5	2.E-06
86	218611_at	IER5	Immediate early response 5	0.5	< 1e-07
87	228638_at	MGC34648	Family with sequence similarity 76, member A	0.4	2.E-07
88	1566403_at	RNU68	RNA, U68 small nucleolar	0.4	< 1e-07
89	227897_at	RAP2B	RAP2B, member of RAS oncogene family	0.4	4.E-07
90	229397_s_at	GRLF1	Glucocorticoid receptor DNA binding factor 1	0.4	3.E-07
91	216609_at	TXN	Thioredoxin	0.4	1.E-07
92	222487_s_at	RPS27L	Ribosomal protein S27-like	0.4	< 1e-07
93	228746_s_at	H41	Hypothetical protein H41	0.4	3.E-06
94	230659_at	EDEM1	ER degradation enhancer, mannosidase alpha-like 1	0.4	3.E-04
95	213872_at	C6orf62	Chromosome 6 open reading frame 62	0.4	5.E-07
96	228030_at	RBM6	RNA binding motif protein 6	0.4	2.E-04
97	230333_at	SAT	Spermidine/spermine N1-acetyltransferase	0.4	5.E-07
98	201694_s_at	EGR1	Early growth response 1	0.3	6.E-07
99	227404_s_at	EGR1	Early growth response 1	0.3	3.E-07
100	212834_at	DDX52	DEAD (Asp-Glu-Ala-Asp) box polypeptide 52	0.3	< 1e-07
101	231193_s_at		CDNA clone IMAGE:4285619	0.3	< 1e-07
102	1559343_at	UBE3A	Ubiquitin protein ligase E3A	0.3	< 1e-07
103	244546_at	CYCS	Cytochrome c, somatic	0.3	< 1e-07
104	220494_s_at			0.3	2.E-05
105	232392_at	SFRS3	Splicing factor, arginine/serine-rich 3	0.3	< 1e-07
106	228834_at	TOB1	Transducer of ERBB2, 1	0.3	9.E-07
107	214395_x_at	EEF1D	Eukaryotic translation elongation factor 1 delta	0.3	1.E-07
108	214041_x_at	RPL37A	Ribosomal protein L37a	0.2	< 1e-07

Table S4. Genotyping of 5 *TOB1* SNPs in patients with mild (n = 62) or severe (n = 74) MS

		Logistic regression		Allele case-control	
Marker	Alleles	Genotype *P* value (FDR)	Trend *P* (FDR)	OR	Allele *P* (FDR)
rs11079937	A/G	0.2957 (0.4928)	0.1197 (0.1995)	1.55	0.075928 (0.1265)
rs9905480	C/T	0.4408 (0.5510)	0.8671 (0.8671)	1.01	0.951641 (0.9516)
rs9303568	C/T	0.9449 (0.9449)	0.7719 (0.8671)	0.93	0.767137 (0.9516)
rs4626	A/G	0.0515 (0.2200)	0.0142 (0.0710)	0.50	0.00882 (0.0441)
rs7221352	A/G	0.088 (0.2200)	0.0789 (0.1972)	1.74	0.02777 (0.0694)

FDR, false discovery rate.

Other Supporting Information Files

Table S1 (XLS)