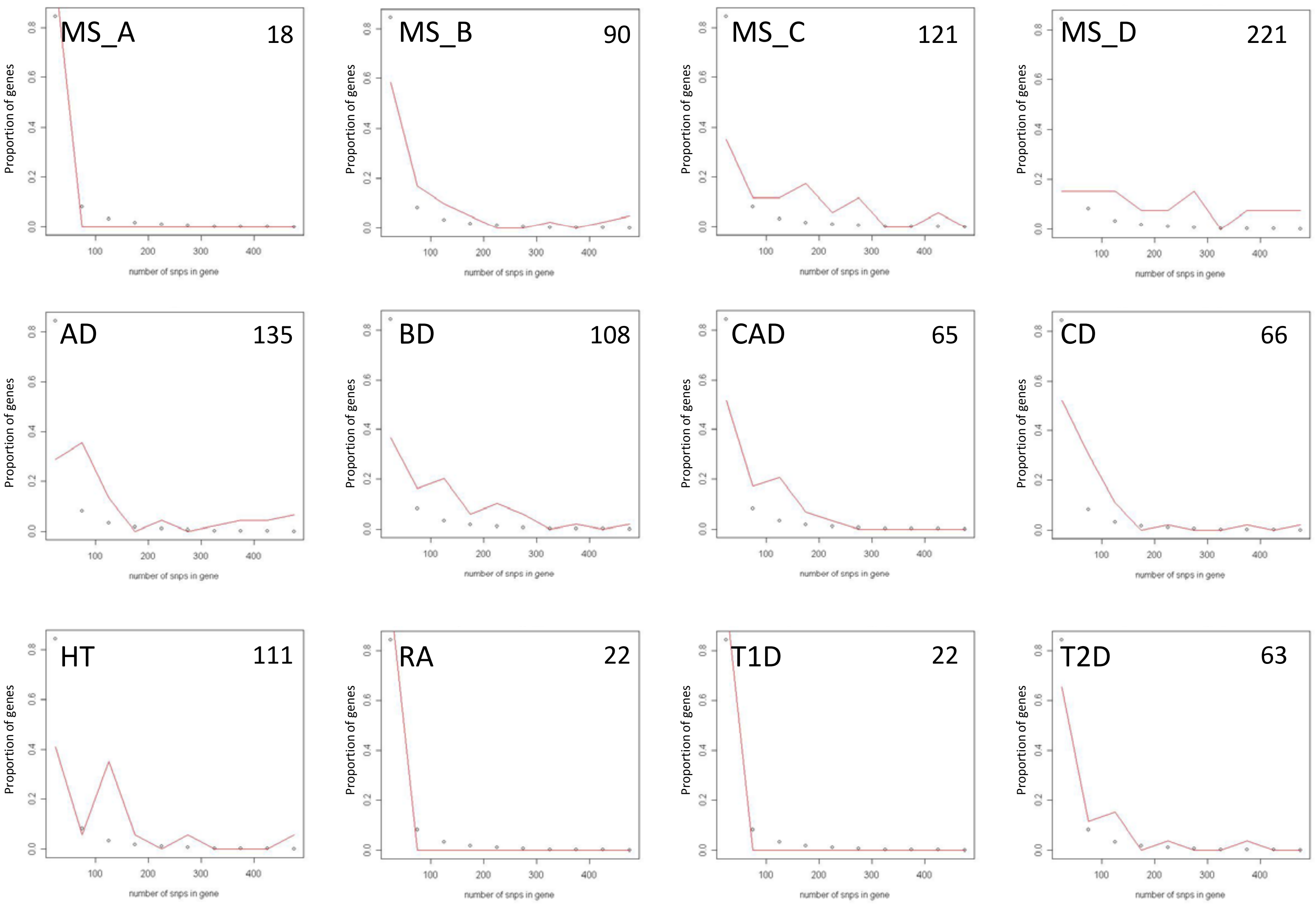

Supplementary Figure 1. Proportion of significant genes in a module as a function of gene size.
The red curve denotes the relationship for the modules described in the manuscript, while the black dots indicate the same relationship for a random sample of genes (background). The module for each disease is indicated in the top left corner and the average gene size (in number of SNPs) for that module is indicated in the top right corner of each panel. The average gene size for the background was 60.

Supplementary Table 1. Module identification in an expanded pathway dataset

The 25 most significant pathway modules in both our own genome scan and the IMSGC genome scan. These broadly identified the same core modules as our PINBPA approach, including immune and neural modules. Putative MS disease mechanisms are represented by a different color.

Rank	GeneMSA				IMSGC		PathwayID	Pathway Source: Pathway_Name	GeneMSA Genotypic P value gene summary			GeneMSA Trend P value gene summary			IMSGC P value gene summary		
	Geno_P	Geno_P_FDR	Trend_P	Trend_P_FDR	P-value	P_FDR			Pathway_genes	No_genes	Sig_genes	Pathway_genes	No_genes	Sig_genes	Pathway_genes	No_genes	Sig_genes
1	2.2E-03	3.2E-01	3.3E-03	3.3E-01	1.1E-10	4.2E-07	411	GO:Antigen Presentation: BP	25	18	9	25	18	11	25	20	11
2	1.4E-03	3.2E-01	9.6E-04	2.5E-01	3.5E-08	6.8E-05	408	GO:Antigen Presentation, Exogenous Antigen: BP	16	9	6	16	9	8	16	13	6
3	1.8E-05	2.3E-02	1.8E-05	2.2E-02	7.1E-08	9.1E-05	3572	NetPro:Morphogenesis:Neurogenesis	89	53	29	89	53	37	89	75	46
4	9.8E-04	3.2E-01	8.8E-04	2.5E-01	2.5E-07	2.4E-04	407	GO:Antigen Presentation, Exogenous Antigen Via MHC Class II: BP	11	7	6	11	7	7	11	9	6
5	1.8E-01	5.8E-01	1.3E-01	5.7E-01	5.3E-07	4.0E-04	413	GO:Antigen Processing: BP	17	14	6	17	14	8	17	12	8
6	7.9E-05	7.6E-02	9.1E-05	7.0E-02	1.9E-06	1.2E-03	438	GO:Axon Guidance: BP	76	48	28	76	48	29	76	62	42
7	1.1E-01	5.7E-01	4.4E-02	5.2E-01	2.6E-06	1.4E-03	613	GO:Detection Of Biotic Stimulus: BP	22	14	5	22	14	7	22	18	9
8	2.8E-03	3.2E-01	1.9E-03	3.0E-01	3.8E-06	1.8E-03	410	GO:Antigen Presentation, Peptide Antigen: BP	8	6	5	8	6	5	8	7	6
9	3.3E-02	5.4E-01	2.1E-02	4.7E-01	1.8E-05	7.2E-03	619	GO:Detection Of External Stimulus: BP	53	33	12	53	33	16	53	42	20
10	1.5E-02	4.6E-01	1.3E-02	4.4E-01	1.9E-05	7.2E-03	622	GO:Detection Of Pest, Pathogen Or Parasite: BP	9	7	4	9	7	5	9	7	5
11	1.7E-01	5.7E-01	1.3E-01	5.7E-01	2.3E-05	8.1E-03	508	GO:Cell Recognition: BP	21	17	6	21	17	8	21	16	11
12	9.1E-02	5.7E-01	3.2E-02	5.0E-01	4.3E-05	1.4E-02	624	GO:Detection Of Stimulus: BP	80	46	15	80	46	22	80	64	33
13	1.3E-03	3.2E-01	2.3E-04	1.5E-01	5.3E-05	1.6E-02	2925	Jubilant:Responsive Genes--Pain	74	47	24	74	47	30	74	68	44
14	1.1E-01	5.7E-01	2.7E-02	4.8E-01	8.3E-05	2.1E-02	1506	GO:Regulation Of T Cell Differentiation: BP	25	15	5	25	15	9	25	24	9
15	3.0E-04	1.6E-01	3.6E-04	1.7E-01	8.9E-05	2.1E-02	501	GO:Cell Fate Determination: BP	26	17	10	26	17	10	26	19	14
16	1.7E-06	6.7E-03	6.8E-07	2.6E-03	8.9E-05	2.1E-02	500	GO:Cell Fate Commitment: BP	86	54	30	86	54	34	86	70	41
17	1.3E-05	2.3E-02	2.2E-06	4.2E-03	1.0E-04	2.3E-02	1226	GO:Positive Regulation Of Development: BP	81	48	30	81	48	36	81	72	38
18	2.8E-01	6.3E-01	1.5E-01	5.8E-01	1.2E-04	2.5E-02	399	GO:Angiogenesis: BP	99	66	23	99	66	34	99	87	48
19	1.0E-01	5.7E-01	1.2E-01	5.7E-01	1.4E-04	2.8E-02	663	GO:Embryonic Pattern Specification: BP	35	20	10	35	20	13	35	28	18
20	1.9E-03	3.2E-01	3.0E-03	3.3E-01	1.8E-04	3.4E-02	3542	NetPro:Lymphocyte activation:Natural killer cell activation	50	27	15	50	27	16	50	44	18
21	5.0E-02	5.4E-01	3.8E-02	5.2E-01	1.9E-04	3.5E-02	1660	GO:T Cell Differentiation: BP	44	28	11	44	28	16	44	42	15
22	3.7E-02	5.4E-01	1.9E-01	5.9E-01	2.2E-04	3.8E-02	3835	Glutamate receptors	61	43	17	61	43	19	61	51	31
23	1.9E-01	5.8E-01	2.0E-01	5.9E-01	2.8E-04	4.7E-02	412	GO:Antigen Processing, Exogenous Antigen Via MHC Class II: BP	6	4	2	6	4	3	6	5	4
24	3.2E-01	6.6E-01	1.2E-01	5.7E-01	3.2E-04	4.8E-02	3767	NetPro:Transmembrane receptor activity:Glutamate receptor activity	38	21	9	38	21	11	38	34	24
25	1.9E-04	1.2E-01	4.9E-05	4.7E-02	3.2E-04	4.8E-02	1214	GO:Positive Regulation Of Cell Differentiation: BP	59	34	21	59	34	25	59	52	27

Disease Hypothesis:
Green: Neurogenesis
Red: Known MS pathways
Orange: Immune hypothesis
Blue: Cell fate and differentiation