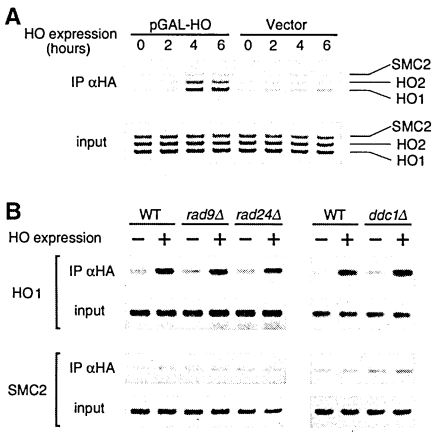

Fig. 5. Association of Mec1 with sites near the HO-induced DSB. (**A**) Kinetics of Mec1 association with DSB. (**B**) Effect of the *rad9Δ*, *rad24Δ*, and *ddc1Δ* mutations on Mec1 association with DSB. Cells transformed with pGAL-HO or the control vector were processed and subjected to a chromatin immunoprecipitation assay, as in Fig. 2B (A) and Fig. 2C (B). Strains used (*11*) contain *MATα* and *MEC1-HA*.

the association of Mec1 with DNA lesions remains to be determined. ATR and hRad9 are human homologs of Mec1 and Ddc1, respectively (*1*), and localize to nuclear foci that may contain regions of damaged DNA (*27*, *28*). Because homologs of the checkpoint genes have been identified in other species, it is likely that the mechanism described here is conserved in the checkpoint control among eukaryotic cells.

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17. Yeast cells were cultured in medium containing 2% sucrose, and then one-half of the culture was maintained in sucrose and the other half was incubated with 2% galactose to induce *HO* expression. Cells were converted to spheroplasts with the use of oxalyticase (50 μg/ml) in 50 mM Hepes-KOH (pH 7.5); 100 mM NaCl; 0.4 M sorbitol; 50 mM NaF; 5 mM PNPP; 1 mM Na3VO4; 0.5 mM PMSF; aprotinin (13 μg/ml); leupeptin (5 μg/ml); pepstatin (5 μg/ml); and 1 mM benzamidine. Spheroplasts were lysed by adding Triton X-100 (0.25%) and were subsequently cross-linked with 1% formaldehyde for 15 min at 4°C. Immunoprecipitation of cross-linked DNA was performed essentially as described (*29*) with the use of monoclonal antibody 12CA5 to HA. DNA was also purified from the whole cell extract (designated "input"). PCR was done in 50-μl volumes containing 1/25 of the anti-HA antibody immunoprecipitates or 1/1200 of input, respectively. The PCR products were separated in 2% agarose gels and were stained with ethidium bromide. The sequences of primers for the are as follows: HO1 set at *MATα* locus, 5′-CCAGATTTGTATTAGACGAGGGACGGAG-TGA-3′ and 5′-AGAGGGTCACAGCACTAATACAGC-TCGTAAT-3′; HO2 set at *MATα* locus, 5′-GGTG-TCCTCTGTAAGGTTTAGTACTTTTGT-3′ and 5′-CA-CAGATGAGTTTAAATCCAGCATACTAGACA-3′; and *SMC2* locus 5′-AAGAGAAACTTTAGTCAAAACAT-GGG-3′ and 5′-CCATCACATTATACTAACTACGG-3′.
18. Cells were processed and incubated with mouse antibody to HA (16B12; Babco, Richmond, CA). Antibody binding was detected using Cy3-conjugated anti-mouse antibody (Jackson ImmunoResearch, West Grove, PA).
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30. We thank M. P. Longhese, G. Lucchini, and T. Weinert for materials; we also thank J. Haber, H. Araki, M. Lamphier, N. F. Lowndes, and H. Masumoto for critical reading, discussion, and suggestion. Supported by grants from the Ministry of Education, Science, Sports and Culture of Japan.

26 June 2001; accepted 20 August 2001

The Plasticity of Dendritic Cell Responses to Pathogens and Their Components

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Dendritic cells are involved in the initiation of both innate and adaptive immunity. To systematically explore how dendritic cells modulate the immune system in response to different pathogens, we used oligonucleotide microarrays to measure gene expression profiles of dendritic cells in response to *Escherichia coli*, *Candida albicans*, and influenza virus as well as to their molecular components. Both a shared core response and pathogen-specific programs of gene expression were observed upon exposure to each of these pathogens. These results reveal that dendritic cells sense diverse pathogens and elicit tailored pathogen-specific immune responses.

How organisms respond appropriately to the wide variety of pathogens and antigens they encounter on a daily basis remains a central question in immunology. It has recently been shown that pattern recognition receptors expressed on immune cells contribute to the specific detection of pathogens (*1*, *2*). However, the downstream target genes induced by the different pathogens have not been fully determined. The importance of dendritic cells (DCs) in initiating immune responses led us to investigate at a genetic level how DCs discriminate different pathogens (*3*). DCs reside in an immature state in most tissues, where they recognize and phagocytose pathogens and other antigens (*4*). Direct contact with many pathogens leads to the maturation of DCs, which is characterized by an increase in antigen presentation, expression of costimulatory molecules, and subsequent stimulation of naïve T cells in lymphoid organs (*4*). The extensive reprogramming of DCs during maturation prompted us to measure the corresponding changes in gene expression. We used oligonucleotide microarrays (*5*) to test to what extent DCs discriminate between phylogenetically diverse pathogens and whether the commonly studied molecular components of these pathogens are sufficient to account for the live pathogen response.

Human monocyte-derived DCs (*6*) were exposed to a diverse set of organisms and com-

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pounds: a Gram-negative bacterial species, *E. coli*, and its cell wall component, lipopolysaccharide (LPS); a fungus, *C. albicans*, and yeast cell wall–derived mannan; and an RNA virus, influenza A, and double-stranded RNA (dsRNA). DCs were cultured (*6*) with pathogens or their components between 1 and 36 hours (*7*) and RNA was isolated, labeled, and hybridized to microarrays (*8, 9*). Each pathogen stimulation was repeated in three independent donors, and each component stimulation was repeated in two donors. Genes with expression levels that changed in response to stimuli (termed regulated genes) were selected on the basis of repeated differences in the expression levels of the treated and untreated samples across multiple time points (*10*). Of the ~6800 genes represented on the oligonucleotide array, a total of 1330 genes changed their expression significantly upon encounter with one of the pathogens or components (*10*). Such a large-scale change in gene expression demonstrated that DCs are able to undergo a marked transformation in their cellular phenotype.

Analysis of the individual responses to pathogens showed that a unique number of genes was regulated by each pathogen. Influenza and *E. coli* were able to modulate the expression of exclusive subsets of genes (Fig. 1, A and C) (*11*), whereas *C. albicans* only modulated the expression of a subset of *E. coli*–regulated genes (Fig. 1B). In addition, gene expression was most rapidly induced by *E. coli*, less rapidly by *C. albicans*, and most slowly by influenza (*12*).

The intersection of the three different pathogen responses revealed a common set of 166 highly regulated genes (Fig. 1, A and D). To describe the dynamics of DC response after exposure to any of the three pathogens, we classified these genes according to their kinetics of expression and known biological functions (Fig. 2) (*13*). Immediately after contact with any of the three pathogens, a rapid decline was observed in the transcript levels of genes associated with phagocytosis and pathogen recognition (Fig. 2B). At the same time, there was a transient increase in the expression of immune cytokines, chemokines, and receptors that contribute to the recruitment of monocytes, DCs, and macrophages to the site of infection. Also strongly induced was a set of cytoskeletal genes that may potentially mediate shape change and migratory behavior of activated DCs. The induction of signaling genes and transcription factors in the middle phase may be involved in preparing the DC to be receptive to regulatory signals in the lymphatics and lymph nodes. In addition, several antigen processing and presentation genes were induced to high levels in a sustained fashion. Genes involved in generating reactive oxygen species (ROS) were induced across the time course, which suggests that infecting organisms are killed throughout DC maturation and migration. Finally, during the late phase, chemokine receptors known to mediate responses to lymph node chemokines, thereby mediating DC migration, were up-regulated (*14*). The set of 166 genes described here thus constitutes part of a core DC response. This response is elicited independently of pathogen characteristics and unfolds as a temporally ordered cascade that modulates both innate and adaptive immune responses (Fig. 2C).

In contrast, analysis of the *E. coli*–specific genes (Table 1 and Fig. 1E) showed that DCs also strongly and rapidly up-regulated most innate immune genes on the array, including inflammatory cytokines, neutrophil- and monocyte-attracting chemokines, and prostaglandin pathway components. This potent inflammatory response probably is partially counteracted by interleukin-10 (IL-10) that is induced in the middle phase. At later times, genes that regulate the adaptive immune response were induced, including T cell–stimulating genes, secreted cytokines, and a subset of chemokines that are thought to attract naïve T_H2 T helper cells (*15*). An unexpected class of cytokine receptors that share a

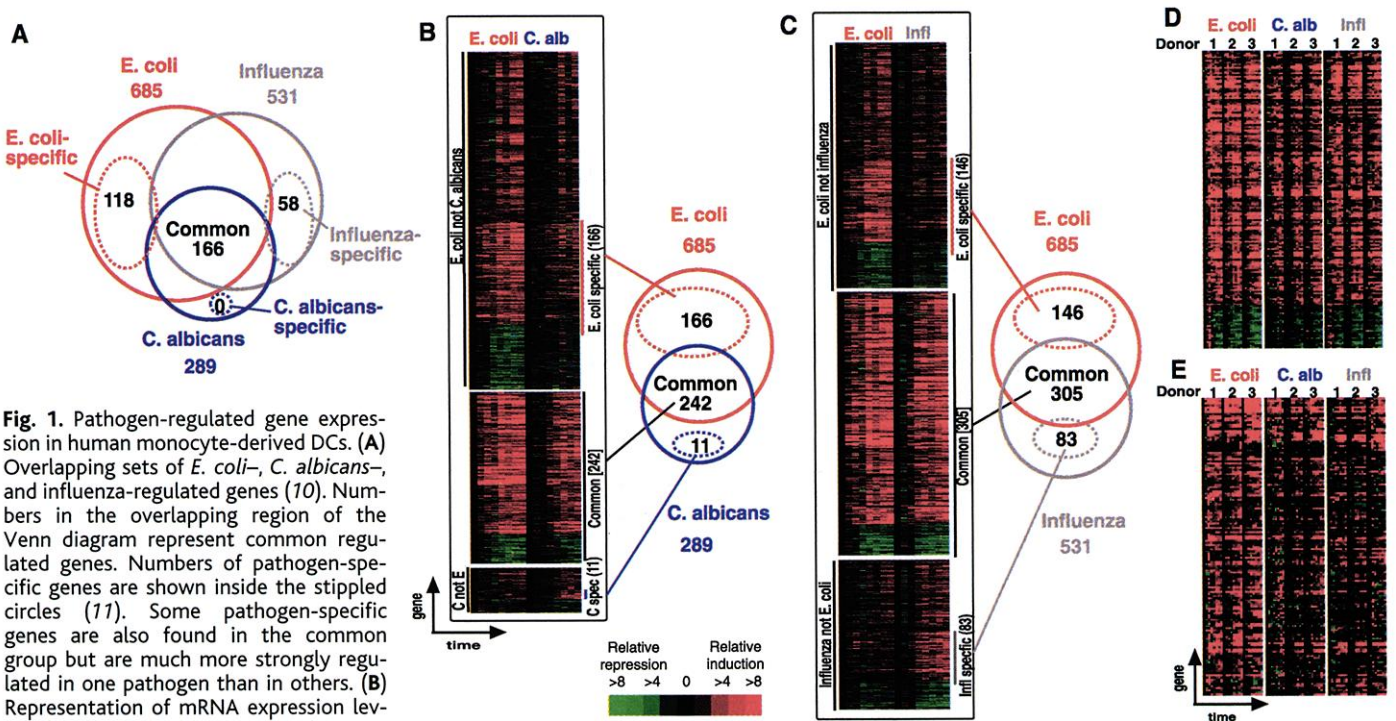


Fig. 1. Pathogen-regulated gene expression in human monocyte-derived DCs. (**A**) Overlapping sets of *E. coli*–, *C. albicans*–, and influenza-regulated genes (*10*). Numbers in the overlapping region of the Venn diagram represent common regulated genes. Numbers of pathogen-specific genes are shown inside the stippled circles (*11*). Some pathogen-specific genes are also found in the common group but are much more strongly regulated in one pathogen than in others. (**B**) Representation of mRNA expression levels at 0, 1, 2, 4, 8, 12, and 24 hours in response to *E. coli* and *C. albicans*. Each gene is represented by a single row of colored bars, and each time point is represented by a single column. Color bars represent the ratio of hybridization measurements between corresponding time points in the pathogen and control medium profiles, according to the scale shown. Genes are placed in groups corresponding to pairwise overlaps shown in accompanying Venn diagrams. From top to bottom: *E. coli*– but not *C. albicans*–regulated genes; common regulated genes; *C. albicans*– but not *E. coli*–regulated genes. (**C**) Gene profiles and overlaps for *E. coli* and influenza. (**D** and **E**) Gene expression of common response genes [(D), see also Fig. 2] and differential response genes [(E), same genes as in Table 1] in three independent donors.

common γ chain (IL-2R, IL-7R, IL-15R, and IL-4R) were also induced. The expression of these receptors may allow DCs to respond to lymphocyte-derived interleukins within the lymph node.

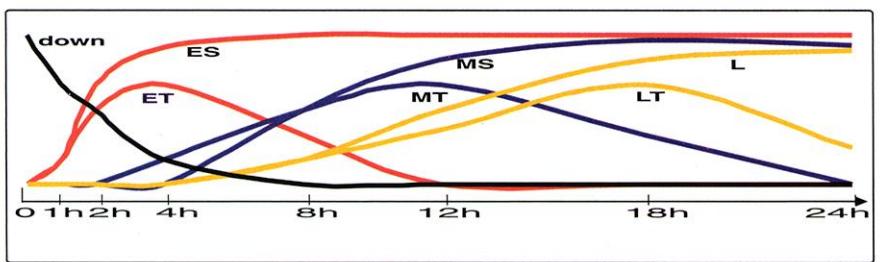
All these immunostimulatory responses may be enhanced through induction of additional induced gene families (Table 1) (*12*)—for example, cell stress genes that modulate levels of antimicrobial ROS, antiapoptotic genes that may extend the lifetime of the infected DC (*16*), and the late-expressing matrix metalloproteases that may allow processing of cytokines and DC migration to lymph nodes (*17*). Genes with undefined roles in DC function were also regulated by *E. coli*, including signaling molecules, transcription factors, adhesion molecules, and many of the glycolytic genes. HIF1α, a known transcription factor of glycolysis genes, was also up-regulated (*18*). Collectively, these diverse changes of gene expression in response to *E. coli* and LPS reflect a significant cellular and immunological reprogramming of the DC.

Relative to the response of DCs to *E. coli*, their response to *C. albicans* was greatly attenuated in many functional categories and constituted a subset of the *E. coli* response, with a much smaller number of immune genes and with no robust *C. albicans*–specific genes (Fig. 1, A and B, and Table 1). Because many of the immune genes are known to be regulated by the transcription factor NF-κB (*19*), this difference may be partially explained by the relatively weak NF-κB up-regulation (Table 1).

DCs regulated a large number of genes in response to influenza, comparable to the number regulated in response to *E. coli*. However, the innate immune response was relatively weak and completely devoid of genes capable of stimulating neutrophils, as confirmed by a neutrophil chemotaxis assay (*12*). The adaptive response to influenza was also distinct from the response to *E. coli*. The antiviral genes—those encoding interferon (IFN) α and β—were strongly induced, as were the interferon-inducible chemokine genes (Table 1). This suggests possible effects on induction and migration of naïve T_H1 cells (*15*). An important subset of genes induced by influenza are linked with the inhibition of the immune response at certain stages. These include proapoptotic genes that may lead to early death of infected cells (*16*) as well as genes encoding mcp-1, which can block IL-12 production in macrophages (*20*); HLA-E, which can inhibit natural killer cells (*21*); Gfrp, a close homolog of a protein that inhibits NO synthesis (*22*); and IDO, which can inhibit T cell activation (*23*). Influenza also modulated the expression of a large set of genes involved in diverse cellular functions and whose contribution to pathogen-host interactions may not have been studied previously (*12*).

To further dissect the ability of DCs to discriminate pathogens, we investigated whether individual pathogen components were sufficient to elicit these differential pathogen responses. Despite additional active molecules known to be present on bacteria, LPS was able to mimic and account for almost the entire bacterial response (Fig. 3A). Unexpectedly, the fungal component mannan mimicked the magnitude and biological character of the bacterial response more closely than it did the fungal or viral response profiles (Fig. 3, A and B) (*12*). Although dsRNA was a less potent stimulator of the bacterial response, it did elicit a strong innate response com-

A



B

Functional Category	EARLY		MIDDLE		LATE	
	Transient	Sustained	Transient	Sustained	Transient	Sustained
Phagocytosis		beta-adaptin,ap2m1, clathrin coat, MMR				
Translation		ribosomal genes, sui1	wars			
Innate immune response and inflammation	tnfa, il6, mip1a, mip1b, a20, cox-2, oas2	il1b, il8, histamineR cox1, rp105	il1rn, ptgir			
Cytoskeleton	macs, b-tubulin,	snl	tctel1			
Apoptosis	ipl	ciap2,casp7	trail, bcl2-a1			
Receptors+adhesion	ccr6	il10ra, cd33	il7r		cd97	nk4
Signaling	ptp4a1,lcp2, minor, pkr,	ptp1b,pim1,traf1,ikba dusp2, fes, syk, lxra adenosineR,plcb2, itpk, ppp1r7,RhoGap4	mx1, mx2, dusp4, igfbp4, ecgf, lgals9, myd88, lyn	adm, plaur. bst2 tnfaip6		
Transcription	irf1, tcpc4, nrf2	atf4	stat1, irf7, irf1, aml2, id2, staf50	myl		
Protein degradation			psma4, psma3			
T cell regulation		icam1	rantes, slam, mcp1, inp10, mig			mcp2
Cell stress and radical homeostasis		ninj1, ncf1	mt2a,hspf4,rcn1	copt2, sod2, thioredoxin	mt1h	
Antigen presentation		pa28a	pa28b	hla, lmp2, tap1, tap2		lmp7, hla
Migration to lymph node						ccr7, cxcr4

C

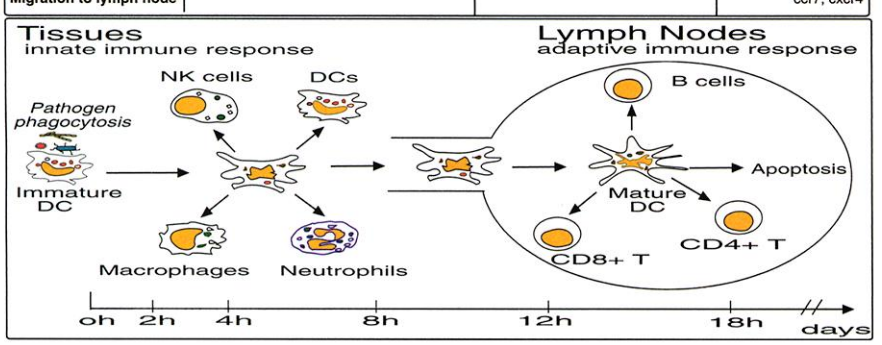


Fig. 2. Expression kinetics of common response genes in DCs. (**A**) Schematic transient (T) and sustained (S) gene expression profiles based on self-organizing map clusters of up-regulated genes (*38*). Temporal clustering of up-regulated genes is based on the expression kinetics of *E. coli*–responsive genes (E, early; M, middle; L, late). Down-regulated genes (down) were placed into a single cluster. (**B**) Function of genes regulated at different times in response to any pathogen; underlined genes are down-regulated; all others are up-regulated. GenBank accession numbers are listed in (*12*). (**C**) Stages in DC life: encounter and phagocytosis of pathogens, activation of the innate immune response, migration to the lymph node, antigen presentation and stimulation of the adaptive immune cells, and apoptosis.

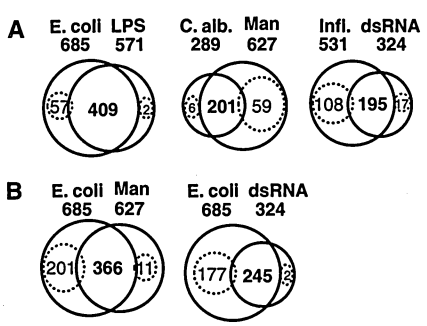


Fig. 3. Relation between pathogen- and component-responsive genes. (**A**) Overlapping sets of pathogen-regulated and corresponding component-regulated genes (as in Fig. 1). (**B**) Comparison of *E. coli*–regulated and other component-regulated genes.

parable to that induced by bacteria, and at the same time elicited aspects seen in the viral response (Fig. 3, A and B) (*12*). Thus, all three components were able to elicit the expression of many innate immune genes as well as most of the genes in the common pathogen response. This finding shows that the core DC program can be triggered by multiple stimuli with diverse molecular structures.

Genome-scale studies of DC transcriptional responses have allowed us to demonstrate the existence of common and differential pathogen recognition pathways. Although there have been reports of changes in gene expression in DCs in response to LPS, the response to pathogens has not been thoroughly investigated (*24, 25*). Differential immune responses to pathogens have been described in clinical and animal studies (*26–28*), and we show here that these responses are reflected by changes in DC gene expression.

The temporal cascade of gene expression in the common response to pathogens [which is also induced by Gram-positive *Staphylococcus aureus (29)*] accounts for core DC functions and delineates the essential role of DCs in linking innate recognition of pathogens with antigen presentation and the development of an adaptive T cell response (*30–33*). The existence of this common response reflects a convergence of pathways from receptors that are known to distinguish some of these components and pathogens. In contrast, the presence of pathogen-specific gene expression in most functional categories (including transcription factors and cytokines) suggests that distinct pathways are activated by different pathogens. These differential responses demonstrate that human monocyte-derived DCs are flexible in their responses and may even exhibit a diversity of responses similar to that of the different DC subtypes (*34, 35*).

The extensive plasticity of the DCs observed in our experiments indicates that the concept of DC maturation cannot be simply defined by the modulation of a standard set of markers (*4*). Instead, we propose that DCs not only are capable of generating a core response to any pathogen, but also exhibit stimulus-specific maturation and activation. For each stimulus, particular subsets of genes are modulated and lead to important physiological consequences. There is likely to be even more differential regulation in vivo, depending on DC subtype, cell interactions, and tissue location. Determining whether these unique responses are advantageous to the pathogen, or to the host, is essential for understanding host-pathogen interactions (*36*). Further studies of these pathogen-regulated genes may thus enhance our understanding of DC maturation and provide future targets for immunotherapy.

Table 1. Functional categories of genes regulated differentially in response to *E. coli*, *C. albicans*, and influenza. Code: +, gene expression is up-regulated in response to pathogen; −, gene expression is not changed; ++ and +++, gene expression is changed at a higher level relative to other pathogens that regulate the same gene (each + denotes increased expression by a factor of ~2.5); +/−, gene expression is regulated in a subset of donors; d, gene expression is down-regulated.

Gene	GenBank accession no.	*E. coli*	*C. albicans*	Influenza
		Innate		
Neutrophil				
il8	Y00787	+++	+	+
gro1	X54489	+++	+	+/−
gro2	M57731	+++	+	+/−
gro3	X53800	++	+/−	+/−
Inflammation				
tnfα	X02910	++	+	+
il1β	X04500	+++	+	+
il6	X04602	++	+	+
il1α	M28983	+	−	−
gcsf	X03656	++	−	−
mip1β	M69203	++	+	++
mip3α/larc	U64197	++	+/−	+/−
mip3β/elc	U77180	+	+/−	+/−
bf	L15702	++	+	+/−
Prostaglandin/leukotriene				
ptgir	D38128	++	+	+
ptger4a	L28175	−	−	+
cox2	U04636	++	+	+
		Adaptive		
T cell: T_H1				
il12b/p40	M65290	++	+	−
itac	U59286	+	+	++
mig	X72755	+	+	++
inp10	X02530	+	+	++
ifnβ1	V00535	+	−	++
ifnα2	J00207	−	−	+
ifnα13	J00210	−	−	+++
ifnα14	V00533	−	−	+
ifnα16	M28585	−	−	+
T cell: T_H2				
tarc	D43767	++	+	+/−
mdc	U83171	+	+	+/−
T cell stimulation				
41bbL	U03398	++	−	+/−
slam	U33017	+++	+	+
cd86	U04343	+	+	+
icam1	M24283	++	+	++
ebi3	L08187	++	+	−
Antigen presentation				
β2m	J00105	++	−	++
lmp10	X71874	+	+	+/−
B cell				
pbef	U02020	+++	+	+
		Immune receptor		
il15rα	U31628	++	+/−	+
il7r	M29696	++	+	+
il2r	X01057	+	+/−	−
il4r	X52425	+	+	+/−
gmcsfr	X17648	+	+/−	−
il3r	D49410	+	+	−
41bb	U03397	+++	+/−	++
tnfr2	M32315	++	−	−
il13rα1	Y10659	++	++	−
cd155	M24406	+++	−	−
cd83	Z11697	++	++	++
		Immune transcription		
nfκb p52	S76638	++	+/−	+
nfκbp50	M58603	++	+/−	++
nfκb p65	L19067	+	+	+
nfκb relB	M83221	+	+/−	−
stat5a	U43185	++	+	−

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6. Elutriated human monocytes (Advanced Biotechnology Inc.) were differentiated into DCs for 7 days in standard conditions with granulocyte-macrophage colony-stimulating factor (GM-CSF) and IL-4 (*12*, *30*).
7. Pathogens or their components were added to DC cultures (10^7 cells per plate per time point) at day 7 at the following amounts: *E. coli* SD54 (ATCC) [multiplicity of infection (MOI) 5:1], *Influenza* A/PR/8/34 (750 HAU/ml), *Candida albicans* HLC54 (5:1 MOI), LPS from *E. coli* 055:B5 (1 μg/ml, Sigma L-2880), polyinosine-polycytidine (25 μg/ml, Pharmacia; endotoxin levels were *S. cerevisiae* (1 mg/ml, Sigma M-7504). See (*12*).
8. Total RNA at each time point was isolated, labeled, and prepared for hybridization to HuGeneFL oligonucleotide arrays (Affymetrix) using standard methods (*12*, *37*).
9. Gene expression measurements were stored, analyzed, and visualized using a set of database and analysis tools developed in the lab. Messenger RNA expression kinetics and induction levels were validated with enzyme-linked immunosorbent assay (ELISA) measurement of tumor necrosis factor (TNF) α, IL-12/p40, IL-10, and MCP-1 protein levels (*12*).
10. A scoring system was developed to measure significant change in stimulated expression levels relative to control time course. We collected a time series of mRNA fluorescence levels, $R = \{R_1, R_2, R_3, \ldots, R_n\}$, in DCs exposed to each pathogen or compound, and a control series of mRNA levels, $C = \{C_1, C_2, C_3, \ldots, C_n\}$, in untreated DCs from the same donor. R_i and C_i are steady-state mRNA hybridization measurements ("average difference" in Affymetrix terminology) at the *i*th time point; *n* is the total number of time points. We devised a score, $S_i = (R_i - \mu_C)/\sigma_C$, to measure deviation of the stimulated expression level at one time point, R_i, from the mean, μ_C, of all the time points in the control time course. By using σ_C, the standard deviation of the control time course, the score penalizes genes with high noise in the media control, thus allowing us to extract the most robust data. Up-regulated and down-regulated genes were selected according to criteria described in (*12*).
11. Stimulus-specific genes (Figs. 1 and 3, stippled circles) were selected if the ratio of relative expression levels between stimuli was larger than 2.5, or if the data passed a stringent stimulus-specific filter based on the score (*12*).
12. Supplementary information is available on *Science* Online (www.sciencemag.org/cgi/content/full/294/5543/870/DC1) and our lab's Web site (http://web.wi.mit.edu/hacohen/dc).
13. A self-organizing map algorithm (*38*) was used to cluster genes on the basis of similarity of their temporal expression profiles and allowed us to classify genes into six groups: genes that peak at early, middle, or late phases of the time course, and, for each of these, genes that are expressed transiently or in a sustained fashion (Fig. 2A). We also assigned each of the regulated genes to functional categories according to the public databases and the Proteome annotated database (Human PSD, kindly provided through a collaboration with Proteome Inc.).
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Table 1. *Continued*

Gene	GenBank accession no.	*E. coli*	*C. albicans*	Influenza
stat4	L78440	++	+	–
stat3	L29277	+	+	+/–
irf2	X15949	+	–	+
irf4	U52682	+	+/–	+/–
isgf3	M87503	+	+/–	+
csda	M24069	++	–	–
		Glycolysis and energy		
eno1	M14328	+	–	d
pk3	X56494	++	–	+/–
tpi	J04603	+	–	–
gys	J04501	+	–	d
pgm1	M83088	+	+/–	d
gk	X69886	+	+/–	–
pfkp	D25328	+	–	–
pgk1	V00572	+	–	+/–
g3pdh	X01677	+	–	+/–
ldh1	X02152	+	–	+/–
pgd	U30255	+	–	+/–
pgam1	J04173	+	+	+
hif1α	U22431	+	–	+/-
		Apoptosis		
Inhibitor				
pai2	M31551	++	–	–
iex-1	S81914	++	+	–
tax1bp1	U33821	+	–	+/–
flip	AF005775	++	+	+/–
bag1	Z35491	+	+	+/–
ciap2	U37546	++	++	+
bcl2-a1	U29680	++	+	+
mcl1	L08246	+	–	+
tau	X56468	+/–	+/–	++
Activator				
casp4	U28014	++	+	+/–
nip3	U15174	++	+/–	–
trail	U37518	+	+	++
fas	X63717	+	+	+
casp5	U28015	+	–	+
bak1	U16811	+/–	+/–	+
pmaip1	D90070	+	–	++
casp10	U60519	+/–	+	+
		Growth factors and receptors		
tgfa	X70340	+	–	–
ndp	X65724	+++	–	–
wnt5a	L20861	+++	+/–	–
activinβa	X57579	+++	++	+
p2x4	AF000234	+	+	–
vdr	J03258	+	+/–	–
		Tissue remodeling		
mmp9	J05070	+/–	+	–
mmp7	L22524	++	–	–
mmp3	X05232	+	–	–
mmp19	X92521	+	+/–	+/–
mmp14	Z48481	++	–	+/–
mmp12	L23808	++	+	–
mmp10	X07820	+	–	–
mmp1	X54925	+	–	–
lad1	U42408	+	–	+/–
extl2	U76189	+/–	+	+/–
collagen-a1	M55998	+	–	–
tnr	X98085	+	–	+/–
		Cell stress		
mt1g	J03910	+++	+/–	+/–
mt1e	M10942	+++	+/–	+/–
btg2	U72649	++	+/–	–
fth1	L20941	++	+	–
quiescin	L42379	++	+/–	–
cagb	M26311	++	–	+/–

Table 1. *Continued*

Gene	GenBank accession no.	*E. coli*	*C. albicans*	Influenza
ddit1	M60974	++	–	+/–
map3k4	D86968	++	+/–	+/–
mt1l	X76717	++	–	+/–
mt1h	X64177	++	+	+
mt2a	V00594	++	+	+
hspa1a	M11717	++	+/–	++
ninj1	U72661	++	+	++
sod2	X07834	++	+	++
atox1	U70660	+	+	–
hspa6	X51757	+	+/–	–
krs1	U26424	+	+/–	–
mt1a	K01383	++	–	–
mt1f	M10943	+	–	–
rtp	D87953	++	+/–	–
cyp450db1	X07619	+	+/–	+/–
gst12	U46499	+	–	+/–
hsf4	D87673	+	–	+/–
hspa4	L12723	+	–	+/–
dusp1	X68277	+	–	+
mtf	X78710	+	–	+
hsp70	U10284	+/–	–	+
hsp27	Z23090	–	+/–	+++
cbr1	J04056	+/–	+	+
		Immune inhibitors		
mcp1	S69738	+	++	++
il10	U16720	++	–	–
hla-e	X56841	–	–	+
gfrp	U78190	d	–	+
ido	M34455	++	+/–	++

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39. We thank T. Golub, M. Gaasenbeek, and C. Ladd for resources and training for microarray experiments; F. Lewitter and K. Roach for contributions to data analysis and bioinformatics; J. Richmond, J. Nau, and Q. Feng for advice and reagents; and D. Sabatini, G. Fink, T. Golub, L. Van Parijs, M. Albert, and R. Khosravi-Far for discussions and critical reading of the manuscript. Supported by grants from the Whitehead Institute Fellows Program, Affymetrix, Bristol Myers Squibb, Millennium Pharmaceuticals, Rippel Foundation, and Hascoe Foundation.

12 July 2001; accepted 17 August 2001