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rived from the three major Eurasian founder haplogroups, M, N, and R, which are also found alongside one another to the west in the Indian subcontinent (15) as well as throughout continental Asia (25, 28).

The very similar ages of haplogroups M, N, and R indicate that they were part of the same colonization process [see (23)]. This most likely involved the exodus of a founding group of several hundred individuals (27) from East Africa, some time after the appearance of haplogroup L3 ~85,000 years ago, followed by a period of mutation and drift during which haplogroups M, N, and R evolved and the ancestral L3 was lost. Although the details of this period remain to be elucidated, the next stage is much clearer. The presence in each region of the same three founder haplogroups, but differentiated into distinct subhaplogroups, indicates that there was a rapid coastal dispersal from ~65,000 years ago around the Indian Ocean littoral and on to Australasia. Firm minimum archaeological age estimates are somewhat more recent—~50,000 years for Australia (30) and ~45,000 years for southeast Asia (31)—but early evidence may have been lost to sea level rises. Moreover, human populations may then have diffused from the coast into the continental interiors more gradually, leaving a greater archaeological signature on the landscape as they grew in size.

This evidence suggests that this coastal trail was likely the only route taken during the Pleistocene settlement of Eurasia by the ancestors of modern humans, and that the primary dispersal process, at least from India to Australasia, was very rapid. A founder analysis of western, southern, and eastern Eurasian and Australasian complete mtDNAs suggested a shallow gradient of arrival times, from ~66,000 years ago in India to ~63,000 years ago in Australasia (table S4). Assuming a distance of ~12,000 km, this allowed us to estimate a dispersal rate of ~4 km/year from point estimates, a little lower than estimates for the more recent expansion into the Americas (32). An approximate lower bound on the dispersal rate is ~0.7 km/year, comparable to the recolonization of Europe after the ice age (33).

By contrast with South Asians, eastern Eurasians, and Australasians, western Eurasians have a high level of haplogroup-level diversity within haplogroups N and R, but lack haplogroup M almost entirely (34). The colonization of western Eurasia has usually been thought to have been the result of a “northern route” dispersal out of Africa, through North Africa and the Levant (4), but the close similarity of the mtDNA founder age to that of India (table S4) suggests that it was most likely the result of an early offshoot of colonization along the southern route, followed by a lengthy pause until the climate improved (26) and the ancestors of western Eurasians were able to

enter the Levant and Europe. This implies that the subsequent Upper Paleolithic “revolution” in western Eurasia was one regional indication of the emergence of modern humans, rather than a radical break with the past (35).

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36. Supported by United Productions and the Discovery Channel, the British Academy, the Royal Society, the University of Huddersfield, the Wellcome Trust, the Italian Ministry of the University (Progetti Ricerca Interesse Nazionale 2003), Progetto CNR-MIUR Genomica Funzionale-Legge 449/97, Grandi Progetti di Ateneo (Università La Sapienza), the Muzium Negara Malaysia (Kuala Lumpur), and the Universiti Putra Malaysia. We thank the Malaysian participants for providing cheek-swab samples and J. Clegg and A. S. Sofro for Indonesian samples.

## Supporting Online Material

www.sciencemag.org/cgi/content/full/308/5724/1034/DC1  
Materials and Methods  
Fig. S1  
Tables S1 to S4  
References

14 January 2005; accepted 24 March 2005  
10.1126/science.1109792

## Induction of Protein Secretory Pathway Is Required for Systemic Acquired Resistance

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In plants, systemic acquired resistance (SAR) is established as a result of NPR1-regulated expression of pathogenesis-related (PR) genes. Using gene expression profiling in *Arabidopsis*, we found that in addition to controlling the expression of PR genes, NPR1 also directly controls the expression of the protein secretory pathway genes. Up-regulation of these genes is essential for SAR, because mutations in some of them diminished the secretion of PR proteins (for example, PR1), resulting in reduced resistance. We provide evidence that NPR1 coordinately regulates these secretion-related genes through a previously undescribed cis-element. Activation of this cis-element is controlled by a transcription factor that is translocated into the nucleus upon SAR induction.

SAR is a plant immune response that is induced after a local infection and confers resistance throughout the plant to a broad spectrum

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of pathogens (1). Induction of SAR requires accumulation of the endogenous signaling molecule salicylic acid (SA), which activates gene expression mediated by the master regulator protein NPR1 [Nonexpressor of pathogenesis-related (PR) genes 1, also known as NIM1] (2). Exogenous application of SA triggers the translocation of NPR1 into the nucleus. Once in the nucleus, NPR1 interacts with TGA transcription factors to mediate gene expression.

Treatment of plants with SA alters the expression of a large array of genes (3–5). Among these, only some are regulated by NPR1 and therefore specific to SAR. The most-studied NPR1 targets are *PR* genes, which encode small, secreted or vacuole-targeted proteins with antimicrobial activities (6).

To identify additional NPR1 target genes, we used the *35S::NPR1-GR* transgenic line generated in the *npr1-3* mutant (7). In this transgenic plant, nuclear translocation of NPR1-GR (GR, glucocorticoid receptor) requires not only SA but also dexamethasone (Dex). Treating *35S::NPR1-GR* plants first with SA and then with Dex specifically activates NPR1 target genes. With the use of a known NPR1 primary target, *PR1*, experimental conditions were optimized with the inclusion of the translation inhibitor cycloheximide (Chx) to achieve maximal induction of NPR1 target genes in the absence of de novo protein synthesis (fig. S1).

Using Affymetrix GeneChips (8200 genes), we identified putative NPR1 primary target genes by comparing transcriptional profiles of *npr1* and *npr1/35S::NPR1-GR* that were both treated with SA and then Chx/Dex (fig. S1). Duplicate experiments were performed independently and the data were analyzed with both MAS5.0 and dChip programs. Genes that showed a consistent difference in their pattern of expression (induction or repression) and low *P*-values (<0.05) in both replicates were considered for further analysis (table S1). Many of the induced genes can be classified into groups according to their known or deduced functions. One group (Table 1) contains genes known to be involved in defense, including several *PR* genes. Another group encodes members of the protein secretory pathway (9 of the 49 genes with >2-fold induction or 18 of the 120 genes with >1.6-fold induction), most of which are endoplasmic reticulum (ER)-localized proteins (8, 9). These secretion-related genes include those encoding the Sec61 translocon complex, which provides a channel for proteins to cross the ER membrane, and a signal recognition particle (SRP) receptor, which directs proteins with a signal peptide to the translocon complex. NPR1 also regulates many genes encoding ER-resident chaperones, such as BiP2 and glucose regulated protein 94 (GRP94), as well as co-chaperones including defender against apoptotic death 1 (DAD1) (10), calnexins (CNXs), calreticulins (CRTs), and protein disulfide isomerases (PDIs). These proteins function in the cotranslational folding and modification (e.g., disulfide bond formation and glycosylation) of nascent polypeptides destined for the apoplast or various organelles. Other genes in this group encode a Golgi-associated membrane trafficking protein; a clathrin, which is involved in packaging secretory proteins into small vesicles; and a vacuolar sorting receptor.

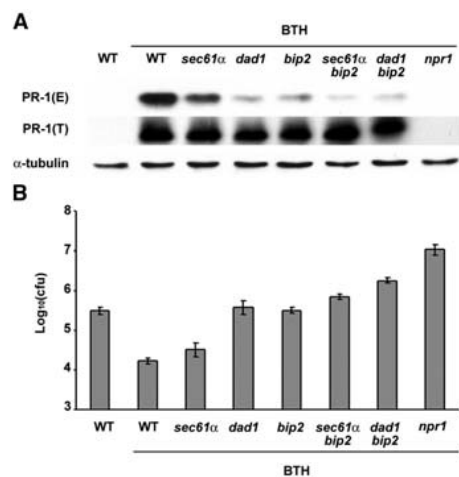
Taken as a group, the secretion-related genes showed statistically significant up-regulation in both experiments using a mixed-model analysis of variance (ANOVA) ( $P = 0.003$ ) (11). Furthermore, the induction of many of these genes by SA via the endogenous NPR1 was confirmed by RNA blot analysis, real-time reverse transcription-polymerase chain reaction (RT-PCR) (fig. S2), and with data from public microarray databases, such as the Stanford Microarray Database (12).

Although several previous studies have noted the induction of a few individual secretion-related genes by plant defense elicitors, the importance of this induction has only been speculated on (13–17) and the regulatory mechanism is not known. During SAR, there is a massive buildup of PR proteins in vacuoles and the apoplast. The basal activity of the protein secretory pathway may not be sufficient to accommodate the marked increase in PR protein synthesis. Therefore, we hypothesized that a coordinated up-regulation in the protein secretory machinery is required to ensure proper folding, modification, and transport of PR proteins. Consistent with this hypothesis, the ER-resident gene, *BiP*, was shown to be induced before the accumulation of PR1 (fig. S3) (16).

To provide genetic evidence that the up-regulation of the secretion-related genes is essential for SAR, we identified knockout mutants in five secretion-related genes from the Salk Institute transferred DNA (T-DNA) insertion collection (18). Mutants of a *calnexin* (Salk\_044381; At5g07340) and a *PDI* (Salk\_046705; At2g47470) gene showed no significant change in induced resistance. Because the *Arabidopsis* genome contains six calnexin and the related calreticulin genes, and more than 20 *PDI* genes, the lack of a phenotype in these mutants is likely due to functional redundancy. On the other hand, T-DNA insertions in *BiP2* (Salk\_047956), *DAD1* (Salk\_046070), and *SEC61α* (Salk\_034604) all compromised the plant's ability to efficiently secrete PR1 after treating with benzothiadiazole *S*-methyl ester (BTH, an SA analog) (Fig. 1A). The reduction in PR protein secretion directly correlates with impaired resistance against the bacterial pathogen *Pseudomonas syringae* pv. *maculicola* ES4326 (Fig. 1B). In the *sec61α bip2* and *dad1 bip2* double mutants, less PR1 was secreted and more pathogen growth was detected compared with the single mutants. Thus, an intact and responsive protein secretory pathway is required for SAR.

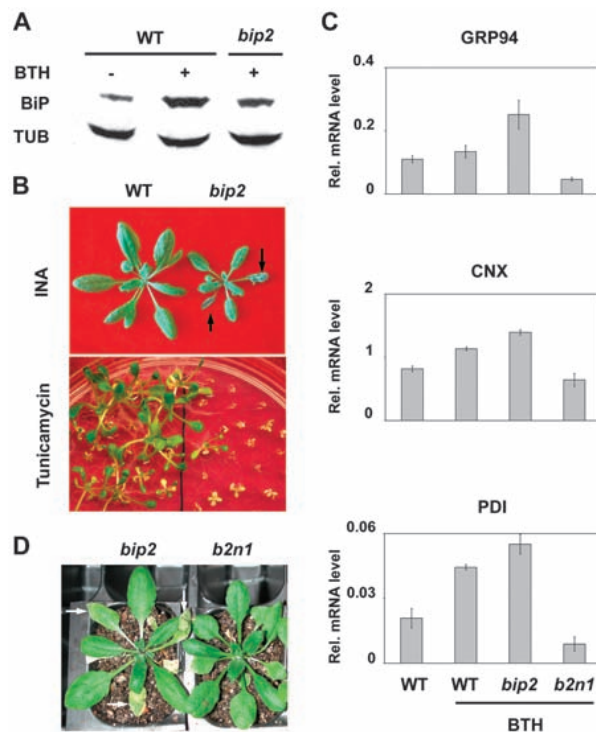
**Table 1.** A partial list of primary target genes of NPR1 identified in the microarray experiments. Data from two independent biological replicates are presented. Fold changes (F. C.) and *P*-values were calculated with the MAS 5.0 package, and similar results were obtained with dChip (21). Both groups of genes are shown to be significantly induced by a mixed-model ANOVA test with  $P = 7.6 \times 10^{-14}$  for the defense genes and  $P = 0.003$  for the secretory pathway genes.

Gene description	Locus	Replicate 1		Replicate 2	
		F. C.	<i>P</i> -value	F. C.	<i>P</i> -value
<i>Defense</i>					
PR-1	At2g14610	42.2	$1.0 \times 10^{-6}$	256.0	0
PR-5	At1g75040	14.9	0	2.6	0
Endochitinase	At2g43570	2.1	$1.8 \times 10^{-4}$	2.5	0
Putative disease resistance protein	At4g12010	6.1	$5.2 \times 10^{-3}$	2.6	$2.4 \times 10^{-4}$
Disease resistance protein RPP8	At5g43470	2.5	$9.2 \times 10^{-5}$	2.0	0
Beta-1,3-glucanase	At4g34480	2.0	$9.9 \times 10^{-5}$	2.8	$1.0 \times 10^{-6}$
Chitinase	At2g43570	2.1	$1.8 \times 10^{-4}$	2.5	0
Peroxidase	At5g64120	2.1	$4.7 \times 10^{-5}$	2.6	0
Endoxylglucan transferase	At5g57550	3.5	$1.1 \times 10^{-5}$	29.9	0
<i>Protein folding and secretion</i>					
Signal recognition particle receptor	At2g45770	4.9	$3.1 \times 10^{-5}$	6.1	0
Sec61α subunit	At2g34250	2.1	$5.4 \times 10^{-5}$	1.5	0
Sec61β subunit	At2g45070	1.4	$4.0 \times 10^{-2}$	1.3	$1.0 \times 10^{-2}$
BiP2	At5g42020	3.2	$7.0 \times 10^{-6}$	2.5	0
GRP94	At4g24190	7.5	0	2.3	0
DAD1	At1g32210	3.0	$1.0 \times 10^{-6}$	2.0	0
Protein disulfide-isomerase (PDI)	At2g47470	3.2	$3.1 \times 10^{-5}$	2.0	$1.0 \times 10^{-6}$
Protein disulfide-isomerase (PDI)	At3g54960	1.6	$8.0 \times 10^{-4}$	3.0	$1.0 \times 10^{-6}$
Calreticulin 3	At1g08450	4.0	0	2.3	0
Calreticulin	At1g09210	4.3	$1.0 \times 10^{-6}$	3.1	0
Calnexin1	At5g61790	6.1	$4.3 \times 10^{-5}$	2.6	0
Calnexin 2	At5g07340	1.4	$5.0 \times 10^{-6}$	2.1	$1.2 \times 10^{-5}$
Ribophorin I	At2g01720	3.7	$8.0 \times 10^{-6}$	1.5	$1.0 \times 10^{-6}$
Tetratricoredoxin	At4g22670	3.2	0	1.9	0
Cyclophilin	At2g47320	4.0	$2.0 \times 10^{-6}$	1.4	$7.9 \times 10^{-5}$
Clathrin-coat assembly protein	At1g10730	3.7	$5.8 \times 10^{-2}$	2.0	$4.7 \times 10^{-5}$
Transmembrane trafficking protein	At1g14010	4.3	$2.2 \times 10^{-4}$	2.0	$1.0 \times 10^{-6}$
Vacuolar sorting receptor	At1g30900	7.0	$1.0 \times 10^{-5}$	3.5	0



**Fig. 1.** Effects of mutations in secretion-related genes on PR1 protein secretion and resistance against *Pseudomonas syringae* pv. *maculicola* ES4326 (*Psm* ES4326). (A) Immunoblot of PR1 protein in the secretion-related gene mutants. Intercellular wash fluid (IWF) was collected from equal amounts of plant tissue treated with BTH or untreated. As a control, total protein was extracted. Secreted (E) and total (T) PR1 was examined using separate immunoblots with an antibody raised against this protein. An antibody against  $\alpha$ -tubulin was then used to probe the total protein blot to confirm equal loading of the samples. The same antibody was also used to probe the IWF blot to demonstrate that no intracellular protein ( $\alpha$ -tubulin) leaked out of the cell during IWF preparation (21). This experiment was repeated three times with similar results. (B) Growth of *Psm* ES4326 in the secretion-related gene mutants after BTH induction. Plants were induced with 60  $\mu$ M BTH 24 hours before infiltration with *Psm* ES4326 (optical density at 600 nm = 0.001). Uninduced WT plants were infiltrated at the same time. Bacterial growth was monitored 2 days after infection (27). Error bars represent 95% confidence limits of log-transformed data from eight independent samples. cfu, colony-forming units.

The importance of this coordinated induction of PR and secretion-related genes by NPR1 was further demonstrated by additional characterization of the *bip2* mutant. In *Arabidopsis*, there are three *BiP* genes (19, 20). Knocking out the NPR1-regulated *BiP2* gene resulted in reduced accumulation of total BiP protein after BTH induction (to ~50% of the wild-type level) (Fig. 2A). As a result, the *bip2* mutant is not only impaired in BTH-induced resistance (Fig. 1B), but also is hypersensitive to treatment of BTH or 2,6-dichloroisonicotinic acid (INA, another SA analog). Application of these chemicals at high concentrations to the *bip2* mutant resulted in a rapid tissue collapse not seen in wild-type (WT) or untreated mutant (Fig. 2B) (21). We believe that in the *bip2* plants, the increased PR protein synthesis is not accompanied by a sufficient increase in BiP protein, causing intracellular accumulation of unfolded proteins, leading to an acute unfolded protein response (UPR) in the form of cell death. In mammalian cells, free BiP binds the



**Fig. 2.** UPR in the *bip2* mutant after BTH, INA, and tunicamycin treatment. (A) Total BiP protein levels in WT and the *bip2* knockout mutant after BTH treatment. BiP protein was detected with a polyclonal antibody (anti-BiP, Santa Cruz Biotechnology) and  $\alpha$ -tubulin (TUB) was probed as a loading control. (B) Upper panel: Leaf collapse, marked by arrows, observed overnight after INA treatment. Lower panel: Three-week-old seedlings treated with tunicamycin (0.3  $\mu$ g ml<sup>-1</sup>) for 5 days during germination. (C) Induction of UPR marker genes in *bip2* and *bip2 npr1* (*b2n1*). Real-time RT-PCRs were performed to examine the relative mRNA levels (Rel. mRNA level) of *GRP94*, *CNX* (At5g61790), and *PDI* (At1g21750) normalized to that of ubiquitin. Error bars represent standard deviations from three PCR results. (D) Rescue of the BTH-induced leaf collapse phenotype in *bip2* by *npr1*.

UPR sensor Ire1 (a kinase and endonuclease on the ER membrane) and prevents it from dimerizing and activating the UPR. When unfolded proteins accumulate, BiP dissociates from Ire1 and binds the unfolded proteins, thus freeing Ire1 to activate UPR (22). Indeed, in the *bip2* mutant, several UPR marker genes, which are also NPR1-responsive, are hyperactivated after BTH treatment (Fig. 2C). The *bip2* mutant plants are also more sensitive to inducers of UPR, such as tunicamycin, which causes misfolding of proteins by inhibiting glycosylation (23). Whereas WT plants recovered from tunicamycin treatment, *bip2* plants failed to do so (Fig. 2B).

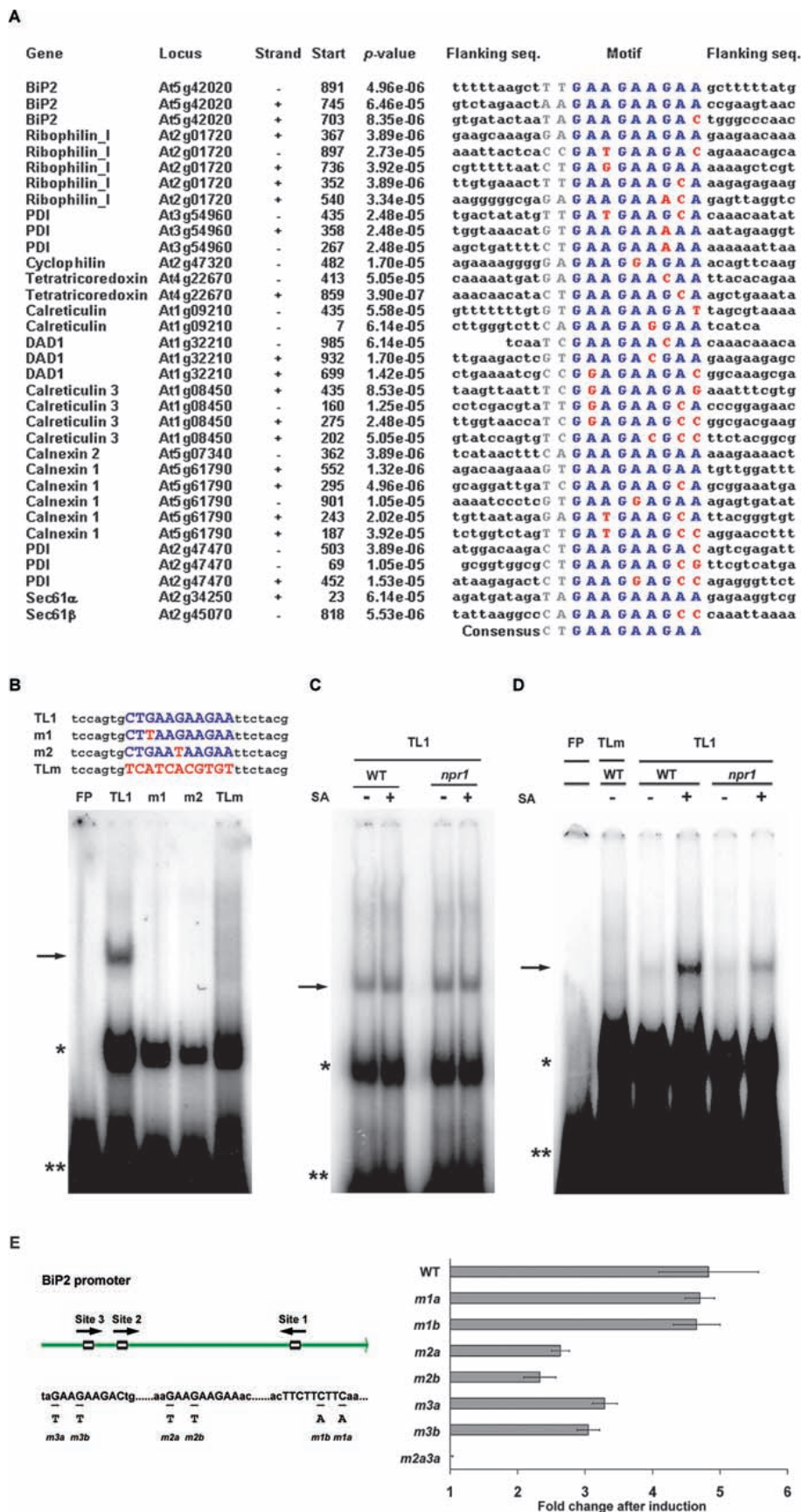
To determine whether the UPR observed in *bip2* was caused by insufficient processing of PR proteins, we introduced the *bip2* mutation into the *npr1* background, in which BTH-induced PR gene expression is blocked. Both BTH-induced UPR marker gene expression and cell death were diminished in the *bip2 npr1* double mutant (Fig. 2, C and D). These genetic data clearly illustrate the detrimental effects that can occur when SAR is induced in plants without a sufficient increase in protein folding and secretion capability.

Because the entire protein secretory pathway is coordinately up-regulated by NPR1 during SAR, the regulatory mechanism may involve common elements. To search for such elements, we focused on the 13 ER-resident genes listed in Table 1 and analyzed their promoter regions (1 kb upstream of the start codon) using the MEME program (24). A consensus sequence, designated *TLI* (CTGAAGAAGAA), was overrepresented in the promoter regions of all 13 NPR1-responsive ER-resident genes surveyed (Fig. 3A) ( $P = 0.02$ ), but was ab-

sent from related genes not up-regulated by NPR1, such as the other *DAD* (*At2g35520*) and *Sec61a* (*At1g78720*).

In an electrophoretic mobility shift assay (EMSA), the *TLI* element was shown to have a specific protein-binding activity, which was completely abolished with changes in the core sequence (*m1*, *m2*, and *TLm* in Fig. 3B). When whole-cell extracts were used, this binding activity was not affected by SA treatment in either WT or *npr1* mutants (Fig. 3C; only *npr1-1* is shown). When nuclear extracts were used instead, the specific binding was enhanced in SA-treated samples, suggesting that the *TLI*-binding protein translocates into the nucleus upon SAR induction (Fig. 3D). Moreover, this translocation was facilitated by NPR1, as indicated by a less profound enhancement of *TLI* binding after SA treatment in *npr1*. Because the induced binding was not completely abolished in *npr1*, we do not exclude the possibility that NPR1 also controls the activation of the *TLI*-binding protein. All of these data are consistent with the facts that the induction of secretion-related genes does not require de novo protein synthesis and that NPR1 is also translocated to the nucleus after SAR induction.

To demonstrate the biological activity of *TLI*, we generated reporter constructs in which the coding sequence of  $\beta$ -glucuronidase (*GUS*) is driven by either the WT *BiP2* promoter or mutant constructs with changes in each of the promoter's three *TLI* elements (Fig. 3E; Sites 1, 2, and 3). These constructs were transformed into WT plants, and the effect of each mutation on promoter activity was analyzed through a GUS assay. As expected, the reporter driven by the WT *BiP2* promoter showed a 4.8-fold



increase in expression after treatment with INA. When transformed into *npr1*, the WT *BiP2* promoter::GUS reporter showed no induction by INA, consistent with the result from the RNA

blot analysis (fig. S2) (21). Whereas mutations in Site 1 had little effect on the inducibility of the promoter, mutations in Sites 2 and 3 significantly reduced the induction of the *GUS* gene.

**Fig. 3.** Characterization of the *TL1* element. (A) Discovery of a conserved sequence (*TL1*) in the promoters of all 13 NPR1-regulated ER-resident protein genes (1 kb upstream of the translation start codon) using MEME (24). Blue and gray letters represent highly and moderately conserved nucleotides identified by the program, respectively. Variations from the consensus sequence are marked in red. (B) EMSA using whole-cell protein extracts and <sup>32</sup>P-labeled oligonucleotides *TL1*, *m1*, *m2*, and *TLM*. The arrow indicates the specific DNA-protein band, the single asterisk marks a nonspecific band, and double asterisks indicate the free probes. FP, free probe without protein extract. (C) EMSA of *TL1* using whole-cell extracts prepared from WT and *npr1-1* with and without SA induction. (D) EMSA of *TL1* using nuclear extracts prepared from WT and *npr1-1* with and without SA treatment. (E) Mutant analysis of the *BiP2* promoter. The three putative *TL1* elements found in the *BiP2* promoter (Sites 1, 2, and 3) are indicated by small rectangles and their orientations shown by black arrows. The coding sequence is on the right (green arrow). WT and mutant (*m1a*, *m1b*, *m2a*, *m2b*, *m3a*, *m3b*, and *m2a3a*; the altered nucleotides are underlined) *BiP2* promoters were cloned upstream of the *GUS* coding sequence and transformed into plants. Eight independent T<sub>2</sub> lines were pooled for each construct, and the inducibility of the promoter by INA was measured by quantitative GUS assay. Fold changes were determined using GUS activity ratios between induced and uninduced samples. Error bars represent standard deviations of three measurements.

Because Sites 2 and 3 are adjacent (30 base pairs apart) (Fig. 3E), we examined whether they can function cooperatively to confer full induction of *BiP2*. Indeed, when both sites were mutated, the reporter showed no induction after INA treatment (Fig. 3E, *m2a3a*).

Taken together, our microarray analysis, EMSA, and promoter mutagenesis data suggest that *TL1* is indeed a cis-element involved in SA induction of secretion-related genes via NPR1. The transcription factor that controls *TL1* is unlikely a TGA factor because *TL1* is distinct from the TGA-binding *as-1* element. Furthermore, in a *tga2 tga5 tga6* triple mutant, the induction of *PR* genes is diminished (25), whereas secretion-related genes are still induced (fig. S4). Therefore, we believe that NPR1 regulates secretion-related and *PR* genes through different transcription factors and cis-elements.

Our finding sheds new light on the induction mechanism of SAR by demonstrating that NPR1 not only directly induces the *PR* genes but also prepares the cell for secretion of the *PR* proteins by first making more secretory machinery components. A similar phenomenon is also observed in mammals in which the secretory machinery in B cells is up-regulated before the B cells start secreting antibodies (26). Further study may clarify whether this commonality reflects any conserved regulatory mechanisms.

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28. We thank P. Benfey, W. Durrant, J. Siedow, T. P. Sun, D. Thiele, and L. Tyler for critical readings of the manuscript and helpful discussion and X. Li for providing the *tga2 tga5 tga6* triple mutant. This project is supported by a NSF 2010 grant and a grant from the U.S. Department of Agriculture.

#### Supporting Online Material

[www.sciencemag.org/cgi/content/full/308/5724/1036/DC1](http://www.sciencemag.org/cgi/content/full/308/5724/1036/DC1)

Materials and Methods

Figs. S1 to S4

Table S1

References and Notes

16 December 2004; accepted 25 February 2005

10.1126/science.1108791

## On the Origin of Leprosy

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Leprosy, a chronic human disease with potentially debilitating neurological consequences, results from infection with *Mycobacterium leprae*. This unculturable pathogen has undergone extensive reductive evolution, with half of its genome now occupied by pseudogenes. Using comparative genomics, we demonstrated that all extant cases of leprosy are attributable to a single clone whose dissemination worldwide can be retraced from analysis of very rare single-nucleotide polymorphisms. The disease seems to have originated in Eastern Africa or the Near East and spread with successive human migrations. Europeans or North Africans introduced leprosy into West Africa and the Americas within the past 500 years.

Comparative genomics enables us to establish solid genealogical relationships with greater precision than ever before. Leprosy (1) has plagued human populations for thousands of years and puzzled scientists since the identification of its etiological agent, *Mycobacterium leprae*, by Hansen in 1873 (2). The main difficulties of working with *M. leprae* are that it cannot be grown in axenic culture and that its doubling time in tissue is slow, nearly 13 days (3). It was only when it was discovered that the nine-banded armadillo, *Dasypus novemcinctus*, could be infected (4) that sufficient quantities of *M. leprae* were obtained for biological and immunological analysis. Comparison of the genome sequence of

the armadillo-passaged strain of *M. leprae* from Tamil Nadu, India (TN strain) with that of the close relative *Mycobacterium tuberculosis* (5), led to a major breakthrough (6). *M. leprae* was shown to have embarked upon a path of reductive evolution in which the genome underwent downsizing and accumulated more than 1130 pseudogenes. The concomitant loss of catabolic and respiratory functions appears to have resulted in severe metabolic constraints (6, 7).

To establish whether all strains of *M. leprae* had undergone similar events and to determine their level of relatedness, we used technological approaches that have successfully detected polymorphic regions in the *M. tuberculosis*

complex (8–10). First, genomic DNA, prepared from seven different strains of leprosy bacilli (Table 1), was hybridized to microarrays corresponding to the complete genome of the TN strain, but no evidence for further gene loss was uncovered in these isolates (fig. S1). Second, to establish whether differences existed in the copy number of insertion-sequence-like, dispersed repetitive sequences, quantitative polymerase chain reaction was performed to target the repetitive sequences RLEP, REPLEP, LEPREP, and LEPRPT (11). Again, within the limits of sensitivity of this approach, no differences were detected between the TN strain and the other isolates (fig. S2).

A major source of variability in tubercle bacilli is the mycobacterial interspersed repetitive unit (MIRU), which serves as the basis of a robust typing system that exploits differences in the variable number of the tandem repeats

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**Table 1.** Strains of armadillo-derived *M. leprae* and VNTR profile.

Strain	Patient's country of origin	Source	3-Hexa	21-TTC	9-GTA	14-AT	15-AT	17-AT	18-AT
Tamil Nadu*	India	IP	3	21	9	14	15	17	18
Africa	Ethiopia	IP	3	29	8	14	19	13	13
India 2	India	IP	3	15	11	18	14	13	9
Br4923	Brazil	NHDP	3	12	12	20	20	15	18
NHDP98	Mexico	CSU/NHDP	3	10	9	22	14	11	12
Thai-53	Thailand	CSU/NHDP	3	15	9	16	17	10	13
NHDP63	USA	CSU/NHDP	3	10	10	18	18	13	16

\*Numbers refer to the repeat copy number for the Tamil Nadu strain (11), whereas numbers in the rest of the table are the copy numbers found in the respective isolates. IP, Institut Pasteur; NHDP, National Hansen's Disease Program; CSU, Colorado State University.