



PLANT SCIENCE

Functional diversification of a wild potato immune receptor at its center of origin

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Plant cell surface pattern recognition receptors (PRRs) and intracellular immune receptors cooperate to provide immunity to microbial infection. Both receptor families have coevolved at an accelerated rate, but the evolution and diversification of PRRs is poorly understood. We have isolated potato surface receptor Pep-13 receptor unit (PERU) that senses Pep-13, a conserved immunogenic peptide pattern from plant pathogenic *Phytophthora* species. PERU, a leucine-rich repeat receptor kinase, is a bona fide PRR that binds Pep-13 and enhances immunity to *Phytophthora infestans* infection. Diversification in ligand binding specificities of PERU can be traced to sympatric wild tuber-bearing *Solanum* populations in the Central Andes. Our study reveals the evolution of cell surface immune receptor alleles in wild potato populations that recognize ligand variants not recognized by others.

Plant cell surface pattern recognition receptors (PRRs) and intracellular immune receptors cooperate to provide robust resistance to microbial infection (1–3). The synergistic activation of plant immunity by spatially separated plant immune receptors suggests their coevolution. A strong correlation in the number of genes encoding surface and intracellular immune receptors observed across the plant lineage supports the concept of mutual potentiation of immune responses initiated in different plant cell compartments (4, 5).

It is assumed that pathogen pressure in ecological niches drives plant immune receptor evolution (5, 6), but evidence for diversification of plant PRR sequences and functions among natural plant populations is lacking. We hypothesized that a PRR might recognize Pep-13, a conserved microbial immunogenic 13-amino-acid fragment from a cell wall glycoprotein (GP42) with transglutaminase (TG) activity (7–9). TGs are produced by several plant-pathogenic oomycete *Phytophthora* species, including *P. infestans*, the causal agent of potato late blight disease and the Great Irish Famine (10–12). Pep-13 triggers a hypersensitive response and other immunity-associated responses in diverse

plant species, including the solanaceous host plant, potato (*10*).

Potato PERU senses oomycete-derived pattern Pep-13

We screened a collection of wild *Solanum* species and cultivated potato genotypes for cell death induction when infiltrated with Pep-13 or its structural derivative, Pep-25 (7, 13). To identify the Pep-13-receptor by a map-based cloning approach, we crossed genotype *Solanum tuberosum* Group Phureja DM 1-3 516 R44 (DM) and genotype *S. tuberosum* RH89-039-16 (RH) (Fig. 1A). DM is a Pep-13/Pep-25-sensitive genotype, which was previously used to establish the potato reference genome (14). RH is a Pep-13/Pep-25-insensitive genotype. We back-crossed the F1 generation 3240-4 to the RH parent and used the resulting F2 population (3648) for genetic mapping (15). Pattern sensitivity segregated in a 1:1 ratio, suggesting that a single, dominant gene encodes the corresponding receptor (fig. S1A). Pep-13/Pep-25 sensitivity was previously mapped to the top of chromosome 3 (13), and subsequent marker-assisted fine-mapping yielded a 55.2-kb fragment containing 7 open reading frames, three of which encode leucine-rich repeat receptor kinases (LRR-RKs a-c) (fig. S1B). LRR-RKs consist of an extracellular LRR domain, a transmembrane-spanning domain, and an intracellular serine/threonine protein kinase domain, which is absent in LRR receptor proteins (LRR-RPs). LRR ectodomain-containing receptors are the predominant type of plant PRRs known to date and have evolved to recognize primarily proteinaceous microbial patterns or phytochemicals (16–18).

To determine which LRR-RK candidate gene sequence confers Pep-13 sensitivity, we performed transient expression assays in the solanaceous model plant, *Nicotiana benthamiana*. *Agrobacterium* infection-mediated expression

of LRR-RK b—but not LRR-RK a or c-encoding cDNA sequences—resulted in plant cell death after treatment with either Pep-13 or GP42 (Fig. 1B). We thus designated LRR-RK b Pep-13 receptor unit (PERU). PERU is a canonical plant LRR-RK that hosts an ectodomain composed of 27 LRRs linked by a transmembrane domain to an intracellular serine-threonine protein kinase domain (fig. S2). Stable expression of PERU cDNA in Pep-13-insensitive potato cultivar Atlantic resulted in Pep-13-inducible cell death, production of reactive oxygen species (ROS) and accumulation of the plant stress hormone, ethylene (Fig. 1, C to E, and fig. S3). These responses were not observed in wild-type (WT) Atlantic or in control lines transformed with empty vector only. Inactivation of the PERU locus in Pep-13-sensitive DM by CRISPR-Cas9 mutagenesis provided direct proof for a causal role of PERU in Pep-13 pattern recognition. To abolish PERU gene expression, genotype DM was stably transformed with CRISPR-Cas9 and 4 sgRNA, CRISPR lines were genotyped, and deletion and frameshift mutations were found, resulting in loss of Pep-13-induced cell death, ROS burst, and ethylene production (Fig. 1, F to H). In sum, these results document a role for potato PERU in Pep-13 pattern recognition.

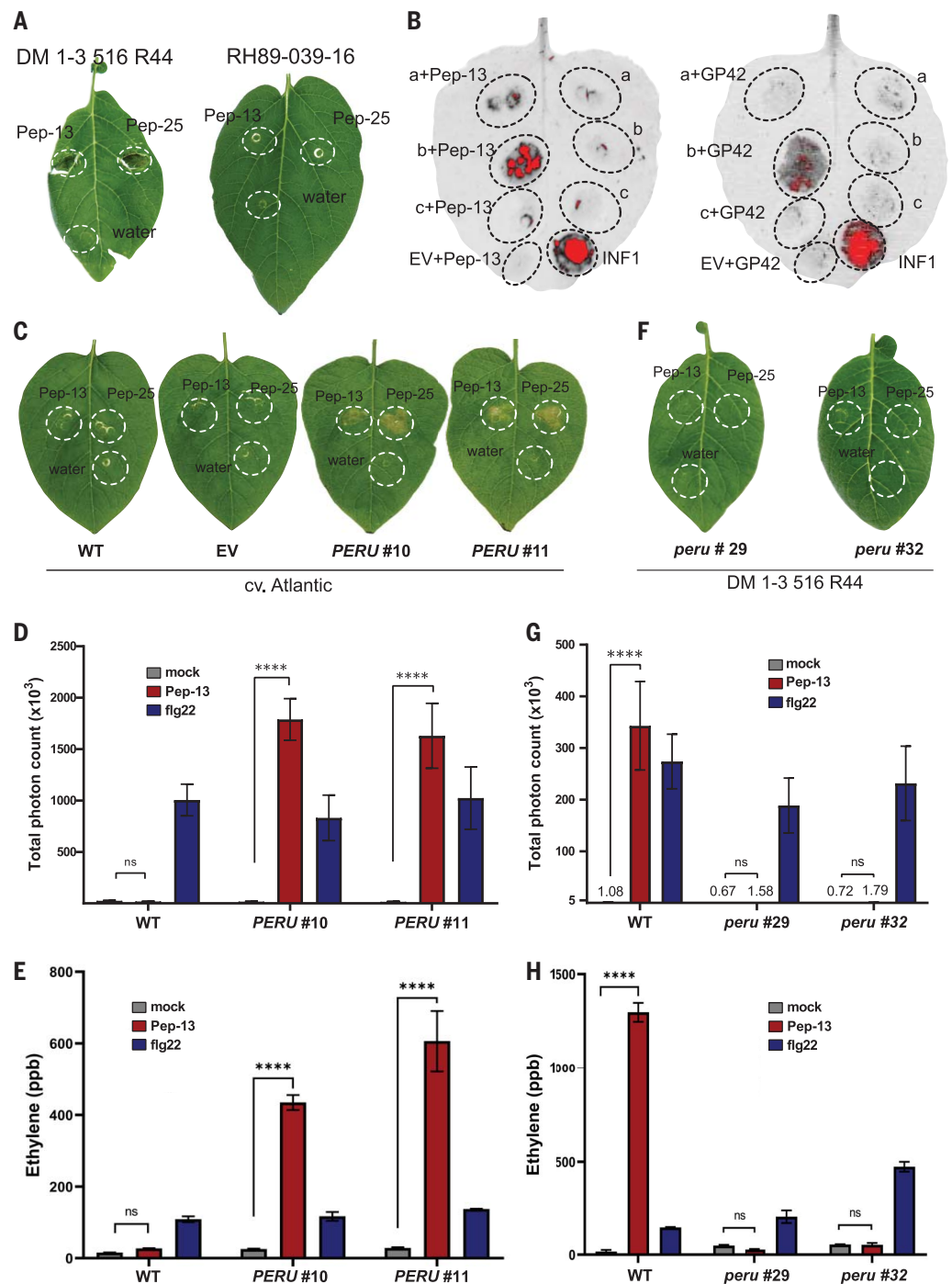
A PERU-SERK3 complex mediates Pep-13/Pep-25-induced defenses and plant cell death

LRR-type PRRs recognize their cognate ligands by binding to their LRR ectodomains (19). We investigated ligand-receptor binding in vitro and in planta. To test for physical interaction of PERU and Pep-25 in vitro, we incubated recombinant hexa-histidine (His₆)-tagged PERU LRR ectodomain protein (PERU^{LRR}-His₆) with biotinylated Pep-25 (Pep-25-bio) before treatment with the homo-bifunctional cross-linker ethylene glycol bis (succinimidyl succinate) (EGS) to stabilize the ligand-receptor complex (8). Pep-25-bio is as active as Pep-25 (fig. S4). Following PERU^{LRR}-His₆ immunoprecipitation, bound Pep-25-bio was visualized by streptavidine/anti-streptavidine antisera (fig. S5). A large molar excess of free Pep-13 competitively abolished ligand-receptor complex formation, which suggests direct and specific ligand binding by PERU^{LRR}. The affinity constant of the ligand/receptor interaction ($K_D = 88.9$ nM) is close to ligand concentrations required for immune activation in *p35S::PERU-expressing* Pep-13-insensitive *Solanum hjertingii* or in Pep-13-sensitive potato DM ($EC_{50} = 9.8$ nM or 44 nM respectively), indicating that the PERU ectodomain is sufficient for ligand binding (fig. S5). To analyze the Pep-25-bio/PERU interaction in planta, we treated leaves of *N. benthamiana* plants expressing green fluorescent protein (GFP)-tagged PERU (*p35S::PERU-GFP*) with ligand prior to EGS treatment. Precipitation of PERU-GFP protein and subsequent detection of bound ligand corroborated

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Fig. 1. PERU confers response to

Pep-13. (A) The genotype DM 1-3 516 R44 (DM) shows cell death response upon infiltration of Pep-13 and Pep-25 whereas the genotype RH89-039-16 (RH) does not. (B) Representative *N. benthamiana* leaves co-agroinfiltrated with the candidate genes “a,” “b,” or “c,” and Pep-13 or the full-length glycoprotein GP42, show that candidate “b” confers cell death to Pep-13 (left leaf) and GP42 (right leaf), whereas candidates “a” and “c” do not. Cell death was visualized by a red light imaging system at 3 days post infiltration (47). (C) Potato cultivar Atlantic (WT) is insensitive to Pep-13/25, transgenic Atlantic expressing *PERU* (*PERU* #10 and *PERU* #11) show cell death after Pep-13/25 infiltration, cv. Atlantic transformed with empty vector (EV) is included as negative control. (D) Total ROS production, and (E) Ethylene accumulation after treatment with 1 μ M Pep-13, flg22 or water as control in potato cv. Atlantic WT, EV, *PERU* #10 and #11. (F) CRISPR lines *peru* #29 and #32 are insensitive to Pep-13/25. (G) Total ROS production, and (H) Ethylene accumulation after treatment with 1 μ M Pep-13, flg22, or water as control, in DM (WT) and lines *peru* #29 and *peru* #32. Data were analyzed using one-way analysis of variance (ANOVA) with Tukey’s test, (*****P*-value \leq 0.0001). All experiments were performed three times with similar results and representative experiments are shown.



ligand-receptor binding observed in vitro (Fig. 2A). Again, excess of Pep-13 abolished ligand binding. We did not observe an inhibitory effect when a biologically inactive Pep-13 mutant peptide, Pep-13W231A (tryptophan residue 231 mutated to alanine, amino acid numbering corresponds to full-length GP42 sequence) (10), was used as a competitor (Fig. 2A). Notably, a W231A mutant of GP42 not only abolished its plant defense-eliciting activity but also reduced its TG activity by 98.5% (10). Altogether, these data

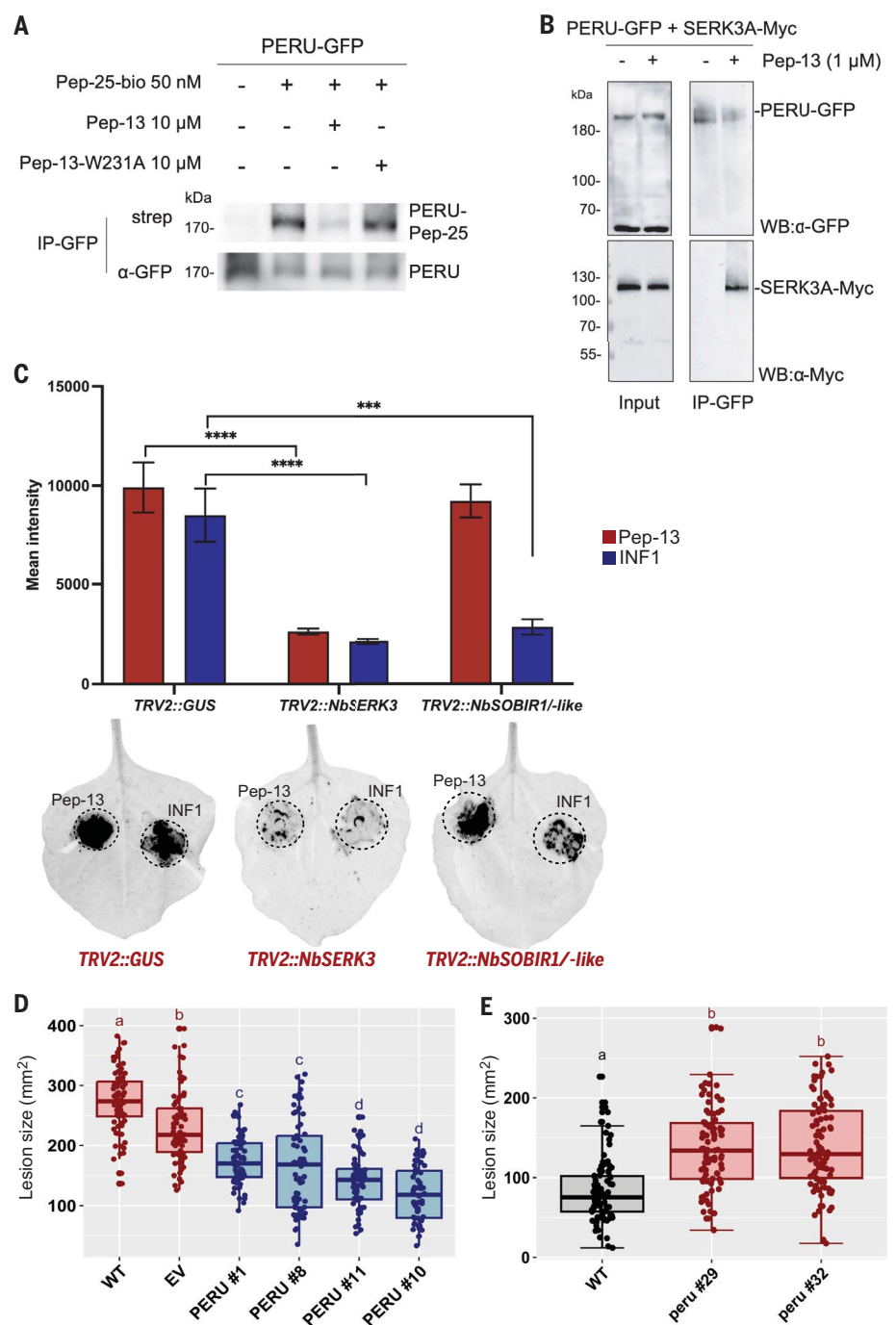
demonstrate specific binding of Pep-13 to its high-affinity binding site, PERU.

The LRR-RK BAK1/SERK3 (BRASSINOSTEROID INSENSITIVE 1-ASSOCIATED KINASE/SOMATIC EMBRYOGENESIS RECEPTOR KINASE 3) forms ligand-induced receptor/co-receptor complexes with plant LRR-RK-type PRRs (17, 18, 20). We found Pep-13 pattern-induced complex formation of PERU and SERK3A after transient coexpression of *p35S::PERU^{DM}-GFP* and *p35S::SERK3A^{DM}-Myc* in

N. benthamiana plants (Fig. 2B). Virus-induced gene silencing of *SERK3* (*TRV::NbSERK3*) in *N. benthamiana* resulted in a massive reduction in Pep-13-induced hypersensitive cell death and ROS production in *TRV::NbSERK3* plants (Fig. 2C and fig. S6), suggesting that PERU recruits SERK3 in a pattern-dependent manner. Silencing of SOBIR1 (SUPPRESSOR OF BAK1-INTERACTING KINASE1) (*TRV::NbSOBIR1-like*), which is exclusively required for the function of LRR-RP-type PRRs, did not

Fig. 2. PERU recognizes Pep-13, is dependent on SERK3, and confers enhanced resistance to *Phytophthora infestans*.

(A) Binding of biotinylated Pep-25 to PERU. PERU-GFP transiently expressed in *N. benthamiana* served as receptor, Pep-25-bio peptide as ligand, and unlabeled Pep-13 and Pep-13W231A peptides as competitors. Streptavidin-AP (strep) was used to detect ligand binding to receptor. (B) PERU-GFP and SERK3^{DM}-Myc were transiently expressed in *N. benthamiana* and treated with Pep-13 or water as control. Proteins were subjected to coimmunoprecipitation with GFP trap beads and immunoblotting with tag-specific antibodies. This experiment was performed in duplicate with similar results. (C) Cell death induced by Pep-13 peptide and INF1 protein (as control) in TRV2::NbSERK3 *N. benthamiana* leaves was significantly reduced compared with TRV2::GUS. Pep-13-induced cell death was not reduced in leaves treated with TRV2::NbSOBIR1-like. Representative leaves are shown at the bottom. Data were analyzed using one-way ANOVA with Tukey's test, (*****P*-value ≤ 0.0001, ****P*-value < 0.001, ***P*-value < 0.01). (D) Leaves of cv. Atlantic WT, and transgenic EV (negative control), PERU #1, #8, #10, and #11 intact plants were spot-inoculated with *P. infestans* strain Dinteloord, and lesion sizes measured at 4 dpi. All transgenic lines expressing PERU showed smaller lesions than WT or EV. (E) DM (WT) and CRISPR lines *peru* #29 and #32 were spot-inoculated with *P. infestans* strain Dinteloord. Lesion sizes were measured at 4 dpi. Larger lesions were observed in the CRISPR lines *peru* #29 and #32. Data were analyzed using one-way ANOVA with Tukey's test (*P*-value ≤ 0.05), different letters indicate significant differences. All experiments were performed 3 times with similar results and representative results are shown.



affect Pep-13-induced cell death formation. By contrast, *Phytophthora infestans* elicitor INF1-induced cell death mediated by activation of LRR-RP-type ELR (ELICITIN RESPONSE) (21) is reduced in both TRV2::NbSERK3 and TRV2::NbSOBIR1-like plants (Fig. 2C).

In solanaceous *N. benthamiana*, activation of plant immunity and cell death by LRR-RP-type PRRs requires lipase-like ENHANCED DISEASE SUSCEPTIBILITY 1 (EDS1) (22) and helper NUCLEOTIDE-BINDING LRR (hNLR) REQUIRED FOR HYPERSENSITIVE RESPONSE-

ASSOCIATED CELL DEATH 2, 3, and 4 (NRC2, NRC3, NRC4) (23, 24). Because LRR-RK-type PRRs have not previously been implicated in activating plant cell death in any plant system, we tested whether these proteins are required for PERU signaling. *N. benthamiana* plants transiently expressing *p35S::PERU^{DM}* developed cell death symptoms upon infiltration of Pep-13 or GP42 (Fig. 1B) and produced ethylene upon treatment with Pep-25 (fig. S4). Transient expression of *p35S::PERU^{DM}-GFP* in *N. benthamiana* mutants lacking EDS1 and related PHYTO-

ALEXIN-DEFICIENT 4 (PAD4) (25, 26) or hNLRs NRC2/3/4 (23) had no reducing effect on elicitor-induced cell death and ethylene production (fig. S7). Altogether, we find substantial differences in the molecular mechanisms controlling plant immune responses upon activation of different classes of LRR-type PRRs in this plant.

PERU confers enhanced resistance to *P. infestans*

Potato varieties used in agricultural production are often susceptible to major plant pathogens,

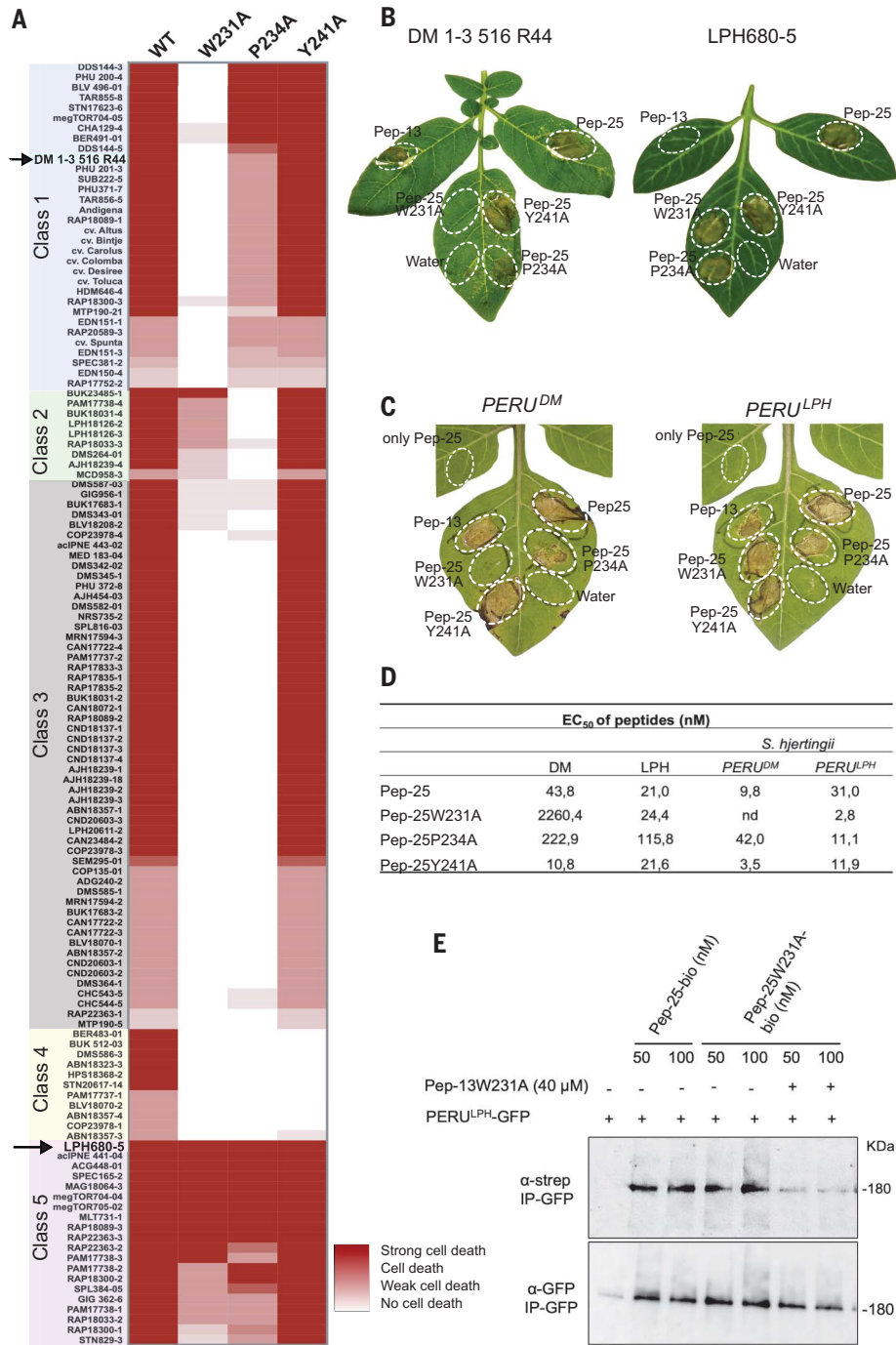


Fig. 3. Functional diversification of PERU in *Solanum* section *Petota*. (A) Heat map of cell death responses of *Solanum* accessions to Pep-25 (WT) and Pep-25W231A, Pep-25P234A, Pep-25Y241A mutants reveals five different classes (1 to 5) of recognition specificities. DM 1-3 516 R44 (class 1) and LPH680-5 (class 5) are marked with arrows. (B) Cell death induction by Pep-13, Pep-25, and mutants in DM and LPH plants. In DM, Pep-25W231A induces no cell death, and Pep-25P234A induces weaker cell death whereas in LPH, Pep-25W231A and Pep-25P234A-induced cell death is similar to that caused by Pep-25. (C) PERU^{DM} or PERU^{LPH} were transiently expressed in Pep-13-insensitive *S. hjertingii* by agroinfiltration. Infiltration of Pep-13/25 and Pep-25 mutant peptides yielded the same response pattern as observed in DM and LPH plants. (D) EC₅₀ values were determined by quantification of elicitor-induced production of ethylene in DM or LPH plants, and in *S. hjertingii* plants transiently transformed with either PERU^{DM} or PERU^{LPH}. nd, not determined. (E) Receptor/ligand binding assays show that PERU^{LPH} specifically bound both Pep-25-bio and Pep-25W231A-bio as ligands, and Pep-13W231A efficiently competes for ligand binding to PERU^{LPH}. All experiments were performed 3 times with similar results and representative experiments are shown.

including species of the genus *Phytophthora* (27). Genetic engineering provides one way of increasing plant resistance in crop plants. Ectopic expression of plant PRRs is known to confer novel microbial pattern recognition specificities and enhanced pathogen resistance to crop plants (16, 21, 28, 29). For infection assays with the virulent *P. infestans* isolate, Dinteloord, we obtained four potato cultivar Atlantic lines stably expressing *p35S::PERU*, and two DM lines stably transformed with CRISPR-Cas9 and 4 sgRNA to disable *PERU* gene expression. By scoring disease lesions four days post infection we found that *PERU*-transgenic lines were significantly less damaged when compared with WT plants or to lines transformed with vector only (Fig. 2D). Likewise, CRISPR-Cas9-generated *peru* mutant lines were significantly more susceptible to infection when compared with WT DM (Fig. 2E). Hence, *PERU* confers quantitative resistance against the pervasive potato late blight pathogen.

Diversification of PERU ligand specificities in wild potato populations

Pep-13/25-induced plant defenses have been studied in parsley and potato cell suspensions, as well as in leaves of a cultivated potato clone, Désirée (7, 10). Alanine scanning mutagenesis of Pep-13 sequences revealed that mutant Pep-13W231A abolished elicitor activity, mutation of proline 234 (Pep-13P234A) reduced it, and replacement of the remaining amino acid residues (including tyrosine 241, Pep-13Y241A) did not significantly affect activities of the mutant peptides (7, 8, 10). We found the same pattern of ligand responses in the Pep-25-sensitive genotype DM, which was used for *PERU* identification (Figs. 1A, 3A, and data S1). To determine the frequency of biologically active *PERU* alleles in *Solanum* sect. *Petota* (30), we analyzed 476 genotypes corresponding to 98 species (97 wild, and 1 cultivated potato species) for cell death triggered by Pep-25 and its described mutant variants (data S1). 350 (74%) of these genotypes did not develop cell death in response to Pep-25, indicating that most wild *Solanum* genotypes in this collection lack an active *PERU* allele (data S1). Pep-25 and its mutants were tested for cell death induction on all 126 Pep-25-sensitive genotypes (Fig. 3A). Overall, we observed at least five different recognition specificities, including substantial qualitative and quantitative variations in their abilities to respond to Pep-25 and its mutants. Wild potato genotypes grouped in class 1 include DM and exhibit the same ligand response patterns as described for cultivated potato cultivar Désirée previously (7, 8, 10) (Fig. 3A). These accounted for 25% of all Pep-25-sensitive genotypes (Fig. 3A). Other genotypes showed responsiveness to Pep-13W231A but failed to respond to Pep-13P234A and Pep-13Y241A (class 3),

genotype-specific properties account for altered PERU ligand binding specificities, we transiently expressed *PERU*^{DM} or *PERU*^{LPH}-encoding sequences in Pep-13-insensitive *S. hjertingii*. Again, infiltration of Pep-25 WT and mutant peptides yielded the same response pattern as observed previously (Fig. 3B), with all Pep-25 mutants inducing cell death in *PERU*^{LPH} plants only (Fig. 3C). Thus, differences in ligand specificities of PERU proteins from *PERU*^{DM} or *PERU*^{LPH}-expressing plants are features of the receptor proteins themselves rather than of co-receptors or other auxiliary factors.

We further analyzed biological activities of Pep-25 and its mutants by quantifying elicitor-induced production of the stress hormone ethylene in *PERU*^{DM} or *PERU*^{LPH} potato plants and in *S. hjertingii* plants transiently transformed with either *PERU* allele (Fig. 3, D and E). Determination of elicitor concentrations required to induce half-maximal ethylene production (EC₅₀) corroborated qualitative data from cell death assays (Fig. 3, B and C). Pep-25W231A proved as active as Pep-25 only when tested on *PERU*^{LPH}-expressing plants. We found substantially reduced or no activity of this peptide in plants expressing *PERU*^{DM} (Fig. 3, D and E). In agreement with that, *PERU*^{LPH} plants bound both Pep-25-bio and Pep-25W231A-bio in receptor-ligand binding assays (Fig. 3E). Likewise, Pep-13W231A efficiently blocked ligand binding to *PERU*^{LPH} (Fig. 3E), but not to *PERU*^{DM} (Fig. 2A). Altogether, our data obtained from ligand binding assays and from plant defense activation studies confirm that *PERU*^{DM} and *PERU*^{LPH} encode related LRR-RK immune receptors that have diversified in ligand specificities. Our findings further suggest that functional diversification has occurred within this immune receptor family during evolution, resulting in *PERU* alleles that recognize Pep-13 variants not recognized by others.

Evolutionary history of PERU

To obtain information about the origin of *PERU* alleles, we studied their geographic distribution and genetic variation (Fig. 4). We developed a computational pipeline to extract *PERU* sequences from 6,630,292 predicted proteins from 124 Solanaceae genome assemblies and for comparison extracted sequences of FLS2 (FLAGELLIN-SENSING 2), a conserved LRR-RK that detects bacterial flagellin (fig. S8 and data S2) (3). Both *PERU* and FLS2 clustered in well-supported clades within the LRR-RK subgroup XII indicating a monophyletic origin within the Solanaceae (fig. S9) (5). All plant LRR-RK-type PRRs currently known fall into this clade, including *Arabidopsis* FLS2 and EF-TU RECEPTOR (EFR), or rice Xa21 (16, 31). This pipeline yielded 114 *PERU* clade sequences from 17 species and 180 FLS2 clade sequences from 33 species with the *PERU* clade sequences exhibiting markedly more diversity than the

FLS2 clade (fig. S9 and data S3, S4, and S5). The same primers employed to isolate *PERU* (DM) facilitated the isolation of 26 responsive homologs and 25 nonresponsive homologs (data S6). The amplified and genome-extracted sequence datasets were then combined for phylogenomic analyses, which revealed that the *PERU* sequences encoding Pep-13-responsive *PERU* alleles fall into one clade whereas the non-responsive homologs are scattered throughout the tree (Fig. 4A and fig. S10, A and B). The *PERU*^{LPH} sequences are embedded within a tighter *PERU*^{DM} clade indicating that evolution of a new ligand specificity and, hence, functional diversification has occurred within the *PERU* receptor family of *Solanum* (Fig. 4A and fig. S10A). Our phylogenomics analyses of *PERU* sequences further suggest that potato *PERU*^{DM} and the PEP-13 receptor in parsley are distinct proteins, although they share similar ligand specificities (Fig. 3) (7, 10).

Metazoan and plant immune receptors have been targeted by positive, diversifying selection, which accelerates the divergence between homologous proteins (32, 33). To identify amino acids under diversifying selection in the proteins encoded by *PERU* alleles, we applied maximum likelihood models of codon substitution using the program codeml from PAML (34, 35). We found a total of 11 residues (S118, E172, L194, Q198, R245, E339, E391, L392, A416, Q489, R590) to be under positive selection according to the three models tested (table S1). We further used AlphaFold2 to predict the tertiary structure of the *PERU*^{DM} ectodomain (fig. S11). All residues but one (S118) found to be under positive selection are located on the concave side of the LRR structure, consistent with observations made for binding of the bacterial flagellin epitope flg22 to the *Arabidopsis* LRR-RK FLS2 (36). As observed for other immune receptors, diversifying selection may have driven functional diversification of *PERU* receptors in wild potato populations.

We further observed that Pep-25-insensitive genotypes were found across the American continent ranging from the US to Chile and Argentina (Fig. 4B). By contrast, Pep-25 sensitivity clustered among species belonging to the section Tuberosa or Piurana—which thrive predominantly in the Andean region of Bolivia and Peru (Fig. 4C)—which suggests that the *PERU* receptor family arose in this region. Wild potatoes carrying *PERU*^{LPH} alleles also cluster in this region, suggesting that functional diversification of *PERU* alleles in wild potato populations has occurred at its center of origin. *PERU* alleles from multiple potato cultivars used today for crop production all cluster with *PERU*^{DM} (Fig. 4A and fig. S10A), suggesting that *PERU* has been maintained during domestication (13).

Discussion

In this study, we characterize potato *PERU* as a bona fide plant PRR conferring *P. infestans*

recognition. *PERU* binds Pep-13/25 patterns that are conserved among species of the genus *Phytophthora*, hetero-dimerizes with BAK1 in a ligand-dependent manner, mediates activation of plant immunity, and increases resistance to a devastating potato disease.

Different ligand response specificities observed among wild *Solanum* accessions indicate that functional diversification within this PRR family has occurred at the site of origin of the predominant allele, *PERU*^{DM}. The explicit use of wild potato populations instead of plant materials that have undergone substantial genetic rearrangements during crop breeding implies that natural forces have been major drivers of immune receptor diversification. The Pep-13 pattern is widespread and highly conserved among plant-associated oomycetes (10), a trait that has likely facilitated the evolution of plant PRRs that recognize it. Although residue W231 is invariant in known sequences of *Phytophthora* TGs, polymorphisms affecting the elicitor activity of WT Pep-13 might occur as pathogen pressure in defined ecological niches is assumed to shape immune receptor reservoirs in metazoans and plants (5). It is thus conceivable that functional diversification of *PERU* was driven by escape mutations within *Phytophthora* Pep-13 patterns that enable Pep-13-producing pathogen strains to elude recognition by the predominant allele, *PERU*^{DM}. Microbial evasion strategies to avoid plant immune activation encompass alterations within immunogenic patterns, thus disabling their recognition by plant PRRs (37, 38). In turn, individual plant species have evolved to perceive polymorphic patterns or, alternatively, structurally unrelated immunogenic molecules (39–43). Likewise, phylogenetically distinct PRRs have evolved in different plant species to recognize structurally unrelated epitopes within individual microbial patterns (44, 45).

We report here the identification of a potato cell surface PRR from the Central Andes and its natural origin in wild potatoes. Our analysis highlights PRR diversification in sympatric, natural potato populations.

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ACKNOWLEDGMENTS

We acknowledge our colleagues T. Bisseling, J. Flegmann, E. Jacobsen, T. Lahaye, R. Lozano-Durán, J. E. Parker, D. Weigel, and S. Wolf for critical reading. We thank D. Huigen for assistance with crossing and greenhouse work organization; H. Wieggersma and H. Smid for excellent plant care; J. Kourelis and Y. Sugihara for assistance with the phylogenomics, J. Win for advice with PAML analysis; S. Landeo for help with ROS assays; J. Schaart, W. de Martinez and D. Monino Lopez for help with CRISPR-Cas constructs cloning; I. Pereira-Bertram for culturing *Solanum* plants; Matthieu Joosten for VIGS constructs; Geert Kessel for providing *P. infestans* isolates; A. Andriani for help with disease tests; J. Stüttmann for providing *N. benthamiana edsI, pad4* and *edsI pad4* lines, and T. Marti Ferrando for help with molecular work. We recognize the ‘Apoplasmic interactions’ session of the 17th IS-MPMI meeting in Portland 2016 that led to initiating the search for the Pep-13 receptor. We dedicate this work to the late D. Scheel, who started the study on Pep-13. **Funding:** This work was supported by the following: Peruvian Council for science, technology and technological innovation (CONCYTEC) FONDECYT contract 129-2017 (to Y.C.T.A.); Deutsche Forschungsgemeinschaft grant CRC1101-D10 and Nu70/17-1 (to T.N.); The Gatsby Charitable Foundation BBSRC, UK, BBS/E/J/000PR9795; BBSRC, UK, BBS/E/J/000PR9796; BBSRC, UK, BS/E/J/000PR9798. **Author contributions:** Conceptualization: Y.C.T.A., A.T., X.L., P.J.W., S.K., V.G.A.A.V., and T.N. Methodology: V.G.A.A.V., T.N.,

Y.C.T.A., A.T., and A.P. Investigation: Y.C.T.A., L.Z., C.H., A.T., N.J.R., A.P., H.P., and N.S. Resources: A.T., D.W., and M.J.M.P. Visualization: Y.C.T.A., A.T., A.P., and R.B. Writing—original draft: Y.C.T.A., T.N., and V.G.A.A.V. Writing—review and editing: Y.C.T.A., L.Z., A.T., S.K., T.N., and V.G.A.A.V. Funding acquisition: R.G.F.V., S.K., T.N., and V.G.A.A.V. **Competing interests:** S.K. receives funding from industry and cofounded a start-up company (Resurrect Bio Ltd.) on plant disease resistance. S.K. has filed patents on plant disease resistance. All other authors declare that they have no competing interests. **Data and materials availability:** Sequences of cloned homologs were deposited in the National Center for Biotechnology Information database, www.ncbi.nlm.nih.gov (accession nos. OQ999431 to OQ999482). All other data, sequences, datasets, and scripts for the phylogenomic analyses are available in the manuscript, the supplementary material or deposited at Zenodo (46). Most of the wild *Solanum* accessions were in possession of WUR Plant Breeding before Nagoya rules applied, part of the material was obtained later from the Center of Genetic Resources, The Netherlands for which we refer to Access and Benefit-Sharing (<https://www.absfocalpoint.nl/en/absfocalpoint.htm>) at their website (<https://cgngenis.wur.nl>). **License information:** Copyright © 2023 the authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original US government works. <https://www.sciencemag.org/about/science-licenses-journal-article-reuse>

SUPPLEMENTARY MATERIALS

science.org/doi/10.1126/science.adg5261
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Submitted 4 January 2023; accepted 11 July 2023
10.1126/science.adg5261



Functional diversification of a wild potato immune receptor at its center of origin

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Science, **381** (6660), .

DOI: 10.1126/science.adg5261

Editor's summary

The oomycete *Phytophthora infestans* devastates potato crops, most famously during the Great Irish Famine of the mid-1800s. Torres Ascurra *et al.* examined wild potato variants from across the Americas and identified a pattern recognition receptor called PERU, which recognizes a *P. infestans* peptide. When PERU binds a protein fragment from *P. infestans*, the potato plant can mount an immune response. The authors established that different alleles of PERU from wild Andean potato relatives have different sensitivities to the *P. infestans* peptide. Their work provides mechanistic insight into *P. infestans* immunity, thus paving the way for improved crop resilience to a disease that has been challenging to control. —Madeleine Seale

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