PathoPlant[®]: A Database on Plant-Pathogen Interactions

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ABSTRACT: Pathogen recognition and signal transduction during plant pathogenesis is essential for the activation of plant defense mechanisms. To facilitate easy access to published data and to permit comparative studies of different pathogen response pathways, a database is indispensable to give a broad overview of the components and reactions so far known. PathoPlan® has been developed as a relational database to display relevant components and reactions involved in signal transduction related to plant-pathogen interactions. On the organism level, the tables 'plant', 'pathogen' and 'interaction' are used to describe incompatible interactions between plants and pathogens or diseases. On the molecular level, plant pathogenesis related information is organized in PathoPlant's main tables 'molecule', 'reaction' and 'location'. Signal transduction pathways are modeled as consecutive sequences of known molecules and corresponding reactions. PathoPlant entries are linked to associated internal records as well as to entries in external databases such as SWISS-PROT, GenBank, PubMed, and TRANSFAC®. PathoPlant is available as a web-based service at http://www.pathoplant.de.

KEYWORDS: Database, plant, pathogen, phytopathogen, interaction, signal transduction, signal perception, pathway, virulence, resistance, susceptibility, avirulence factor, plant defense

INTRODUCTION

When plants are challenged by a pathogen infection, early local defense reactions and delayed systemic responses are activated in order to counteract the pathogen attack. Among the early local responses, the hypersensitive response (HR) leads to a local programmed cell death in order to deprive the pathogens of their nutrition base [Greenberg, 1997; Pontier *et al.*, 1998]. This defense strategy, which is particularly successful towards biotrophic bacteria and fungi as well as towards viruses, is based on pathogen recognition and cell-to-cell communication in the tissue adjacent to the site of infection [Thomma *et al.*, 2001]. Later on, the plant can develop systemic acquired resistance (SAR) leading to resistance throughout the whole plant in an unspecific manner towards a broad spectrum of pathogens. In the case of SAR, the signal is transmitted from the infected tissue into the whole plant for induction of overall defense gene expression [Ryals *et al.*, 1994]. This demonstrates that signal perception in initial pathogen recognition and signal transduction to initiate further defense responses is essential for plants to counteract phytopathogens [Nürnberger and Scheel, 2001].

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Virulence of the pathogen or resistance of the plant is race-specific. The gene-for-gene hypothesis postulates that a specific avirulence signal from the pathogen is recognized by a corresponding plant resistance gene product resulting in a defense response of the plant [Hammond-Kosack and Jones, 1997]. It has been shown for the tomato-*Pseudomonas syringae* pv. *tomato* interaction that the presence of the resistance gene Pto and avirulence gene avrPto determines gene-for-gene specificity in this plant-pathogen interaction [Scofield *et al.*, 1996; Tang *et al.*, 1996]. In a potentially compatible interaction, i.e. an interaction of a virulent pathogen with a susceptible plant, the plant's susceptibility or the virulence of the pathogen is dependent on the strain of the pathogen and the variety of the plant. So far, no comprehensive database has been developed that combines and interconnects information on signal transduction components on molecular level and specific plant-pathogen interactions on organism level.

The TRANSPATH[®] database is a database on signal transduction pathways with a focus on pathways involved in the regulation of transcription factors in mammals, mainly human, mouse and rat [Schacherer et al., 2001; Krull et al., 2003; Choi et al., 2004]. It is linked to the TRANSFAC® database that represents a comprehensive database on eukaryotic transcription factors and their respective DNA-binding sites [Matys et al., 2003]. Organisms from which the transcription factors are derived are not restricted to vertebrates. Also factors from insects, nematodes, fungi, and plants are annotated in TRANSFAC. In contrast, the PRODORIC database organizes information on gene expression of prokaryotes and integrates this information into regulatory networks [Münch et al., 2003]. The GeneNet database harbors data on gene regulation of sets of genes functioning in a coordinated manner to control vital processes in organisms of all types including plants [Kolchanov et al., 2000; Kolchanov et al., 2002]. These databases are not specific for plant-pathogen interactions. Thus, the PathoPlant[®] database has been created to link specific plants and pathogens with the corresponding signal transduction pathways during their interactions. The objectives of PathoPlant are to give a comprehensive overview about specific plant-pathogen interactions and to link this information to signal perception and transduction components. This may allow identification of missing links in signal transduction pathways, deduction of the function of novel proteins by comparison with known signal transduction pathways, estimation of virulence of pathogens and resistance of plants by analysis of similar plant-pathogen interactions, and finally, may contribute to the development of strategies for improving resistance of plants by genetic engineering after identification of the missing signal transduction component or resistance factor in a compatible interaction.

SYSTEM AND METHODS

The PathoPlant database structure was initially established in UML and then implemented as a relational database on a Microsoft SQL Server 2000 System. The structure of PathoPlant basically consists of the main tables 'plant', 'pathogen', and 'interaction' on the organism level and of the main tables 'molecule', 'reaction', and 'location' on the molecular level (Fig. 1). On molecular signal transduction level, the structure of the PathoPlant database is partly based on the TRANSPATH database [Krull *et al.*, 2003] which has been adapted and extended to meet the specific requirements for a phytopathological database. In contrast to TRANSPATH, PathoPlant models not only signal transduction components and reactions between molecules but covers also interactions between plants and pathogens and therefore enables linking of specific signal transduction reactions on molecular level to the corresponding specific interactions between the organisms.

Molecular signal perception and signal transduction mechanisms are stored in the table 'reaction' that is linked to the corresponding entries of the participating molecules in the table 'molecule'. The table

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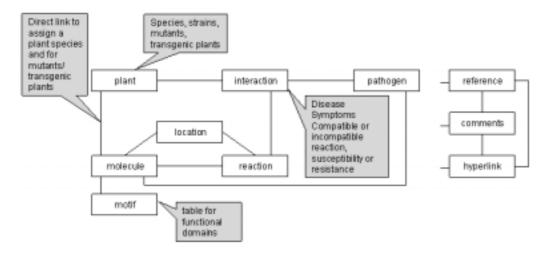


Fig. 1. Part of the E/R-diagram of the PathoPlant database with the main tables and comments on selected tables.

'location' was created to store information where a molecule is located or a reaction takes place and can be recorded on organ, on tissue type as well as on organelle level. If known, the table 'motif' linked to a molecule entry provides a description of the functional domains of a protein. On organism level, information on the plants and pathogens involved in plant-pathogen interactions is organized in the tables 'plant' and 'pathogen'. Data about the interactions between the organisms is stored in the table 'interaction'. In this table, specific data on the type of interaction, virulence of the pathogen, resistance or susceptibility of the plant, and disease symptoms are given. The organisms as well as the interactions are classified hierarchically enabling navigation to the more specific or more general record.

Via the table 'reference', entries are linked to the related publications where the information was extracted from. Links to external databases are established through the table 'hyperlink'. The table 'annotate' was included to display linkable comments such as a cross reference to a pathway map. The entries in the table 'reaction' are qualified according to the material and method employed in the experimental procedure to determine the accuracy of the mechanism stated in the database. Therefore, the table 'quality' was introduced into the database structure and linked to the tables 'reaction' and 'location'. A scoring system that is analogous to the system used in the TRANSPATH database [Schacherer *et al.*, 2001; Krull *et al.*, 2003; Choi *et al.*, 2004] automatically assigns a quality value to each combination of material and method. This system is also used to assess the accuracy of the location information provided. In total, the PathoPlant database consists of 49 tables including link tables.

IMPLEMENTATION AND WEB INTERFACE

An interactive web interface implemented on an Apache web server running on a Linux operation system was developed for access via internet at http://www.pathoplant.de. The web interface enables direct access to the information stored in the database through multiple search functions. A specific signal transduction component from the table 'molecule', a plant, a pathogen, or a plant-pathogen interaction can be searched by directly submitting the search term in the 'Quick search' form. This term will be found if present in the fields for the 'name', 'full name' or 'synonym'. The 'Advanced search' form allows restriction of the submitted search term to specific attributes. Multiple queries can be combined using either the AND or the OR operator. A result list displays the matching entries in a table where

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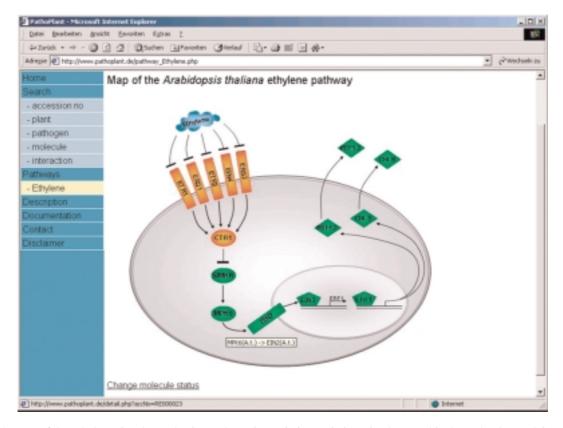


Fig. 2. Map of the Ethylene signal transduction pathway in Arabidopsis thaliana implemented in the PathoPlant web interface.

they are directly linked to the corresponding record displays. Furthermore, the search can be refined by submitting additional search terms to specific attributes that are then applied for a search within the results list. This process can be repeated with the resulting list if necessary. If the accession number of a specific entry is known, e.g. from a previous database query, the search by accession number offers a rapid way that leads directly to the corresponding record. For plant species, pathogen species, and interactions between organisms, a graphical search function enables comfortable access without necessity of knowing the precise determinations resulting in a list of all available organisms and interactions.

The entries are directly accessible from the search results list. The record display is divided into a section with general information and a section with links to other related entries in PathoPlant and links to external databases. In the case of signal transduction components, a link leads to a graphical overview displaying the related pathway molecules and reactions (Fig. 2). In this pathway map, each molecular component and each reaction is linked to the corresponding record.

DATABASE CONTENT

Currently, 104 interaction records related to 47 plant and 29 pathogen entries with the corresponding references and hyperlinks are annotated in PathoPlant. The current database content of the PathoPlant database is displayed in Table 1 (status as of September 2004). All information annotated in PathoPlant is extracted manually out of published literature. In the case of reactions between molecules and location

Table 1

Database content of the PathoPlant database, status as of September 2004		
Table	No. of records	
plant	47	
pathogen	29	
interaction	104	
molecule	50	
reaction	26	
reference	205	
comment	19	
hyperlink	439	

of molecules and reactions, the re-	esults are assessed automatically by a sco	oring system to determine
the reliability of the information.	This score depends on the material and th	e method employed in the
underlying experiment.		

An example of a signal transduction pathway annotated in PathoPlant is the ethylene pathway in Arabidopsis thaliana shown in Fig. 2. Ethylene is a plant hormone not only acting as a signal molecule in plant development [Abeles et al., 1992] but is also involved in the plant's defense response [Knoester et al., 1998; Lund et al., 1998; Penninckx et al., 1998; Devadas et al., 2002]. Furthermore, the ethylene pathway is one of the best characterized signal transduction pathways in plants. Therefore, proteins from Arabidopsis thaliana related to ethylene signal perception and signal transduction were annotated and displayed graphically in a pathway map (Fig. 2). In this map, signal transduction molecules are displayed as green symbols if their status is active, and inactive molecules are shown in red. According to this, the arrows between the molecules indicate activation, and the blunt-ended lines represent inhibition. Ethylene is recognized by five homologous membrane-bound receptors that are negatively regulated by ethylene and inactivated by the binding of the signal molecule resulting in a reverted signal in the presence of ethylene indicated as red molecules in Fig. 2 [Chang et al., 1993; Hua et al., 1995; Hua et al., 1998; Sakai et al., 1998]. These inactive receptors do not transmit the signal on CTR1 [Kieber et al., 1993; Clark et al., 1998], a MAP kinase kinase kinase, which in consequence is also inactive in the presence of ethylene. CTR1 represents the starting point of a MAP kinase cascade. The presence of a cascade has been proposed since the identification of CTR1 but the missing members were unknown [Stepanova and Ecker, 2000; Wang et al., 2002]. It was demonstrated recently that a MAP kinase kinase and a MAP kinase expressed in stress-induced plants are the missing components in this cascade of the ethylene pathway [Ouaked et al., 2003]. In the course of signal transmission through this cascade, the signal is reverted again resulting in active (green in Fig. 2) MPK6 in the presence of ethylene. The signal is then transmitted via EIN2 into the nucleus [Alonso et al., 1999] and the transcription factor EIN3 activates expression of primary ethylene responsive genes [Chao et al., 1997]. Among them, a second transcription factor, ERF1, is expressed driving expression of secondary ethylene responsive genes like beta-chitinase and plant defensin as pathogenesis related proteins [Solano et al., 1998]. The changed status of the molecules in the absence of ethylene is displayed by clicking on the link 'Change molecule status' below the map (Fig. 2).

PathoPlant is focused in the initial annotation phase on different ecotypes of *Arabidopsis thaliana*, different strains of *Pseudomonas syringae* and is describing the specific interactions between these organisms as well as the corresponding avirulence proteins. *Pseudomonas syringae* pv. *tomato* not only infects tomato plants causing bacterial speck disease but is also able to infect *Arabidopsis thaliana* [Dong *et al.*, 1991]. The interactions of different *Pseudomonas syringae* pv. *tomato* strains with diverse ecotypes of *Arabidopsis thaliana* are in accordance with the gene-for-gene hypothesis that postulates

corresponding avirulence genes of the pathogen and resistance genes of the plant resulting in a dependence of resistance or susceptibility on the encounter of a specific pathogenic strain with the matching ecotype of a plant [Whalen *et al.*, 1991]. The *Arabidopsis thaliana-Pseudomonas syringae* interaction has evolved into a model system to study bacterial interactions with plants (Ausubel *et al.*, 1995]. New screening methods for potential avirulence genes have been developed using *Arabidopsis thaliana* and *Pseudomonas syringae* as model organisms [Guttman *et al.*, 2002; Greenberg and Vinatzer, 2003]. Additionally, the genomic sequencing of *A. thaliana* ecotype Columbia and strain DC3000 from *P. syringae* pv. *tomato* has been completed recently [Arabidopsis Genome Initiative, 2000; Buell *et al.*, 2003].

The PathoPlant database content is continuously extended and updated. In the future, links to expression data from published microarray experiments with *Arabidopsis thaliana* after treatment with phytopathogens and elicitors will be incorporated into PathoPlant. The recent establishment of the AthaMap database may provide an attractive opportunity to identify target genes regulated in plantpathogen interactions based on common regulatory elements in their promoters [Steffens el al., 2004].

CONCLUSION

Signal perception and signal transduction is essential for plants to recognize a pathogen and counteract the pathogen's infection. PathoPlant has been developed as a new database that combines information of specific plant-pathogen interactions on organism level and data about signal transduction on molecular level related with plant pathogenesis. PathoPlant will help to predict the function of newly discovered proteins and will help to place them in the context of a signal transduction network. By comparing susceptible with resistant plant species or races, PathoPlant may enable the development of new resistance strategies via genetic engineering.

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