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Salicylic Acid and Plant Immunity

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ABSTRACT: The plant immune system consists of two interconnected tiers of receptors, one outside and one inside the cell. Both systems sense the intruder, respond to the intrusion and optionally signal to the rest of the plant and sometimes to neighboring plants that the intruder is present. Salicylic Acid (SA) is one of a wide variety of phenolic compounds bearing a hydroxyl group or its derivative that are synthesized by plants. The strongest evidence supporting SA's role as a critical defense signal has come from analyses of plants in which endogenous SA levels were altered. The first of these studies utilized transgenic tobacco or Arabidopsis expressing the bacterial nahG gene, encoding the SA-metabolizing enzyme salicylate hydroxylase. SA treatment was subsequently found to induce PR (pathogenesis-related) gene expression and/or resistance to viral, bacterial, and fungal pathogens in many plant species. It induced the same set of genes in tobacco and Arabidopsis as was activated during SAR (systemic acquired resistance). In tobacco mosaic virus (TMV) resistant, SA levels increased more than 20-fold in the inoculated leaves and over 5-fold in the systemic leaves; in both sets of leaves these increases preceded or paralleled PR gene expression. Similarly, SA levels increased 10- to 100-fold in the phloem exudates of cucumber inoculated with tobacco necrosis virus, Colletotrichum lagenarium, or Pseudomonas syringae, and these increases preceded SAR development and induction of a defense-associated peroxidase activity. Additional evidence supporting a signaling role for SA came from the demonstration that high temperature growth conditions suppressed disease resistance, PR expression and SA accumulation in TMV-resistant tobacco.

Keywords: Plant Immunity, Salicylic Acid, systemic resistance, SAR (systemic acquired resistance).

INTRODUCTION

Plant disease resistance is crucial to the reliable production of food, and it provides significant reductions in agricultural use of land, water, fuel and other inputs. Plants in both natural and cultivated populations carry inherent disease resistance, but this has not always protected them. The late blight Irish potato famine of the 1840s was caused by the oomycete *Phytophthora infestans*. The world's first mass-cultivated banana cultivar Gros Michel was lost in the 1920s to Panama disease caused by the fungus *Fusarium oxysporum*. The wheat stem, leaf, and yellow stripe rust epidemics spreading from East Africa into the Indian subcontinent were caused by rust fungi *Puccinia graminis* and *P. striiformis*. Other epidemics include Chestnut blight, as well as recurrent severe plant diseases such as Rice blast, Soybean cyst nematode, Citrus canker (Dangl *et al.,* 2013).

Plant pathogens can spread rapidly over great distances, vectored by water, wind, insects, and humans. Across large regions and many crop species, it is estimated that diseases typically reduce plant yields by 10% every year in more developed nations or agricultural systems, but yield loss to diseases often exceeds 20% in less developed settings, an estimated 15% of global crop production.

However, disease control is reasonably successful for most crops. Disease control is achieved by use of plants that have been bred for good resistance to many diseases, and by plant cultivation approaches such as crop rotation, pathogen-free seed, appropriate planting date and plant density, control of field moisture and pesticide use (Dangl *et al.,* 2013).

EARLY HISTORY OF SALICYLATES

Plants are a rich source of natural medicines. Indeed, people often fail to realize that many currently used drugs, including digitalis, quinine, taxol, the opiates codeine and morphine, and aspirin [a synthetic derivative of salicylic acid (SA)] are derived from plants. Of these, aspirin is one of the most successful and widely used drugs. An estimated 43 million Americans, which translates into roughly one-fifth of the population, take aspirin on a regular basis.

Not only does aspirin reduces pain, inflammation, and fever, but prophylactic use lowers the risk of heart attack, stroke, and certain cancers. Long before salicylates (the general term for derivatives of SA) were identified, plants containing these compounds in large quantities were used medicinally. In the fourth century B.C., Hippocrates encouraged women to chew willow leaves to relieve the pain of childbirth (Raskin, 1992). The use of salicylate-containing plants for therapeutic purposes continued to develop throughout the ancient world, from Rome and Asia, to the New World, where Native Americans used compresses containing extracts of willow bark to relieve pain Vane and Botting (1992). Despite the popularity of willow bark as a folk remedy, its medicinal effects were not clinically studied until the mid-1700s by the Reverend Edward Stone in Oxfordshire, England. More than a half century later, French and German scientists competed to isolate the active ingredient in willow bark. In 1828, a German scientist, Johann A. Buchner, purified a small quantity of a yellowish substance he called salicin. Ten years later, Raffaele Piria, an Italian chemist working in Paris, split salicin into a sugar and an aromatic compound that could be converted into an acid he named acide salicylice. Other natural sources of SA were discovered around this time, but the demand for SA as a pain reliever rapidly outstripped production capability. SA was first chemically synthesized by Hermann Kolbe and coworkers in 1859; improvements to the synthetic process eventually led to large-scale production of cheaply priced SA, which led to even greater medicinal use.

However, the bitter taste and unpleasant side effects, such as chronic stomach inflammation, made long-term use of SA for conditions such as arthritis difficult. Subsequent research by Felix Hoffmann, an employee of the Bayer pharmaceutical company, revealed that acetylation of SA yielded a compound that was better tolerated, yet retained the medicinal qualities of SA. The impracticality of marketing this over the- counter painkiller as acetylsalicylic acid led to the selection in 1899 of the trade name aspirin.

SALICYLIC ACID AS A PLANT SIGNAL/HORMONE

SA is one of a wide variety of phenolic compounds bearing a hydroxyl group or its derivative that are synthesized by plants. Traditionally, plant phenolics were classified as secondary metabolites, as they were thought to be relatively unimportant or waste products. However, this concept changed drastically with the discovery that phenolics have many important functions. For example, certain phenolics are involved in lignin biosynthesis; others serve as allelopathic compounds, regulate plant responses to abiotic stimuli, or play critical roles in plant disease resistance either by functioning as preformed or inducible antimicrobial defense compounds termed phytoalexins or by signaling defense activation (Humphreys and Chapple 2002, M´etraux and Raskin 1993, Raskin, 1992). SA, in particular, influences seed germination, seedling establishment, cell growth, respiration, stomatal closure, senescence-associated gene expression, responses to abiotic stresses, basal thermotolerance, nodulation in legumes, and fruit yield. Its effect on some of these processes may be indirect because SA alters the synthesis of and/or signaling by other plant hormones including jasmonic acid (JA), ethylene (ET), and auxin (see Relationship to Other Defense Signals below). In addition, SA functions as a key signal in regulating thermogenesis and disease resistance (Clarke *et al.,* 2004, Klessig and Malamy 1994, Mateo 2004, Metwally *et al.,* 2003, Morris 2000).

THE PLANT IMMUNE SYSTEM

The plant immune system consists of two interconnected tiers of receptors, one outside and one inside the cell. Both systems sense the intruder, respond to the intrusion and optionally signal to the rest of the plant and sometimes to neighboring plants that the intruder is present. The two systems detect different types of pathogen molecules and classes of plant receptor proteins. The first tier is primarily governed by pattern recognition receptors that are activated by recognition of evolutionarily conserved pathogen or microbial–associated molecular patterns (PAMPs or MAMPs, here P/MAMP). Activation of PRRs leads to intracellular signaling, transcriptional reprogramming, and biosynthesis of a complex output response that limits colonization. The system is known as PAMP-Triggered Immunity (PTI). (Jones and Dangl 2006, Dodds and Rathjen 2010). The second tier (again, primarily), effector-triggered immunity (ETI), consists of another set of LRRs, the nucleotide-binding LRRs (NLRs). They operate within the cell, encoded by R genes. The presence of specific pathogen “effectors” activates specific NLR proteins that limit pathogen proliferation. Receptor responses include ion channel gating, oxidative burst, cellular redox changes, or protein kinase cascades that directly activate cellular changes (such as cell wall reinforcement or antimicrobial production), or activate changes in gene expression that then elevate other defensive responses. Plant immune systems show some mechanistic similarities with the immune systems of insects and mammals, but also exhibit many plant-specific characteristics. Plants can sense the presence of pathogens and the effects of infection via different mechanisms than animals Boyd (2012).

GENES INVOLVED

Gene expression is controlled at both transcriptional and post-transcriptional levels. RNA-binding proteins (RBP) are involved in multiple post-transcriptional processes. After protein-coding genes are transcribed into pre-mRNA by RNA polymerase II, processing and modification steps, such as splicing, are required to produce functional mRNA that is ready for export from the nucleus to the cytoplasm. The cytoplasmic mRNAs can be translated or degraded (Lorkovic, 2009). RBP can regulate all of these processes. For example, approximately 30% of *Arabidopsis* genes are thought to be alternatively spliced, and RBP, such as serine/arginine-rich (SR) proteins, are involved in selection of splice sites and recruitment of the splicing machinery to selected splice sites (Reddy, 2007). Plant RBP are characterized by the presence of RNA-binding domains, such as the RNA recognition motif (RRM) or the K-homology (KH) domain (Lorkovic, 2009). The *Arabidopsis* genome contains more than 200 putative RBP genes, and some of them have been shown to be involved in abiotic stress responses and flowering (Lorkovic and Barta, 2002, Kim *et al.*, 2005, Kim *et al.*, 2007). A large percentage of genes in the plant genome respond transcriptionally to pathogen attack (Tao *et al.*, 2003, Thilmony *et al.*, 2006). In addition to reprogramming of transcription, post-transcriptional regulation also plays a role in the plant immune response. For example, alternatively spliced transcript forms of both *N* and *RPS4 R* genes are required for their full function (Dinesh-Kumar and Baker, 2000, Zhang and Gassmann (2003). A glycine-rich RBP family member, GRP7, was shown to be involved in the plant immune response (Fu *et al.*, 2007). GRP7 is required for defense against *P. syringae* pathogens and is targeted by the effector HopU1 for mono-ADP-ribosylation (Fu *et al.*, 2007). In addition, GRP7 is involved in many other biological processes, such as seed germination, cold response, stomata opening and closing, circadian rhythm (Staiger, 2003, Schoning, 2007) and flowering (Streitner, 2008). Discovery of RNA-binding proteins involved in plant immunity will contribute to our understanding of post-transcriptional regulation in plant responses to pathogens.

Plants have evolved R genes (resistance genes) whose products allow recognition of specific pathogen effectors, either through direct binding or by recognition of the effector's alteration of a host protein (Jones and Dangl, (2006). These virulence factors drove co-evolution of plant resistant genes to combat the pathogens' Avr (avirulent) genes. Many R genes encode NB-LRR proteins (nucleotide-binding/leucinerich repeat domains, also known as NLR proteins or STAND proteins, among other names). R gene products control a broad set of disease resistance responses whose induction is often sufficient to stop further pathogen growth/spread. Each plant genome contains a few hundred apparent R genes. Studied R genes usually confer specificity for particular pathogen strains. As first noted by Harold Flor in his mid-20th century formulation of the gene-for-gene relationship, the plant

R gene and the pathogen Avr gene must have matched specificity for that R gene to confer resistance, suggesting a receptor/ligand interaction for Avr and R genes (Numberger, 2004). Alternatively, an effector can modify its host cellular target (or a molecular decoy of that target) activating an NLR associated with the target or decoy. Plant breeders frequently rely on R genes to obtain useful resistance, although the durability of this resistance can vary by pathogen, pathogen effector and R gene. The presence of an R gene can place significant selective pressure on the pathogen to alter or delete the corresponding avirulence/effector gene. Some R genes show evidence of stability over millions of years while other R genes, especially those that occur in small clusters of similar genes, can evolve new pathogen specificities over much shorter intervals (Friedman and Baker, 2007). RNA silencing-based resistance is a powerful tool for engineering resistant crops. The advantage of RNAi (interfering RNA) as a novel gene therapy against fungal, viral and bacterial infection in plants lies in the fact that it regulates gene expression via messenger RNA degradation, translation repression and chromatin remodelling through small noncoding RNAs. Mechanistically, the silencing processes are guided by processing products of the double-stranded RNA (dsRNA) trigger, which are known as small interfering RNAs and microRNAs (Karthikeyan, 2013). Against viruses, plants often induce pathogen-specific gene silencing mechanisms mediated by RNA interference. This is a simple form of adaptive immunity (Ding and Voinnet (2007). Plant immune systems also can respond to an initial infection in one part of the plant by physiologically elevating the capacity for a successful defense response in other parts. Such responses include systemic acquired resistance, largely mediated by salicylic acid-dependent pathways, and induced systemic resistance, largely mediated by jasmonic acid-dependent pathways (Spoel, 2012).

SALISYLIC ACID IS AN ENDOGENOUS RESISTANCE SIGNAL

A possible role for SA in signaling disease resistance was first suggested by White and coworkers, who demonstrated that injecting leaves of resistant tobacco with SA or aspirin stimulated

PR (pathogenesis-related) protein accumulation and enhanced resistance to tobacco mosaic virus (TMV) infection, manifested by a 90% reduction in lesion number.

SA treatment was subsequently found to induce *PR* gene expression and/or resistance to viral, bacterial, and fungal pathogens in many plant species. Furthermore, it induced the same set of genes in tobacco and *Arabidopsis* as was activated during SAR (systemic acquired resistance). SA was initially proposed to act by mimicking an endogenous phenolic signal for resistance; however, analyses of SA levels in cucumber and tobacco argued that it was the actual defense signal. In TMV resistant (but not TMV-susceptible) tobacco, SA levels increased more than 20-fold in the inoculated leaves and over 5-fold in the systemic leaves; in both sets of leaves these increases preceded or paralleled *PR* gene expression (Malamy *et al.,* 1990). Similarly, SA levels increased 10- to 100-fold in the phloem exudates of cucumber inoculated with tobacco necrosis virus, *Colletotrichum lagenarium*, or *Pseudomonas syringae*, and these increases preceded SAR development and induction of a defense-associated peroxidase activity (M´etraux *et al.,* 1990 and Rasmussen *et al.,* 1991). Additional evidence supporting a signaling role for SA came from the demonstration that high temperature growth conditions (>28◦C) suppressed disease resistance (including HR development), *PR* expression and SA accumulation in TMV-resistant tobacco (Yalpani, *et al.,* 1991). Shifting these plants to room temperature led to a dramatic increase in SA levels, which preceded lesion formation and *PR-1* expression. Furthermore, the highly elevated SA levels found in certain plants and genetic mutants correlated with their enhanced resistance to pathogen infection. The strongest evidence supporting SA's role as a critical defense signal has come from analyses of plants in which endogenous SA levels were altered. The first of these studies utilized transgenic tobacco or *Arabidopsis* expressing the bacterial *nahG* gene, encoding the SA-metabolizing enzyme salicylate hydroxylase. Following pathogen infection, these plants were unable to accumulate high SA levels, and they failed to develop SAR or express *PR* genes in the systemic leaves; instead, they displayed heightened susceptibility to both virulent and avirulent pathogens (Vernooij *et al.,* 1994). Both disease resistance and *PR* expression were restored in these plants by treatment with the SA synthetic analog, 2,6-dichloro-isonicotinic acid (INA). Subsequent studies revealed that plants defective for SA biosynthesis displayed a similar phenotype. Tobacco or *Arabidopsis* with suppressed *PAL* expression or mutations in *SID2/EDS16* (encodes ICS1) or *SID1/EDS5* (encodes a member of the MATE transporter family required for SA accumulation) displayed enhanced pathogen susceptibility and/or failed to develop SAR or systemically express *PR* genes. Like *nahG* plants, resistance and *PR* expression were restored by treatment with SA or INA. Overexpression of enzymes involved in SA metabolism, including SA glucosyltransferase 1 (AtSGT1) or SA methyltransferase (OsBSMT1), in transgenic *Arabidopsis* also led to reduced endogenous SA levels, reduced *PR* expression and enhanced susceptibility to pathogens. By contrast, overexpression of bacterial SA biosynthetic genes in transgenic tobacco conferred highly elevated SA levels, constitutive *PR* expression, and enhanced resistance (Wildermuth *et al.,* 2001).

Plant breeding for disease resistance

Plant breeders emphasize selection and development of disease-resistant plant lines. Plant diseases can also be partially controlled by use of pesticides and by cultivation practices such as crop rotation, tillage, planting density, disease-free seeds and cleaning of equipment, but plant varieties with inherent (genetically determined) disease resistance are generally preferred. Breeding for disease resistance began when plants were first domesticated. Breeding efforts continue because pathogen populations are under selection pressure for increased virulence, new pathogens appear, evolving cultivation practices and changing climate can reduce resistance and/or strengthen pathogens, and plant breeding for other traits can disrupt prior resistance. A plant line with acceptable resistance against one pathogen may lack resistance against others. Breeding for resistance typically includes:

_ Identification of plants that may be less desirable in other ways, but which carry a useful disease resistance trait, including wild strains that often express enhanced resistance.

_ Crossing of a desirable but disease-susceptible variety to another variety that is a source of resistance.

_ Growth of breeding candidates in a disease conducive setting, possibly including pathogen inoculation.

Attention must be paid to the specific pathogen isolates, to address variability within a single pathogen species.

_ Selection of disease-resistant individuals that retain other desirable traits such as yield, quality and including other disease resistance traits.

Resistance is termed *durable* if it continues to be effective over multiple years of widespread use as pathogen populations evolve. "Vertical resistance" is specific to certain races or strains of a pathogen species, is often controlled by single R genes and can be less durable.

Hoizontal or broad-spectrum resistance against an entire pathogen species is often only incompletely effective, but more durable, and is often controlled by many genes that segregate in breeding populations.

Crops such as potato, apple, banana and sugarcane are often propagated by vegetative reproduction to preserve highly desirable plant varieties, because for these species, outcrossing seriously disrupts the preferred traits.

See also asexual propagation. Vegetatively propagated crops may be among the best targets for resistance improvement by the biotechnology method of plant transformation to manage genes that affect disease resistance.

Scientific breeding for disease resistance originated with Sir Rowland Biffen, who identified a single recessive gene for resistance to wheat yellow rust. Nearly every crop was then bred to include disease resistance (R) genes, many by introgression from compatible wild relatives (Dangl *et al.*, 2013, Corina *et al.*, 2009).

REFERENCES

Dangl, J.L.; Horvath, D.M.; Staskawicz, B.J. (2013). "Pivoting the Plant Immune System from Dissection to Deployment". *Science* **341**(6147): 746. doi:10.1126/science.1236011.

Raskin I. (1992). Role of salicylic acid in plants. *Annu. Rev. Plant Physiol.* **43**: 439–63.

Vane JR, Botting RM. (1992). The history of aspirin. In *Aspirin and Other Salicylates*, ed. JR Vane, RM Botting, **1**: 3–16. London: Chapman & Hall.

Humphreys J.M., Chapple, C. (2002). Rewriting the lignin roadmap. *Curr. Opin. Plant Biol.* **5**: 224–29.

M´etraux JP and Raskin I. (1993). Role of phenolics in plant disease resistance. In *Biotechnology in Plant Disease*

Control, ed. *I Chet*, **11**: 191–209. New York: John Wiley & Sons.

Raskin I. (1992). Role of salicylic acid in plants. *Annu. Rev. Plant Physiol.* **43**: 439–63.

Clarke SM, Mur LAJ, Wood JE, Scott IM. (2004). Salicylic acid dependent signaling promotes basal thermotolerance but is not essential for acquired thermotolerance in *Arabidopsis thaliana*. *Plant J.* **38**: 432–47.

Klessig DF, Malamy J. (1994). The salicylic acid signal in plants. *Plant Mol. Biol.* **26**: 1439–58.

Mateo A,M¨ uhlenbock P,R´esterucci C, Chang CCC, Miszalski Z, et al. (2004). *Lesion Simulating Disease 1* is required for acclimation to conditions that promote excess excitation energy. *Plant Physiol.* **136**: 2818–30.

Metwally A, Finkemeier I, Georgi M, Dietz KJ. (2003). Salicylic acid alleviates the cadmium toxicity in barley seedlings. *Plant Physiol.* **132**: 272–81.

Morris K, Mackerness SAH, Page T, John CF, Murphy AM, et al. (2000). Salicylic acid has a role in regulating gene expression during leaf senescence. *Plant J.* **23**: 677–85.

Jones, J. D.; Dangl, J.L. (2006). "The plant immune system". *Nature* **444**(7117): 323–329. Bibcode:2006Natur.444..323J. doi:10.1038/nature05286. PMID 17108957.

Dodds, P. N.; Rathjen, J. P. (2010). "Plant immunity: Towards an integrated view of plant–pathogen interactions". *Nature Reviews Genetics* **11** (8): 539. doi:10.1038/nrg2812.

Boyd, Jade (2012). A bit touchy: Plants' insect defenses activated by touch. Rice University.

Lorkovic, Z. J. (2009). Role of plant RNA-binding proteins in development, stress response and genome organization. *Trends Plant Sci.* **14**: 229-236.

Reddy, A. S. (2007). Alternative splicing of pre-messenger RNAs in plants in the genomic era. *Annu. Rev. Plant Biol.* **58**: 267-294.

Lorkovic, Z. J., and Barta, A. (2002). Genome analysis: RNA recognition motif (RRM) and K homology (KH) domain RNA-binding proteins from the flowering plant *Arabidopsis thaliana*. *Nucleic Acids Res.* **30**: 623-635.

Kim, Y. O., Kim, J. S., and Kang, H. (2005). Cold-inducible zinc finger-containing glycine-rich RNA-binding protein contributes to the enhancement of freezing tolerance in *Arabidopsis thaliana*. *Plant J.* **42**: 890-900.

Kim, J. S., Park, S. J., Kwak, K. J., Kim, Y. O., Kim, J. Y., Song, J., Jang, B., Jung, C. H., and Kang, H. (2007). Cold shock domain proteins and glycine-rich RNA-binding proteins from *Arabidopsis thaliana* can promote the cold adaptation process in *Escherichia coli*. Nucleic Acids Res. **35**: 506-516.

Tao, Y., Xie, Z., Chen, W., Glazebrook, J., Chang, H. S., Han, B., Zhu, T., Zou, G., and Katagiri, F. (2003). Quantitative nature of *Arabidopsis* responses during compatible and incompatible interactions with the bacterial pathogen *Pseudomonas syringae*. *Plant Cell*, **15**: 317-330.

Thilmony, R., Underwood, W., and He, S.Y. (2006). Genome-wide transcriptional analysis of the *Arabidopsis thaliana* interaction with the plant pathogen *Pseudomonas syringae* pv. *tomato* DC3000 and the human pathogen *Escherichia coli* O157:H7. *Plant J.* **46**: 34-53.

Dinesh-Kumar, S. P., and Baker, B. J. (2000). Alternatively spliced N resistance gene transcripts: Their possible role in *Tobacco mosaic virus* resistance. Proc. Natl. Acad. Sci. U.S.A. **97**: 1908-1913.

Zhang, X. C., and Gassmann, W. (2003). RPS4-mediated disease resistance requires the combined presence of RPS4 transcripts with full-length and truncated open reading frames. *Plant Cell* **15**: 2333-2342.

Fu, Z.Q., Guo, M., Jeong, B.R., Tian, F., Elthon, T.E., Cerny, R.L., Staiger, D., and Alfano, J.R. (2007). A type III effector ADP-ribosylates RNA-binding proteins and quells plant immunity. *Nature*, **447**: 284-288.

Staiger, D., Zecca, L., Wieczorek Kirk, D. A., Apel, K., and Eckstein, L. (2003). The circadian clock regulated RNA-binding protein AtGRP7 autoregulates its expression by influencing alternative splicing of its own pre-mRNA. *Plant J.* **33**: 361-371.

Schoning, J. C., Streitner, C., Page, D. R., Hennig, S., Uchida, K., Wolf, E., Furuya, M., and Staiger, D. (2007). Auto-regulation of the circadian slave oscillator component AtGRP7 and regulation of its targets is Vol. **23**, No. 12, 2010 / 1583 impaired by a single RNA recognition motif point mutation. *Plant J.* **52**: 1119-1130.

Streitner, C., Danisman, S., Wehrle, F., Schoning, J. C., Alfano, J. R., and Staiger, D. (2008). The small glycine-rich RNA binding protein AtGRP7. promotes floral transition in *Arabidopsis thaliana*. *Plant J.* **56**: 239-250.

Jones, J.D., Dangl, J.L. (2006). "The plant immune system". *Nature* **444**(7117): 323–329. Bibcode:2006Natur.444..323J. doi:10.1038/nature05286. PMID 17108957.

Numberger, T.; Brunner, F., Kemmerling, B., and Piater, L.; Kemmerling, B; Piater, L (2004). "Innate immunity in plants and animals: striking similarities and obvious differences". *Immunological Reviews* **198**: 249–266. doi:10.1111/j.0105-2896.2004.0119.x. PMID 15199967.

Friedman, A. R.; Baker, B. J. (2007). "The evolution of resistance genes in multi-protein plant resistance systems". *Current Opinion in Genetics & Development* **17**(6): 493–9. doi:10.1016/j.gde.2007.08.014. PMID 17942300.

Karthikeyan, A.; Deivamani, M.; Shobhana, V. G.; Sudha, M.; Anandhan, T. (2013). "RNA interference: Evolutions and applications in plant disease management". *Archives of Phytopathology and Plant Protection* **46**(12): 1430. doi:10.1080/03235408.2013.769315.

Ding, S. W. and Voinnet, O. (2007). "Antiviral Immunity Directed by Small RNAs". *Cell* **130**(3): 413–426. doi:10.1016/j.cell.2007.07.039. PMC 2703654. PMID 17693253.

Spoel, Steven H.; Dong, Xinnian (2012). "How do plants achieve immunity? Defence without specialized immune cells". *Nature Reviews Immunology* **12** (2): 89–100. doi:10.1038/nri3141. PMID 22273771.

Klessig DF, Malamy J. (1994). The salicylic acid signal in plants. *Plant Mol. Biol.* **26**: 1439–58.

Malamy J, Klessig DF. (1992). Salicylic acid and plant disease resistance. *Plant J.* **2**: 643–54.

Raskin I. (1992). Role of salicylic acid in plants. *Annu. Rev. Plant Physiol.* **43**: 439–63.

Malamy J, Carr JP, Klessig DF, Raskin I. (1990). Salicylic acid: a likely endogenous signal in the resistance response of tobacco to viral infection. *Science* **250**: 1002–4.

M´etraux JP, Signer H, Ryals J,Ward E,Wyss-Benz M, (1990). Increase in salicylic acid at the onset of systemic acquired resistance in cucumber. *Science* **250**: 1004–6.

Rasmussen JB, Hammerschmidt R, Zook MN. (1991). Systemic induction of salicylic acid accumulation in cucumber after inoculation with *Pseudomonas syringae* pv. *syringae*. *Plant Physiol.* **97**: 1342–47.

Yalpani N, Silverman P,Wilson TMA, Kleier DA, Raskin I. (1991). Salicylic acid is a systemic signal and an inducer of pathogenesis-related proteins in virus-infected tobacco. *Plant Cell* **3**: 809–18.

Vernooij B, Friedrich L, Morse A, Reist R, Kolditz-Jawhar R, (1994). Salicylic acid is not the translocated signal responsible for inducing systemic acquired resistance but is required in signal transduction. *Plant Cell* **6**: 959–65.

Wildermuth MC, Dewdney J,Wu G, Ausubel FM. (2001). Isochorismate synthase is required to synthesize salicylic acid for plant defence. *Nature* **414**: 562–71.

Corina Vlot, A; D'M. A. Dempsey and Klessig, Daniel F. (2009). Salicylic Acid, a Multifaceted Hormone to Combat Disease. *Annu. Rev. Phytopathol.* 2009.**47**: 177-206.