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Review

Hormone Signaling Networks Open Multiple Routes for Immunity and Disease in Plants

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Abstract

Plant hormones are small signaling molecules that regulate almost every aspect of plant life cycle. Plant pathogens alter hormonal balance of the host to cause disease. In response, host redefines hormone signaling networks to cope with the invading pathogen. Biotrophic pathogens are generally sensitive to salicylic acid mediated defense responses, whereas necrotrophic pathogens are deterred through jasmonate/ethylene pathways. Interaction between these pathways is regarded as central backbone of plant immunity. Classic hormones such as auxin, gibberellin, and cytokinin either promote salicylic acid or jasmonates mediated networks of immunity in plants. Here, we advocate a network biology perspective and emphasize the application of systems biology approaches for a comprehensive understanding of plant-pathogen interactions.

Keywords
Plant immunity, Phytohormones, Plant-pathogen interaction, Hormone immune networks

Phytohormones are small signaling molecules that are essential for the regulation of plant growth, development, reproduction as well as stress responses. They act in concert and their interactions with regulatory proteins modulate cellular networks in response to external and internal cues [1-2]. Typical phytohormones are abscisic acid (ABA), auxins, cytokinins (CK), ethylene (ET) and gibberellic acid (GA) (Figure 1). The role of these hormones in governing dynamics of growth and development has already been established [3]. However small molecules with signaling properties such as jasmonates (JAs) and salicylic acid (SA) are also considered as phytohormones [2]. Their importance in regulating immune dynamics has been well studied. Reciprocally, the involvement of the former hormones group in immunity and that of latter in growth has also recently been known [1-3]. These new trends in the investigation of plant hormone signaling strongly emphasize that the control of plant growth, development and defense is linked in a complex signaling network (Figure 1). Crosstalk among these various pathways plays a pivotal role in system responses to internal and external cues. Regarding immunity and disease, phytohormes are shared weaponry, exploited by pathogens to propagate and utilized by the host to mitigate the development of infection [4].

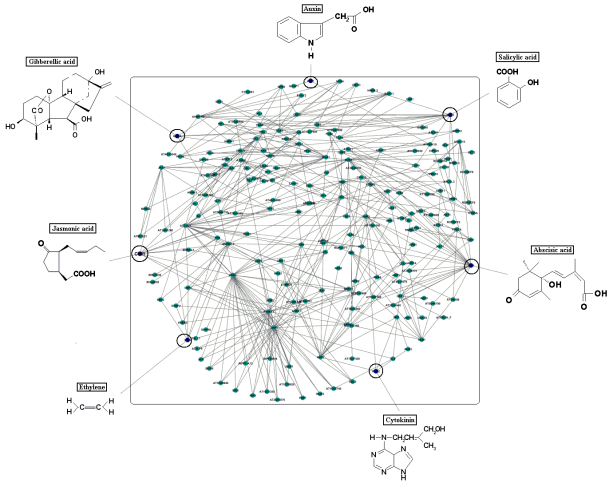

Figure 1: Hormonal interplays in plant immunity mediate complex signaling networks. Plant pathogens alter host hormone balance to cause the disease. Plant hormones are small signaling molecules (chemical structures depicted around the network). They interact with cellular receptors (small molecule-protein interaction: encircled nodes in the network) to transmit their corresponding signals for the induction of gene expression as signaling output of the system. Transduction of hormone signaling is not a linear process, signaling pathways either reinforce or inhibit each others. Plant hormone immune signaling is a fine tuned balance where cross talk among pathways through interacting proteins creat dynamic environnet in cellular system. Plant PPI (protein-protein interaction) databases can be exploited for the investigation of such complex interactions. Here, we used the STRING-database (http://string-db.org/) for the reconstruction of a hormone-signaling network by using the individual hormone receptors as inputs to the database. A combined interaction score greater than 0.7 (p-values for Bayesian confidence score) as well as an experimental validation of the interaction was fixed as criteria for the selection of interactions. This results in a network of 207 nodes (interactors) and 430 interactions. We used the network biology tool Cytoscape version 2.8.3 (www.cytoscape.org) for the visualization of our hormonal network (phytohormones chemical structures, receptors in circles,

nodes in light green and interactions in grey: see Supplementary table for further details).

In nature, plants are always challenged by a plethora of harmful pathogens and pests, including among them are viruses, bacteria, oomycetes, nematodes, fungi and herbivores. Based on their life style, plant pathogens are broadly categorized into necrotrophs, biotrophs and hemibiotrophs [5]. Necrotrophs first destroy host cells and afterwards feed on dead carcasses of the cells. Contrarily, biotrophs keep the host cells alive and acquire nutrients from living tissues. Some plant pathogens bear dual lifestyles; they reprogram host cellular machinery for their establishment and subsequently destroy host cells for feeding and are called hemibiotrophs [2,5].

Plants have evolved multi-layers robust immune systems [1,6]. They perceive the presence of invading pathogen and devise an effective deterrence strategy. Plant cellular receptors warrant the presence of microbial patterns such as flagellin, chitin, glycoproteins and lipopolysaccharides. These microbial determinants are known as pathogen-associated molecular patterns (PAMPs) [6]. PAMPs interact with pattern-recognition receptors (PRRs), which initiate the activation of a basal resistance that is called PAMP-triggered immunity [2,6]. PTI is transient and fragile immune response and can easily be dampened down by pathogens that have acquired the ability to infect their cognate host. In order to suppress PTI these pathogens have acquired effector (the pathogenecity factors from the "effectorome") molecules that are delivered into the host cell [6,7]. In response, plant based mobile cellular receptors called resistance (R) proteins that recognize these effectors, resulting in robust immune response known as effector-triggered immunity (ETI) [2,7]. No matter whether it is immune defense against pathogen infection through PTI and/or ETI or pathogen mediated host susceptibility, phytohormones play always a critical role in governing the dynamics of plant-pathogen interactions [1,3,8]. Biotrophic pathogens are generally sensitive to SA mediated defense responses, whereas JA and ET pathways commonly deter necrotrophic pathogens. The SA, JA/ET response pathways are mutually antagonistic and serve as the backbone of the plant immune defense system, whereas other plant hormones either potentiate or inhibit the balance between them [3,4].

The growth promoting hormone auxin enhances the growth of biotrophic pathogen *H. arabidopsidis* and hemibiotrophic pathogen *P. syringae* in infected *Arabidopsis* leaves [9-11]. On the contrary repression of auxin responses promotes *Arabidopsis* susceptibility to necrotrophic pathogen [12]. Moreover, auxin has been demonstrated to affect JA production and the expression of genes involved in JA biosynthesis [13]. To cause susceptibility of the host auxin counter balance SA mediated defense against biotrophic pathogens [10,14]. Additionally, SA independent mechanism for auxin mediated susceptibility has also recently been described [15]. Reciprocally, SA signaling interferes with auxin response, specifically represses the auxin receptor gene TIR1 [2,10]. These findings suggest that despite a central signal of plant growth and development auxin also influences immune dynamics of plant-pathogen interactions. Therefore, auxin pathway is closely connected to the SA-JA/ET immune signaling network. Likewise, ABA signaling plays not only important role in controlling plant growth and development but equally instrumental in plant pathogen interaction [16]. ABA has been shown to reduce plant resistance against infection with necrotrophic pathogens by attenuating JA mediated gene expression and its production [17]. Moreover, enhanced ABA responses also counter regulate SA mediated resistance against biotrophic pathogens [18]. Therefore ABA also influences the SA-JA balance in plant immune networks. Recently, gibberellins were shown to hook up to the SA-JA/ET network as well. Gibberellins control the degradation of growth-repressing DELLA proteins which negatively regulate plant immune responses against biotrophic pathogens [19]. Contrarily, ABA gives stability to DELLA proteins. The stability of DELLA proteins prioritizes JA based responses over SA [1,19]. Therefore, DELLA proteins are responsible for the integration of multiple signals that modulate balance between SA and JA in regulating immune dynamics of the plant. Relatively new player in the field of plant immunity is plant hormone cytokinin. Like other classic plant hormones cytokinin functions as essential modulator of growth and development in plants [20]. However its implications in influencing the balance between SA and JA in immune signalling are still not well understood. In *Arabidopsis*, the member of type-B cytokinin response regulator ARR2 has been shown to interact with the SA pathway at the level of TGA3 and promotes resistance against infection with *Pst* DC3000 [8,21]. Moreover, type-A cytokinin response regulators have been shown to counter regulate the SA mediated immune defense against pathogen infection [22]. These studies show a link between cytokinin signalling and SA pathway of resistance in plants whereas the interaction between cytokinin and the JA sector of immunity has not been congruently analyzed.

The preceding discussion is merely a glimpse of the actual details involved in plant hormone immune networks. The enormous amount of expert knowledge produced by several numbers of laboratories on plant hormone signaling in the last few decades substantially enhanced our understanding regarding the role of individual hormones in plant immunity (Figure 1). In essence, plant hormones act in concert and their combined action formulate system's response to the prevailing internal or external cues. Plant immunity "ZIG-ZAG" paradigm [6] is well established. Now it is high time to focus on "Network-Network" paradigm where immunity and susceptibility mediate distinct

cellular networks in the host during infection. Intricate interactions between plant and pathogen simultaneously affect each other's cellular networks. Post genomic era calls upon an inclusive approach which should integrate complex hormone immune signaling data for a comprehensive understanding of variable systems such as plant and pathogen. Application of systems biology tools in the investigation of plant-pathogen interactions will further advance the field of plant immunity beyond classical approaches toward addressing the open questions otherwise remained unanswered due to capacity concerns. Exploitation of public databases on genomics, transcriptomics, proteomics and metabolomics with efficient biocomputing skills will certainly expedite relatively slow pace of advancement in plant immunity as compared to growth and development.

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