Trends in Plant Science

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Review

Sensing Danger: Key to Activating Plant Immunity

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In both plants and animals, defense against pathogens relies on a complex surveillance system for signs of danger. Danger signals may originate from the infectious agent or from the host itself. Immunogenic plant host factors can be roughly divided into two categories: molecules which are passively released upon cell damage ('classical' damage-associated molecular patterns, DAMPs), and peptides which are processed and/or secreted upon infection to modulate the immune response (phytocytokines). We highlight the ongoing challenge to understand how plants sense various danger signals and integrate this information to produce an appropriate immune response to diverse challenges.

Metazoan and Plant Immunity – Shared Principles

Multicellular eukaryotic organisms employ sophisticated, multilayered immune systems to ward off microbial infection. In higher vertebrates, immediate activation of pathogen-nonspecific innate immunity is required for and followed by activation of adaptive immune responses [1]. Lower vertebrates, crustaceans, insects, and plants rely solely on innate immune systems to stop pathogen ingress and proliferation [2–5].

Proper recognition of a potentially deadly threat is key to execution of effective immune responses [6–10]. The concept of 'self versus non-self' discrimination, first proposed in 1949, and later refined by Janeway ('self versus infectious non-self'), recognized microbe-derived (foreign non-self) structures as immunogenic triggers of metazoan host defenses, whereas host-derived structures were considered to be tolerated by the host immune system ('stranger model') [11–13]. In 1997 the term pathogen-associated molecular pattern (PAMP) was coined for microbe-derived patterns (elicitors) of metazoan innate immunity [14]. PAMPs, also referred to as microbe-associated molecular patterns (MAMPs), are recognized through structurally diverse plasma membrane or intracellular pattern recognition receptors (PRRs) such as the Toll-like receptors (TLRs) [7,9,15].

While the self versus non-self concept of immune activation prevailed for a long time, it failed to account for a phenomenon termed sterile inflammation – immune activation in the absence of infection [16,17]. In fact, numerous host tissue-derived molecules released in pathological conditions such as tissue injury, trauma, or non-apoptotic cell death have been shown to trigger immune responses very similar to those activated upon PAMP recognition [16]. In the literature such patterns are inconsistently referred to as DAMPs, danger signals, alarmins, or self-antigens. Key examples of such host-derived (endogenous) immunogens are ATP, heat-shock protein 70, hyaluronic acid, mitochondrial or nuclear DNA, and high mobility group box (HMBG) nuclear proteins (for an extensive list see [15,16,18]). Notably, many of these patterns are recognized by the same class of PRRs (e.g., TLRs) through which PAMPs are recognized [15,18,19], suggesting co-evolution of perception systems for either pattern type. This insight has given rise to the 'danger hypothesis' [20] which suggests that the metazoan immune system has evolved to recognize all types of molecules regarded as signature of danger rather

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Innate immune systems in metazoans and plants share a similar conceptual logic.

The innate immune system is designed to sense all types of danger signals rather than only distinguishing between self and non-self.

Exogenous (non-host) and endogenous (host/self) danger signals are perceived by similar pattern recognition receptors. These danger signals most likely act together to bring about an appropriate immune response.

Host-derived immunogenic factors can be divided into primary endogenous danger signals, which are passively released upon host damage, and secondary endogenous danger signals, which are actively processed and released upon tissue damage and other stimuli.

Plant secondary endogenous danger signals modulating the immune response have similar characteristics to metazoan cytokines, and should thus be termed phytocytokines.

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than to discriminate between self and non-self. Following this logic, both endogenous DAMPs and microbe-derived PAMPs are considered to be danger signals [16,21–23] (Figure 1).

Innate immune systems in metazoans and plants share a similar conceptual logic [24]. Recognition through plant PRRs of microbe (viruses, bacteria, fungi, oomycetes), nematode, insect herbivore, or parasitic plant-derived patterns and subsequent immune activation is referred to as pattern- or PAMP-triggered immunity (PTI) (Figure 1). Recognition of host-derived damage-associated elicitors is also a hallmark of plant PTI, and is mediated by PRRs resembling sensors for PAMPs [25–28]. PTI provides protection against invaders that are unable to subvert the immune system of a given plant [6,8]. However, host-adapted pathogens have evolved means (effectors) to suppress PTI and colonize their hosts [29–31]. In turn, plants have evolved immune receptors capable of sensing microbial effectors or effector-induced perturbations of host structures. This 'second layer' of defense has been termed effector-triggered immunity (ETI) [4,32,33]. The discovery and characterization of diverse immunogenic triggers and their receptors has revealed ambiguities in the distinction between PAMPs and effectors, as well as between ETI and PTI [34]. Limitations of the ETI/PTI model have sparked the idea that the plant immune system is a general means to cope with invasion or danger [34–36]. Indeed, applying the term danger to describe plant immunity would foster a holistic view of immunity as a general feature of higher eukaryotes.

We review here recent progress in plant immunity research on how plants sense and respond to tissue damage inflicted by microbial infection or herbivory. We divide immunogenic plant factors roughly into two categories: primary endogenous danger signals which are passively released upon host damage ('cell debris'), and secondary endogenous danger signals that are actively processed and released upon tissue damage and other stimuli, and discuss these in the context of metazoan tissue-derived danger signals.

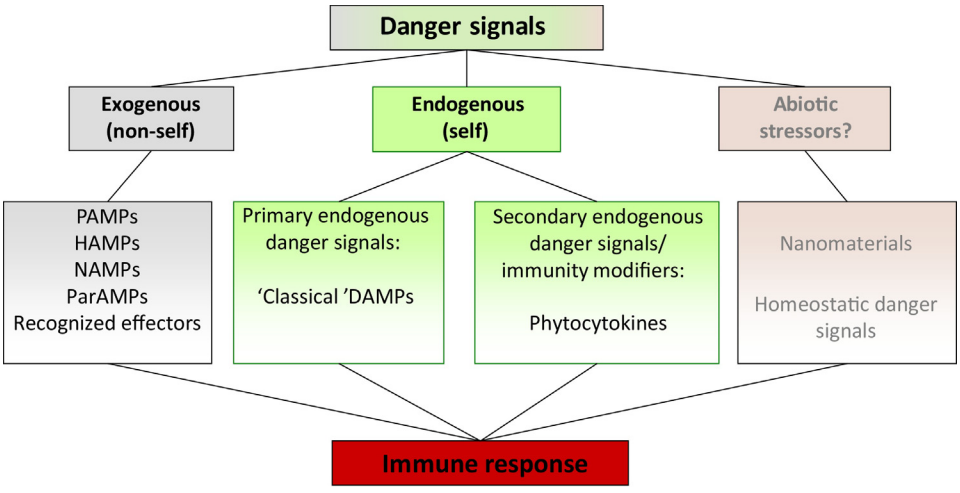

Figure 1. Immunogenic Patterns Implicated in Danger Perception and Activation of Plant Immunity. Danger signals can be divided into exogenous signals derived from 'non-self' and endogenous signals originating from the host 'self'. Exogenous danger signals include molecular patterns from pathogens/microbes (PAMPs or MAMPs), herbivores (HAMPs), nematodes (NAMPs), parasitic plants (ParAMPs), and possibly from viruses, as well as effectors from host-adapted pathogens. In animal systems, abiotic factors such as nanomaterials and homeostatic danger signals have also been described to act as danger signals; however, this has not yet been well established in plants. In contrast to exogenous danger signals, endogenous danger signals originate from the organism itself and comprise primary and secondary signals. Primary danger signals can be regarded as the 'classical' damage-associated molecular patterns (DAMPs) because they are only released upon cellular damage. Secondary endogenous danger signals are processed peptides that act as immunity modifiers and should be termed 'phytocytokines'.