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Editorial

Systemic Immunity in Plants: Biochemical Signals and the Challenge for Practical Application

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Firstly, we would like to thank the EC Agriculture Journal for the invitation to collaborate with an editorial article in which we will present a plant immunity issue.

At present the world faces enormous and unresolved challenges in many respects. According to the UN Food and Agricultural Organization, one of these serious challenges is undernourishment of about 1 billion people including 300 million children, of the global population of 7 billion [1]. This can increase not only the health risk and mortality of the population but moreover, undermine global economic stability. One of the highest risks to world agricultural production along with shortage of water supply and climate change, is pest, weed and pathogen control, especially under low investment and intensity production conditions. However, plants offer natural, genetically coded biochemical mechanisms that can help to survive these biotic and abiotic stress conditions and consequently help address the human over-population of the Earth. One of these mechanisms in plants is the so called *systemic acquired resistance* (SAR) or its synonymously used up-to-date term, *systemic immunity* [2-4]. But what does systemic immunity (SI) in fact mean? This brief overview illuminates SI mainly from the signalling and practical points of view.

Systemic immunity is an inducible defence mechanism that provides protection in distant, pathogen-free parts of plants against a broad range of pathogens (Figure 1). In practice, SI has been recognised as a strategy to control plant pathogens due to several features A) phylogenetic stability (present not only in angiosperms and gymnosperms, but in non-vascular plants as well) [5] B) long-term effectiveness during the vegetation period (once activated) [6] and C) transgenerational effectiveness [7]. Additionally, both in transgenerational and single generational cases, the defence mechanisms are induced more rapidly and intensively in SI plants than in control plants after being challenged with a pathogen (i.e. they display so called "prepared state" during defense priming). However, it is important to note that the mechanism via which DNA methylation regulates SI within a single generation may differ from transgenerational SI responses [8]. This "immune memory" is based upon posttranslational modification of histone and results in changes of the structure of chromatin.

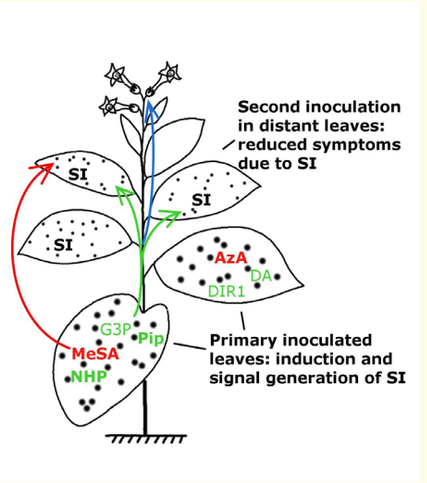

Figure 1: *Schematic view of the development of systemic immunity (SI) in plants. Putative signal molecules: methyl salicylate (MeSA), lipid transfer protein DIR1 (Defective in Induced Resistance1), dehydroabietinal (DA), glycerol-3-phosphate (G3P) or G3P-dependent factor, azelaic acid (AzA), pipecolic acid (Pip) and its derivative, N-hydroxy-pipecolic acid (NHP) move from the infected leaves to pathogen-free parts of the plant where they induce SI against broad range of biotrophic and hemibiotrophic pathogens (second infection). Pip and NHP are highlighted. The arrows indicate the movement of signal molecules via phloem transport or the air (putative volatile compounds for airborne signals). Compounds in red and green coloured letters are former and present signal candidates, respectively. The blue arrow indicates transgenerational SI signalling where the epigenetic information is inherited and present in the next generation (modified from [2]).*

Other key biochemical events during SI induction are the generation and movement of multiple signal transduction compounds (Figure 1) responsible for the manifestation of resistance mechanisms in pathogen-free parts of plants. From the viewpoint of practical chemical induction of SI, signalling compounds are also of primary importance. Before addressing these signal transduction compounds, via which plants can transfer information from their infected to non-infected parts (leaves) we should focus on another important feature of SI, its aspecific nature. Thus the putative mobile SI signal(s) is neither plant- nor pathogen-specific. Present studies, independent of signalling, support former views detected in *Arabidopsis* in this respect: TMV (tobacco mosaic virus) infection can induce SI against the same virus, other viral and bacterial pathogens in tobacco [2]. This feature is also important for practical applicability of SI.

In the last two decades, several compounds have been identified as putative SI signals or important factors for movement of long-distance SI signals in *Arabidopsis* and tobacco (Figure 1). These include compounds with very different chemical structures like methyl salicylate (MeSA), the lipid transfer protein DIR1 (Defective in Induced Resistance1), dehydroabietinal (DA), azelaic acid (AzA), glycerol-3-phosphate dependent factor (G3P), the lysine catabolite amino acid, pipecolic acid (Pip), and its derivative, N-hydroxi-pipecolic acid (NHP) [2-4].

As a last step during SI induction, after signal generation, movement, and perception, the manifestation of SI (defence priming) in pathogen-free leaves (Figure 1) is associated with a massive transcriptional and metabolic reprogramming [9]. However, the functional roles of some of these compounds in SI signal transduction were later questioned [10,11]. Moreover, genetic studies with different SI-deficient mutants and silenced lines rather support the idea that some of these compounds are activated only when SI is induced in darkness after primary inoculation. In addition, although the amount of AzA doubled in phloem exudate of TMV infected tobacco leaves, external AzA treatment could not induce resistance neither to viral nor bacterial pathogens, independent of light conditions [11]. Nevertheless, the crucial role of light conditions in SI signalling and induction is in agreement with the putative role of chloroplasts in signal generation [2]. Although it is not clear whether the same or different signalling is reponsible for single and transgenerational effects.

One of the most promising signal candidates of SI is L-pipecolic acid (Pip), a heterocyclic non-protein amino acid. Former genetic studies with an *ald1* mutant indicated the key role of an aminotransferase (ALD1) in local and systemic defence responses, but the function of Pip was discovered only later on. In fact, detailed studies indicated that A) the ALD1 gene product shows *in vitro* substrate preference to lysine, a putative precursor of Pip biosynthesis B) the biosynthesis of Pip in *Arabidopsis* is dependent on a functional *ALD1* locus and C) the ALD1 enzyme acts as a first step during lysine catabolism and this route leads to the formation of Pip [3,9,12]. Furthermore, *ALD1* transcript accumulates in the pathogen-inoculated and distant pathogen-free leaves [12]. The local and systemic immune defects of *ald1* mutant *Arabidopsis* after bacterial inoculation could be rescued by external application of Pip. From the viewpoint of signal transduction during SI response, it is important to note that strong Pip accumulation was found in petiolar exudate of SI-inducing *Pseudomonas syringae* inoculated leaves in *Arabidopsis* [12]. Later studies indicated the massive local accumulation of Pip in tobacco leaves after two local necrotic viral infections as well as its putative role in systemic induction of SI [2]. Consequently, Pip could be an important player in SI induction in a range of plants against various pathogens [2].

In two recent publications a new SI signalling compound, N-hydroxy-pipecolic acid (NHP, Figure 1) a N-oxygenation product of Pip, was described [13,14]. Furthermore, local, sustained activation of MPK3 and MPK6 MAPKs (mitogen activated protein kinase) and their phosphorylation target, WRKY33 transcription factor are also required for Pip accumulation in *Arabidopsis* [15]. It would also be interesting to test the roles of avirulent pathogen and/or elicitor activated MAPKs [16,17] of tobacco in SI induction.

Regarding the practical applicability of Pip it is important to test the effectiveness of a putative SI signal compound under hydroponic growth conditions against pathogen infection. Therefore we tested the effect of Pip in two nutrient solutions (Hoagland and a commercial product, Wuxal S) against viral infection (Figure 2). Although in both cases hydroponic growth conditions themselves increased resistance

to TMV infection as compared to growth in soil, transient (24h) application of 2 - 10 mM Pip induced systemic resistance against necrotic symptoms of TMV infection in tobacco leaves (about 50% reduction in lesion size). Effectiveness of Pip application via the root system was also reported after soil tests in *Arabidopsis* [12]. The flexible and transient induction criteria are important points as induction of SI would be economical only under high pathogen pressure and/or intensive cultivation conditions (mainly in indoor growth conditions). This is especially due to the long-term energy dissipation "cost" of permanent reprogramming of plant gene expression and metabolism during SI induction. For this purpose, the simulation of crop parameters under stress conditions via plant growth and yield process models is also required [18]. Alternatively, transient and site-directed activation of certain SI-inducible genes would pave the way for practical application of this phenomenon.

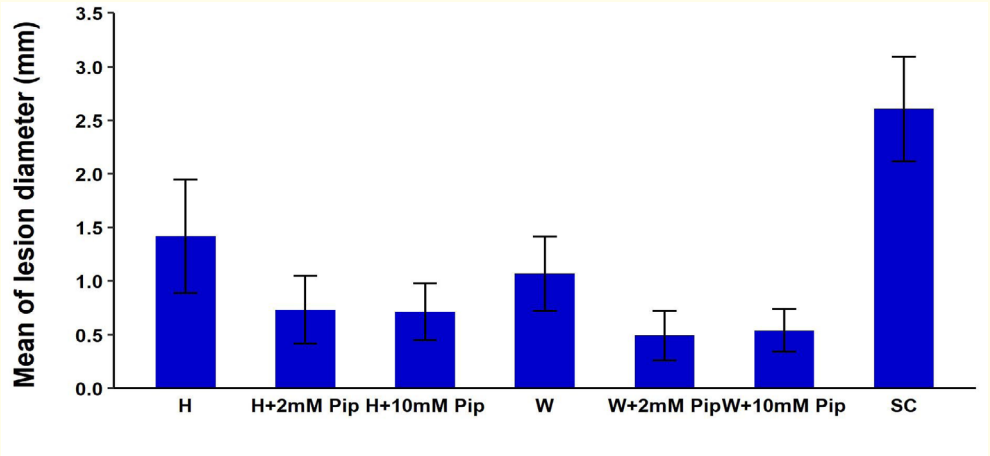

Figure 2: *Systemic effect of transient (24h) pipecolic acid (Pip) application under hydroponic conditions in two nutrient solutions: one fourth strength Hoagland solution (H) or 0.1% WuxalR Super (W) (Aglukon Specialdünger Gmbh, Düsseldorf, Germany) on the resistance of TMV infection in tobacco (N. tabacum Xanthi nc plants). Soil was used as a control system (SC). TMV infection was performed two days after transient hydroponic application of Pip. Plants (4 per treatment) were kept under controlled light conditions [11]. Lesion diameter of TMV infection on leaves 2 and 4 were evaluated four days after infection as we have described earlier [11].*

Although considerable progress has been made in the identification of signalling compounds of SI and their functional aspects in different plants, further efforts should focus not only on theoretical aspects but on practical application methods.

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