Keeping it in the family: Transgenerational memories of plant defence

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Abstract

Plants possess a sophisticated array of systems with which to sense and respond to their internal and external environment. Biological changes triggered by such systems represent examples of phenotypic plasticity. One aspect of phenotypic plasticity that has recently emerged is transgenerational priming of plant defence responses – the persistence of induced resistance responses across generations. There has been a recent surge in interest in epigenetic mechanisms as a basis for phenotypic plasticity, including the ability for such epigenetic changes to be inherited across generations. In this review, we focus on the evidence that attack by pests and disease can stimulate plant defence responses that increase levels of resistance not only in attacked plants, but in their offspring, and discuss mechanisms by which environmental stress signals can be inherited. Finally, we consider the implications of transgenerational defence responses for plants in natural and agricultural systems.

Keywords

Disease resistance; Environment; Epigenetics; DNA Methylation; Acclimatization

Review Methodology

Sources were identified by regular examination of primary research journals during the course of our own research and by the examination of citation lists in relevant articles.

Epigenetics as a component of plant memory

Plants, as sessile organisms, need to sense and adapt to heterogeneous environments and have developed sophisticated mechanisms to allow them to do this, including changes in morphology, cellular physiology, gene regulation and genome stability [1]. A common feature of plant responses to environmental stress is that exposure to an initial stress influences later responses. This implies that the first exposure generates some form of "memory" which is used to enhance tolerance to future stressful events [2]. The mechanisms by which such memories are generated and maintained are still under intense scrutiny and debate, but one key component is epigenetics. Plant epigenetics has recently gained unprecedented interest, not only as a subject of basic research but also as a possible new source of beneficial traits for plant breeding [3]. The term epigenetics is generally used to refer to the study of heritable change in gene expression that is independent of DNA sequence variation [4-5], but is commonly used more broadly to include regulation of gene expression via changes in chromosome structure. Such change can occur at the DNA level through DNA methylation of cytosine residues, or at the level of chromatin by post-translational modifications of histones that influence the accessibility of the DNA to transcriptional activation. Epigenetic changes can result in altered gene transcription, and are an important mechanism in regulating gene expression during development and in response to environmental cues, including those arising from biotic and abiotic stress [6-8]. Such epigenetic information represents a form of transcriptional memory associated with cell fate decisions, developmental switches, or stress responses [7].

Environmental cues are perceived and transmitted by a myriad of plant signal transduction pathways that enable adaptation to environmental challenges [9]. It is becoming increasingly clear from observations of animals and human populations, that environmental cues such as diet or exposure to environmental toxins can generate adaptation at the genome level based on epigenetic imprints, which can either be short-lived or persistent, resulting in their transmission into subsequent generations [10-11]. In plants too, epigenetic variation is likely to contribute to both short-term phenotypic plasticity and the longer-term adaptive capacity of plant species [12]. Thus, epigenetic changes could potentially contribute to the ability of plants to succeed in variable environments [12]. Chromatin modifications which alter the transcriptional capacity of a gene are a normal part of the environmental regulation of gene

expression. Most stress-induced modifications are reset to the basal level once the stress is relieved, while some may be more stable, that is, may be carried forward as a "stress memory." Chromatin modifications may be transmitted as a heritable cellular memory across mitotic cell divisions (within the lifetime of an individual), or even across meiotic cell divisions, resulting in transgenerational epigenetic inheritance [8,13-17]. The recognition of a mechanism that can generate natural variation in response to specific environmental stimuli which then influences phenotypes in subsequent generations is stimulating renewed interest from a range of biologists and ecologists in this somewhat Lamarckian concept.

Transgenerational Induction of Defence

In the case of plant defence against biotic stress, the suggestion that disease could affect resistance responses in progeny of infected plants was first made over three decades ago, when it was found that that inoculation with tobacco mosaic virus (TMV), led to increased resistance in progeny of infected tobacco (*Nicotiana tabacum*) [18]. Other studies found that plants attacked by herbivores or pathogens produced seeds with elevated levels of defensive secondary metabolites compared with uninfested control plants [19-20]. A series of papers by Agrawal and co-workers demonstrated that insect herbivory in wild radish (*Raphanus raphanistrum*), led to induced resistance in seedlings of progeny plants [21-23]. However, there were also impacts on fitness associated with this transgenerational defence response when plants were grown in the field, suggesting altered resource allocation. No direct mechanism for induced defence was identified, and the observed increase in resistance was transient. Such effects could all have been accounted for by maternal effects – the provisioning of seeds with resources from the mother plant produced in response to stress. Whilst of ecological importance, maternal effects are regarded as distinct from *bone fide* transgenerational inheritance, which acts via phenotypes expressed directly by the offspring generation. Indeed, many only regard phenotypes that can be observed in the 2^{nd} generation removed from the stress as true transgenerational inheritance, since the germ line of the immediate offspring generation can potentially experience the original stress whilst forming within the parent plant.

More recently, some well-characterised examples of heritable responses to protect future generations against biotic stress have emerged, several of which strongly implicate epigenetic control. It has been confirmed that TMV infection of tobacco causes increased resistance in

the progeny generation. What is more, resistance is broad-spectrum, providing protection against bacterial (*Pseudomonas syringae*) and oomycete (*Phytophthora nicotianae*) pathogens in addition to TMV [24]. Three parallel studies in particular provided new insights into transgenerationally induced resistance [25-27]. Here, the emphasis is on priming of induced resistance. The sensitization during biotic stress of future responses is referred to as priming [28-29]. Priming boosts the plant's defensive capacity and establishes a heightened state of alert [29-30]. Priming can be triggered biologically, such as in healthy plant parts of pathogen-infected or herbivore-damaged plants, or chemically, by low doses of the defence hormones salicylic acid (SA) and JA, or synthetic compounds such as β-aminobutyric acid (BABA) [31-33]. In primed plants, cellular defences are not activated immediately by the priming agent, but retain some form of "memory" of the priming event, which allows their expression to be more rapidly and/or strongly activated upon perception of a later biotic stress signal. Increasingly, it is becoming recognised that priming is at least in part, regulated epigenetically [15,30].

Recently it was been shown that the progeny of the parental plants primed by treatment with BABA or infection with avirulent *P. syringae* bacteria, show enhanced expression of SA-dependent defence genes and stronger resistance to infection by both virulent *P. syringae* and the downy mildew pathogen *Hyaloperonospora arabidopsidis* [25]. Remarkably, these transgenerationally primed plants were also "primed to be primed" because when treated with BABA themselves, their offspring showed yet higher levels of priming than first generation primed plants [25]. Similarly, chemical elicitation of barley (*Hordeum vulgare*) with acibenzolar-S-methyl or saccharin also primed the subsequent generation for resistance to leaf blotch, caused by the fungal pathogen, *Rhynchosporium commune* [34].

Luna et al., [26] also demonstrated priming of the progeny generation when parental Arabidopsis plants were subjected to repeated inoculations with virulent *P. syringae*. In this study, not only was the primed state passed to the immediate offspring generation, but increased disease resistance could be detected in the grandchildren of the original infected plants, and was therefore inherited over one stress-free generation. This observation means that maternal effects could not account for the increased resistance, indicating that the phenomenon is truly epigenetically-regulated. In support of this idea, it was shown that transgenerational priming was associated with chromatin modifications at the promoters of the SA-regulated genes, *PATHOGENESIS-RELATED1*, *WRKY6*, and *WRKY53*. Furthermore,

evidence was provided for a role of DNA methylation, because the DNA methylation-related *drm1drm2cmt3* triple mutant, which is mutated in *DOMAINS REARRANGED METHYLASE1 AND 2 AND CHROMOMETHYLASE3* and exhibits hypomethylation of genomic DNA, exhibits a constitutively elevated acquired resistance phenotype but is not responsive to further priming by parental stress [26]. Hence it is possible that transgenerational priming may be inherited via hypomethylation of defence genes that confer SA-dependent pathogen resistance.

In parallel with the observations of transgenerational disease resistance described above, persistence of herbivore-induced resistance has also been demonstrated. In a field experiment with *Lotus wrangelianus*, terHorst and Lau [35], showed that both plant resistance to herbivores and reproductive fitness were dependent on exposure to insect herbivory and intraspecific competition in the parental environment. A more detailed mechanistic study found that in Arabidopsis and tomato (*Solanum lycopersicum*), parental herbivory resulted in increased resistance to insect herbivores in offspring, and that this phenomenon required JA signaling [27]. Intriguingly, Arabidopsis mutants compromised in their ability to produce small interfering RNAs (siRNAs), did not transmit the herbivore-induced resistance to the next generation, indicating an important role for siRNAs in heritable resistance to insect herbivory [27].

Together, these studies clearly demonstrate that priming for enhanced biotic stress resistance extends to future generations, and suggest that epigenetic mechanisms, including DNA methylation, chromatin remodeling and small RNA signalling, play key functions in regulating transgenerational plant immunity. These exciting discoveries provide a basis from which to uncover the molecular basis of how plants are able to protect their offspring against future biotic threats without making changes to their DNA sequence.

DNA methylation in Transgenerational stress memories

Due to its potential role in adaptation, there is an increasing interest in studying the transgenerational inheritance of environmentally induced changes that can confer increased biotic stress tolerance. When considering possible epigenetic mechanisms for transgenerational stress memories, it is crucial that changes in the epigenetic modification are not only mitotically heritable but also meiotically heritable [14]. On current evidence it is

suggested that while histone modifications are mitotically heritable [36] they are not meiotically heritable [37]. Hence, it appears unlikely that changes in histone modifications could mediate a transgenerational stress memory. In contrast, changes in DNA methylation can be meiotically heritable in plants and are therefore considered a plausible mechanism by which transgenerational stress memories may be transmitted between generations, given their influence on transcription [38-39]. Beyond the role for DNA methylation in transient responses to stress conditions, it is becoming increasingly clear that modifications to the DNA methylome can be maintained through the plant's lifespan and into the following generation(s) [38-43], giving them the potential to encode stress imprints and transgenerational stress memories. As intimated earlier, several studies indicate that epigenetic mechanisms are important for transgenerational defence priming. Biotic stress from insects and pathogens, as well as plant defence signalling molecules such as JA or SA, can elicit the production of small RNAs (sRNAs) [44] and methylation changes that lead to epiallelic variation in the Arabidopsis genome [26]. High resolution, genome-wide profiling of the DNA methylation landscape in Arabidopsis, shows that global disruption of establishment and maintenance of DNA methylation in a set of mutants including *drm1/drm2/cmt3* and *methyltransferase1* (*met1*), enhances resistance to bacteria and induces wide spread dynamic changes in methylation [45]. Moreover, the *drm1/drm2/cmt3* mutant, which is reduced in DNA methylation at non-CpG sites, was found to mimic the priming phenotype of progeny from *Pseudomonas syringae*-infected wild-type plants [45]. Since *P. syringae* triggers DNA hypomethylation in Arabidopsis [45-46], it is plausible that transgenerational priming of SA-dependent defence is based on reduced DNA methylation of regulatory genes.

In contrast to the advantageous stress resistance phenotypes discussed thus far, environmentally-induced, transgenerationally heritable epigenetic traits in plants may also be associated with negative consequences. For example, transgenerational priming of SA-dependent defences was associated with a negative impact on JA-dependent defences in Arabidopsis [26]. Thus, accumulation of epigenetic information reflecting the 'stress memories' of previous generations could impair responses to current environmental challenges [8]. A genetic screen in Arabidopsis identified a mechanism by which such negative consequences of environmentally-induced epigenetic changes may be constrained. Two genes involved in chromatin remodelling, *DEFICIENT IN DNA METHYLATION 1* (*DDM1*) and *MORPHEUS' MOLECULE 1* (*MOM1*), were found to prevent the transmission

of stress-induced transcriptional changes through meiosis. Whilst abiotic stress-induced changes in gene expression were rapidly silenced after stress in wild-type plants, in *ddm1/mom1* double mutants, stress-induced gene expression was maintained into the progeny generation [8]. Thus, *DDM1* and *MOM1* may function to limit transgenerational impacts of stress.

Ecological Implications

In the field, when plants are growing in competition with other plant species and are subject to a wide range of biotic and abiotic threats, individual phenotypes are of central importance in mediating ecological interactions. As such, transgenerational inheritance of altered stress responses may be an important facet of phenotypic plasticity [15]. To have evolved, transgenerational induced defences must have benefits that outweigh costs in at least some environments. Presumably, transgenerational responses are most effective when the parental environment is predictive of the offspring environment – in other words, when the offspring are likely to encounter the same stress as the parents and will therefore benefit from enhanced resistance or tolerance. Another assumption would be that epigenetic stress imprints should gradually be erased in stress-free environments, when the costs of priming would become burdensome. If it were adaptive in the evolutionary sense, transgenerational defence priming, would be predicted to influence interspecies competitive interactions and plant community dynamics [47]. Such interactions remain to be examined, and the ecological significance (or otherwise) of transgenerational defence priming for plants and their associated communities is only just starting to be explored.

Outlook

To date, there are still relatively few characterised examples of transgenerational epigenetic inheritance of plant defence. Although knowledge about the possible mechanisms is steadily emerging, there are still many open questions. Perhaps one of the most attractive applications of transgenerational defence priming is in the potential to address some of the current problems in the area of agricultural pest management.

In agriculture, transgenerational priming of plant defences has the potential to contribute to sustainable intensification. Plant induced resistance provides broad spectrum protection against pests and pathogens, and is durable. Once induced, priming can be maintained throughout the life of a plant, and so primed crops should require fewer pesticide applications in order to reach similar levels of protection. By reducing pesticide inputs, integration of transgenerational priming into existing crop protection schemes could provide multiple benefits to both growers and to the environment. Beyond this, the identification of imprinted "epialleles" associated with defence priming could provide molecular markers to assist in the optimisation of resistance-inducing seed treatments of crops. Such treatments would not require alteration of the genetic make-up of elite crop varieties, and would offer an attractive alternative to the time-consuming introgression of new genes by traditional breeding. The exploitation of epiallele variation for the selection of agronomically-important traits has in fact already been demonstrated. High-yielding lines of *Brassica napus* were selected from an isogenic population on the basis of high energy use efficiency as a consequence of changes in DNA methylation (*i.e.* epialleles) that were stably-inherited for at least eight generations [48]. In the model system, Arabidopsis, a population of so-called epigenetic recombinant inbred lines (epiRILs) have been extensively studied to identify traits that are likely regulated epigenetically. This population is derived from a genetic cross between a wild-type background and a mutant deficient in DNA methylation [49]. The resultant progeny are therefore near-isogenic, but inherit different portions of demethylated chromosomal DNA. Heritable variation within this epiRIL population has been identified for a range of morphological and developmental traits and responses to environmental conditions, including drought, salinity and nutrient levels, and responses to the defence hormones JA and SA [49-52]. Together, these studies provide clear evidence that epigenetically-inherited traits that do not require novel germplasm can be used to alter plant phenotypes.

Thus, we stand at the beginning of an exciting new avenue of research, in which the mechanisms, ecological significance, and potential applications of transgenerational plant defence are only just beginning to be revealed.

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References

1. Lang-Mladek C, Popova O, Kiok K, Berlinger M, Rakic B, Aufsatz W, et al. Transgenerational inheritance and resetting of stress-induced loss of epigenetic gene silencing in Arabidopsis. Molecular Plant 2010; 3:594-602

2. Bruce TJA, Matthes MC, Napier JA, Pickett JA. Stressful "memories" of plants: Evidence and possible mechanisms. Plant Science 2007 ;173:603-608.

3. Mirouze M, Paszkowski J. Epigenetic contribution to stress adaptation in plants. Current Opinion in Plant Biology 2011; 14:267-274.

4. Berger SL, Kouzarides T, Shiekhattar R, Shilatifard A. An operational definition of epigenetics. Genes and Development 2009; 23:781-783.

5. Haig D. The (dual) origin of epigenetics. Cold Spring Harbor Symposium 2004; 69:67-70.

6. Bonasio R, Tu S, Reinberg D. Molecular signals of epigenetic states. Science 2010; 330:612-616.

7. Zhang, C, Hsieh, T-F. Heritable epigenetic variation and its potential. Applications for crop improvement. Plant Breeding Biotechonology 2013; 1:307-319.

8. Iwasaki M, Paszkowski J. Identification of genes preventing transgenerational transmission of stress-induced epigenetic states. Proceedings of the National Academy of Sciences of the United States of America 2014; 111:8547-8552.

9. Mirouze M, Paszkowski J. Epigenetic contribution to stress adaptation in plants. Current Opinion in Plant Biology 2011; 14:267-274.

10. Anway MD, Cupp AS, Uzumcu M, Skinner MK. Epigenetic transgenerational actions of endocrine disruptors and male fertility. Science 2005; 308:1466-1469.

11. Rando OJ, Verstrepen KJ. Timescales of genetic and epigenetic inheritance. Cell 2007; 128:655-668.

12. Brautigam K, Vining KJ, Lafon-Placette C, Fossdal CG, Mirouze M, Marcos JG, et al. Epigenetic regulation of adaptive responses of forest tree species to the environment. Ecology and Evolution 2013; 3:399-415.

13. Saze H. Epigenetic memory transmission through mitosis and meiosis in plants. Seminars in Cell & Developmental Biology 2008; 19:527-536.

14. Chinnusamy V, Zhu JK. Epigenetic regulation of stress responses in plants. Current Opinion in Plant Biology 2009; 133-139.

15. Holeski LM, Jander G, Agrawal AA. Transgenerational defense induction and epigenetic inheritance in plants. Trends in Ecology & Evolution 2012; 27:618-626.

16. Baulcombe DC, Dean C. Epigenetic regulation in plant responses to the environment. Cold Spring Harbor Perspectives in Biology 2014; 6:a019471.

17. Kinoshita T, Seki M. Epigenetic memory for stress response and adaptation in plants. Plant & Cell Physiology 2014; 55:1859-1863.

18. Roberts DA. Acquired resistance to tobacco mosaic virus transmitted to the progeny of hypersensitive tobacco. Virology 1983; 124:161-163.

19. Lammerink J, Macgibbon DB, Wallace AR. Effect of the cabbage aphid (*Brevicoryne brassicae*) on total glucosinolate in the seed of oilseed rape (*Brassica napus*). New Zealand Journal of Agricultural Research 1984; 27:89-92.

20. Shattuck VI. Glucosinolates and glucosinolate degradation in seeds from turnip mosaic-virus-infected rapid cycle *Brassica campestris* L. plants. Journal of Experimental Botany 1993; 44:963-970.

21. Agrawal AA, Laforsch C, Tollrian R. Transgenerational induction of defences in animals and plants. Nature 1999; 401:60-63.

22. Agrawal AA. Transgenerational consequences of plant responses to herbivory: an adaptive maternal effect? The American Naturalist 2001; 157:555-569.

23. Agrawal AA. Herbivory and maternal effects: Mechanisms and consequences of transgenerational induced plant resistance. Ecology 2002; 83:3408-3415.

24. Kathiria P, Sidler C, Golubov A, Kalischuk M, Kawchuk LM, Kovalchuk I. Tobacco mosaic virus infection results in an increase in recombination frequency and resistance to viral, bacterial, and fungal pathogens in the progeny of infected tobacco plants. Plant Physiology 2010; 153:1859-1870.

25. Slaughter A, Daniel X, Flors V, Luna E, Hohn B, Mauch-Mani B. Descendants of primed Arabidopsis plants exhibit resistance to biotic stress. Plant Physiology 2012; 158:835-843.

26. Luna E, Bruce TJ, Roberts MR, Flors V, Ton J. Next-generation systemic acquired resistance. Plant Physiology 2012; 158:844-853.

27. Rasmann S, De Vos M, Casteel CL, Tian D, Halitschke R, Sun JY, et al. Herbivory in the previous generation primes plants for enhanced insect resistance. Plant Physiology 2012; 158:854-863.

28. Conrath U, Pieterse CM, Mauch-Mani B. Priming in plant-pathogen interactions. Trends in Plant Science 2002; 7:210-216.

29. Conrath U. Molecular aspects of defence priming. Trends in Plant Science 2011; 16:524-531.

30. Pastor V, Luna E, Ton J, Cerezo M, Garcia-Agustin P, Flors V. Fine tuning of reactive oxygen species homeostasis regulates primed immune responses in Arabidopsis. Molecular Plant-Microbe Interactions 2013; 26:1334-1344.

31. Zimmerli L, Jakab G, Metraux JP, Mauch-Mani B. Potentiation of pathogen-specific defense mechanisms in Arabidopsis by beta-aminobutyric acid. Proceedings of the National Academy of Sciences of the United States of America 2000; 97:12920-12925.

32. Flors V, Ton J, van Doorn R, Jakab G, Garcia-Agustin P, Mauch-Mani B. Interplay between JA, SA and ABA signalling during basal and induced resistance against *Pseudomonas syringae* and *Alternaria brassicicola*. The Plant Journal 2008; 54:81-92.

33. Zimmerli L, Hou BH, Tsai CH, Jakab G, Mauch-Mani B, Somerville S. The xenobiotic beta-aminobutyric acid enhances Arabidopsis thermotolerance. The Plant Journal 2008; 53:144-156.

34. Walters DR, Paterson L. Parents lend a helping hand to their offspring in plant defence. Biology Letters 2012; 8:871-873.

35. terHorst CP, Lau JA. Direct and indirect transgenerational effects alter plant-herbivore interactions. Evolutionary Ecology 2012; 26:1469-1480.

36. Kouskouti A, Talianidis I. Histone modifications defining active genes persist after transcriptional and mitotic inactivation. The EMBO Journal 2005; 24:347-357.

37. Kouzarides T. Chromatin modifications and their function. Cell 2007; 128:693-705.

38. Bossdorf O, Arcuri D, Richards CL, Pigliucci M. Experimental alteration of DNA methylation affects the phenotypic plasticity of ecologically relevant traits in *Arabidopsis thaliana*. Evolutionary Ecology 2010; 24:541-553.

39. Verhoeven KJ, Jansen JJ, van Dijk PJ, Biere A. Stress-induced DNA methylation changes and their heritability in asexual dandelions. New Phytologist 2010; 185:1108-1118.

40. Johannes F, Porcher E, Teixeira FK, Saliba-Colombani V, Simon M, Agier N, et al. Assessing the impact of transgenerational epigenetic variation on complex traits. PLoS Genetics 2009; 5:e1000530.

41. Kinoshita Y, Saze H, Kinoshita T, Miura A, Soppe WJ, Koornneef M, et al. Control of *FWA* gene silencing in *Arabidopsis thaliana* by SINE-related direct repeats. The Plant Journal 2007; 49:38-45.

42. Mathieu O, Reinders J, Caikovski M, Smathajitt C, Paszkowski J. Transgenerational stability of the Arabidopsis epigenome is coordinated by CG methylation. Cell 2007; 130:851-862.

43. Rangwala SH, Elumalai R, Vanier C, Ozkan H, Galbraith DW, Richards EJ. Meiotically stable natural epialleles of Sadhu, a novel Arabidopsis retroposon. PLoS Genetics 2006; 2:e36.

44. Mosher RA, Melnyk CW. siRNAs and DNA methylation: seedy epigenetics. Trends in Plant Science 2010; 15:204-210.

45. Dowen RH, Pelizzola M, Schmitz RJ, Lister R, Dowen JM, Nery JR, et al. Widespread dynamic DNA methylation in response to biotic stress. Proceedings of the National Academy of Sciences of the United States of America 2012; 109:E2183-2191.

46. Pavet V, Quintero C, Cecchini NM, Rosa AL, Alvarez ME. Arabidopsis displays centromeric DNA hypomethylation and cytological alterations of heterochromatin upon attack by *Pseudomonas syringae*. Molecular Plant-Microbe Interactions 2006; 19:577-587.

47. Clark JS. Individuals and the variation needed for high species diversity in forest trees. Science 2010; 327:1129-1132.

48. Hauben M, Haesendonckx B, Standaert E, Van Der Kelen K, Azmi A, Akpo H, et al. Energy use efficiency is characterized by an epigenetic component that can be directed through artificial selection to increase yield. Proceedings of the National Academy of Sciences of the United States of America 2009; 106:20109-20114.

49. Johannes F, Porcher E, Teixeira FK, Saliba-Colombani V, Simon M, Agier N, et al. Assessing the impact of transgenerational epigenetic variation on complex traits. PLoS Genetics 2009; 5:e1000530.

50. Kooke R, Johannes F, Wardenaar R, Becker F, Etcheverry M, Colot V, et al. Epigenetic basis of morphological variation and phenotypic plasticity in *Arabidopsis thaliana*. The Plant Cell 2015; 27:337-348.

51. Latzel V, Zhang Y, Karlsson Moritz K, Fischer M, Bossdorf O. Epigenetic variation in plant responses to defence hormones. Annals of Botany 2012; 110:1423-1428.

52. Zhang YY, Fischer M, Colot V, Bossdorf O. Epigenetic variation creates potential for evolution of plant phenotypic plasticity. New Phytologist 2013; 197: 314-322.