Opening the Door to Epigenetics in PCP

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Background

The term "epigenetics" was coined in 1942 by the British developmental biologist Conrad H. Waddington and is derived from a combination of "epigenesis" and "genetics". Waddington defined the term of epigenetics as "the branch of biology that studies the causal interactions between genes and their products, which bring the phenotype into being" (Waddington 1942). He believed that the biological disciplines of development and genetics should be integrated, despite the fact that these fields were at the time considered to be totally distinct branches of biology. Waddington had the foresight to predict that fertilized zygotes developed into differentiated cells, tissues and individuals according to the information provided by their genes, cell-cell communications, and also environmental cues, by using the metaphorical illustration of an epigenetic landscape (Goldberg et al. 2007). Thus during the course of development of an organism, cell fate is determined not only by genes but also by other (epigenetic) factors, which underlies the notion of "epigenesis". A number of epigenetic factors have now been identified resulting in a more modern definition of "epigenetics" as heritable changes in gene expression or cellular phenotypes caused by mechanisms other than changes in DNA sequence.

For over 60 years, plant researchers performing classical genetic studies in maize and more modern molecular techniques in Arabidopsis have significantly contributed to the discovery of "epigenetic" phenomena, such as paramutation (Brink 1958), imprinting (Kermicle 1970), control of transposon activity (McClintock 1984), and gene silencing (e.g. see Baulcombe 2004; Matzke et al. 2009), long before their underlying molecular mechanisms were even known. These phenomena were considered exceptions to Mendelian genetics since the outcomes of genetic segregation often appeared to contest Mendel's predicted laws of inheritance. However, recent discoveries of the underlying molecular pathways have altered the original perception of these epigenetic phenomena as a layer on top of Mendelian genetics, which plays a major role in the control of gene expression. While many aspects of these molecular epigenetic controls, namely DNA methylation, histone modifications, small RNAs and non-coding RNAs, are common to both mammals and plants; plant researchers have contributed greatly to the discovery of such mechanisms. More recent studies in Arabidopsis thaliana have been key to revealing the molecular nature of some of these components, which have proven to be remarkably relevant to mammals and other organisms. Such factors include the chromatin remodeling factor DDM1, the CG DNA methylation maintenance factor VIM1/UHRF1, the base-excision DNA demethylase DEMETER, and silencing components via small RNAs (Law and Jacobsen 2010).

Molecular Mechanisms of Plant Epigenetics

This special focus issue of Plant & Cell Physiology explores the fast-moving topic of Plant Epigenetics and includes reviews and original articles reporting on this exciting and growing field of research, as well as highlighting new directions in epigenetic studies. For instance, novel components of epigenetic mechanisms are forever being discovered in plants, some of which are comprehensively reviewed by Saze et al. (2012 and see p. 766). In particular, the authors focus on the control of DNA methylation in plants by DNA methyltransferases, small RNAs, and histone modifications, and also discuss the relationship between DNA methylation and transposon inactivation. Complementary work by Eun et al. (2012 and see p. 857) also describes inactivation/activation of nDart1 transposons being dependent on DNA methylation status.

Unlike in animals, plants develop germ cells late in their life cycle. In addition, many different plant tissues emerge continuously from meristematic cells. The differences in their life cycles and patterns of development may in part account for the fact that plants and animals show considerable differences in certain aspects of their epigenetic mechanisms, despite sharing many of the same basic epigenetic components. For example, genome-wide resetting of DNA methylation in zygote or germ cells has thus far not been found in plants. However, genome-wide demethylation does occur in the companion

cells of the egg and sperm cells, that is the central cell of the female gametophyte and the vegetative cell of the male gametophyte. On pages 817–823, Gutierrez-Marcos and Dickinson (2012) describe epigenetic control of male and female lineages during sexual reproduction, an exciting topic in plant biology. Both plants and mammals display sexual dimorphisms for the expression of selected genes. This parent-of-origin pattern of gene expression is epigenetically determined by a phenomenon restricted to flowering plants and mammals known as genomic imprinting (Feil and Berger 2007). DNA methylation is commonly used for the control of genomic imprinting in both kingdoms thereby providing a typical example of convergent evolution. However, in mammals, gene imprints are erased and subsequently reinforced by *de novo* DNA methylation, whereas in *Arabidopsis thaliana*, *de novo* methyltransferases are not required for imprinting (Cao and Jacobsen 2002). Instead, gene activation by the DNA demethylase DEMETER and a chromatin related factor SSRP1 control the imprinted expression of several genes (Gehring et al. 2006; Ikeda et al. 2011; Kinoshita et al. 2004). This mechanism is discussed in the review by Ikeda (2012 and see pp. 809–816), which also describes the discovery of novel imprinted genes from recent plant genome-wide analyses–some of which show conservation in rice, maize and *Arabidopsis thaliana*.

Epigenetic Memory and Adaptation

Given that plants are sessile organisms, rapid perception and adaptation to environmental changes are important strategies for their survival. A critical topic of study in *Arabidopsis thaliana* with respect to adaptation is the vernalization response. If plants are to bloom in spring, they must perceive and create a memory of the winter experience in order to achieve proper timing of flowering. In *Arabidopsis*, perception and memory operate at the chromatin level to control the flowering repressor and MADS-box transcription factor *FLOWERING LOCUS C (FLC)* (Kim et al. 2009). On pages 785–793, the review article by Buzas et al. (2012) elaborates on *FLC* genetic architecture in relation to its role as a key target sequence of the Polycomb repressive complex to confer this environmental epigenetic memory. In addition, the research article on pages 834–846 by Yun et al. (2012) proposes a novel role for the histone H3K4 methyltransferase, *ATXR3/SDG2*, in the vernalization response.

Other types of environmental stresses also affect plant development at the cellular and whole-organism level. On pages 794–800 Kim et al. (2012b) review emerging evidence that the histone deacetylase HDA6 (in combination with DNA methyltransferases) plays a role in the integration of environmental signals through modification of chromatin status. While on pages 824–833 Matsunaga et al. (2012) describe transposition of Arabidopsis ONSEN transposable elements by heat stress, which might be a source of adaptive genetic and epigenetic variation under long-term environmental changes.

An outstanding fundamental question regarding plant response to stress is how can plants "remember" past events in the absence of a structure that functions similar to the central nervous system of animals? While chromatin memory controlled by the Polycomb Repressive Complex may provide part of the answer, other candidate key players and mechanisms are beginning to emerge. For instance, a recent report by Ding et al. (2012) showed that plants can retain a memory of drought stress via their chromatin status. Similarly, on pages 847–856 Kim et al. (2012a) demonstrate that during recovery from drought stress an active H3K4 methylation chromatin mark is gradually decreased, while occupancy of RNA polymerase II and H3K9 acetylation are rapidly decreased. These processes may contribute to a chromatin memory that allows a more rapid response to future drought stress.

Perspectives: Transgenerational Inheritance of Acquired Characters and Genome-Wide Analysis Using More Sensitive Methods

Several reports describing changes to chromatin marks that are induced by stress or certain environmental stimuli, show that these are heritable through mitotic cell divisions within the plant but are rarely transmitted meiotically to progeny, e.g. vernalization-related chromatin marks are reset in the next generation (Kim et al. 2009). Much attention is now focused on identifying transgenerational chromatin memory in plants that is induced by environmental cues. By contrast, in *Drosophila* it has been clearly shown that heat stress-induced heterochromatin disruption can be inherited by the next generation (Seong et al. 2011). To date, several studies in plants have reported stress-induced heritable changes in chromatin, however, in their critical review Pecinka and Mittelsten Scheid (2012 and see pp. 801–808) cautiously note the important limitations of these studies. It is envisaged that our awareness and understanding of the phenomenon of transgenerational inheritance of acquired characters will undoubtedly be improved in the near future as the underlying epigenetic mechanism(s) are discovered in both plants and animals.

Another main challenge for plant researchers is the development of higher resolution methods for carrying out genome-wide epigenetic analyses. Several early investigations to determine plant epigenetic landscapes of aboveground tissues have been undertaken in conjunction with mutation analysis of epigenetic components (Zhang et al. 2006; Zilberman et al. 2007). However, epigenome information almost certainly changes in response to distinct environmental stimuli and developmental cues. Therefore, more refined temporal and spatial analyses will be required in the future. For example, investigations into the resetting of chromatin marks, genome-wide DNA demethylation, and small RNA biogenesis in the companion cells of female and male germ cells during sexual reproduction will require development of specialized methods. Ultimately, strategies for decoding the epigenetic information in single

cell types at selected time points will increase our overall comprehension of the extent to which epigenetics influences plant function – not just at the single-cell but also at the whole-organism level. Without doubt, this special focus issue of *Plant and Cell Physiology* will stimulate further debate on the significant and far-reaching implications of epigenetic regulation in plants.

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