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Gene regulation in response to DNA damage ☆

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ABSTRACT

To deal with different kinds of DNA damages, there are a number of repair pathways that must be carefully orchestrated to guarantee genomic stability. Many proteins that play a role in DNA repair are involved in multiple pathways and need to be tightly regulated to conduct the functions required for efficient repair of different DNA damage types, such as double strand breaks or DNA crosslinks caused by radiation or genotoxins. While most of the factors involved in DNA repair are conserved throughout the different kingdoms, recent results have shown that the regulation of their expression is variable between different organisms. In the following paper, we give an overview of what is currently known about regulating factors and gene expression in response to DNA damage and put this knowledge in context with the different DNA repair pathways in plants. This article is part of a Special Issue entitled: Plant gene regulation in response to abiotic stress.

1. Introduction

Analysis of the expression levels of different genes under various conditions gives us multiple hints as to how, where, when and by what factors genes are regulated. Although there are various methods for analyzing expression levels, for example, powerful microarray hybridization, sensitive real-time PCR or the fluorescent imaging of proteins, the pathways responsible for regulating and signaling the DNA damage repair mechanisms are still poorly understood in plants. Only a handful of transcription factors that are involved in these repair processes have been described. Irradiation or treatment with genotoxins that cause DNA alterations and therefore later on mutations, is used for studying the DNA damage response in plants [1–13]. Several studies that used expression arrays to study transcriptome alterations in response to DNA damaging agents in *Arabidopsis* have previously been reported [10,14–19]. Approximately 16,200 genes out of 27,000 showed a signal higher than the background level in a high-density array when the plants were treated with the double strand break (DSB) inducing genotoxin, bleomycin, and the crosslink inducing genotoxin, mitomycin C (MMC) [10]. Further details about gene regulation in response to DNA damage have been obtained by comparing microarray studies of wildtype plants and plants with mutations in their DNA repair genes [20–23].

To maintain genomic integrity, plants have several DNA repair mechanisms to respond to different types of DNA damage. Most of these DNA repair pathways are, in principle, conserved between all kingdoms of life. The base excision repair (BER) and the nucleotide excision repair (NER) pathway are activated by damage at nucleotides. Besides the NER pathway, plants are also equipped with photolyases, which can specialize in recovery from UV-induced damages at nucleotides. Furthermore, two main pathways have evolved to repair dangerous DNA double strand breaks: the non-conservative, non-homologous end joining (NHEJ) pathway and the conservative, homologous recombination (HR) pathway, which can repair DSBs accurately and depends on the presence of a homologous sequence in the genome (Fig. 1).

2. Signaling factors of DNA repair

The protein kinases ATM (ataxia telangiectasia mutated) and ATR (ataxia telangiectasia and Rad3 related) play a central role in the signaling in eukaryotes [24–29]. ATM and ATR are kinases that mediate the signal cascade following DNA damage. The ATM kinase is activated by DNA damage, such as DSBs, and activates downstream signaling pathways, leading to the repair of DNA, transient arrest of the cell cycle, and inhibition of DNA replication. The ATR kinase, on the other hand, is activated by stalled replication forks, which can occur either spontaneously or after genotoxic stress, UV irradiation or hydroxyurea exposure [30]. In response, ATR regulates the slowing of the cell cycle during S-Phase, and the G2/M progression [31]. ATM kinases are well studied in mammals (for review see [31,32]).

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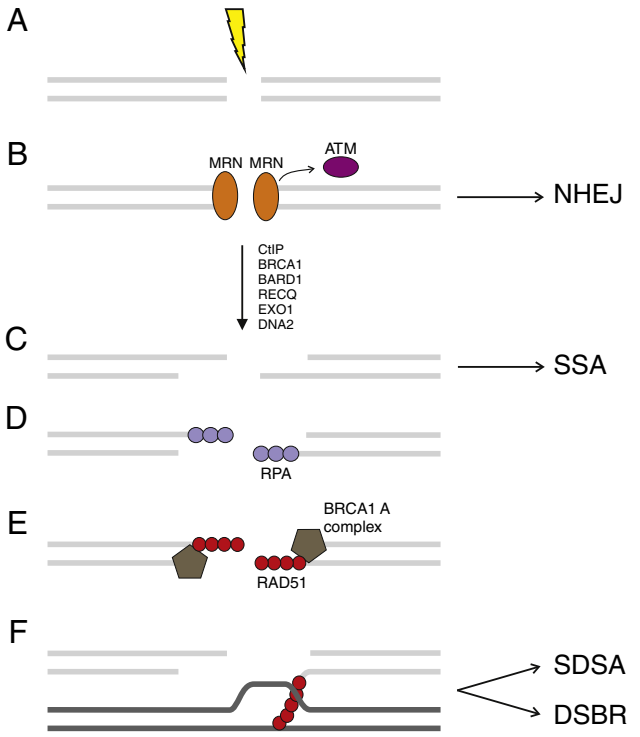

Fig. 1. Initial steps of the repair of double strand breaks in animal somatic cells. (A) Following a double strand break occurs, (B) the MRN complex can identify the DNA ends and activates ATM and ATR. Alternatively, the DSB can be repaired directly via nonhomologous end joining (NHEJ) by ligating the ends together. This pathway, however, is non-conservative, and some sequence alterations may occur at the double strand break ends. (C)With the help of several other proteins, the 5′ ends are resected. The following intermediate containing 3′ overhangs can be used for single strand annealing (SSA) if the break occurred in a repetitive sequence. (D) Otherwise, the single stranded DNA is loaded with RPA, which is later replaced by RAD51. For this step, the BRCA1 A complex is needed. (E). Next follows the invasion of the nucleofilament into a homologous sequence (F). The damage can then be repaired via the synthesis dependent strand annealing (SDSA) model or the double strand break repair (DSBR) model.

In contrast to other eukaryotes, the initial response to DNA damage is still poorly understood in plants. Nevertheless, there have been several studies on the functions of ATM and ATR in *Arabidopsis thaliana*. Single mutants of either AtATM or AtATR are viable and show no developmental defects other than reduced fertility in At*atm* mutants [33]. In mammals, however, a single mutated protein results in embryonic lethality, in case of *atr* [34], while an *atm* mutation causes growth defects and infertility [35]. Only double At*atm* and At*atr* mutants show sterility [36]. This pattern makes studying these proteins in *Arabidopsis* very interesting. Furthermore, it has been shown that AtATM is involved in the transcriptional response primarily after double strand breaks, while AtATR plays a role in signaling after replication blocking lesions [22]. Additionally, both plant At*atm*- and At*atr*-mutants show an increased sensitivity to ionizing radiation just like their mammalian counterparts [22]. Altogether these points suggest distinct and redundant functions for AtATM and AtATR and that especially AtATM is involved in changing gene expression following DNA damage.

In animals, there is a transcription factor, called p53, that exhibits a critical role in orchestrating the response to DNA damage and that is a well known tumor suppressor (reviewed in [37]). No homolog of this protein has been identified in plants; however, a transcription factor, AtSOG1 (suppressor of gamma response 1), that governs similar functions was found in *Arabidopsis* some time ago [38,39]. AtSOG1 is activated by AtATM and AtATR and is responsible for a large proportion of the transcriptional changes in response to DNA damage. Because of its important role as a transcription factor, it was discussed as a possible analog to the critical transcription factor p53 in animals in some aspects, although AtSOG1 and p53 share no sequence homology [40]. AtSOG1 is an NAC (*NAM*, *ATAF1*, and *CUC2*) domain protein that is unique to plants; it appears to be the important transcription factor downstream of AtATM and AtATR and is required to alter gene expression following a double strand break at almost all of the induced genes [39]. However, its own transcription is not enhanced by DNA damage [22].

AtATM and AtATR also control cell cycle checkpoints, and two genes that participate in this task have been identified: the previously mentioned transcription factor, At*SOG1*, and the protein kinase, At*WEE1* [39,41]. AtWEE1 is the main intra-S-phase checkpoint regulator. Homozygous At*wee1* mutants show a prolonged S-phase upon replication stress and, therefore, a delayed cell cycle progression. Furthermore, it is an inhibitor of premature xylem formation and as such plays a role in development as well [42]. Microarray studies have shown that AtWEE1, despite being an important cell cycle regulator, is dispensable for the up-regulation of DNA damage related genes after damage induction as well as for the repair of DSBs [42].

The mammalian DNA POL θ and its homolog, *Drosophila* MUS308, were reported to be involved in tolerance of DNA damage [43,44] and prevention of chromosome breakage [45]. A homolog has also been found in *Arabidopsis*, TEBICHI (TEB) [46]. AtTEB possess both a helicase and a DNA polymerase domain [46]. It was discussed that TEB might regulate the expression of euchromatic genes through chromatin remodeling [47]. In plants, AtTEB genetically interacts with AtATR. The expression of a number of tandem and dispersed duplicated genes, as well as genes near *Helitron* transposons, is activated in At*teb* mutants. A number of γ-irradiation-inducible genes show increased expression in At*teb* mutants and are even further up-regulated in *teb*/*atr* double mutants, suggesting that TEB and ATR prevent the formation or accumulation of DSBs or other types of DNA damage during DNA replication [47]. The results of this study suggest that At*teb* mutants activate the ATR-mediated DNA replication checkpoint, which is then followed by a cell cycle arrest at the G2/M transition. Furthermore, for about three-quarters of the genes regulated by both, the difference in expression was more pronounced in a At*teb*/*Atatr* double mutant than in a At*teb* mutant alone, suggesting that the molecular phenotype of At*teb* with regards to gene expression is enhanced by At*atr* [47].

3. Double strand breaks

DSBs occur naturally in all cells but also occur as a result of exposure to exogenous factors, such as radiation or DNA damaging substances.

To deal with DNA double strand breaks, plants possess two main pathways: non-homologous end joining (NHEJ) and homologous recombination (HR) [48–52]. NHEJ has been shown to be the dominant repair mechanism in somatic cells of both plants and animals [53,54], but it has been postulated that both pathways compete with each other depending on the cell type, developmental stage, phase of cell cycle and also on the type of DNA ends at a break [55–59].

To recognize a DSB, it was shown that the MRE11/RAD50/NBS1 (MRN) (in yeast MRE11/RAD50/XRS2 [MRX]) complex can identify and bind sites of DNA damage, unwind them and subsequently recruit and activate ATM and ATR via NBS1, resulting in further signal transduction in yeast and humans [60–64]. ATM then phosphorylates many proteins involved in DNA repair, translation initiation, telomere factors, replication initiation, and checkpoint control (reviewed in [32]) to maintain genome stability. Although the MRN complex is conserved between mammals and plants [65,66], it is still unclear whether all functions are also conserved but the involvement of ATR

and MRN in DNA damage signaling was recently shown in plants, too [67].

To quantify the change in gene expression after DNA damage, microarray studies were conducted after induction of double strand breaks by γ-rays [20,22]. Table 1 shows up-regulated genes that are involved in DNA damage repair and whether this up-regulation is dependent on AtATM, AtATR or AtSOG1. It can be concluded from the results that the kinase, AtATM, and the transcription factor, AtSOG1, are especially needed for transcriptional changes after the induction of double strand breaks.

However, there is not only up-regulation but also repression of gene transcripts after the induction of double strand breaks. In general, genes involved in basic cellular activities, cytoskeleton and cell cycle progression are down-regulated; again, this is primarily through the function of AtATM and is rarely through AtATR.

In total, genes involved in DNA metabolism, DNA repair, replication, chromatin remodeling, and cell cycle control show higher expression after treatment with double strand break inducers. Taken together, the up-regulation and repression of these genes after DNA damage are dependent on AtATM and AtSOG1, but only in rare cases is it dependent on AtATR. Because the genes involved in HR are especially transcriptionally up-regulated, we will concentrate on this mechanism first.

3.1. Homologous recombination

After a DSB is recognized, the 5′ ends are resected to produce single-stranded 3′ overhangs (Fig. 1C). In animals, many proteins have been shown to be involved in this process, for example, the MRN complex and CtIP in a complex with the tumor suppressors, BRCA1 and BARD1, in the first resection step; afterwards, more proteins, such as a RECQ-helicase, are needed for a full resection [68]. In *Arabidopsis*, a CtIP homolog exists with the name AtCOM1 [69]; additionally, there are BRCA1 and BARD1 homologs [70–72]. Also, *Arabidopsis* has several RECQ-helicases [73,74].

The single-stranded 3′ overhangs subsequently are coated with RPA (replication protein A) (Fig. 1D). It is possible that ATR is also recruited to the site of DNA damage via ATRIP (ATR interacting protein), which binds to RPA-coated ssDNA. ATR is activated and can, for example, arrest the cell cycle or block replication [75–78]. Eventually, RPA is replaced by RAD51, which facilitates strand invasion into the homologous template. This replacement is dependent on the BRCA1-A complex, which recruits RAD51 into the proximity of the DSB (Fig. 1E). In humans members of this complex include BARD1, BRCA2, and PALB2 (also known as FANCN; for an overview see [79]) among others. RPA is actually a heterotrimeric complex, and in *Arabidopsis*, there are five large RPA subunit homologs, as well as two annotated examples each of the medium and small subunits [80]. Because *RAD51* is essential for the eukaryotic HR machinery, it is not surprising that a homolog in *Arabidopsis* was detected and its transcription is highly induced following γ-irradiation [22,81]. As in animals, there are six other RAD51 paralogs with many different functions present in *Arabidopsis* [81,82] and as far as they have been tested, only some of them showed an up-regulation after genotoxic stress: AtRAD51B gets slightly induced after cisplatin treatment or γ-irradiation [83] and AtRAD51C and AtXRCC3 were up-regulated after treatment with γ-irradiation [84]. For the remaining three paralogs (AtRAD51D, AtDMC1 and AtXRCC2) no induction of gene expression after treatment with genotoxins was observed, yet ([10] data available at http://jsp.weigelworld.org/expviz/expviz.jsp).

After the ssDNA is loaded with RAD51, the filament can find homologous sequences and invade them by displacing the second strand of the template and generating a so-called "D-loop" (displacement loop) (Fig. 1F). A DNA polymerase then elongates the invasive ssDNA by using the sequence from the donor strand as template. The next step follows one of the two HR models, either the double strand break repair (DSBR) model or the synthesis-dependent strand-annealing (SDSA) model. In the DSBR model, a double Holliday junction occurs and needs to be resolved. Depending on the mechanism by which the double Holliday junction is resolved, the result can either be a crossover or a gene conversion; the result of the SDSA model is always a gene conversion (topic reviewed in [54,85–87]).

In γ-irradiated plant cells, the gene that is most up-regulated is At*BRCA1*, which is induced an average of several hundred fold, pointing to its importance in the repair of DSBs [22]. Interestingly, the most prominent interaction partner of BRCA1, namely BARD1, is not induced. This is surprising because all of the functions of mammalian BRCA1 have thus far described it as existing as a heterodimer with BARD1 [79]. AtRAD51, an essential protein for DSB repair via HR, is also strongly up-regulated. It was recently demonstrated that another putative plant BRCA1-A complex partner, BRCC36, which shows deubiquitinating activity in humans [88,89], is duplicated in *Arabidopsis* [90]. Both BRCC36 homologs in *Arabidopsis* show a weak up-regulation after DSB induction via γ-irradiation, which indicates that both homologs play a role in DNA damage repair [90]. Other up-regulated genes include the At*PARP* genes, which are involved in BER, the At*RECQ3* helicase, the At*WEE1* checkpoint regulator, and two of the five At*RPA70* (large subunit of RPA) homologs are also up-regulated.

The single strand annealing (SSA) pathway can also be used to repair a double strand break that has occurred in a repetitive sequence [51]. In SSA, 3′ overhangs are produced by 5′ digestion, and the overhangs can anneal to another repeat with complementary sequence, resulting in a healed break. This process makes SSA a non-conservative pathway because the genetic information between the two repeats is lost.

3.2. Non-homologous end joining

NHEJ is non-conservative and often produces short deletions and insertion because it involves joining broken ends back together without regard for absolute DNA sequence fidelity. The end joining pathway is also interesting because it is involved in T-DNA integration during transformation [31,91–96]. Recent results indicate that at least four different end joining pathways operate in plants [97]. However,

Table 1
List of selected DNA repair genes with a change in gene expression after genotoxic stress. Sources: [22,39,10,20,41,201,211].

Gene	*Arabidopsis* locus	Change of expression after genotoxic stress	ATM dependency	ATR dependency	SOG1 dependency
BRCA1	At4g21070	+++	x	–	x
RAD51	At5g20850	+++	x	–	x
XRI1	At5g48720	+++	x	–	x
CYB1;1	At4g37490	+++	x	–	x
PARP1	At4g02390	+++	x	–	x
SYN2	At5g40840	+++	x	–	x
GMI1	At5g24280	+++	x	–	x
PARP2	At2g31320	++	x	–	x
RAD17	At5g66130	++	x	–	x
POL2A	At1g08260	++	x	–	x
RECQ3	At4g35740	++	x	–	x
POLD4	At1g09815	++	x	–	x
RPA70A	At2g06510	+	x	–	x
RPA70C	At5g45400	+	x	–	x
WEE1	At1g02970	+	x	–	x

Listed are selected, up-regulated genes involved in DNA repair after induction of double strand breaks. It has been shown that the up-regulation is dependent on the protein kinases, ATM (ataxia telangiectasia mutated), and the transcription factor, SOG1 (suppressor of gamma response 1), but not on ATR (ataxia telangiectasia and Rad3 related). +++ = strong up-regulation, ++ = medium up-regulation, + = weak up-regulation.

only one of these pathways is known in detail. We will concentrate on this well-characterized classical pathway here.

The first step in the classical NHEJ pathway is the recognition and binding of the broken DNA ends by a KU70–KU80 heterodimer [98]. The KU proteins prevent large-scale degradation of the DNA ends and bring the free DNA ends into close proximity [93,99]. In mammals, a third protein, the DNA-dependent protein kinase catalytic subunit (DNA-PK_{cs}), binds to the KU heterodimers at both DNA ends; however, this protein is absent in plants. The KU/DNA-PKcs complex tethers the two ends of the DNA molecule [99,100]. KU may also recruit other proteins involved in NHEJ repair to the DNA ends and may interact with other proteins involved in DNA repair or DNA damage signaling [101,102]. For example, mammalian KU70 interacts with MRE11, a component of the MRN complex, which is involved in DNA end processing in NHEJ and HR [103]. DNA ligase 4 (LIG4) and XRCC4 (LIF1) catalyze the ligation of the DSB.

AtXRCC4 and AtLIG4 have been isolated and characterized, and it was shown that the proteins interact with each other and that the transcription of *LIG4* is induced by γ-irradiation [7,104]. *Arabidopsis* homologs of yeast MRE11 and RAD50 have also been isolated [3,105]. At*mre11* mutant lines are hypersensitive to genotoxic agents and in contrast to yeast, the telomeres in the At*mre11* mutant lines are longer than those in wildtype plants. This suggests that plants possess an additional alternative mechanism for telomere length maintenance [106]. The mutant lines of At*mre11* in which the T-DNA disturbs the strongly conserved 5′ region of the gene show severe developmental defects and are sterile [106]. At*RAD50* mRNA is expressed in all cell tissues analyzed; however, stronger levels were found in fast growing cells, such as cell-suspension cultures, young primary roots and flowering structures. Furthermore, AtRAD50 is essential in meiotic cells because At*rad50* plants are sterile [3]. However, At*RAD50* does not show a change in expression level in response to treatment with the radiomimetic compound, methylmethane sufonate (MMS), or with the DSB-inducing genotoxin, bleomycin, or the interstrand-crosslink inducing genotoxin, MMC ([3], [10] data available at http://jsp.weigelworld.org/expviz/expviz.jsp). Furthermore, At*RAD50* deficient cells are sensitive to treatment with MMS [3]. Note that the expression level of a gene is not the only important factor for its function in DNA repair because it could be possible that essential DNA repair proteins are constitutively expressed in plant tissues in an attempt to avoid damages at replication forks.

The At*MRE11* and At*NBS1* genes have been characterized, and it was shown that At*NBS1* expression increases slightly 3 h after irradiation with 100 Gy [107]. KU homologs have also been characterized in *A. thaliana*. AtKU80 was shown to be able to interact with AtKU70, and the KU dimer was shown to interact with DNA ends. Mutant lines of At*KU80* are sensitive to DSB-inducing agents, such as bleomycin [108,109]. At*ku70* mutant lines are hypersensitive to DNA damaging agents and it was found, that the telomeres are much longer in At*ku70* plants than in the wildtype plants [110]. The expression levels of At*KU70* and At*KU80* are similar in all plant tissues tested (roots, rosette, leaves, stalks, bract leaves, flowers and cell culture), but their expression levels are lower under normal growth conditions [109]. Exposure to the DSB-inducing genotoxin, bleomycin, or the methylating agent, methylmethane sufonate (MMS), increased the amounts of At*KU70* and At*KU80* mRNAs more than threefold after 1 h [109]. The rapid transcriptional activation of *KU* genes appears to be clearly associated with the generation of DSBs and with repair of the DNA damage [109].

Interestingly, after abscisic acid (ABA) treatment, the expression levels of the At*KU* genes were decreased by roughly 50% after 6 h and were restored to the control level after 8 h of treatment [111]. Furthermore, At*KU* gene expression gradually decreased as ABA concentration increased. Through screening of factors downstream of ABA treatment, it was shown that down-regulation of At*KU* expression by ABA is potentially mediated by the phospholipase Dα (PLDα) and p38-type mitogen-activated protein kinases MAPK6 cascading pathways and the ABA insensitive (ABI3 and ABI5) transcription factors, which regulate various aspects of seed maturation and gene expression [111,112]. In contrast, auxins and gibberelic acid (GA) stimulate At*KU* expression up to two fold. However, At*KU* repression by ABA is not antagonized by auxins and GA. [111]. Perhaps the At*KU* genes are regulated by different phytohormones to prevent NHEJ in different stages of plant development. Interestingly, a change in At*KU70* expression was found in a search of ATM-dependent expression changes [20].

Following the recognition of a DSB, an additionally mechanism must decide which repair pathway, HR or NHEJ, should be used. The array results indicate that genes whose products are involved in the HR pathway are more likely to be up-regulated than the ones involved in NHEJ [20]. The expression of HR proteins in plants is probably cell cycle dependent, similar to DT40 chicken and mammalian cells [113–117] and therefore requires a tight gene regulation. Unfortunately, due to experimental limitations no detailed analysis on the influence of the cell cycle on the DNA damage response has been performed in plants to date.

4. Single strand damages

There are various endogenous and exogenous factors that cause damage to only one strand of the genetic material. The UV component of sunlight threatens all living beings on earth by damaging DNA. The main damages resulting from UV light are pyrimidine dimers, which can be divided into the major induced photoproducts: cyclobutane pyrimidine dimers (CPD) and pyrimidine (6–4) pyrimidone dimers ((6–4) photoproducts; (6–4)PPs). CPDs are the major class of pyrimidine dimers (75%) induced by UV damage [118]. Plants try to avoid such lesions but must repair them when they occur. Avoidance mechanisms include the accumulation of shielding compounds, which are synthesized after UV-B irradiation, such as UV-absorbing secondary metabolites and free radical scavengers [119]. For example, mutant *Arabidopsis* plants with increased levels of flavonoids and other phenolic compounds exhibit tolerance to otherwise lethal UV-B levels [120].

Endogenous factors are mostly reactive oxygen species (ROS), which can be generated by toxic agents, such as Paraquat and menadione experimentally [121]. However, the vast bulk of ROS are generated by normal cellular metabolism [122,123]. Also in plants, ROS are generated as by-products of the most essential energy-generating processes: photosynthesis and respiration. Chloroplasts, peroxisomes, and mitochondria are the main organellar ROS producers [124–127]. Although there are several mechanisms to convert these compounds into oxygen and water, this conversion is not 100% efficient, and residual peroxides persist in the cell [127]. The common ROS (reactive oxygen species) are $O2^{\bullet -}$ (superoxide radical), OH• (hydroxyl radical), and H_2O_2 (hydrogen peroxide). Every cell experiences up to 10^5 spontaneous DNA lesions per day [128].

ROS induce a variety of DNA damages. Over one hundred different DNA modifications caused by ROS have been identified *in vitro* [129]. First, there are several different oxidized bases, such as 8-oxoadenine, 8-oxoguanine and thymine glycol. Some base adducts can cause point mutations. Also, the deoxyribose of the nucleotides can be oxidized by ROS, which results in, e.g., deoxyribonolactone or phospoglycolate. Furthermore, single strand breaks (SSBs) and DSBs can be induced by ROS [130–132].

To research the repair of such lesions, ethyl methane sulfonate (EMS) or MMS is often used to treat mutant lines that are deficient in important DNA repair proteins in plants.

4.1. Base excision repair

Damaged bases are preferentially repaired by the base excision repair (BER) pathway, which is widely conserved between bacteria,

plants and humans. BER is a multistep process in which a protein called DNA glycosylase initially removes the damaged base [133,134]. A couple of DNA glycosylases have been characterized in plants, e.g., a 3-methyladenine-specific DNA glycosylase [135]. This specific DNA glycosylase showed the highest expression in tissues that are undergoing rapid growth and cell division [136]. Biochemical and genetic evidence has shown that BER in plants performs a key role in epigenetic regulation through active DNA demethylation induced by 5-methylcytosine DNA glycosylases [137–139]. Methylation of genes is an epigenetic modification which is associated with gene silencing in eukaryotes. DNA methylation defects in mammals lead to embryonic lethality and in plants they can lead to pleiotropic morphological defects (reviewed in [140]). Although methylation is in most cases a stable epigenetic mark, reduced levels were observed during development in plants and mammals (reviewed in [141]). This is because of the demethylation of genes, which is achieved by DNA glycosylase activity, probably in combination with the BER pathway [141–144].

The usual function of a DNA glycosylase is to excise damaged or incorrect bases by generating an abasic (apurinic/apyrimidinic, AP) site [145,146]. Bifunctional glycosylases have an additive AP lyase activity and can further catalyze the cleavage of the sugar phosphate chain to cut out the abasic residue. There are at least nine *Arabidopsis* genes encoding bifunctional DNA glycosylases, and an AP lyase activity has been demonstrated *in vitro* for seven of these (AtMMH, AtNTH1, AtOGG1, AtDME, AtROS1, AtDML2 and AtDML3) [137–139,147–150]. Only the expression of At*OGG1* and At*MMH* was analyzed in detail after treatment with γ-irradiation, H_2O_2 or Paraquat and it was found out that they are not induced [151]. One explanation for this finding could be that there is enough protein constitutively produced to ensure the removal of 8-oxoG under oxidative conditions. Alternatively, the regulation could be post-transcriptional [151].

After base excision, it is necessary to remove the AP site to generate 3' OH termini [152]. This reaction is performed by means of AP endonucleases. The *Arabidopsis* genome encodes three AP endonucleases, which show homology to AP endonuclease genes of bacteria, yeast and animals (At*ARP*, At*APE1L* and At*APE2*) [153]. An interesting finding was that AtAPE1L and AtAPE2 play an essential role in embryonic development of plants. This role may reflect the importance of DNA repair in the embryo, or it may represent a function of AP endonucleases in the modification of DNA to activate expression of specific genes [153].

After the AP endonuclease cuts the DNA backbone, the resulting gap has to be filled in by a DNA polymerase, and the nick has to be sealed by a complex that includes DNA ligase III and X-ray repair cross-complementing group 1 (XRCC1). XRCC1 interacts with LIG III and other BER proteins in mammalian cells to coordinate different steps of the repair. The *Arabidopsis* genome encodes an *XRCC1* homolog [154]. It has been proposed that AtXRCC1 plays an important role in the repair of DSB in a presumably parallel NHEJ pathway to the AtKU proteins [155]. Furthermore At*XRCC1* shows an ATM kinase-dependent expression change after γ-irradiation, which confirms the idea that AtXRCC1 has an important function in the DSB repair pathway in plants [20]. The XRCC1 homolog in rice, OsXRCC1, has been shown to bind to single and double stranded DNA and to interact with PCNA *in vivo* [156].

There are two different mechanisms to fill in the resulting SSB. It can be filled in by inserting a single nucleotide into the gap (short-patch [SP] repair) or by DNA synthesis of several nucleotides (long patch [LP] repair) [157]. In humans, the filling of the SP gap is performed by Polymerase β [158]. *Arabidopsis* lacks any clear POL β homolog, but it has been proposed that its role could be fulfilled by a homolog of another polymerase, termed POL λ [159,160]. POL λ from rice shows DNA polymerase activity, and its expression is associated with cell proliferation in meristematic and meiotic tissues [161]. In LP repair, the gap is filled by the replicative DNA POL δ or ε by creating a flap-structure that is excised by the 5' flap endonuclease, FEN1, before ligation [162].

Another protein that has a role in BER and other strand break events is PARP1 (poly [ADP-ribose] polymerase-1). PARP1 is a nuclear protein that, when bound to DNA strand breaks, catalyzes the formation of branched polymers of poly(ADP-ribose) using NAD+ as a substrate. Polymers of ADP-ribose are transferred to a limited number of protein acceptors involved in modulating chromatin architecture or in DNA metabolism [31,163,164]. In plants, PARP activity has been demonstrated by the incorporation of labeled NAD^+ into poly(ADP-ribose) in nuclei of rapidly dividing tissues, such as root tips, germinating seedlings and tobacco cell suspensions (for review see [165]).

Two PARP homologs are characterized in *Arabidopsis*: AtPARP1 and AtPARP2 [166]. It was shown that mRNA of both *PARP* homologs in *Arabidopsis* shows a massive accumulation induced by ionizing radiation (IR); this accumulation is transient and dose-dependent, and the mRNA concentration returns to near basal levels 10–12 h after irradiation [2]. Additionally, both genes showed a very high expression rate when plants were treated with a mixture of bleomycin and mitomycin C, though At*PARP1* shows a much higher expression rate than At*PARP2* in roots and aerial plant parts ([10] data available at http://jsp.weigelworld.org/expviz/expviz.jsp). This is a clear hint that AtPARP1 and AtPARP2 play a role in the repair of damage induced by ionizing radiation, as well as genotoxins. Therefore, *PARP1* or *PARP2* mRNA could be a marker to investigate if plants are under genotoxic or irradiation stress. A study in soybeans gives suggests that PARP2 plays a general role in the response to oxidative stress, while the *PARP1* gene is more specifically activated by DNA strand breaks [2,167]. PARP1 has also been shown to be involved in an alternative NHEJ pathway in mammals [168].

4.2. Photoreactivation

Other than bacteria, only plants, with their sessile live style that makes them especially vulnerable to irradiation, harbor functional photolyase genes in their genome. The photolyase/chryptochrome family is commonly categorized as flavoproteins. These are proteins that contain a flavin cofactor. Members maintain genetic integrity by taking advantage of blue light to restore UV-induced photoproducts, such as CPDs or (6–4)PP, to intact bases. Once the substrate is bound, light is required to excite the $FADH^-$ either directly or via energy transfer. The photoexcited flavin ($FADH^-$) transfers an electron to the CPD, the two CPD bonds split and the electron returns to the flavin.

A. thaliana contains two kinds of photolyases that are specific for photoreactivation of either CPDs or (6–4)PPs [169–172].

There are two specific photolyases for CPD reversal encoded in the *Arabidopsis* genome: photolyase 1 (PHR1) and photolyase 2 (PHR2). A. Batschauer's group showed that expression of the photolyase, Sa*PHR1*, from *Sinapis alba* is light induced [173]. *PHR1* expression in *Arabidopsis* is also controlled by light [174]. Recently, it was shown that there is a link between photomorphogenesis and DNA repair via light induction of the PHR1 photolyase gene by the elongated hypocotyl 5 (AtHY5) and HY5-homolog (AtHYH) transcription factors. In contrast, the negative regulators of photomorphogenesis, de-etioleated 1 (DET1) and constitutive photomorphogenic 1 (AtCOP1), repress At*PHR1* and At*UVR3* gene expression in darkness [175]. Interestingly, in rice, *PHR1* expression is not restricted to dividing cells and can also be detected in mature tissues [176]. The results of that study indicate that BER and NER correlate with proliferating cells, while photoreactivation also protects post-mitotic cells [176]. The *Arabidopsis* CPD photolyase protein, PHR1, is most abundant in floral tissues with intermediate levels present in leaf tissue and very low levels evident in roots; it is present only at low levels in young, 7-day-old seedlings and increases between 7 and 14 days before declining in the leaves of mature plants [174].

(6–4)PPs are removed by another photolyase enzyme, AtUVR3 [172]. The *Arabidopsis* (6–4)PP photolyase showed that this protein has a very similar tissue distribution to that of the CPD photolyases. The (6–4)PP photolyase was detected in all tissues except for the roots with the highest levels detected in siliques [174], and it was present at all leaf ages examined [174].

In rice, the sensitivity to UV-B radiation varies among cultivars [177]. It was shown that the capacity to repair CPDs in UV-resistant rice is significantly higher than that in UV-sensitive rice and that this is due to an alteration of CPD photolyase activity resulting from mutations in the CPD photolyase gene [178–180]. In contrast to the (6–4)PP photorepair activity, which is constitutively active in *Arabidopsis* seedlings, the CPD photorepair requires preceding exposure of the seedlings to visible light for optimal expression [181]. The differential regulation of the expression of the (6–4)PP photolyase versus the CPD photolyase indicates that the two lesions are photoreactivated via two independent pathways.

Depletion of photolyase activity in *Arabidopsis* leads to incomplete CPD photoreactivation and defects in root growth after irradiation [170,172,174]. Conversely, an increase in CPD photolyase activity can minimize the growth-inhibitory effect of UV-B in *Arabidopsis* and *Oryza sativa* [182,183].

4.3. Nucleotide excision repair

Plants are equipped with genes for the nucleotide excision repair (NER) pathway. This pathway belongs to the so-called “dark repair pathways” as the proteins function independently from light.

NER involves recognition of especially bulky lesions that distort the helix structure, incision on the damaged strand, excision of 25–32 oligonucleotides around the distortion containing oligonucleotides, DNA synthesis and ligation [184,185]. There are two subpathways of NER: the transcription-coupled repair (TCR) and the global genomic repair (GGR) pathways. While GGR repairs DNA damage over the entire genome, TCR only repairs the transcribed DNA strand in expressed regions. The operators of the NER are called nucleotide excision repair factors (NEFs). The functions and structures of the involved genes and proteins are highly conserved between different eukaryotes [186,187]. The damage detection factor in yeast for the GGR is called NEF4 and consists of a heterodimer of RAD7 and RAD16. In *A. thaliana*, there are a several *RAD7* and *RAD16* homologs encoded in the genome (our own unpublished data and [188–190]). None of these homologs are characterized so far. The yeast NEF1 complex consists of RAD14, which could be another detector of DNA damages because it shows a high affinity to UV damaged DNA [191], and the endonuclease complex RAD1/RAD10. The ability to build a complex with RAD14 is of paramount importance for the targeting of this nuclease complex to lesion sites in vivo [192]. RAD23 and RAD4 form the NEF2 complex [193]. The endonuclease RAD2 and the transcription factor TFIIH of RNA Polymerase II make up the NEF3 complex [194]. NEF1, NEF2 and NEF3 are essential for TCR. GGR needs NEF4 to detect damages in nontranscribed regions. A number of proteins that are homologous to NER proteins have been detected in the *Arabidopsis* genome (for review, see [195]).

Analysis of TFIIH or its subunits indicates remarkable versatility. TFIIH participates not only in NER but also in transcription by RNA Polymerase II and possibly RNA Polymerase I, cell cycle control, and regulation of nuclear receptor activity [196–199]. It has also been implicated in the transcriptional response to DNA damage and translation initiation [200,201]. In human cells, TFIIH is a complex consisting of 10 required proteins, including XPB, XPD, p62, p52, p44, p34 and p8 [202,203]. There are different TFIIH subunits involved in NER that have been characterized, such as AtXPB1, AtXPB2, AtXPD and p44 (AtGTF2H2 and AtXPD) [204–208]. At*XPD* (also known as At*UVH6*) appears to be expressed at low levels in all tissues, as would be expected for a gene required for general transcription [207]. A comparison between the 5′ UTRs of At*XPB1* and At*XPB2* in the Col-0 ecotype detected significant differences, but both 5′ UTRs contain putative TATA boxes which have the capacity do drive constitutive gene expression of both genes. At*XPB1* and At*XPB2* are probably not induced by UV-B-induced DNA damage [205]. The promoter region of the *Arabidopsis p44* homolog, At*GTF2H2*, and At*XPD* contain multiple *cis*-elements, including ACGT, ACCTA, H-box, myeloblastosis (Myb), Myb recognition element (MRE), SET binding factor 1 (SBF-1) and TCA [14]. These promoter elements have previously been shown to be involved in light regulation or stress responses. [14,209–213]. While Vornarx et al. saw no changes in the expression level of these genes after UV irradiation, Molinier et al. did [15,208]. Evidently, the UV dose, length and the time point for measurement are important for detecting changes in expression of DNA repair genes.

Both endonucleases RAD1 and RAD10 that are involved in NEF1 have homologs encoded in the *Arabidopsis* genome, called At*RAD1* (or At*UVH1*) and At*ERCC1*, respectively. Expression of At*RAD1* was detected in all tissues with the highest level being found in flower bud tissue and the lowest level in leaf tissue [214]. The *Arabidopsis RAD10* homolog, At*ERCC1*, is also expressed in all tissues [215] but shows no expression changes following treatment with UV light [16]. The same result was found for the yeast RAD10 homolog, which is also not inducible after treatment with 4-nitroquinoline 1-oxide (4NQO). Human lung cancer cells also show no correlation between mRNA expression of ERCC1 and chemosensitivity to cisplatin and carboplatin [216,217]. In lily (*Lilium longiflorum*), it is interesting to note that *ERCC1* expression is up-regulated in the male germline cells of plants. Exposure of pollen released from the anther to solar UV-radiation and other environmental mutagens, as well as its enhanced susceptibility to dehydration, could eventually lead to DNA damage [218]. It is therefore possible that the up-regulation of the *ERCC1* homolog in lily generative cells indicates that DNA repair must be very active in such cells to protect germline DNA from mutations [219].

Additionally, a RAD23 homolog that makes up the yeast NEF2 complex along with RAD4 has been characterized in plants. In carrot (*Daucus carota*), there exist two *RAD23* homologs similar to *Arabidopsis* [220]. Both of these are expressed in all organs and tissue types, but transcript levels in carrot do not change up to 48 h after UV-C irradiation. This is similar to the *RAD23* human homologs [221] but differs from the regulation of the yeast gene [222]. The caltractin-like protein (CENTRIN2, AtCEN2) appears to be acting as an upstream regulator of the NER pathway in *Arabidopsis* because several components of the NER pathway were found to be transcriptionally altered in the mutant. This appears to be a switch mechanism that is relatively high in the hierarchy of DNA repair regulation [21]. HsCEN2 plays a role in the NER pathway, as well [223]. AtCEN2 contains four EF-hand calcium-binding sites. The ‘EF-hand’ domain is an important and highly conserved entity of the intracellular $Ca2^{+}$ receptor proteins that trigger cellular responses. At*CEN2* expression was detected in different organs, such as leaves and roots and was detected at a lower level in stems, flower buds and flowers [21]. Furthermore, the At*UVR3* photolyase was found to be down-regulated in the untreated At*cen2* mutant, whereas genes involved either directly or indirectly in double strand break repair (*RAD51* and *ATM*) were found to be up-regulated in the *centrin* mutant [21]. This finding leads to the hypothesis that AtCEN2 may be a global player for a switch mechanism between different DNA repair pathways.

5. E2F transcription factors

E2F/DP heterodimers are a family of transcription factors (TF) that are highly conserved in plants and mammals. In *Arabidopsis*, six E2F transcription factors have been identified [224]. These TF can be divided into typical (E2Fa-E2Fc) and atypical (E2Fd-E2Ff) E2Fs. The typical E2Fs contain one DNA-binding domain and one protein-

binding domain to bind its dimerization partner (DP) protein. The DP protein contains another DNA-binding domain, which allows for a stronger, high-affinity binding to promoters of genes that are regulated by E2F transcription factors. The atypical E2Fs (also known as DP-E2F-like [DEL] proteins) lack a dimerization domain to bind to the DP protein; instead, they have a duplicated DNA-binding domain, which allows them to bind to the same consensus element as the typical E2F TFs. The binding region of E2Fs is TTTSSCGS (where S is C or G) [225–229]. Interestingly, the atypical E2Fs possess no clear transcriptional activation domain, and they are therefore classified as transcriptional repressors [224,230].

The atypical E2Fe/DEL1 TF is involved as a specific inhibitor of endoreduplication [227,231]. The role of endoreduplication in DNA repair is still poorly understood but is a matter of discussion. One function for endoreduplication has been postulated in DNA stress tolerance [232,233]. It was speculated that if endoreduplicating cells possess more copies of genes then they could better bypass deleterious mutations. One target of the E2Fe/DEL1 TF is the *CCS52A2* gene, which encodes a CDH1-related activator of the anaphase-promoting complex (APC) ubiquitin ligase. If E2Fe/DEL1 is present, the APC activity is reduced and specific G2-M-cyclins that drive mitosis accumulate. However, if E2Fe/DEL1 is repressed, the APC, in cooperation with CCS52A2, destroys the mitotic cyclin complexes and stimulates endoreduplication [227,230]. Therefore, these plants show increased vitality following UV-B treatment compared to treated wildtype plants, likely due to their endoreduplicational background.

Interestingly, it was also shown that DSBs induce endoreduplication and that this process is dependent on the previously mentioned AtATM, AtATR, and AtSOG1 [234].

Recently, it was shown that the photolyase, AtPHR1, is also a target gene of the E2Fe/DEL1 TF. It is well described that the E2Fe/DEL1 TF represses the expression of At*PHR1*, which leads to a lower repair rate of CPDs in DNA [230]. Treatment with UV-B strongly down-regulates the expression of *E2Fe/DEL1*, possibly due to preventing that cells with damaged DNA enter the dividing process to avoid mutations. Thus At*PHR1* expression is up-regulated to repair new damages and to dispose and ensure the progression of the endocycle, which might lead to a higher UV resistance in the plant [230].

In the last several years, some arrays were performed to uncover genes that have an E2F TF binding site [10,228,229]. Surprisingly, a large number of genes were found that display E2Fa-DPa (regular E2F TF)-dependent expression, such as replication enzymes, origin factors, and enzymes that are involved in chromatin structure, cell cycle and DNA repair ([228,229] also see Table 2). Genes involved in DNA repair are affected in all known DNA repair pathways (see Table 2). All of the following genes which are involved in DNA damage repair were up-regulated in plants that over-express the E2Fa-DPa transcription factor: *ARP*, *PARP1*, *PARP2* which are involved in BER. The UV repair *UVR3* (6–4)PP photolyase, the NER putative Sc*RAD16* homolog, and the aforementioned *RAD51C*, *BRCA1*, *BARD1* and *SOG1* genes are up-regulated, too. In translesion synthesis and postreplicative repair (PRR), which are active at stalled replication forks to overcome lesions and ensure completion of replication, the catalytic subunit of POL ζ, namely, *REV3*, *PCNA1* and *PCNA2* and the helicase, *RAD5A*, are up-regulated in plants in which *E2Fa TFs* are over expressed [229]. This finding emphasizes the universal and fundamental function of the E2F transcription factors, especially in the regulation of DNA damage repair.

Table 2
List of DNA damage repair genes that possess at least one putative E2F binding site and are upregulated in plants in which the E2Fa transcription factor is over expressed. Sources: [195,196].

Gene	*Arabidopsis* locus	Putative repair pathway	Number of putative E2F binding sites	E2Fa ^{OE} dependent expression
BRCA1	At4g21070	HR	1	+++
WEE1	At1g02970	Signaling	n.f.	+++
BARD1	At1g04020	HR	1	+++
PARP1	At4g02390	BER, HR	n.f.	++
RAD51C	At2g45280	HR	1	++
UVR3	At3g15620	PR	1	++
RAD17	At5g66130	Signaling	1	++
PCNA2	At2g29570	PRR	1	++
POLH (POL η)	At5g44740	TLS	2	++
RAD5A	At5g22750	PRR, HR	1	+
PCNA1	At1g07370	PRR	2	+
ARP	At2g41460	BER	3	+
RECQ4A	At1g10930	HR, RF	1	+
PARP2	At2g31320	BER	1	+
RECQ4B	At1g60930	HR	1	+
REV3	At1g67500	TLS	2	+
SOG1	At1g25580	Signaling	1	+
CDKB1;1	At3g54180	Signaling	1	+
BRCA2 (V)	At5g01630	HR	1	+
RAD51B	At2g28560	HR	2	+

Listed are selected genes that are involved in DNA damage repair signaling, homologous recombination (HR), base excision repair (BER), photoreactivation (PR), postreplicative repair (PRR) and translesion synthesis (TLS). Nearly all of these genes exhibit at least one putative E2F binding site upstream of the ATG start codon. In two genes, no E2F binding site has been found (n.f.). Additionally, the up-regulated expression of these genes is classified as strong (+++), medium (++) or weak (+) in plants that over expressed (OE) the E2Fa transcription factor.

6. Conclusion

In this review, we summarized the current knowledge about gene regulation in response to DNA damage in plants. We primarily concentrated on genes involved in DNA repair. A large number of these genes are induced by DNA damage, which indicates that transcription is an important level of regulation for DNA damage repair in plants. The ATM kinase and the SOG1 transcription factor play important roles in this process. Additionally, the transcription factor, E2Fa, is involved in the regulation of DNA repair genes. Some genes, such as *BRCA1*, *RAD51* or *PARP1*, are transcriptionally induced by orders of magnitude in response to DNA damage. This finding gives us the opportunity to screen for their up-regulation as an indication of the accumulation of DNA damage in backgrounds with mutated genes to understand the genes' possible role in genome maintenance (for example, see [235]).

Nevertheless, many questions remain that should be addressed in the future. An interesting issue that has barely been studied in plants [31,58,59] is whether or not there are organ or cell specific responses or whether specific states of the cell cycle are involved in the regulation of genes in response to DNA damage. Another important aspect of gene expression is the regulation of the protein level by degradation in the 26S proteasome, which we did not cover in this review. A very prominent protein in humans, p53, which is an important cell cycle regulator, is regulated via polyubiquitination and subsequent degradation. In the future, additional research on protein levels should be performed. It will be very interesting to identify target proteins of ubiquitin E3 ligases, which are responsible for the specificity of the ubiquitin transfer. Nearly 1,300 genes in the *Arabidopsis* genome are predicted to encode for E3 components [236–238], and some of them are involved in DNA repair, such as At*RAD5A* or At*BRCA1* [239–241].

In light of these open questions, it appears that our current knowledge on the regulation of genes in response to DNA damage is just the tip of an iceberg of unknown complexity.

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References

[1] I.P. Chen, A. Mannuss, N. Orel, F. Heitzeberg, H. Puchta, A homolog of ScRAD5 is involved in DNA repair and homologous recombination in *Arabidopsis*, Plant Physiol. 146 (2008) 1786–1796.

[2] G. Doucet-Chabeaud, C. Godon, C. Brutesco, G. de Murcia, M. Kazmaier, Ionising radiation induces the expression of PARP-1 and PARP-2 genes in *Arabidopsis*, Mol. Genet. Genomics 265 (2001) 954–963.

[3] M.E. Gallego, M. Jeanneau, F. Granier, D. Bouchez, N. Bechtold, C.I. White, Disruption of the *Arabidopsis* RAD50 gene leads to plant sterility and MMS sensitivity, Plant J. 25 (2001) 31–41.

[4] A. Mannuss, S. Dukowic-Schulze, S. Suer, F. Hartung, M. Pacher, H. Puchta, RAD5A, RECQ4A, and MUS81 have specific functions in homologous recombination and define different pathways of DNA repair in *Arabidopsis thaliana*, Plant Cell 22 (2010) 3318–3330.

[5] H. Puchta, P. Swoboda, S. Gal, M. Blot, B. Hohn, Somatic intrachromosomal homologous recombination events in populations of plant siblings, Plant. Mol. Biol. 28 (1995) 281–292.

[6] E.J. Vonarx, H.L. Mitchell, R. Karthikeyan, I. Chatterjee, B.A. Kunz, DNA repair in higher plants, Mutat. Res. 400 (1998) 187–200.

[7] C.E. West, W.M. Waterworth, Q. Jiang, C.M. Bray, *Arabidopsis* DNA ligase IV is induced by gamma-irradiation and interacts with an *Arabidopsis* homologue of the double strand break repair protein XRCC4, Plant J. 24 (2000) 67–78.

[8] F. Hartung, S. Suer, T. Bergmann, H. Puchta, The role of AtMUS81 in DNA repair and its genetic interaction with the helicase AtRecQ4A, Nucleic Acids Res. 34 (2006) 4438–4448.

[9] F. Hartung, S. Suer, H. Puchta, Two closely related RecQ helicases have antagonistic roles in homologous recombination and DNA repair in *Arabidopsis thaliana*, Proc. Natl. Acad. Sci. U. S. A. 104 (2007) 18836–18841.

[10] I.P. Chen, U. Haehnel, L. Altschmied, I. Schubert, H. Puchta, The transcriptional response of *Arabidopsis* to genotoxic stress — a high-density colony array study (HDCA), Plant J. 35 (2003) 771–786.

[11] F. Heitzeberg, I.P. Chen, F. Hartung, N. Orel, K.J. Angelis, H. Puchta, The Rad17 homologue of *Arabidopsis* is involved in the regulation of DNA damage repair and homologous recombination, Plant J. 38 (2004) 954–968.

[12] N. Sanchez-Pons, S. Irar, N. Garcia-Muniz, C.M. Vicient, Transcriptomic and proteomic profiling of maize embryos exposed to camptothecin, BMC Plant Biol. 11 (2011) 91.

[13] U. Markmann-Mulisch, E. Wendeler, O. Zobell, G. Schween, H.H. Steinbiss, B. Reiss, Differential requirements for RAD51 in *Physcomitrella patens* and *Arabidopsis thaliana* development and DNA damage repair, Plant Cell 19 (2007) 3080–3089.

[14] M. Brosche, M.A. Schuler, I. Kalbina, L. Connor, A. Strid, Gene regulation by low level UV-B radiation: identification by DNA array analysis, Photochem. Photobiol. Sci. 1 (2002) 656–664.

[15] J. Molinier, E.J. Oakeley, O. Niederhauser, I. Kovalchuk, B. Hohn, Dynamic response of plant genome to ultraviolet radiation and other genotoxic stresses, Mutat. Res. 571 (2005) 235–247.

[16] J. Kilian, D. Whitehead, J. Horak, D. Wanke, S. Weinl, O. Batistic, C. D'Angelo, E. Bornberg-Bauer, J. Kudla, K. Harter, The AtGenExpress global stress expression data set: protocols, evaluation and model data analysis of UV-B light, drought and cold stress responses, Plant J. 50 (2007) 347–363.

[17] Y. Kim, Analysis of gene expression upon DNA damage in *Arabidopsis*, J. Plant Biol. 49 (2006) 298–302.

[18] L. Jiang, Y. Wang, L. Björn, S. Li, UV-B-induced DNA damage mediates expression changes of cell cycle regulatory genes in *Arabidopsis* root tips, Planta 233 (2011) 831–841.

[19] J.T. Ascencio-Ibanez, R. Sozzani, T.J. Lee, T.M. Chu, R.D. Wolfinger, R. Cella, L. Hanley-Bowdoin, Global analysis of *Arabidopsis* gene expression uncovers a complex array of changes impacting pathogen response and cell cycle during geminivirus infection, Plant Physiol. 148 (2008) 436–454.

[20] L. Ricaud, C. Proux, J.P. Renou, O. Pichon, S. Fochesato, P. Ortet, M.H. Montane, ATM-mediated transcriptional and developmental responses to gamma-rays in *Arabidopsis*, PLoS One 2 (2007) e430.

[21] J. Molinier, C. Ramos, O. Fritsch, B. Hohn, CENTRIN2 modulates homologous recombination and nucleotide excision repair in *Arabidopsis*, Plant Cell 16 (2004) 1633–1643.

[22] K.M. Culligan, C.E. Robertson, J. Foreman, P. Doerner, A.B. Britt, ATR and ATM play both distinct and additive roles in response to ionizing radiation, Plant J. 48 (2006) 947–961.

[23] T. Cools, A. Iantcheva, A.K. Weimer, S. Boens, N. Takahashi, S. Maes, H. Van den Daele, G. Van Isterdael, A. Schnittger, L. De Veylder, The *Arabidopsis thaliana* checkpoint kinase WEE1 protects against premature vascular differentiation during replication stress, Plant Cell 23 (2011) 1435–1448.

[24] K. Savitsky, A. Bar-Shira, S. Gilad, G. Rotman, Y. Ziv, L. Vanagaite, D.A. Tagle, S. Smith, T. Uziel, S. Sfez, M. Ashkenazi, I. Pecker, M. Frydman, R. Harnik, S.R. Patanjali, A. Simmons, G.A. Clines, A. Sartiel, R.A. Gatti, L. Chessa, O. Sanal, M.F. Lavin, N.G. Jaspers, A.M. Taylor, C.F. Arlett, T. Miki, S.M. Weissman, M. Lovett, F.S. Collins, Y. Shiloh, A single ataxia telangiectasia gene with a product similar to PI-3 kinase, Science 268 (1995) 1749–1753.

[25] N.J. Bentley, D.A. Holtzman, G. Flaggs, K.S. Keegan, A. DeMaggio, J.C. Ford, M. Hoekstra, A.M. Carr, The *Schizosaccharomyces pombe* rad3 checkpoint gene, EMBO J. 15 (1996) 6641–6651.

[26] K.A. Cimprich, T.B. Shin, C.T. Keith, S.L. Schreiber, cDNA cloning and gene mapping of a candidate human cell cycle checkpoint protein, Proc. Natl. Acad. Sci. U. S. A. 93 (1996) 2850–2855.

[27] D. Shechter, V. Costanzo, J. Gautier, Regulation of DNA replication by ATR: signaling in response to DNA intermediates, DNA Repair (Amst.) 3 (2004) 901–908.

[28] E.U. Kurz, S.P. Lees-Miller, DNA damage-induced activation of ATM and ATM-dependent signaling pathways, DNA Repair (Amst.) 3 (2004) 889–900.

[29] K. Czornak, S. Chughtai, K.H. Chrzanowska, Mystery of DNA repair: the role of the MRN complex and ATM kinase in DNA damage repair, J. Appl. Genet. 49 (2008) 383–396.

[30] A. Sancar, L.A. Lindsey-Boltz, K. Unsal-Kacmaz, S. Linn, Molecular mechanisms of mammalian DNA repair and the DNA damage checkpoints, Annu. Rev. Biochem. 73 (2004) 39–85.

[31] R.T. Abraham, Cell cycle checkpoint signaling through the ATM and ATR kinases, Genes Dev. 15 (2001) 2177–2196.

[32] Y. Shiloh, The ATM-mediated DNA-damage response: taking shape, Trends Biochem. Sci. 31 (2006) 402–410.

[33] V. Garcia, H. Bruchet, D. Camescasse, F. Granier, D. Bouchez, A. Tissier, AtATM is essential for meiosis and the somatic response to DNA damage in plants, Plant Cell 15 (2003) 119–132.

[34] E.J. Brown, D. Baltimore, ATR disruption leads to chromosomal fragmentation and early embryonic lethality, Genes Dev. 14 (2000) 397–402.

[35] Y. Xu, T. Ashley, E.E. Brainerd, R.T. Bronson, M.S. Meyn, D. Baltimore, Targeted disruption of ATM leads to growth retardation, chromosomal fragmentation during meiosis, immune defects, and thymic lymphoma, Genes Dev. 10 (1996) 2411–2422.

[36] K. Culligan, A. Tissier, A. Britt, ATR regulates a G2-phase cell-cycle checkpoint in *Arabidopsis thaliana*, Plant Cell 16 (2004) 1091–1104.

[37] D.W. Meek, Tumour suppression by p53: a role for the DNA damage response? Nat. Rev. Cancer 9 (2009) 714–723.

[38] S.B. Preuss, A.B. Britt, A DNA-damage-induced cell cycle checkpoint in *Arabidopsis*, Genetics 164 (2003) 323–334.

[39] K. Yoshiyama, P.A. Conklin, N.D. Huefner, A.B. Britt, Suppressor of gamma response 1 (SOG1) encodes a putative transcription factor governing multiple responses to DNA damage, Proc. Natl. Acad. Sci. U. S. A. 106 (2009) 12843–12848.

[40] T. Furukawa, M.J. Curtis, C.M. Tominey, Y.H. Duong, B.W. Wilcox, D. Aggoune, J.B. Hays, A.B. Britt, A shared DNA-damage-response pathway for induction of stem-cell death by UVB and by gamma irradiation, DNA Repair (Amst.) 9 (2010) 940–948.

[41] K. De Schutter, J. Joubes, T. Cools, A. Verkest, F. Corellou, E. Babiychuk, E. Van Der Schueren, T. Beeckman, S. Kushnir, D. Inze, L. De Veylder, *Arabidopsis* WEE1 kinase controls cell cycle arrest in response to activation of the DNA integrity checkpoint, Plant Cell 19 (2007) 211–225.

[42] T. Cools, A. Iantcheva, A.K. Weimer, S. Boens, N. Takahashi, S. Maes, H. Van den Daele, G. Van Isterdael, A. Schnittger, L. De Veylder, The *Arabidopsis thaliana* checkpoint kinase WEE1 protects against premature vascular differentiation during replication stress, Plant Cell. 23 (2011) 1435–1448.

[43] J.B. Boyd, K. Sakaguchi, P.V. Harris, mus308 mutants of *Drosophila* exhibit hypersensitivity to DNA cross-linking agents and are defective in a deoxyribonuclease, Genetics 125 (1990) 813–819.

[44] A. Ukai, T. Maruyama, S. Mochizuki, R. Ouchida, K. Masuda, K. Kawamura, M. Tagawa, K. Kinoshita, A. Sakamoto, T. Tokuhisa, O.W. J, Role of DNA polymerase theta in tolerance of endogenous and exogenous DNA damage in mouse B cells, Genes Cells 11 (2006) 111–121.

[45] N. Shima, S.A. Hartford, T. Duffy, L.A. Wilson, K.J. Schimenti, J.C. Schimenti, Phenotype-based identification of mouse chromosome instability mutants, Genetics 163 (2003) 1031–1040.

[46] S. Inagaki, T. Suzuki, M.A. Ohto, H. Urawa, T. Horiuchi, K. Nakamura, A. Morikami, *Arabidopsis* TEBICHI, with helicase and DNA polymerase domains, is required for regulated cell division and differentiation in meristems, Plant Cell 18 (2006) 879–892.

[47] S. Inagaki, K. Nakamura, A. Morikami, A link among DNA replication, recombination, and gene expression revealed by genetic and genomic analysis of TEBICHI gene of *Arabidopsis thaliana*, PLoS Genet. 5 (2009) e1000613.

[48] M. Chiurazzi, A. Ray, J.F. Viret, R. Perera, X.H. Wang, A.M. Lloyd, E.R. Signer, Enhancement of somatic intrachromosomal homologous recombination in *Arabidopsis* by the HO endonuclease, Plant Cell 8 (1996) 2057–2066.

[49] H. Puchta, Double-strand break-induced recombination between ectopic homologous sequences in somatic plant cells, Genetics 152 (1999) 1173–1181.

[50] G. Shalev, A.A. Levy, The maize transposable element Ac induces recombination between the donor site and an homologous ectopic sequence, Genetics 146 (1997) 1143–1151.

[51] R. Siebert, H. Puchta, Efficient repair of genomic double-strand breaks by homologous recombination between directly repeated sequences in the plant genome, Plant Cell 14 (2002) 1121–1131.

[52] Y.L. Xiao, T. Peterson, Intrachromosomal homologous recombination in *Arabidopsis* induced by a maize transposon, Mol. Gen. Genet. 263 (2000) 22–29.

[53] R.G. Sargent, M.A. Brenneman, J.H. Wilson, Repair of site-specific double-strand breaks in a mammalian chromosome by homologous and illegitimate recombination, Mol. Cell. Biol. 17 (1997) 267–277.

[54] H. Puchta, The repair of double-strand breaks in plants: mechanisms and consequences for genome evolution, J. Exp. Bot. 56 (2005) 1–14.

[55] J.H. Barlow, M. Lisby, R. Rothstein, Differential regulation of the cellular response to DNA double-strand breaks in G1, Mol. Cell 30 (2008) 73–85.

[56] M. Shrivastav, L.P. De Haro, J.A. Nickoloff, Regulation of DNA double-strand break repair pathway choice, Cell Res. 18 (2008) 134–147.

[57] C. Zierhut, J.F. Diffley, Break dosage, cell cycle stage and DNA replication influence DNA double strand break response, EMBO J. 27 (2008) 1875–1885.

[58] A. Boyko, J. Filkowski, D. Hudson, I. Kovalchuk, Homologous recombination in plants is organ specific, Mutat. Res. 595 (2006) 145–155.
[59] A. Boyko, F. Zemp, J. Filkowski, I. Kovalchuk, Double-strand break repair in plants is developmentally regulated, Plant Physiol. 141 (2006) 488–497.
[60] T. Uziel, Y. Lerenthal, L. Moyal, Y. Andegeko, L. Mittelman, Y. Shiloh, Requirement of the MRN complex for ATM activation by DNA damage, EMBO J. 22 (2003) 5612–5621.
[61] J.H. Lee, T.T. Paull, ATM activation by DNA double-strand breaks through the Mre11-Rad50-Nbs1 complex, Science 308 (2005) 551–554.
[62] E. Olson, C.J. Nievera, A.Y. Lee, L. Chen, X. Wu, The Mre11-Rad50-Nbs1 complex acts both upstream and downstream of ataxia telangiectasia mutated and Rad3-related protein (ATR) to regulate the S-phase checkpoint following UV treatment, J. Biol. Chem. 282 (2007) 22939–22952.
[63] R.S. Williams, G. Moncalian, J.S. Williams, Y. Yamada, O. Limbo, D.S. Shin, L.M. Groocock, D. Cahill, C. Hitomi, G. Guenther, D. Moiani, J.P. Carney, P. Russell, J.A. Tainer, Mre11 dimers coordinate DNA end bridging and nuclease processing in double-strand-break repair, Cell 135 (2008) 97–109.
[64] A. Dupre, L. Boyer-Chatenet, J. Gautier, Two-step activation of ATM by DNA and the Mre11-Rad50-Nbs1 complex, Nat. Struct. Mol. Biol. 13 (2006) 451–457.
[65] J.Y. Bleuyard, M.E. Gallego, C.I. White, Meiotic defects in the *Arabidopsis* rad50 mutant point to conservation of the MRX complex function in early stages of meiotic recombination, Chromosoma 113 (2004) 197–203.
[66] W.M. Waterworth, C. Altun, S.J. Armstrong, N. Roberts, P.J. Dean, K. Young, C.F. Weil, C.M. Bray, C.E. West, NBS1 is involved in DNA repair and plays a synergistic role with ATM in mediating meiotic homologous recombination in plants, Plant J. 52 (2007) 41–52.
[67] S. Amiard, C. Charbonnel, E. Allain, A. Depeiges, C.I. White, M.E. Gallego, Distinct roles of the ATR kinase and the Mre11-Rad50-Nbs1 complex in the maintenance of chromosomal stability in *Arabidopsis*, Plant Cell 22 (2010) 3020–3033.
[68] A.V. Nimonkar, J. Genschel, E. Kinoshita, P. Polaczek, J.L. Campbell, C. Wyman, P. Modrich, S.C. Kowalczykowski, BLM-DNA2-RPA-MRN and EXO1-BLM-RPA-MRN constitute two DNA end resection machineries for human DNA break repair, Genes Dev. 25 (2011) 350–362.
[69] C. Uanschou, T. Siwiec, A. Pedrosa-Harand, C. Kerzendorfer, E. Sanchez-Moran, M. Novatchkova, S. Akimcheva, A. Woglar, F. Klein, P. Schlogelhofer, A novel plant gene essential for meiosis is related to the human CtIP and the yeast COM1/SAE2 gene, EMBO J. 26 (2007) 5061–5070.
[70] S. Lafarge, M.H. Montane, Characterization of *Arabidopsis thaliana* ortholog of the human breast cancer susceptibility gene 1: AtBRCA1, strongly induced by gamma rays, Nucleic Acids Res. 31 (2003) 1148–1155.
[71] W. Reidt, R. Wurz, K. Wanieck, H.H. Chu, H. Puchta, A homologue of the breast cancer-associated gene BARD1 is involved in DNA repair in plants, EMBO J. 25 (2006) 4326–4337.
[72] O. Trapp, K. Seeliger, H. Puchta, Homologs of breast cancer genes in plants, Front. Plant Sci. 2 (2011).
[73] F. Hartung, H. Puchta, The RecQ gene family in plants, J. Plant Physiol. 163 (2006) 287–296.
[74] A. Knoll, H. Puchta, The role of DNA helicases and their interaction partners in genome stability and meiotic recombination in plants, J. Exp. Bot. 62 (2011) 1565–1579.
[75] K.E. Adams, A.L. Medhurst, D.A. Dart, N.D. Lakin, Recruitment of ATR to sites of ionising radiation-induced DNA damage requires ATM and components of the MRN protein complex, Oncogene 25 (2006) 3894–3904.
[76] M. Cuadrado, B. Martinez-Pastor, M. Murga, L.I. Toledo, P. Gutierrez-Martinez, E. Lopez, O. Fernandez-Capetillo, ATM regulates ATR chromatin loading in response to DNA double-strand breaks, J. Exp. Med. 203 (2006) 297–303.
[77] L. Zou, S.J. Elledge, Sensing DNA damage through ATRIP recognition of RPA-ssDNA complexes, Science 300 (2003) 1542–1548.
[78] P.R. Sweeney, A.B. Britt, K.M. Culligan, The *Arabidopsis* ATRIP ortholog is required for a programmed response to replication inhibitors, Plant J. 60 (2009) 518–526.
[79] M.S. Huen, S.M. Sy, J. Chen, BRCA1 and its toolbox for the maintenance of genome integrity, Nat. Rev. Mol. Cell Biol. 11 (2010) 138–148.
[80] R.W. Shultz, V.M. Tatineni, L. Hanley-Bowdoin, W.F. Thompson, Genome-wide analysis of the core DNA replication machinery in the higher plants *Arabidopsis* and rice, Plant Physiol. 144 (2007) 1697–1714.
[81] M.P. Doutriaux, F. Couteau, C. Bergounioux, C. White, Isolation and characterisation of the RAD51 and DMC1 homologs from *Arabidopsis thaliana*, Mol. Gen. Genet. 257 (1998) 283–291.
[82] J.Y. Bleuyard, M.E. Gallego, F. Savigny, C.I. White, Differing requirements for the *Arabidopsis* Rad51 paralogs in meiosis and DNA repair, Plant J. 41 (2005) 533–545.
[83] K. Osakabe, K. Abe, H. Yamanouchi, T. Takyuu, T. Yoshioka, Y. Ito, T. Kato, S. Tabata, S. Kurei, Y. Yoshioka, Y. Machida, M. Seki, M. Kobayashi, K. Shinozaki, H. Ichikawa, S. Toki, *Arabidopsis* Rad51B is important for double-strand DNA breaks repair in somatic cells, Plant. Mol. Biol. 57 (2005) 819–833.
[84] K. Osakabe, T. Yoshioka, H. Ichikawa, S. Toki, Molecular cloning and characterization of RAD51-like genes from *Arabidopsis thaliana*, Plant. Mol. Biol. 50 (2002) 71–81.
[85] A.J. Hartlerode, R. Scully, Mechanisms of double-strand break repair in somatic mammalian cells, Biochem. J. 423 (2009) 157–168.
[86] N. Nassif, J. Penney, S. Pal, W.R. Engels, G.B. Gloor, Efficient copying of nonhomologous sequences from ectopic sites via P-element-induced gap repair, Mol. Cell. Biol. 14 (1994) 1613–1625.
[87] J.W. Szostak, T.L. Orr-Weaver, R.J. Rothstein, F.W. Stahl, The double-strand-break repair model for recombination, Cell 33 (1983) 25–35.
[88] E.M. Cooper, C. Cutcliffe, T.Z. Kristiansen, A. Pandey, C.M. Pickart, R.E. Cohen, K63-specific deubiquitination by two JAMM/MPN+ complexes: BRISC-associated Brcc36 and proteasomal Poh1, EMBO J. 28 (2009) 621–631.
[89] G. Shao, D.R. Lilli, J. Patterson-Fortin, K.A. Coleman, D.E. Morrissey, R.A. Greenberg, The Rap80-BRCC36 de-ubiquitinating enzyme complex antagonizes RNF8-Ubc13-dependent ubiquitination events at DNA double strand breaks, Proc. Natl. Acad. Sci. U. S. A. 106 (2009) 3166–3171.
[90] A.S. Block-Schmidt, S. Dukowic-Schulze, K. Wanieck, W. Reidt, H. Puchta, BRCC36A is epistatic to BRCA1 in DNA crosslink repair and homologous recombination in *Arabidopsis thaliana*, Nucleic Acids Res. 39 (2011) 146–154.
[91] V.V. Gorbunova, A.A. Levy, How plants make ends meet: DNA double-strand break repair, Trends Plant Sci. 4 (1999) 263–269.
[92] H. van Attikum, P. Bundock, P.J. Hooykaas, Non-homologous end-joining proteins are required for *Agrobacterium* T-DNA integration, EMBO J. 20 (2001) 6550–6558.
[93] M.R. Lieber, The biochemistry and biological significance of nonhomologous DNA end joining: an essential repair process in multicellular eukaryotes, Genes Cells 4 (1999) 77–85.
[94] H. van Attikum, P. Bundock, R.M. Overmeer, L.Y. Lee, S.B. Gelvin, P.J. Hooykaas, The *Arabidopsis* AtLIG4 gene is required for the repair of DNA damage, but not for the integration of *Agrobacterium* T-DNA, Nucleic Acids Res. 31 (2003) 4247–4255.
[95] H. van Attikum, P.J. Hooykaas, Genetic requirements for the targeted integration of *Agrobacterium* T-DNA *in Saccharomyces cerevisiae*, Nucleic Acids Res. 31 (2003) 826–832.
[96] M. Dafny-Yelin, A. Tovkach, T. Tzfira, Integration of *Agrobacterium* T-DNA in Plant Cells, in: I. Meier (Ed.), Functional Organization of the Plant Nucleus, vol. 14, Springer, Berlin / Heidelberg, 2009, pp. 157–186.
[97] C. Charbonnel, E. Allain, M.E. Gallego, C.I. White, Kinetic analysis of DNA double-strand break repair pathways in *Arabidopsis*, DNA Repair (Amst.) 10 (2011) 611–619.
[98] W.S. Dynan, S. Yoo, Interaction of Ku protein and DNA-dependent protein kinase catalytic subunit with nucleic acids, Nucleic Acids Res. 26 (1998) 1551–1559.
[99] R.B. Cary, S.R. Peterson, J. Wang, D.G. Bear, E.M. Bradbury, D.J. Chen, DNA looping by Ku and the DNA-dependent protein kinase, Proc. Natl. Acad. Sci. U. S. A. 94 (1997) 4267–4272.
[100] M. Yaneva, T. Kowalewski, M.R. Lieber, Interaction of DNA-dependent protein kinase with DNA and with Ku: biochemical and atomic-force microscopy studies, EMBO J. 16 (1997) 5098–5112.
[101] L.K. Lewis, M.A. Resnick, Tying up loose ends: nonhomologous end-joining in *Saccharomyces cerevisiae*, Mutat. Res. 451 (2000) 71–89.
[102] S.A. Nick McElhinny, C.M. Snowden, J. McCarville, D.A. Ramsden, Ku recruits the XRCC4-ligase IV complex to DNA ends, Mol. Cell. Biol. 20 (2000) 2996–3003.
[103] W. Goedecke, M. Eijpe, H.H. Offenberg, M. van Aalderen, C. Heyting, Mre11 and Ku70 interact in somatic cells, but are differentially expressed in early meiosis, Nat. Genet. 23 (1999) 194–198.
[104] M.L. Heacock, R.A. Idol, J.D. Friesner, A.B. Britt, D.E. Shippen, Telomere dynamics and fusion of critically shortened telomeres in plants lacking DNA ligase IV, Nucleic Acids Res. 35 (2007) 6490–6500.
[105] F. Hartung, H. Puchta, Isolation of the complete cDNA of the Mre11 homolog of *Arabidopsis* (accession no. AJ243822) indicates conservation of DNA recombination mechanisms between plants and other eucaryotes, Plant Physiol. 121 (1999) 312.
[106] P. Bundock, P. Hooykaas, Severe developmental defects, hypersensitivity to DNA-damaging agents, and lengthened telomeres in *Arabidopsis* MRE11 mutants, Plant Cell 14 (2002) 2451–2462.
[107] N. Akutsu, K. Iijima, T. Hinata, H. Tauchi, Characterization of the plant homolog of Nijmegen breakage syndrome 1: involvement in DNA repair and recombination, Biochem. Biophys. Res. Commun. 353 (2007) 394–398.
[108] C.E. West, W.M. Waterworth, G.W. Story, P.A. Sunderland, Q. Jiang, C.M. Bray, Disruption of the *Arabidopsis* AtKu80 gene demonstrates an essential role for AtKu80 protein in efficient repair of DNA double-strand breaks in vivo, Plant J. 31 (2002) 517–528.
[109] K. Tamura, Y. Adachi, K. Chiba, K. Oguchi, H. Takahashi, Identification of Ku70 and Ku80 homologues in *Arabidopsis thaliana*: evidence for a role in the repair of DNA double-strand breaks, Plant J. 29 (2002) 771–781.
[110] P. Bundock, H. van Attikum, P. Hooykaas, Increased telomere length and hypersensitivity to DNA damaging agents in an *Arabidopsis* KU70 mutant, Nucleic Acids Res. 30 (2002) 3395–3400.
[111] P.F. Liu, W.C. Chang, Y.K. Wang, H.Y. Chang, R.L. Pan, Signaling pathways mediating the suppression of *Arabidopsis thaliana* Ku gene expression by abscisic acid, Biochim. Biophys. Acta 1779 (2008) 164–174.
[112] R.R. Finkelstein, S.S. Gampala, C.D. Rock, Abscisic acid signaling in seeds and seedlings, Plant Cell 14 (2002) S15–S45 (Suppl).
[113] F. Delacote, B.S. Lopez, Importance of the cell cycle phase for the choice of the appropriate DSB repair pathway, for genome stability maintenance: the trans-S double-strand break repair model, Cell Cycle 7 (2008) 33–38.
[114] K. Rothkamm, I. Kruger, L.H. Thompson, M. Lobrich, Pathways of DNA double-strand break repair during the mammalian cell cycle, Mol. Cell. Biol. 23 (2003) 5706–5715.
[115] Y. Saintigny, F. Delacote, D. Boucher, D. Averbeck, B.S. Lopez, XRCC4 in G1 suppresses homologous recombination in S/G2, in G1 checkpoint-defective cells, Oncogene 26 (2007) 2769–2780.
[116] M. Takata, M.S. Sasaki, E. Sonoda, C. Morrison, M. Hashimoto, H. Utsumi, Y. Yamaguchi-Iwai, A. Shinohara, S. Takeda, Homologous recombination and non-homologous end-joining pathways of DNA double-strand break repair have

overlapping roles in the maintenance of chromosomal integrity in vertebrate cells, EMBO J. 17 (1998) 5497–5508.
[117] A. Hartlerode, S. Odate, I. Shim, J. Brown, R. Scully, Cell cycle-dependent induction of homologous recombination by a tightly regulated I-SceI fusion protein, PLoS One 6 (2011) e16501.
[118] A.B. Britt, DNA damage and repair in plants, Annu. Rev. Plant Physiol. Plant. Mol. Biol. 47 (1996) 75–100.
[119] M.A.K. Jansen, V. Gabab, B.M. Greenberg, Higher plants and UV-B radiation: balancing damage, repair and acclimation, Trends Plant Sci. 3 (1998) 131–135.
[120] K. Bieza, R. Lois, An *Arabidopsis* mutant tolerant to lethal ultraviolet-B levels shows constitutively elevated accumulation of flavonoids and other phenolics, Plant Physiol. 126 (2001) 1105–1115.
[121] H. Kappus, H. Sies, Toxic drug effects associated with oxygen metabolism: redox cycling and lipid peroxidation, Experientia 37 (1981) 1233–1241.
[122] B.N. Ames, Endogenous oxidative DNA damage, aging, and cancer, Free. Radic. Res. Commun. 7 (1989) 121–128.
[123] B.N. Ames, M.K. Shigenaga, T.M. Hagen, Oxidants, antioxidants, and the degenerative diseases of aging, Proc. Natl. Acad. Sci. U. S. A. 90 (1993) 7915–7922.
[124] K. Apel, H. Hirt, Reactive oxygen species: metabolism, oxidative stress, and signal transduction, Annu. Rev. Plant Biol. 55 (2004) 373–399.
[125] F. Van Breusegem, J.F. Dat, Reactive oxygen species in plant cell death, Plant Physiol. 141 (2006) 384–390.
[126] E. Vranova, D. Inze, F. Van Breusegem, Signal transduction during oxidative stress, J. Exp. Bot. 53 (2002) 1227–1236.
[127] R. Mittler, S. Vanderauwera, M. Gollery, F. Van Breusegem, Reactive oxygen gene network of plants, Trends Plant Sci. 9 (2004) 490–498.
[128] J.H. Hoeijmakers, DNA damage, aging, and cancer, N. Engl. J. Med. 361 (2009) 1475–1485.
[129] M. Dizdaroglu, Oxidative damage to DNA in mammalian chromatin, Mutat. Res. 275 (1992) 331–342.
[130] M.L. Hegde, T.K. Hazra, S. Mitra, Early steps in the DNA base excision/single-strand interruption repair pathway in mammalian cells, Cell Res. 18 (2008) 27–47.
[131] S. Mitra, T. Izumi, I. Boldogh, K.K. Bhakat, J.W. Hill, T.K. Hazra, Choreography of oxidative damage repair in mammalian genomes, Free Radic. Biol. Med. 33 (2002) 15–28.
[132] N. Yang, H. Galick, S.S. Wallace, Attempted base excision repair of ionizing radiation damage in human lymphoblastoid cells produces lethal and mutagenic double strand breaks, DNA Repair (Amst.) 3 (2004) 1323–1334.
[133] J.C. Fromme, A. Banerjee, G.L. Verdine, DNA glycosylase recognition and catalysis, Curr. Opin. Struct. Biol. 14 (2004) 43–49.
[134] K.W. Caldecott, Mammalian DNA single-strand break repair: an X-ra(y)ted affair, Bioessays 23 (2001) 447–455.
[135] A. Santerre, A.B. Britt, Cloning of a 3-methyladenine-DNA glycosylase from *Arabidopsis thaliana*, Proc. Natl. Acad. Sci. U. S. A. 91 (1994) 2240–2244.
[136] L. Shi, R. Kent, N. Bence, A.B. Britt, Developmental expression of a DNA repair gene in *Arabidopsis*, Mutat. Res. 384 (1997) 145–156.
[137] F. Agius, A. Kapoor, J.K. Zhu, Role of the *Arabidopsis* DNA glycosylase/lyase ROS1 in active DNA demethylation, Proc. Natl. Acad. Sci. U. S. A. 103 (2006) 11796–11801.
[138] M. Gehring, J.H. Huh, T.F. Hsieh, J. Penterman, Y. Choi, J.J. Harada, R.B. Goldberg, R.L. Fischer, DEMETER DNA glycosylase establishes MEDEA polycomb gene self-imprinting by allele-specific demethylation, Cell 124 (2006) 495–506.
[139] T. Morales-Ruiz, A.P. Ortega-Galisteo, M.I. Ponferrada-Marin, M.I. Martinez-Macias, R.R. Ariza, T. Roldan-Arjona, DEMETER and REPRESSOR OF SILENCING 1 encode 5-methylcytosine DNA glycosylases, Proc. Natl. Acad. Sci. U. S. A. 103 (2006) 6853–6858.
[140] J.A. Law, S.E. Jacobsen, Establishing, maintaining and modifying DNA methylation patterns in plants and animals, Nat. Rev. Genet. 11 (2010) 204–220.
[141] J.K. Zhu, Active DNA demethylation mediated by DNA glycosylases, Annu. Rev. Genet. 43 (2009) 143–166.
[142] Z. Gong, T. Morales-Ruiz, R.R. Ariza, T. Roldan-Arjona, L. David, J.K. Zhu, ROS1, a repressor of transcriptional gene silencing in *Arabidopsis*, encodes a DNA glycosylase/lyase, Cell 111 (2002) 803–814.
[143] Y. Ikeda, T. Kinoshita, DNA demethylation: a lesson from the garden, Chromosoma 118 (2009) 37–41.
[144] J. Penterman, D. Zilberman, J.H. Huh, T. Ballinger, S. Henikoff, R.L. Fischer, DNA demethylation in the *Arabidopsis* genome, Proc. Natl. Acad. Sci. U. S. A. 104 (2007) 6752–6757.
[145] J.T. Stivers, Y.L. Jiang, A mechanistic perspective on the chemistry of DNA repair glycosylases, Chem. Rev. 103 (2003) 2729–2759.
[146] D.O. Zharkov, A.P. Grollman, The DNA trackwalkers: principles of lesion search and recognition by DNA glycosylases, Mutat. Res. 577 (2005) 24–54.
[147] M.V. Garcia-Ortiz, R.R. Ariza, T. Roldan-Arjona, An OGG1 orthologue encoding a functional 8-oxoguanine DNA glycosylase/lyase in *Arabidopsis thaliana*, Plant. Mol. Biol. 47 (2001) 795–804.
[148] T. Ohtsubo, O. Matsuda, K. Iba, I. Terashima, M. Sekiguchi, Y. Nakabeppu, Molecular cloning of AtMMH, an *Arabidopsis thaliana* ortholog of the *Escherichia coli* mutM gene, and analysis of functional domains of its product, Mol. Gen. Genet. 259 (1998) 577–590.
[149] A.P. Ortega-Galisteo, T. Morales-Ruiz, R.R. Ariza, T. Roldan-Arjona, *Arabidopsis* DEMETER-LIKE proteins DML2 and DML3 are required for appropriate distribution of DNA methylation marks, Plant. Mol. Biol. 67 (2008) 671–681.
[150] T. Roldan-Arjona, M.V. Garcia-Ortiz, M. Ruiz-Rubio, R.R. Ariza, cDNA cloning, expression and functional characterization of an *Arabidopsis thaliana* homologue of the *Escherichia coli* DNA repair enzyme endonuclease III, Plant. Mol. Biol. 44 (2000) 43–52.
[151] A.L. Dany, A. Tissier, A functional OGG1 homologue from *Arabidopsis thaliana*, Mol. Genet. Genomics 265 (2001) 293–301.
[152] B. Demple, L. Harrison, Repair of oxidative damage to DNA: enzymology and biology, Annu. Rev. Biochem. 63 (1994) 915–948.
[153] T.M. Murphy, M. Belmonte, S. Shu, A.B. Britt, J. Hatteroth, Requirement for abasic endonuclease gene homologues in *Arabidopsis* seed development, PLoS One 4 (2009) e4297.
[154] R.M. Taylor, A. Thistlethwaite, K.W. Caldecott, Central role for the XRCC1 BRCT I domain in mammalian DNA single-strand break repair, Mol. Cell. Biol. 22 (2002) 2556–2563.
[155] C. Charbonnel, M.E. Gallego, C.I. White, Xrcc1-dependent and Ku-dependent DNA double-strand break repair kinetics in *Arabidopsis* plants, Plant J. 64 (2010) 280–290.
[156] Y. Uchiyama, Y. Suzuki, K. Sakaguchi, Characterization of plant XRCC1 and its interaction with proliferating cell nuclear antigen, Planta 227 (2008) 1233–1241.
[157] P. Fortini, E. Dogliotti, Base damage and single-strand break repair: mechanisms and functional significance of short- and long-patch repair subpathways, DNA Repair (Amst.) 6 (2007) 398–409.
[158] D.K. Srivastava, B.J. Berg, R. Prasad, J.T. Molina, W.A. Beard, A.E. Tomkinson, S.H. Wilson, Mammalian abasic site base excision repair. Identification of the reaction sequence and rate-determining steps, J. Biol. Chem. 273 (1998) 21203–21209.
[159] A.B. Britt, Repair of damaged bases, MD: American Society of Plant Biologists, Rockville, 2002.
[160] M. Garcia-Diaz, O. Dominguez, L.A. Lopez-Fernandez, L.T. de Lera, M.L. Saniger, J.F. Ruiz, M. Parraga, M.J. Garcia-Ortiz, T. Kirchhoff, J. del Mazo, A. Bernad, L. Blanco, DNA polymerase lambda (Pol lambda), a novel eukaryotic DNA polymerase with a potential role in meiosis, J. Mol. Biol. 301 (2000) 851–867.
[161] Y. Uchiyama, S. Kimura, T. Yamamoto, T. Ishibashi, K. Sakaguchi, Plant DNA polymerase lambda, a DNA repair enzyme that functions in plant meristematic and meiotic tissues, Eur. J. Biochem. 271 (2004) 2799–2807.
[162] B. Pascucci, M. Stucki, Z.O. Jonsson, E. Dogliotti, U. Hubscher, Long patch base excision repair with purified human proteins. DNA ligase I as patch size mediator for DNA polymerases delta and epsilon, J. Biol. Chem. 274 (1999) 33696–33702.
[163] D. D'Amours, S. Desnoyers, I. D'Silva, G.G. Poirier, Poly(ADP-ribosyl)ation reactions in the regulation of nuclear functions, Biochem. J. 342 (Pt 2) (1999) 249–268.
[164] S.L. Oei, J. Griesenbeck, M. Schweiger, The role of poly(ADP-ribosyl)ation, Rev. Physiol. Biochem. Pharmacol. 131 (1997) 127–173.
[165] M. O'Farell, ADP-ribosylation reactions in plants, Biochimie 77 (1995) 486–491.
[166] L. Lepiniec, E. Babiychuk, S. Kushnir, M. Van Montagu, D. Inze, Characterization of an *Arabidopsis thaliana* cDNA homologue to animal poly(ADP-ribose) polymerase, FEBS Lett. 364 (1995) 103–108.
[167] Y. Amor, E. Babiychuk, D. Inze, A. Levine, The involvement of poly(ADP-ribose) polymerase in the oxidative stress responses in plants, FEBS Lett. 440 (1998) 1–7.
[168] M. Wang, W. Wu, B. Rosidi, L. Zhang, H. Wang, G. Iliakis, PARP-1 and Ku compete for repair of DNA double strand breaks by distinct NHEJ pathways, Nucleic Acids Res. 34 (2006) 6170–6182.
[169] M. Ahmad, J.A. Jarillo, L.J. Klimczak, L.G. Landry, T. Peng, R.L. Last, A.R. Cashmore, An enzyme similar to animal type II photolyases mediates photoreactivation in *Arabidopsis*, Plant Cell 9 (1997) 199–207.
[170] L.G. Landry, A.E. Stapleton, J. Lim, P. Hoffman, J.B. Hays, V. Walbot, R.L. Last, An *Arabidopsis* photolyase mutant is hypersensitive to ultraviolet-B radiation, Proc. Natl. Acad. Sci. U. S. A. 94 (1997) 328–332.
[171] S. Nakajima, M. Sugiyama, S. Iwai, K. Hitomi, E. Otoshi, S.T. Kim, C.Z. Jiang, T. Todo, A.B. Britt, K. Yamamoto, Cloning and characterization of a gene (UVR3) required for photorepair of 6–4 photoproducts in *Arabidopsis thaliana*, Nucleic Acids Res. 26 (1998) 638–644.
[172] C.Z. Jiang, J. Yee, D.L. Mitchell, A.B. Britt, Photorepair mutants of *Arabidopsis*, Proc. Natl. Acad. Sci. U. S. A. 94 (1997) 7441–7445.
[173] A. Batschauer, A plant gene for photolyase: an enzyme catalyzing the repair of UV-light-induced DNA damage, Plant J. 4 (1993) 705–709.
[174] W.M. Waterworth, Q. Jiang, C.E. West, M. Nikaido, C.M. Bray, Characterization of *Arabidopsis* photolyase enzymes and analysis of their role in protection from ultraviolet-B radiation, J. Exp. Bot. 53 (2002) 1005–1015.
[175] E. Castells, J. Molinier, S. Drevensek, P. Genschik, F. Barneche, C. Bowler, det1-1-induced UV-C hyposensitivity through UVR3 and PHR1 photolyase gene over-expression, Plant J. 63 (2010) 392–404.
[176] S. Kimura, Y. Tahira, T. Ishibashi, Y. Mori, T. Mori, J. Hashimoto, K. Sakaguchi, DNA repair in higher plants; photoreactivation is the major DNA repair pathway in non-proliferating cells while excision repair (nucleotide excision repair and base excision repair) is active in proliferating cells, Nucleic Acids Res. 32 (2004) 2760–2767.
[177] Q. Dai, V.P. Coronel, B.S. Vergara, P.W. Barnes, A.T. Quintos, Ultraviolet-B radiation effects on growth and physiology of four rice cultivars, Crop. Sci. 32 (1992) 1269–1274.
[178] M. Teranishi, Y. Iwamatsu, J. Hidema, T. Kumagai, Ultraviolet-B sensitivities in Japanese lowland rice cultivars: cyclobutane pyrimidine dimer photolyase activity and gene mutation, Plant Cell Physiol. 45 (2004) 1848–1856.
[179] J. Hidema, M. Teranishi, Y. Iwamatsu, T. Hirouchi, T. Ueda, T. Sato, B. Burr, B.M. Sutherland, K. Yamamoto, T. Kumagai, Spontaneously occurring mutations in the cyclobutane pyrimidine dimer photolyase gene cause different sensitivities to ultraviolet-B in rice, Plant J. 43 (2005) 57–67.

[180] A. Yamamoto, T. Hirouchi, T. Mori, M. Teranishi, J. Hidema, H. Morioka, T. Kumagai, K. Yamamoto, Biochemical and biological properties of DNA photolyases derived from utraviolet-sensitive rice cultivars, Genes Genet. Syst. 82 (2007) 311–319.
[181] J.J. Chen, D.L. Mitchell, A.B. Britt, A light-dependent pathway for the elimination of UV-induced pyrimidine (6–4) pyrimidinone photoproducts in *Arabidopsis*, Plant Cell 6 (1994) 1311–1317.
[182] J. Hidema, T. Taguchi, T. Ono, M. Teranishi, K. Yamamoto, T. Kumagai, Increase in CPD photolyase activity functions effectively to prevent growth inhibition caused by UVB radiation, Plant J. 50 (2007) 70–79.
[183] G. Kaiser, O. Kleiner, C. Beisswenger, A. Batschauer, Increased DNA repair in *Arabidopsis* plants overexpressing CPD photolyase, Planta 230 (2009) 505–515.
[184] J.C. Huang, D.L. Svoboda, J.T. Reardon, A. Sancar, Human nucleotide excision nuclease removes thymine dimers from DNA by incising the 22nd phosphodiester bond 5′ and the 6th phosphodiester bond 3′ to the photodimer, Proc. Natl. Acad. Sci. U. S. A. 89 (1992) 3664–3668.
[185] J.G. Moggs, K.J. Yarema, J.M. Essigmann, R.D. Wood, Analysis of incision sites produced by human cell extracts and purified proteins during nucleotide excision repair of a 1,3-intrastrand d(GpTpG)-cisplatin adduct, J. Biol. Chem. 271 (1996) 7177–7186.
[186] S. Prakash, P. Sung, L. Prakash, DNA repair genes and proteins of *Saccharomyces cerevisiae*, Annu. Rev. Genet. 27 (1993) 33–70.
[187] E.C. Friedberg, A.J. Bardwell, L. Bardwell, W.J. Feaver, R.D. Kornberg, J.Q. Svejstrup, A.E. Tomkinson, Z. Wang, Nucleotide excision repair in the yeast Saccharomyces cerevisiae: its relationship to specialized mitotic recombination and RNA polymerase II basal transcription, Philos. Trans. R. Soc. Lond. B Biol. Sci. 347 (1995) 63–68.
[188] A. Flaus, D.M. Martin, G.J. Barton, T. Owen-Hughes, Identification of multiple distinct Snf2 subfamilies with conserved structural motifs, Nucleic Acids Res. 34 (2006) 2887–2905.
[189] H. Shaked, N. Avivi-Ragolsky, A.A. Levy, Involvement of the *Arabidopsis* SWI2/SNF2 chromatin remodeling gene family in DNA damage response and recombination, Genetics 173 (2006) 985–994.
[190] L. Knizewski, K. Ginalski, A. Jerzmanowski, Snf2 proteins in plants: gene silencing and beyond, Trends Plant Sci. 13 (2008) 557–565.
[191] S.N. Guzder, P. Sung, L. Prakash, S. Prakash, Yeast DNA-repair gene RAD14 encodes a zinc metalloprotein with affinity for ultraviolet-damaged DNA, Proc. Natl. Acad. Sci. U. S. A. 90 (1993) 5433–5437.
[192] S.N. Guzder, C.H. Sommers, L. Prakash, S. Prakash, Complex formation with damage recognition protein Rad14 is essential for *Saccharomyces cerevisiae* Rad1–Rad10 nuclease to perform its function in nucleotide excision repair in vivo, Mol. Cell. Biol. 26 (2006) 1135–1141.
[193] S.N. Guzder, V. Bailly, P. Sung, L. Prakash, S. Prakash, Yeast DNA repair protein RAD23 promotes complex formation between transcription factor TFIIH and DNA damage recognition factor RAD14, J. Biol. Chem. 270 (1995) 8385–8388.
[194] Y. Habraken, P. Sung, S. Prakash, L. Prakash, Transcription factor TFIIH and DNA endonuclease Rad2 constitute yeast nucleotide excision repair factor 3: implications for nucleotide excision repair and Cockayne syndrome, Proc. Natl. Acad. Sci. U. S. A. 93 (1996) 10718–10722.
[195] J.B. Hays, *Arabidopsis thaliana*, a versatile model system for study of eukaryotic genome-maintenance functions, DNA Repair (Amst) 1 (2002) 579–600.
[196] J. Chen, S. Larochelle, X. Li, B. Suter, Xpd/Ercc2 regulates CAK activity and mitotic progression, Nature 424 (2003) 228–232.
[197] E. Compe, P. Drane, C. Laurent, K. Diderich, C. Braun, J.H. Hoeijmakers, J.M. Egly, Dysregulation of the peroxisome proliferator-activated receptor target genes by XPD mutations, Mol. Cell. Biol. 25 (2005) 6065–6076.
[198] J. Russell, J.C. Zomerdijk, RNA-polymerase-I-directed rDNA transcription, life and works, Trends Biochem. Sci. 30 (2005) 87–96.
[199] M. Zurita, C. Merino, The transcriptional complexity of the TFIIH complex, Trends Genet. 19 (2003) 578–584.
[200] Y. Takagi, C.A. Masuda, W.H. Chang, H. Komori, D. Wang, T. Hunter, C.A. Joazeiro, R.D. Kornberg, Ubiquitin ligase activity of TFIIH and the transcriptional response to DNA damage, Mol. Cell 18 (2005) 237–243.
[201] H. Yoon, S.P. Miller, E.K. Pabich, T.F. Donahue, SSL1, a suppressor of a HIS4 5′-UTR stem-loop mutation, is essential for translation initiation and affects UV resistance in yeast, Genes Dev. 6 (1992) 2463–2477.
[202] G. Giglia-Mari, F. Coin, J.A. Ranish, D. Hoogstraten, A. Theil, N. Wijgers, N.G. Jaspers, A. Raams, M. Argentini, P.J. van der Spek, E. Botta, M. Stefanini, J.M. Egly, R. Aebersold, J.H. Hoeijmakers, W. Vermeulen, A new, tenth subunit of TFIIH is responsible for the DNA repair syndrome trichothiodystrophy group A, Nat. Genet. 36 (2004) 714–719.
[203] Y. Takagi, H. Komori, W.H. Chang, A. Hudmon, H. Erdjument-Bromage, P. Tempst, R.D. Kornberg, Revised subunit structure of yeast transcription factor IIH (TFIIH) and reconciliation with human TFIIH, J. Biol. Chem. 278 (2003) 43897–43900.
[204] R.M. Costa, P.G. Morgante, C.M. Berra, M. Nakabashi, D. Bruneau, D. Bouchez, K.S. Sweder, M.A. Van Sluys, C.F. Menck, The participation of AtXPB1, the XPB/RAD25 homologue gene from *Arabidopsis thaliana*, in DNA repair and plant development, Plant J. 28 (2001) 385–395.
[205] P.G. Morgante, C.M. Berra, M. Nakabashi, R.M. Costa, C.F. Menck, M.A. Van Sluys, Functional XPB/RAD25 redundancy in *Arabidopsis* genome: characterization of AtXPB2 and expression analysis, Gene 344 (2005) 93–103.
[206] D.T. Ribeiro, C.R. Machado, R.M. Costa, U.M. Praekelt, M.A. Van Sluys, C.F. Menck, Cloning of a cDNA from *Arabidopsis thaliana* homologous to the human XPB gene, Gene 208 (1998) 207–213.
[207] Z. Liu, S.W. Hong, M. Escobar, E. Vierling, D.L. Mitchell, D.W. Mount, J.D. Hall, *Arabidopsis* UVH6, a homolog of human XPD and yeast RAD3 DNA repair genes, functions in DNA repair and is essential for plant growth, Plant Physiol. 132 (2003) 1405–1414.
[208] E.J. Vonarx, E.K. Tabone, M.J. Osmond, H.J. Anderson, B.A. Kunz, *Arabidopsis* homologue of human transcription factor IIH/nucleotide excision repair factor p44 can function in transcription and DNA repair and interacts with AtXPD, Plant J. 46 (2006) 512–521.
[209] L.M. Yu, C.J. Lamb, R.A. Dixon, Purification and biochemical characterization of proteins which bind to the H-box cis-element implicated in transcriptional activation of plant defense genes, Plant J. 3 (1993) 805–816.
[210] R.W. Sablowski, E. Moyano, F.A. Culianez-Macia, W. Schuch, C. Martin, M. Bevan, A flower-specific Myb protein activates transcription of phenylpropanoid biosynthetic genes, EMBO J. 13 (1994) 128–137.
[211] M.A. Lawton, S.M. Dean, M. Dron, J.M. Kooter, K.M. Kragh, M.J. Harrison, L. Yu, L. Tanguay, R.A. Dixon, C.J. Lamb, Silencer region of a chalcone synthase promoter contains multiple binding sites for a factor, SBF-1, closely related to GT-1, Plant. Mol. Biol. 16 (1991) 235–249.
[212] U. Hartmann, W.J. Valentine, J.M. Christie, J. Hays, G.I. Jenkins, B. Weisshaar, Identification of UV/blue light-response elements in the *Arabidopsis thaliana* chalcone synthase promoter using a homologous protoplast transient expression system, Plant. Mol. Biol. 36 (1998) 741–754.
[213] A.P. Goldsbrough, H. Albrecht, R. Stratford, Salicylic acid-inducible binding of a tobacco nuclear protein to a 10 bp sequence which is highly conserved amongst stress-inducible genes, Plant J. 3 (1993) 563–571.
[214] Z. Liu, G.S. Hossain, M.A. Islas-Osuna, D.L. Mitchell, D.W. Mount, Repair of UV damage in plants by nucleotide excision repair: *Arabidopsis* UVH1 DNA repair gene is a homolog of Saccharomyces cerevisiae Rad1, Plant J. 21 (2000) 519–528.
[215] M. Schmid, T.S. Davison, S.R. Henz, U.J. Pape, M. Demar, M. Vingron, B. Scholkopf, D. Weigel, J.U. Lohmann, A gene expression map of *Arabidopsis thaliana* development, Nat. Genet. 37 (2005) 501–506.
[216] L. Bardwell, H. Burtscher, W.A. Weiss, C.M. Nicolet, E.C. Friedberg, Characterization of the RAD10 gene of *Saccharomyces cerevisiae* and purification of Rad10 protein, Biochemistry 29 (1990) 3119–3126.
[217] J. Shimizu, Y. Horio, H. Osada, T. Hida, Y. Hasegawa, K. Shimokata, T. Takahashi, Y. Sekido, Y. Yatabe, mRNA expression of RRM1, ERCC1 and ERCC2 is not associated with chemosensitivity to cisplatin, carboplatin and gemcitabine in human lung cancer cell lines, Respirology 13 (2008) 510–517.
[218] J.F. Jackson, DNA repair in pollen, a review, Mutat. Res. 181 (1987) 17–29.
[219] H. Xu, I. Swoboda, P.L. Bhalla, A.M. Sijbers, C. Zhao, E.K. Ong, J.H. Hoeijmakers, M.B. Singh, Plant homologue of human excision repair gene ERCC1 points to conservation of DNA repair mechanisms, Plant J. 13 (1998) 823–829.
[220] A. Sturm, S. Lienhard, Two isoforms of plant RAD23 complement a UV-sensitive rad23 mutant in yeast, Plant J. 13 (1998) 815–821.
[221] P.J. van der Spek, A. Eker, S. Rademakers, C. Visser, K. Sugasawa, C. Masutani, F. Hanaoka, D. Bootsma, J.H. Hoeijmakers, XPC and human homologs of RAD23: intracellular localization and relationship to other nucleotide excision repair complexes, Nucleic Acids Res. 24 (1996) 2551–2559.
[222] K. Madura, S. Prakash, Transcript levels of the *Saccharomyces* cerevisiae DNA repair gene RAD23 increase in response to UV light and in meiosis but remain constant in the mitotic cell cycle, Nucleic Acids Res. 18 (1990) 4737–4742.
[223] M. Araki, C. Masutani, M. Takemura, A. Uchida, K. Sugasawa, J. Kondoh, Y. Ohkuma, F. Hanaoka, Centrosome protein centrin 2/caltractin 1 is part of the xeroderma pigmentosum group C complex that initiates global genome nucleotide excision repair, J. Biol. Chem. 276 (2001) 18665–18672.
[224] T. Lammens, J. Li, G. Leone, L. De Veylder, Atypical E2Fs: new players in the E2F transcription factor family, Trends Cell Biol 19 (2009) 111–118.
[225] M.E. Chaboute, B. Clement, M. Sekine, G. Philipps, N. Chaubet-Gigot, Cell cycle regulation of the tobacco ribonucleotide reductase small subunit gene is mediated by E2F-like elements, Plant Cell 12 (2000) 1987–2000.
[226] R. Stevens, L. Mariconti, P. Rossignol, C. Perennes, R. Cella, C. Bergounioux, Two E2F sites in the *Arabidopsis* MCM3 promoter have different roles in cell cycle activation and meristematic expression, J. Biol. Chem. 277 (2002) 32978–32984.
[227] K. Vlieghe, V. Boudolf, G.T. Beemster, S. Maes, Z. Magyar, A. Atanassova, J. de Almeida Engler, R. De Groodt, D. Inze, L. De Veylder, The DP-E2F-like gene DEL1 controls the endocycle in *Arabidopsis thaliana*, Curr. Biol. 15 (2005) 59–63.
[228] N. Naouar, K. Vandepoele, T. Lammens, T. Casneuf, G. Zeller, P. van Hummelen, D. Weigel, G. Ratsch, D. Inze, M. Kuiper, L. De Veylder, M. Vuylsteke, Quantitative RNA expression analysis with Affymetrix Tiling 1.0R arrays identifies new E2F target genes, Plant J. 57 (2009) 184–194.
[229] K. Vandepoele, K. Vlieghe, K. Florquin, L. Hennig, G.T. Beemster, W. Gruissem, Y. Van de Peer, D. Inze, L. De Veylder, Genome-wide identification of potential plant E2F target genes, Plant Physiol. 139 (2005) 316–328.
[230] A. Radziejwoski, K. Vlieghe, T. Lammens, B. Berckmans, S. Maes, M.A. Jansen, C. Knappe, A. Albert, H.K. Seidlitz, G. Bahnweg, D. Inze, L. De Veylder, Atypical E2F activity coordinates PHR1 photolyase gene transcription with endoreduplication onset, EMBO J. 30 (2011) 355–363.
[231] T. Lammens, V. Boudolf, L. Kheibarshekan, L.P. Zalmas, T. Gaamouche, S. Maes, M. Vanstraelen, E. Kondorosi, N.B. La Thangue, W. Govaerts, D. Inze, L. De Veylder, Atypical E2F activity restrains APC/CCCS52A2 function obligatory for endocycle onset, Proc. Natl. Acad. Sci. U. S. A. 105 (2008) 14721–14726.
[232] B.A. Edgar, T.L. Orr-Weaver, Endoreplication cell cycles: more for less, Cell 105 (2001) 297–306.
[233] J. Traas, M. Hulskamp, E. Gendreau, H. Hofte, Endoreduplication and development: rule without dividing? Curr. Opin. Plant Biol. 1 (1998) 498–503.

[234] S. Adachi, K. Minamisawa, Y. Okushima, S. Inagaki, K. Yoshiyama, Y. Kondou, E. Kaminuma, M. Kawashima, T. Toyoda, M. Matsui, D. Kurihara, S. Matsunaga, M. Umeda, Programmed induction of endoreduplication by DNA double-strand breaks in *Arabidopsis*, Proc. Natl. Acad. Sci. U. S. A. 108 (2011) 10004–10009.
[235] E.M. Dohmann, M.P. Levesque, L. De Veylder, I. Reichardt, G. Jurgens, M. Schmid, C. Schwechheimer, The *Arabidopsis* COP9 signalosome is essential for G2 phase progression and genomic stability, Development 135 (2008) 2013–2022, doi: 10.1242/dev.020743.
[236] J.M. Gagne, B.P. Downes, S.H. Shiu, A.M. Durski, R.D. Vierstra, The F-box subunit of the SCF E3 complex is encoded by a diverse superfamily of genes in *Arabidopsis*, Proc. Natl. Acad. Sci. U. S. A. 99 (2002) 11519–11524.
[237] J. Smalle, R.D. Vierstra, The ubiquitin 26S proteasome proteolytic pathway, Annu. Rev. Plant Biol. 55 (2004) 555–590.
[238] R.D. Vierstra, The ubiquitin/26S proteasome pathway, the complex last chapter in the life of many plant proteins, Trends Plant Sci. 8 (2003) 135–142.
[239] E. Kraft, S.L. Stone, L. Ma, N. Su, Y. Gao, O.S. Lau, X.W. Deng, J. Callis, Genome analysis and functional characterization of the E2 and RING-type E3 ligase ubiquitination enzymes of *Arabidopsis*, Plant Physiol. 139 (2005) 1597–1611.
[240] S.L. Stone, H. Hauksdottir, A. Troy, J. Herschleb, E. Kraft, J. Callis, Functional analysis of the RING-type ubiquitin ligase family of *Arabidopsis*, Plant Physiol. 137 (2005) 13–30.
[241] E. Mazzucotelli, S. Belloni, D. Marone, A. De Leonardis, D. Guerra, N. Di Fonzo, L. Cattivelli, A. Mastrangelo, The e3 ubiquitin ligase gene family in plants: regulation by degradation, Curr. Genomics 7 (2006) 509–522.