

## PLANT AP2/ERF TRANSCRIPTION FACTORS

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Transcription factors (TFs) play important roles in plant development and its response to the biotic and abiotic stresses. AP2/ERF transcription factors family is unique to plants and a conserved AP2/ERF domain of about 60 amino acids characterized these transcription factors. AP2/ERF genes have been shown to regulate developmental processes and the response of plants to various types of biotic and environmental stress. Here, we summarize the current knowledge of AP2/ERF plant transcription factor family.

*Key words:* Transcription factors, AP2/ERF domain, AP2/ERF transcription factor family

### INTRODUCTION

Transcription factors (TFs) are sequence-specific DNA-binding proteins that are able to activate and/or repress transcription. They often function in networks, in which a regulatory protein controls the expression of another, which in

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turn may modulate the expression of other regulators genes or control genes encoding structural proteins or enzymes. Transcription factors are responsible for the selectivity in gene regulation and are often expressed in tissue-specific, development-stage-specific or *via* stimulus-dependent pathways (LIU *et al.*, 1999; ZHANG 2003; DAVULURI *et al.*, 2003).

A typical plant transcription factor contains, with few exceptions, a DNA-binding domain, an oligomerization site, a transcription-regulation domain, and a nuclear localization signal, although some lack either a transcription regulation domain or specific DNA-binding domain (GOFF *et al.*, 1992; HILL *et al.*, 1996; DOEBLEY and LUKENS 1998). The DNA-binding domain is responsible for the union of the TFs to specific cis-regulatory DNA sequences in the promoters of genes that they regulate. Most transcription factors exhibit only one type of DNA-binding and oligomerization domain, occasionally in multiple copies, but some contain two distinct types of DNA-binding domain. Several plant transcription factors possess both specific and non-specific DNA-binding domains, with the later occasionally necessary for the transactivation of target genes (HERR *et al.*, 1988; HERR and CLEARY, 199; MARTIN and PAZ-ARES, 1997; KAGAYA *et al.*, 1999).

Many plant transcription factors form hetero-and/or homo-oligomers affecting the DNA-binding specificity. Regulation domains and hence, transcription factors functions as either repressors or activators, depending on whether they inhibit or stimulate the transcription of target genes (DIETRICH *et al.*, 1997; YANAGISAWA and SHEEN 1998). The plant transcription factors contain nuclear localization signal (NLS) characterized by a core peptide enriched in Arginine and Lysine. Some plant transcription factors may lack an NLS and they are thought to be imported in the nucleus by dimerizing with proteins that possess these signals (GOLDFARB and LEWANDOWSKA, 1994; LYCK *et al.*, 1997). Engineering of plant transcription factor genes provides a valuable means for genetic manipulation of plants. In this review, we summarize our knowledge about the AP2/ERF transcription factors family, classification of AP2/ERF genes and their function during plant life cycle.

#### AP2/ERF TRANSCRIPTION FACTORS

**Classification of AP2/ERF transcription factors** - Based in the number of copies of AP2/ERF domain and their sequence similarity, The AP2/ERF proteins have been subdivided into five subfamilies (SAKUMA *et al.*, 2002): AP2 subfamily, DREB subfamily, ERF subfamily, RAV subfamily and others. Members of the AP2 subfamily contain two AP2/ERF domains connected by a conserved linker of 25 amino acid such as AP2, ANT, Glossy15, AtBBM and BnBBM. Members of the DREB, ERF and other subgroups contain a single AP2/ERF domain, such as ZmDBFs, NtERFs, AtDREBs, AtCBFs, LePtis, AtEBP and AtERFs (KIZIS and PAGES, 2002; RIECHMANN *et al.*, 2000; SAKUMA *et al.*, 2002). However, the RAV subfamily (RAV: for Related to ABI3/VP1) includes genes that conserved two different DNA-binding domains, AP2/ERF and B3. B3 DNA-

binding domain is conserved in VP1/ABI3) as shown in Fig. 1 (GIRAUDAT *et al.*, 1992; KAGAYA *et al.*, 1999).

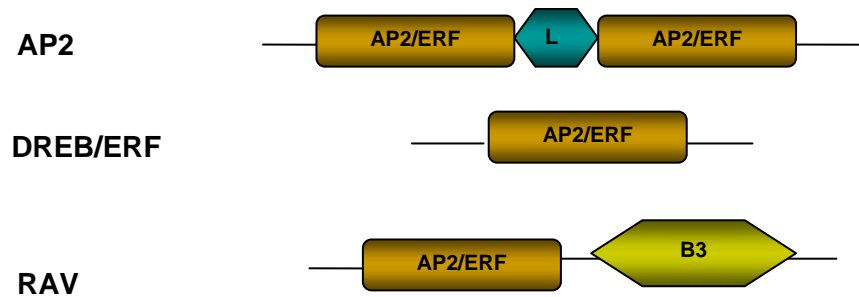


Fig. 1. Schematic illustrations of domain organization of AP2, DREB, ERF and RAV proteins

**AP2/ERF Domain structure** - A conserved AP2/ERF domain of about 60-70 amino acids characterized the AP2/ERF transcription factors with no apparent similarity outside this domain (RIECHMANN and MEYEROWITZ, 1998). The AP2/ERF domain was originally identified in *APETALA2* of *Arabidopsis* (JOFUKU *et al.*, 1994) and *EREBP1* of tobacco (OHME-TAKAGI and SHINSHI, 1995). The AP2/ERF domain is a new type of DNA-binding module that includes two regions: The YRG region (YRG element) of about 20-amino acid-long N-terminal stretch rich in basic and hydrophilic residues. It was proposed to have a role in the DNA binding by making a direct contact with the DNA because of its basic character (OKAMURO *et al.*, 1997).

The RAYD region of about 40-amino acids (RAYD element) in the C-terminal sequence of the domain contains 18 amino acids capable of forming an amphipathic  $\alpha$ -helix and is thought to have an important role for the structure and function of the domain (JOFUKU *et al.*, 1994; OKAMURO *et al.*, 1997). The RAYD element was proposed to mediate protein-protein interactions through  $\alpha$ -helix or to have an alternative role in DNA binding through interactions of hydrophobic face of the  $\alpha$ -helix with the major groove of DNA. DRE-binding proteins contain specific residues within their AP2/ERF domain that may determine their ability to bind the DRE/C-repeat element (JOFUKU *et al.*, 1994; OKAMURO *et al.*, 1997; KIZIS *et al.*, 2000; SAKOMA *et al.*, 2002).

The solution structure of the AP2/ERF domain of AtERF1 bound to the GCC box (5'-AGCCGCC-3') indicated that the protein uses an anti-parallel three-stranded  $\beta$ -sheet to make major groove contacts. The  $\beta$ -sheet packs against an  $\alpha$ -helix that runs approximately parallel to the sheet. This structure is stabilized by an extensive number of hydrophobic contacts. The majority of DNA contacts are made by Arginine and Tryptophan residues located in the  $\beta$ -sheet of the protein (ALLEN *et al.*, 1998).

The existence of repeated DNA-binding domains not unique to AP2/ERF transcription factors. The WRKY family of transcription factors consists of proteins that contain either a single or a repeated DNA-binding domain (RUSHTON *et al.*, 1995). A repeated DNA-binding motif is also found in the MYB family of transcription factors, the MYB DNA-binding domain consists normally of three repeats (R1, R2 and R3) in animal MYB proteins and two repeats (R2 and R3) in plant MYB proteins (MARTIN and PAZ-ARES, 1997).

In other eukaryotes, only a few families of transcription factors with distinct DNA-binding domains include POU-domain proteins (HERR *et al.*, 1988) and Pax proteins (CZERNY *et al.*, 1993), both of which have been studied extensively with respect to how the multiple DNA binding structures contribute to the specificity and affinity of DNA-binding (VERRIJZER *et al.*, 1992; JUN and DESPLAN 1996). The POU-domain consists of two subdomains, a POU-specific domain (POUS) and a POU-type homeo-domain (POUHD), that cooperate functionally as one binding unit (HERR and CLEARY, 1995). The paired-domain (PD) of Pax proteins also consists of two subdomains, PAI and RED, both of which contain a helix-turn-helix (HTH) DNA-binding motif. Many Pax proteins contain a homeo-domain (HD) in addition to PD. Thus, these proteins contain three HTHs and have been shown to recognize different types of target sites using multiple combinations of their HTHs (JUN and DESPLAN, 1996).

### AP2 subfamily

#### R1 (Repeat1)

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-----YRG-----RAYD-----
consensus  .S.YRGVT..R.TGR.E.H.WD.....G.OVYLG.G.D...AARAYD.AA.K..G....NF...Y....
AtAP2      1  S Y R G V T . . R T G R . E H W D . . . . . G O V Y L G G . D T A H A A A R A Y D A A . K . R . S V E A D I N F N I D D Y D D D I 67
Glossy15   1  S Y R G V T . . R T G R . E H W D . . . . . G O V Y L G G . D T A Q A A A R A Y D A A . K . R . R L N A D I N F L L D D K D E N 67
ZmINSP1K1  1  S Y R G V T . . R T G R . E H W D . . . . . G O V Y L G G . D T A H A A A R A Y D A A . K . R . R L D A D I N F L S D S E D D I 67
ANT        1  S Y R G V T . . R T G R . E H W D N S P K K E G H S R K . . . . . G O V Y L G G . D M E E K A A R A Y D A A . K . W . S P T T I N F S A D N . K E K I 77
BnBBM2     1  S Y R G V T . . R T G R . E H W D N S C K R E G Q T R K . . . . . G O V Y L G G . D M E E K A A R A Y D A A . K . W . S P T T I N F S M S E . K E K I 77
AtBBM      1  S Y R G V T . . R T G R . E H W D N S C K R E G Q T R K . . . . . G O V Y L G G . D M E E K A A R A Y D A A . K . W . S P T T I N F S L S E . K E K I 77

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#### Linker

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Consensus  ..M.....E.V..LRR...GF.RG
AtAP2      1  E M K H M T R C E V A S L R R S S G F S R G 25
Glossy15   1  E M K H M T R C E V A S L R R S S G F S R G 25
ZmINSP1K1  1  E M K N M T R C E V A S L R R S S G F S R G 25
ANT        1  K Q M T N L I R E E V H V L R R S S G F S R G 25
BnBBM2     1  K Q M R N W I R E E V H V L R R S S G F S R G 25
AtBBM      1  K R M K D L S R E E V H V L R R S S G F S R G 25

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#### R2 (Repeat2)

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-----YRG-----RAYD-----
Consensus  .S..RGVT..H..G.W.AR.G...G.K..YLG.....EAA.AYD.AA....G..AVTNF...Y....
AtAP2      1  S R G V T . . H . C C W A R G G P L C R K Y Y L G L R D T E V E A A A Y D A A . K C N C K D A V T N F S P S I Y D E E L 68
Glossy15   1  S R R G V T . . H . C C W A R G G L M C R K Y Y L G L M D I T E E A A A Y D A A . K C V S K E A V T N F S A Q S Y K E L 68
ZmINSP1K1  1  S R G R V T . . H . C C W A R G G L L C R K Y Y L G L D S R V E A A A Y D A A . L R F N S R E A V T N F S P S S W A G D 68
ANT        1  S H R G V T R E . H G W A R G H V A C N K D . Y L G T F G L Q E A A A Y D A A . L A F R S T I A V T N F I T R L V W D R 69
BnBBM2     1  S H R G V T R E . H G W A R G H V A C N K D . Y L G T F G L Q E A A A Y D A A . L A F R S T I A V T N F S M N R S W K A 69
AtBBM      1  S H R G V T R E . H G W A R G H V A C N K D . Y L G T F G L Q E A A A Y D A A . L A F R S T I A V T N F S M N R S W K A 69

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Fig 2. cont. on next page ....



tifs) are connected by well conserved linkers (5 or 13 amino acids) that allow the independent structural units to contact with the DNA. The importance of these linkers thus appears to derive primarily from a role in positioning of the DNA-binding domains (WOLFE *et al.*, 2000).

Table 1. Cis-acting elements essential for AP2/ERF proteins

| Cis-element  | Plant specie                   | Protein                | Ref.  |
|--|--------------------------------|------------------------|---|
| Drought Responsive element (DRE/CRT)                             | <i>Arabidopsis thaliana</i>    | DREBs<br>CBFs          | Liu et al., 1998<br>Stockinger et al., 1997<br>Gilmour et al., 1998<br>Haake et al., 2002 |
| 5'TACCGACAT3'  | <i>Zea mays</i>                | DBFs                   | Kizis and Pages 2002  |
|  | <i>Oriza sativa</i>            | OsDREBs                | Dubouzet et al., 2003   |
|  | <i>Triticum aestivum</i>       | TaDREB                 | Shen et al., 2003b  |
|  | <i>Brassica napus</i>          | BnCBFs                 | Gao et al., 2002  |
|  | <i>Atriplex hortensis</i>      | AhDREB1                | Shen et al., 2003a  |
|  | <i>Nicotiana tabaccum</i>      | NtTsi1                 | Park et al., 2001   |
| Low Temperature Responsive Element (LTRE)<br>5' (G/a)(C/t)CGAC3' | <i>Hordeum vulgare</i>         | HvCBF1                 | Xue , 2002  |
| Ethylene Responsive Element (ERE or GCC box)                     | <i>Arabidopsis thaliana</i>    | AtERF1-5<br>AtEBP      | Fujimoto et al., 2000<br>Buttner and Singh 1997   |
| 5'TAAGAGCCGCC3'<br>or<br>5'AGCCGCC3'                             | <i>Nicotiana tabaccum</i>      | NtTsi1<br>NtERF1-4     | Park et al., 2001<br>Takagi and shinshi 1995  |
|  | <i>Lycopersicon esculentum</i> | LeERF1-4<br>LePti4/5/6 | Tournier et al., 2003<br>Zhou et al., 1997  |
|  | <i>Glycine max</i>             | GmEREBP1               | Mazarei et al., 2002  |
| JA- and elicitor-responsive element (JERE)<br>5'-AGACCGCC-3'     | <i>Catharanthus roseus</i>     | CrORCA1-2<br>CrORCA3   | Menke et al., 1999<br>Van der Fits, and Memelink 2000                                     |
| Bipartite sequence<br>5'CAACA-(N)n -CACCTG3'                     | <i>Arabidopsis thaliana</i>    | RAVs                   | Kagaya et al., 1999   |
| ANT consensus site<br>5'gCAC(A/G)N(A/T)TcCC(a/g)<br>ANG(c/t) 3'  | <i>Arabidopsis thaliana</i>    | ANT                    | Nole-Wilson and Krizek, 2000  |

**Cis-acting elements essential for AP2/ERF proteins** - A number of cis-elements have been reported to be recognized by the most of AP2/ERF transcription factors (Table1). The dehydration responsive element (DRE), 5'-TACCGACAT-3', plays an important role in regulating gene expression in response to drought and other types of osmotic stress in *Arabidopsis*. The DRE element was first identified in the promoter of the drought-responsive gene *rd29A* (also, known as *cor78* and *Lti78*) from *Arabidopsis* (YAMAGUCHI-SHINOZAKI and SHINOZAKI, 1994). *rd29A* encodes a protein similar to the late embryogenesis abundant (LEA) proteins, which are induced both during the maturation of embryos and by several types of stress in vegetative tissues and probably function as tolerance effectors. The DRE element is essential of the induction of *rd29A* gene expression not only by osmotic stress such as drought and high salinity but also by low temperature stress but not in the response of this gene to ABA (YAMAGUCHI-SHINOZAKI and SHINOZAKI, 1994).

On the other hand, a *cis*-element with a similar sequence to the DRE, the C-repeat (CRT) responsive element 5'-TGGCCGAC-3' (containing the core 5'-CCGAC-3') was identified in the promoter of the cold-inducible gene *cor15a* from *Arabidopsis* and are essential for the low-temperature responsiveness of many cold-regulated (COR) genes, including the *Arabidopsis* *COR15a* gene, the *Brassica napus* *BN115* gene and the wheat gene *WCS120* (BAKER *et al.*, 1994; JIANG *et al.*, 1996; OUELLET *et al.*, 1998). This motif was also described in the promoters of three other cold regulated genes, *kin*, *kin2* and *rab18* (KURKELA and BORGFRANCK, 1992; LANG and PALVA, 1992). Studies of these genes in ABA-deficient and -insensitive mutants showed activation of the genes during drought and cold stress independently of ABA. However, recent evidence indicates that some DRE/C-repeat motifs behave differently (SHINOZAKI and YAMAGUCHI-SHINOZAKI, 1997; THOMASHOW, 1999).

The DRE2 *cis*-element (5'-ACCGAC-3') was identified in the maize *rab17* promoter and involved in an ABA-dependent response. This site includes the typical core motif and was identified by *in vivo* footprinting analysis of embryos and leaves (BUSK *et al.*, 1997). Differences in DRE2 occupancy were observed after both drought treatment and ABA induction, and *in vivo* analyses showed that DRE2 is important for activation of the *rab17* promoter in both situations (BUSK *et al.*, 1997; BUSK and PAGÉS, 1998). Both ZmDBF1 and ZmDBF2 bound to the DRE2 *cis*-element, ZmDBF1 induced an increase in the GUS reporter gene activity driven by DRE2 in maize callus cells (KIZIS and PAGÉS, 2002).

The tobacco ERFs (EREBPs), the AtEBP, AtERF1-5 and the tomato Pti4/5/6 have been shown to bind to the Ethylene responsive element (ERE, 5'-TAAGAGCCGCC-3') called GCC-box or PR-box, existing in the promoters of many pathogenesis related genes (BUTTNER and SINGH, 1997; SOLANO *et al.*, 1998; BROWN *et al.*, 2003). Also, the tomato ERFs (LeERF1-4) demonstrated different binding capacity to GCC-box (TOURNIER *et al.*, 2003).

On the other hand, a number of *cis* elements that respond to elicitors and Jasmonic acid have been identified. The W-boxes [5'-(T)TGAC(C/T)-3'] from the

promoters of *PR-1* and *Chitinase* CH50 genes are the best characterized. The JERE (5'-AGACCGCC-3') a novel JA- and elicitor-responsive element contains GCC-box motif was reported (FUKUDA and SHINSHI, 1994; RUSHTON *et al.*, 1996; MENKE *et al.*, 1999). The ORCA proteins bound in a sequence-specific manner to the JERE cis element (VAN DER FITS and MEMELINK, 2000). While RAV proteins bind specifically to bipartite recognition sequences composed of two unrelated motifs, 5'-CAACA-3' and 5'-CACCTG-3' (KAGAYA *et al.*, 1999).

DNA binding has not yet been described for any proteins of the AP2 subfamily except ANT gene. These proteins are likely to possess DNA binding specificities that are distinct from those of the DREB, ERF and RAV proteins. The consensus sequence 5'-gCAC(A/G)N(A/T)TcCC(a/g)ANG(c/t)-3' is a DNA binding specificity of ANT. ANT binds as a monomer but at high protein concentrations a higher order complex is also observed. The length of the consensus site suggests that both AP2/ERF repeats (R1 and R2) of ANT contact the DNA and neither AP2/ERF repeat by itself is sufficient for binding to this DNA sequence (KRIZEK, 1999; 2003).

#### FUNCTION OF AP2/ERF TRANSCRIPTION FACTORS

The AP2/ERF transcription factors have several members in many plant species of monocots and dicots. AP2/ERF genes are playing important roles in plant development and in the responses of plants to biotic and abiotic stresses. Members of each subfamily show wide diversity of functions. Proteins from AP2 subfamily have important roles in various stages of plant development (JOFUKU *et al.*, 1994; OKAMURO *et al.*, 1997). The DREB and ERF subfamilies contains proteins that bind to defined cis-regulatory sequences described in many pathogenesis-related (*PR*), cold induced (*COR*) and late embryogenesis abundant (*LEA*) genes, and they form part of the regulatory mechanism of expression of these genes in response to biotic and abiotic (FELIX and MEINS, 1987; OHME-TAKAGI and SHINSHI, 1995; BUSK *et al.*, 1997). While, the RAV subfamily proteins are likely to be involved in some biological processes specially evolved in higher plants (KAGAYA *et al.*, 1999).

**Gene function of DREB subfamily** - Several DRE-binding proteins encoding transcription factors have been identified from Arabidopsis and other plants that specifically interact with the DRE/CRT sequence. Using yeast one-hybrid screening technique genes encoding DRE/CRT binding proteins have been cloned. For example DREBs/CBFs from Arabidopsis (STOCKINGER *et al.*, 1997; GILMOUR *et al.*, 1998), ZmDBFs from Maize (KIZIS and PAGÉS, 2002), BnCBFs from *Brassica napus*, HvCBF1 from Barley (XUE, 2002), OsDREBs from Rice (DUBOUZET *et al.*, 2003), AhDREB1 from *Atriplex hortensis* (SHEN *et al.*, 2003a) and TaDREB1 from Wheat (SHEN *et al.*, 2003b).

The transcription factors DREBs/CBFs specifically interact with the dehydration-responsive element/C-repeat (DRE/CRT) cis-acting element, and control the expression of many stress-inducible genes in Arabidopsis (STOCKINGER *et al.*, 1997; GILMOUR *et al.*, 1998). Also, DREBs/CBFs homologous genes have also



been found in wheat, *Atriplex* and other plants (SHEN *et al.*, 2003a; 2003b). These DREB1/CBFs all contained the AP2/ERF DNA binding-domain, which can recognize the CRT/DRE (BAKER *et al.*, 1994; YAMAGUCHI-SHINOZAKI and SHINOZAKI, 1994). Under normal conditions, neither CBF nor COR genes are expressed. However, when treated with cold (4 °C), the expressions of the CBF genes are induced very early, followed by the expression of CBF-regulated target genes (GILMOUR *et al.*, 1998).

BnCBFs were isolated from *Brassica napus* and function as trans-acting factors in low-temperature responses in *Brassica*, controlling the expression of cold-induced genes through an ABA-independent pathway. TaDREB1 gene was isolated from wheat and is induced by low temperature, salinity and drought; and the expression of Wcs120 that contains DRE motifs in its promoter is closely related to the expression of TaDREB1 (SHEN *et al.*, 2003b). They isolated five cDNAs from Rice for DREB homologs: OsDREB1A, OsDREB1B, OsDREB1C, OsDREB1D, and OsDREB2A. Expression of OsDREB1A and OsDREB1B was induced by cold, whereas expression of OsDREB2A was induced by dehydration and high-salt stresses. The OsDREB1A and OsDREB2A proteins specifically bound to DRE and activated the transcription of the GUS reporter gene driven by DRE in rice protoplasts (DUBOUZET *et al.*, 2003). AhDREB1 was isolated from a halophyte *Atriplex hortensis*. The AhDREB1 gene was expressed in roots, stems and leaves of *A. hortensis*. Salinity induced its expression in roots, but not in other organs (SHEN *et al.*, 2003a).

On the other hand, the DREB2A, DREB2B, CBF4 have been isolated from *Arabidopsis* (LIU *et al.*, 1998; HAAKE *et al.*, 2002). DREB2A and DREB2B were identified based on their ability to bind the CRT/DRE element in vitro and in yeast. The DREB2A and DREB2B are induced by drought stress and are able to induce the expression of genes that contain the CRT/DRE cis-acting element. Overexpression of the DREB2 cDNA in transgenic plants only caused weak induction of the downstream genes and did not result in obvious phenotypes (LIU *et al.*, 1998) CBF4 gene expression is up-regulated by drought stress, ABA treatment, but not by low temperature. Overexpression of CBF4 in transgenic *Arabidopsis* plants results in the activation of CRT/DRE-responsive element containing downstream genes that are involved in cold acclimation and drought adaptation (HAAKE *et al.*, 2002).

ZmDBFs (DBF1 and DBF2) were isolated from maize (KIZIS and PAGES, 2002). Analysis of mRNA accumulation profiles showed that ZmDBF1 is induced during maize embryogenesis and after desiccation, NaCl and ABA treatments in plant seedlings, whereas the ZmDBF2 mRNA is not induced. DNA-binding preferences of ZmDBFs were analysed by electrophoretic mobility shift assays, and showed that both ZmDBF1 and ZmDBF2 bound to the wild-type DRE2 element. Transactivation activity using particle bombardment showed that ZmDBF1 functioned as activator of DRE2-dependent transcription of rab17 promoter by ABA, whereas ZmDBF2 overexpression had a repression action down-regulating not only the basal promoter activity, but also the ABA effect. These results show that

ABA plays a role in the regulation of ZmDBFs activity, and suggests the existence of an ABA-dependent pathway for the regulation of genes through the CRT/DRE element (KIZIS and PAGES, 2002).

The CIP353 cDNA, which encodes a novel cold-inducible protein, from cold-stored tubers of potato. The level of CIP353 transcripts began to increase in tubers 2 weeks after storage at 3 degrees C and continued increasing for at least 3 months during storage. It was reported that the CIP353 is a temperature-dependent and slowly responsive cold-inducible gene of potato (MINE *et al.*, 2003).

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## AP2/ERF BILJNI TRANSKRIPCIONI FAKTORI

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### Izvod

Transkripcioni faktori (TFs) imaju značajnu ulogu u ontogenezi (razvoju) biljke kao i odgovora na uslove biotičkog i abiotičkog stresa. Familija transkripcionih faktora AP2/ERF je unikatna kod biljaka a konzervisani AP2/ERF domen veličine oko 60 aminokiselina je karakteristika ove familije transkripcionih faktora. AP2/ERF geni učestvuju u regulaciji procesa ontogeneze (razvoja) biljke i kontroli odgovora biljke na biotičke i abiotičke faktore spoljne sredine koji izazivaju stresne uslove. U radu je dat pregled poznatih osobina i mehanizam aktivnosti AP2/ERF familije transkripcionih faktora.

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