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RESEARCH HIGHLIGHT

A new role for plant R2R3-MYB transcription factors in cell cycle regulation

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MYB proteins are transcription factors present in all eukaryotes, sharing a common DNA-binding domain that consists of one to three imperfect helix-helix-turn-helix repeats of about 50 amino acids, called R1, R2, and R3 respectively [1]. In animals and yeast these proteins represent a small gene family [1]. Animal R1R2R3-MYB proteins have been described for their role in cell cycle regulation mainly at the G1/S, but also at the G2/M transition, as firstly demonstrated in Drosophila [2].

In plants the MYB superfamily constitutes the most abundant group of transcription factors. From an analysis of the complete *Arabidopsis* genome sequence 198 genes in the *MYB* superfamily were identified, among them 126 are *R2R3-MYB*, 5 are *R1R2R3-MYB*, 64 are *MYB*-related and 3 are atypical *MYB* genes [1]. Plant R1R2R3-MYB proteins, whose repeats are more closely related to the repeats present in vertebrate MYB proteins than to the repeats from plant R2R3-MYB proteins, play a role in the regulation of genes involved in the cell cycle G2/M phase, as shown in tobacco and *Arabidopsis* [3, 4]. They bind to mitosis-specific activator (MSA) elements, present in most promoter sequences of genes specifically expressed in the G2/M phase in *Arabidopsis* [5]. Also the MYB-related CDC5-like proteins, characterized in different species (yeast, animal and AtCDC5 in *Arabidopsis*), harboring a MYB domain with two repeats only distantly related to those of the R2R3-type MYB proteins, control the G2/M transition of the cell cycle [6].

Different members of the most highly represented R2R3-MYB subfamily have been characterized for their roles in the regulation of plant-specific processes, such as phenylpropanoid metabolism, determination of specialized cell morphology, and responses to biotic and abiotic stresses [1]. Until the beginning of this year no clear involvement of R2R3-MYB subfamily members in the regulation of cell cycle was reported, although their role in the local control of cell proliferation was suggested by some authors [7 and references therein]. This year two papers reported a role of two members of this *Arabidopsis* subfamily in the regulation of the cell cycle. These are *AtMYB59*, which is involved in root growth [8] and *DUO1* (*AtMYB125*), encoding a male germline-specific protein [9].

Mu *et al.* [8] reported a detailed analysis of *AtMYB59* in *Cell Research*. *AtMYB59* is preferentially expressed in roots and encodes a protein that has transcriptional activation activity. They found that the expression of AtMYB59 transcription factor in transformed yeast cells altered DNA synthesis and/or chromosome separation, affecting, as a consequence, the cell division process. In fact the proliferation of *AtMYB59*-transformed cells was inhibited and the resulting yeast cells were about threefold longer than the control cells and more than 20% of the *AtMYB59*-transformed cells had double or abnormal nuclei. The authors found that also the DNA content in the yeast cells was altered during the cell division and there was a high percentage of aneuploid and apoptotic cells. Cell division in yeast was affected probably due to the inability to form a cell plate between the two daughter cells or due to the interference of the AtMYB59 protein with the activity of the endogenous CDC5, a MYB-related transcription factor involved in cell cycle progression, as previously mentioned.

The authors demonstrated that the *AtMYB59* gene is preferentially expressed during the S and S to G2 phases in an *Arabidopsis* suspension culture. As the *AtMYB59* gene is preferentially expressed in roots, Mu *et al.* investigated the phenotype of this organ in the *myb59-1* knock-out mutant and in *AtMYB59*-overexpressing lines. They showed an opposite phenotype in the primary root length. In the mutant the root was longer than in the wild-type, while in the overexpressing lines the root was shorter. These phenotypes do not depend on differences in root cell structure or size, but on differences in the percentage of cells at each cell cycle phase with the mutant having only 14%

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of cells at metaphase, the overexpressing line 54% and the wild-type 27%.

One of the probable targets of the AtMYB59 transcription factor is the *CYCB1;1* gene coding for a cyclin B, a regulatory subunit of a cyclin dependent kinase that has a critical role in G2/M progression of the cell cycle [10]. In the *AtMYB59*-overexpressing line *CYCB1;1* gene expression was highly up-regulated, but its expression was only slightly reduced in the *myb59*-1 mutant, indicating only a partial role of AtMYB59 in the regulation of this cyclin. The AtMYB59 protein binds to some potential MYB-binding elements in the *CYCB1;1* gene promoter, but not to the MSA element. Conversely the corresponding tobacco MSA element in the *CYCB1;1* promoter is bound by the R1R2R3-MYB NtmybA1 and NtmybA2 factors that act as positive regulators and by NtmybB working as a repressor [3]. AtMYB59 might control the expression of *CYCB1;1* and maybe other G2/M phase-specific genes, through its binding to the elements identified by Mu *et al.* in a cooperative way with one of the R1R2R3-MYB proteins able to bind to the MSA element [4]. Another possibility is that AtMYB59 acts in a partially redundant fasion with another R2R3-MYB not yet characterized, or with the putative At2g03470 MYB transcription factor, identified as a member of a complex binding to promoter elements of the *CYCB1;1* gene, in combination with transcription factors belonging to other families, such as the HYP protein, which contains a leucine zipper and MYC-type dimerization domains [10].

In another recent paper Brownfield *et al*. showed that the *Arabidopsis* male germline-specific *DUO1* gene, is required for correct male germline differentiation and for male germline cell division, controlling the expression of the G2/M regulator *CYCB1;1* [9]. Expression of the cyclin B as a chimeric gene under the control of the *DUO1* promoter can partially rescue defective germ cell division in the *duo1* mutant.

Therefore the recent papers on *AtMYB59* function in the root [8] and *DUO1* role in the male germline [9] and the hypothesis of involvement of other R2R3MYB members in the local control of cell proliferation [7 and references therein] highlight that R2R3-MYB transcription factors also have a role in the regulation of the cell cycle. Probably in the near future a role in this process will be elucidated for other members of this large subfamily. With the knowledge obtained so far we can speculate that plants have evolved diverse R2R3-MYB proteins to regulate cell cycle progression in an organ-, tissue- or cell-specific way.

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