Commentary

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Novel Aspects of Cell Division Cycle and Apoptosis Regulator 1 (*CDCAR1*) Protein in *Morus notabilis:* An *In silico* Approach

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Abstract

CDCAR1 is a deleted in breast cancer 1 (DBC1) domain containing protein and their molecular roles in the animal system are well characterized. So far study on *CDCAR1* protein not available in plant system. SMART domain based phylogenetic study clearly indicated that the *CDCAR1* protein widely distributed throughout the plant Kingdome. Intron-less *CDCAR1* gene encoded protein comprises five conserved domain and huge intrinsic disorder. Functional annotation of *cis*-regulatory elements (CREs) revealed that a wide range of potential transcription factor binding sites (TFBSs) are present in *CDCAR1* gene promoter. Beside that potential miRNA targets those control post-transcriptional regulation also identified in the present study. Our gene ontogeny (GO) analysis revealed that *CDCAR1* have dynamics role in cellular and metabolic processes. In this study we first report the regulation, functional and structural property of *CDCAR1* transcript and protein which will may help to assist crop improvement by manipulating *CDCAR1*.

Keywords: Phylogeny; *In silico*; *Cis*-regulatory elements; miRNA; Gene ontogeny (GO); *Morus notabilis*

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Introduction

Data-mining bioinformatics and *CDCAR1*

In animal system, the significant role of *CDCAR1* in programmed cell death and other cellular processes have been reported [1]. In plant system, we are first emphasized the characterization, regulation and function of *CDCAR1* in plant using various data-mining bioinformatics. Using the NCBI protein database [2,3] we harvest ninety nine *CDCAR1* protein sequences (homologues to *Morus notabilis CDCAR1* amino acid sequence, NCBI accession number: EXC20006.1) and construct a phylogenetic tree **(Figure 1A).** The *CDCAR1* proteins grouped in to ten clades, from which none of them are characterized previously. Group I family members are comprised Solanaceeae and other putative *CDCAR1* protein. Group 2 having *Helienthus* and *Lactuca* putative and *CDCAR1* like protein. Group 3 comprises Bitavulgaris and *Chenodopodium* putative *CDCAR1* proteins. MeMe Suite tool [4] is implemented to predict the conserved motif *CDCAR1* family proteins. Analyzed data indicates five conserved sites are present across the protein sequence length **(Figure 1B).** Out of five motifs, three are located at the DBC1 domain and the remaining two are situated at the C-terminal site of *CDCAR1* protein. Besides that to understand the folding nature or disorder state of the *CDCAR1* protein, here we have predict the folding nature using the FoldIndex© online tool [5]. The findings of this analysis clearly elucidated that *Morus notabilis CDCAR1* protein has most of the regions that are intrinsically disorder/unfold. Intrinsically disordered regions have a significant contribution to a wide range of cellular processes via molecular interaction [6]. Thus, the *CDCAR1* protein may have a potential fundamental role in the plant system **(Figure 1C).**

Discussion

To understand the transcriptional regulation and promoter structure we have harvested 1kb upstream promoter sequences from the NCBI database. Plant Care [7] database has been used to characterize the *CDCAR1* gene promoter. *Cis*-regulatory elements (CREs) annotation revealed several potential transcription factors such as AP2, C2H2, CAMTA, Dof, GRAS, ERF, EIL, HD-ZIP, HSF, MIKC_MADS and MYB binding sites. Those transcription factors are controlled by various environmental factors (light, salt, heat, drought, wounding), developmental factors (flowering, gravitropism), and cellular metabolites (H_2O_2, auxin, ethylene, gibberellin, cytokinin, salicylic acid, jasmonic acid, cadmium ion, etc.).

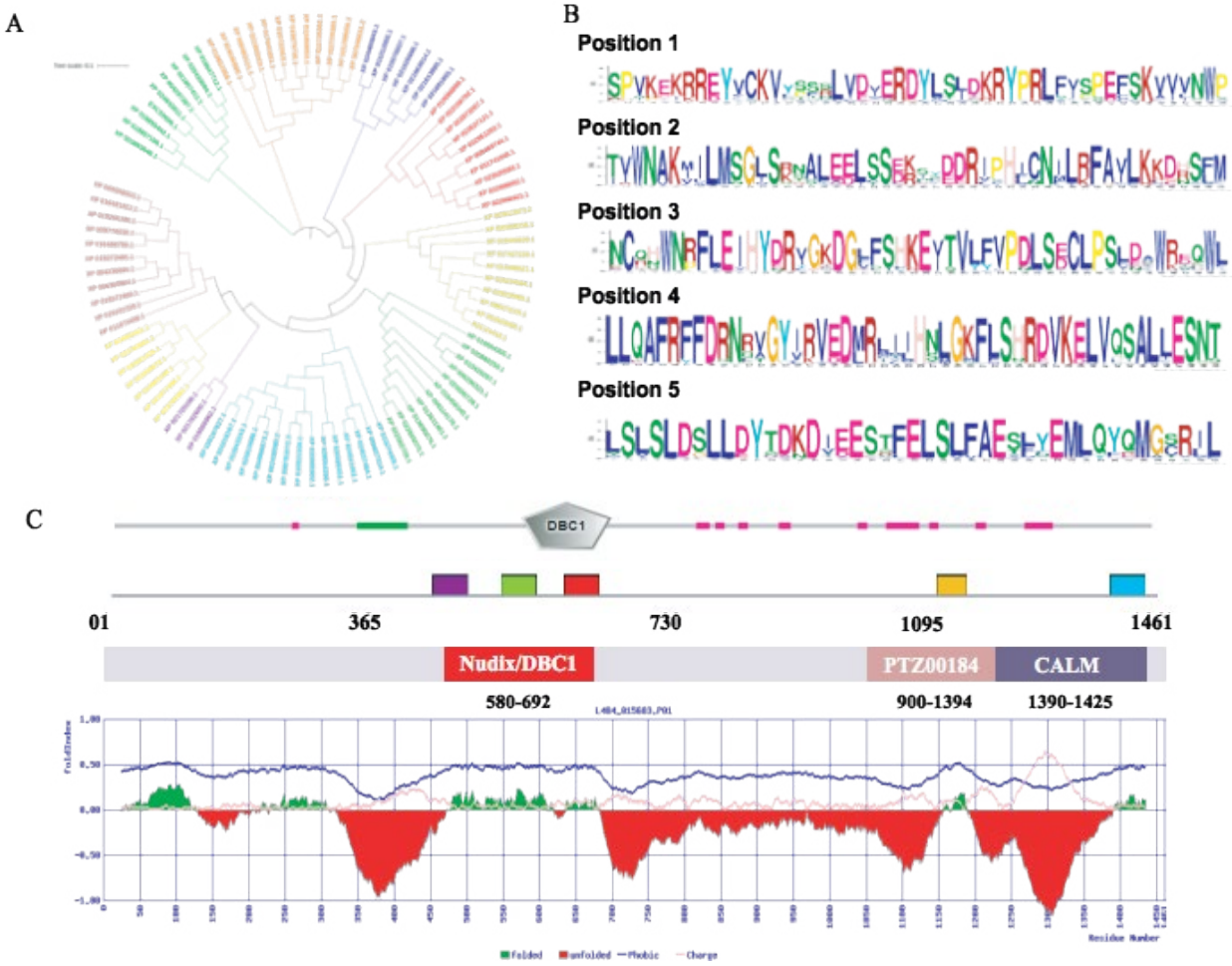

Figure 1 (A) Phylogenetic tree of ninety nine *CDCAR1* protein sequence using SMART [10] and iTOL [3] server. (B) Identified conserved motif s of *CDCAR1* protein family. (C) Domain structure, predicted motif of complete *Morus notabilis CDCAR1* protein along with predicted fold/unfold property.

Furthermore, all putative microRNAs that target *M. notabilis CDCAR1* transcripts are identified, using psRNATarget server [8] (expectation value 4). Identified putative miRNAs are gra-miR8737, gma-miR9752, aly-miR156h-3p, ath-miR836, bdi-miR7735-5p, cca-miR6108e-3p, gma-miR5041-5p, gma-miR9752, gra-miR3267, rgl-miR5577, rgl-miR7800, stu-miR5303e, stu-miR5303f, stu-miR8022 that regulates post-transcription of the *CDCAR1* by translation and cleavage processes. Thus, both CREs and miRNA have potential impacts on regulation at the transcription level.

Gene ontogeny (GO) data have collected from MorusDB [9] to understand the biological and molecular function of the *CDCAR1* protein. Analyzed data revealed that *CDCAR1* involved in several developments and stress-related fundamental processes such as programmed cell death, single-organism process, single-organism cellular process, gene expression, heterocycle metabolic process, nitrogen compound metabolic process, cellular macromolecule metabolic process, organic cyclic compound metabolic process, metabolic process, RNA metabolic process, cellular nitrogen compound metabolic process, primary metabolic process, cellular aromatic compound metabolic process, nucleic acid metabolic process, RNA processing, regulation of biological process. Hence, *CDCAR1* plays a crucial role in cellular, molecular, and biological processes according to *insilico* GO analysis [10].

Conclusion

In the present study, we have emphasized on the phylogenetic relationship, transcript regulation, structural integrity, and functional aspects of *M. notabilis CDCAR1* protein using a good-quality data harvested from publically available databases. Moreover, our present *in silico* investigation briefly represents the novelty of *CDCAR1* protein, which will provide a basic platform for future advanced biotechnological research for crop improvement.

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