

A note on the nomenclatural representation of plant transcription factors, and deviations thereof

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Abstract

Plant transcription factors (TFs) are integral proteins associated with gene transcription. That ability arises after TFs bind to specific DNA sequences, such as promoters, responding positively or negatively to a multitude of endogenous and exogenous factors or stressors. For this reason, in plants, the vast majority of TFs are associated with growth, development, and responses to biotic and abiotic stresses. As is commonly known, the genes coding for TFs are written in uppercase italics, whereas the resulting proteins are written in lowercase, such as *OsWRKY28* and *OsWRKY28*, respectively for a member of the WRKY TF family in rice (*Oryza sativa* L.). However, despite the existence of some conventions for the nomenclature of TFs, some deviation from these norms has been observed in the literature. Several cases are highlighted, primarily related to NAC TFs. These cases emphasize the need for stricter quality control of literature pertaining to the nomenclature of plant TFs.

Keywords: ABA; abiotic stress; bHLH; growth and development; NAC; PubMed; WRKY

Introduction

Plant transcription factors

The function of transcription factors (TFs), which are proteins, is to regulate the transcription of genes (i.e., DNA → mRNA), for example stress-responsive genes (Hrmova and Hussain, 2021), by binding to specific DNA sequences or *cis*-regulatory elements (CREs), such as the promoter (Lai et al., 2020). Differences in binding affinities, the recognition of CREs, and specific genetic alterations, i.e., the complexity of the gene regulatory network, resulted in evolutionary differences, not only between lower plants such as bryophytes (e.g., mosses), and higher plants such as angiosperms, but also between individual species within each of these larger groups (Lai et al., 2020; Romani and Moreno, 2021). Some TFs are common among lower and higher plants, such as the TFs that respond to light signals, PHYTOCHROME INTERACTING FACTOR (PIFs), which form part of the basic helix-loop-helix (bHLH) family of TFs, while other TFs might be more complex in angiosperms, such as the MIKC-type MADS TFs, relative to MADS type I TFs in charophytes or type II TFs in gymnosperms, although some MIKC-type MADS TFs, such as LEAFY (LFY), are present across all three phyla (Lai et al., 2020). To induce a growth-, development- or stress-related response, TFs are integrated into gene regulatory networks, leading to the activation of TFs, depending on the stimulus or signal (Barco and Clay, 2020). Thus, TFs themselves are subject to transcriptional and post-transcriptional regulation (Ng et al., 2018). One common post-transcriptional regulatory process is SUMOylation, in which small ubiquitin-like modifier (SUMO) can influence the association of a TF with chromatin, DNA-binding activity, and even the abundance and localization of TFs (Roy and Sadanandom, 2021).

Broadly, in response to an abiotic stress such as heat, excessive cold, drought, or high salt concentration, complex stress signal pathways induce the phosphorylation or dephosphorylation of TFs, such as the abscisic acid (ABA) and jasmonic acid (JA) signal pathways (Yoon et al., 2020), several of which may act alone, or in concert with other TFs, to exert a response to that stress. If that response involves a developmental event

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that impacts growth, then other growth- and development-related TFs may be activated by another signal cascade, such as somatic embryogenesis (Salaün et al., 2021), until equilibrium is achieved. In the case of excessive stress, a radical response such as plant cell death (PCD) may arise when cellular homeostasis is disrupted due to the accumulation of incorrectly folded or unfolded proteins in the endoplasmic reticulum (ER), and the plant's inability to activate the unfolded protein response (UPR) (Yu et al., 2022). Whereas ER stress can be reversed by proximal UPR, irreversible ER stress activates terminal UPR that then leads to PCD (Yang et al., 2021).

Understandably, different tissues within a plant can also represent distinct developmental events, so the associated TFs that are expressed in each of these tissues, or developmental stages, may be different, as exemplified by cotton (*Gossypium* spp.) (Zhang et al., 2022). Some of those responses might overlap or be seemingly contradictory (Hartmann et al., 2022). Even the balance between life and death, at a cellular scale, and then amplified at a larger (tissue or organ) scale, involves TFs, such as the bZIP28 TF that is involved in the ER-stress-related response in *Arabidopsis thaliana* L. (Yang et al., 2021). For these reasons, it is not uncommon to find TFs common among growth-, development-, and stress-related events, such as the WRKY TFs (Wani et al., 2021), bHLH TFs (Niu and Fu, 2022), or MYB TFs (Wang et al., 2021; Xiao et al., 2021). Consequently, it is possible to increasingly find studies that assess the transcriptional regulation of plant growth-, development-, and stress-related events, in stressed and unstressed environments, and the role that TFs play in those processes.

The objective of this report is not to focus on genetic regulatory aspects of TFs in plants, because those mechanisms are extremely complex and already very well and widely explored in the literature (Blanc-Mathieu et al., 2024; Chow et al., 2024), but rather on a more specific topic that is not frequently discussed, but that serves as a basis for all plant-related TF researchers and studies, specifically the nomenclature and erroneous naming or representation of TFs.

Established convention for plant transcription factors, and deviations therefrom

As is commonly known, the abbreviated form of the names of genes are, in biomedical writing, represented in italics, whereas the protein name is written in standard font, i.e., without italics. There is a convention for naming TFs in plants: except for the genus and species epithet, the TF name is in upper-case letters that are not italicized. In grasses, for example, the TF ZmMYB3 is used to name the MYB family gene number 3 of maize (*Zea mays* L.) (Gray et al. 2009). However, the gene coding for the TF is written in italics, according to the initial rule stated above. Consequently, the gene coding for the rice (*Oryza sativa* L.) WRKY TF family would be written as *OsWRKY*, with the specific protein or gene number appearing at the end, for example, *OsWRKY28* and *OsWRKY28* for the protein and gene, respectively (Wang et al., 2018).

Brian et al. (2021) provided a useful summary of the

methodology that they employed to name new TFs that were discovered after mining the kiwifruit (*Actinidia chinensis* Planch.) genome. They identified 2839 TFs, accounting for about 8.6% of the kiwifruit genome. Following phylogenetic analysis, they discovered many TFs that had already been previously identified and named, and for these, the published names were used. Unknown TFs with no names, except for auxin response factor (ARF) genes, were named based on their descending rank on a phylogenetic tree. The logic to explain their decision was indicated as follows: “This naming method allows genes within subclades to have numbers which are close to each other” (p. 2). In the case of ARF genes, kiwifruit homologues were named based on the closest known *A. thaliana* and tomato (*Solanum lycopersicum* L.) TFs (Brian et al., 2021). A similar approach was employed by Karppinen et al. (2021) for bilberry (*Vaccinium myrtillus* L.) in which TFs related to anthocyanin biosynthesis, and in some cases the genes encoding previously named TFs, were renamed, such as *VmMYBC2.1* to replace *VmMYB1* and *VmMYBPA1.1* to replace *VmMYB2*. Curiously, Karppinen et al. (2021) note that bilberry MYBs were named using the style for grapevine (*Vitis vinifera* L.), to reflect “their proposed functions” (p. 1355). However, Gong et al. (2019) relied on the *A. thaliana* genome to name Chinese white pear (*Pyrus bretschneideri* Rehd.) no apical meristem (NAM), Arabidopsis transcription activation factor (ATAF), and cup-shaped cotyledon (CUC) (NAC) TF-coding genes, suggesting that both closely- and distantly-related plants can serve for nomenclatural purposes, and that the decision lies with the authors, rather than based on a set of established criteria. This nomenclatural flexibility may be one potential source of variation that is noted later on, or that may result in the introduction of errors into plant TF literature related to nomenclature.

The assignment of TFs to new families claims to follow a set of family assignment rules, as is explained in the PlantRegMap plant TF database (Tian et al., 2020). Since these can be complex, readers are directed to the PlantRegMap version 5.0 website for specific details (PlantRegMap, 2024).

Are there any exceptions to the rule?

Despite the conventions stated above, some exceptions can be found, such as the Ruby and Noemi TFs, which are MYB and bHLH TFs, respectively (Allan, 2019; Butelli et al., 2019). In other cases, faced with the lack of clear advice or protocol, despite existing protocols, authors are left to their own devices as to how they should name TFs. For example, referring to the APETALA2/ETHYLENE RESPONSIVE FACTOR (AP2/ERF) TFs of *Saccharum spontaneum* L., Li et al. (2020) stated that “[b]ecause no reliable naming method was defined in previous research on the AP2/ERF family, our naming convention was based on the grouping of 218 sequences and their chromosomal positions”, assigning, as one set of examples, the names SsERF1 to SsERF101 to the 101 ERF subfamily members of the ERF TF family. Jan et al. (2019), who noted that no strict convention for the nomenclature of TFs existed prior to the Gray et al. (2009)

paper, indicated that the number following the DNA-binding domain family name (e.g., WRKY) should indicate the order of discovery, presumably in the literature. This seems to be the case for new discoveries such as the NIGT1/HRS1/HHO TF family in *A. thaliana* and rice, where they are associated with nitrogen and phosphorous use, growth, development and abiotic stress (Li et al., 2021).

Challenges and inconclusive facets of TF nomenclature

One problem of not assigning names to newly discovered TFs, such as through transcriptomic analyses, is that very long gene or protein names may appear in published papers. Moreover, the convention above does not indicate what percentage homology with known TFs in other plant species is needed before a new name can be assigned with certainty. Apparent deviations from stated nomenclatural protocols (e.g., Butelli et al., 2019), or personal decisions that may reveal some bias in the nomenclatural decision (e.g., Karppinen et al., 2021), suggest that while some broad guidelines are currently in place, they are not being effectively monitored, or implemented prior to the publication of a study. One possible reason for this is wide variation in editorial and peer review-based quality control between journals and publishers.

How are conflicting names resolved, such as in established

indexes or in the literature? Is the informal replacement of a gene name in a scientific paper, as was done by Karppinen et al. (2021), standard practice, or is an erratum needed for the original publication to alert readers that the names of genes, or TFs, have changed? What does a researcher do if two names exist for the same TF in the same plant species, and are there any such cases? What if two plant species have the same first letter of the genus and species, such as *Pinus sylvestris* and *Pyrus serrulata*, how is nomenclature resolved, and which plant takes priority? This latter issue is important as more and more TFs get discovered across a wider spectrum of plant species. The author was unable to glean a response to these questions from the literature, but these are issues that need to be formally resolved.

Journal formatting and indexing: Impact on accuracy of transcription factor names, with a focus on italicization

In some biomedical databases, such as PubMed, the metadata of a scientific paper might not be accurately or precisely represented, and even the indicated “how to cite” text might also carry errors (Teixeira da Silva, 2023). These errors, if not carefully screened or verified by readers, may translate into errors in their own papers, and by association, such errors could be carried forward into other papers that cite their paper.

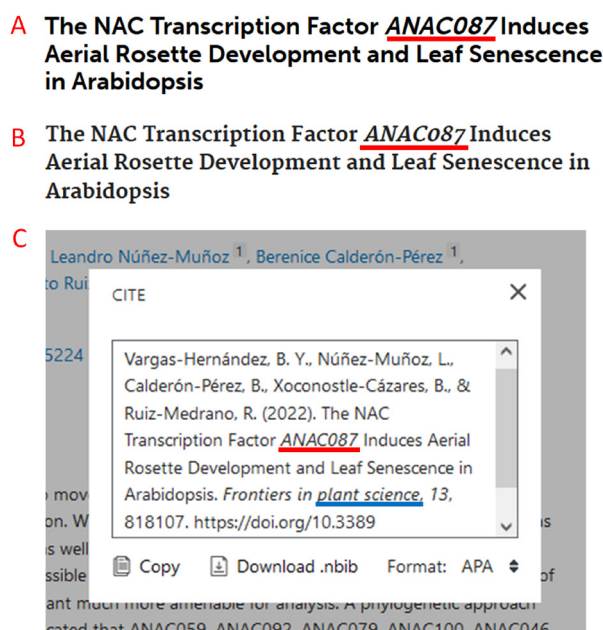


Figure 1. The depiction of type A errors (see text for explanation) in the metadata (title or abstract) of a PubMed-indexed paper related to NAC transcription factors (TFs) in pumpkin (*Cucurbita maxima* Duchesne) (Vargas-Hernández et al., 2022). (A) Error in title (TF written in italics, underlined in red) at original website. (B) The same error in title (underlined in red) at PubMed. (C) The same error in title (underlined in red) in the “cite” function at PubMed (APA style shown); note also an error in the journal’s name (lack of capitalization of the first letters in both words, underlined in blue). Sources of screenshots: (A) <https://www.frontiersin.org/articles/10.3389/fpls.2022.818107/full>; (B, C) <https://pubmed.ncbi.nlm.nih.gov/35283930/>. Dates of screenshots: 10 June 2022 (validated 1 July 2024). Screenshots of any potentially proprietary material, such as the PubMed or Frontiers website, under the fair-use agreement for academic and educational use.

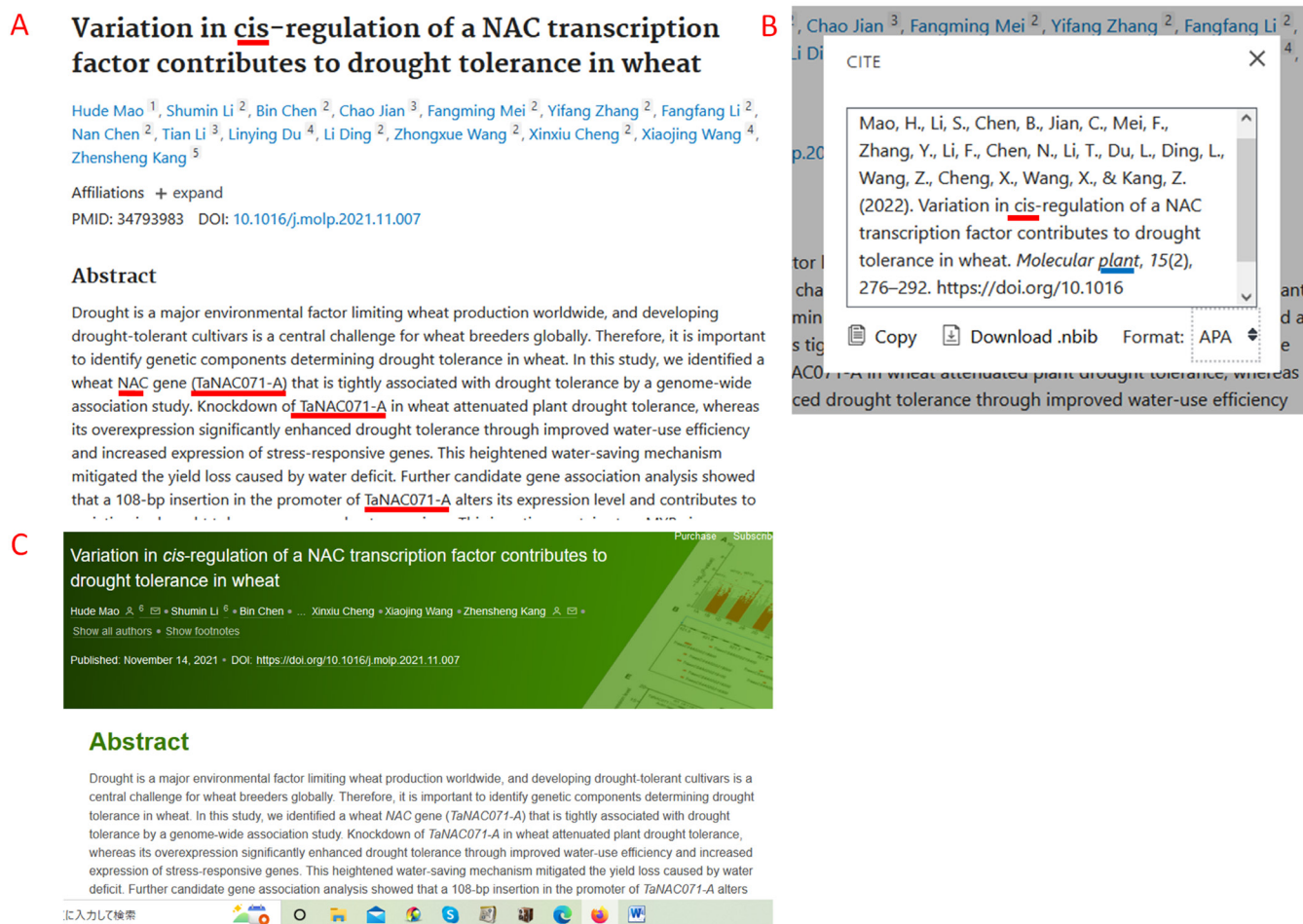


Figure 2. The depiction of type B errors (see text for explanation) in the metadata (title and/or abstract) of a PubMed-indexed paper related to NAC transcription factors (TFs) in wheat (*Triticum aestivum* L.) (Mao et al., 2022). (A) Error in title as well as additional errors in the abstract (lack of italics, underlined in red) at PubMed. (B) The same error in title (underlined in red) at in the “cite” function at PubMed (APA style shown); note also an error in the journal’s name (lack of capitalization of the first letter, underlined in blue). (C) These errors do not exist at the original website. Sources of screenshots: (A, B) <https://pubmed.ncbi.nlm.nih.gov/34793983/>; (C) [https://www.cell.com/molecular-plant/fulltext/S1674-2052\(21\)00438-X](https://www.cell.com/molecular-plant/fulltext/S1674-2052(21)00438-X). Dates of screenshots: 10 June 2022 (validated 1 July 2024). Screenshots of any potentially proprietary material, such as the PubMed or Cell website, under the fair-use agreement for academic and educational use.

Using NAC TFs as the basis to exemplify this issue, the term “plants NAC” was searched (20–25 July 2024) in PubMed, and the results were limited to 2022 (PubMed, 2024). The first 50 of the 348 results for 2022 were screened to identify cases where errors might exist, but no attempt was made to quantify the errors, as such an exercise would require an in-depth bibliometric analysis and complex textual analysis. Essentially, the use of italics to represent TFs in the title of papers served as the primary screening method, and any other errors that were identified, as a by-product of that search, or coincidentally, were also noted, if such information was deemed as useful. Two types of errors were detected. In type A, the error exists in the original paper, and consequently, in the database (here, PubMed). In type B, there are no errors in the original publication (paper and publisher’s website), but an error exists on the database

(PubMed, in this case). The positive control would be where both the original publication, as well as the PubMed metadata, specifically the use of italics and capitalization in TF and/or gene/protein nomenclature, are both accurate and correct, such as Hu et al. (2022). Even so, in that particular case, the accuracy of the cultural and linguistic portrayal of the Chinese authors’ names at/by PubMed is questioned (Teixeira da Silva, 2020). An example of a type A error is in a paper about NAC TF-encoding genes identified in pumpkin (*Cucurbita maxima* Duchesne) (Vargas-Hernández et al., 2022). In this case, referring exclusively to title and abstract metadata, italics has been used to represent the TF, rather than the TF-encoding gene. In this case, the error is evident in the HTML text of the original publication (Fig. 1A) and on PubMed (Fig. 1B), as well as in the PubMed “Cite” function (Fig. 1C). For this reason,

the error has been represented with a “[sic]” in the reference list of this paper, to alert readers that a representation error exists. Another example of a type A error is Xu et al. (2022), on the NAC genes induced by nitrate and the impact on lateral root formation in *A. thaliana*, in which the TF (protein) was represented in italics in the original, as well as in PubMed. A figure is not presented for this case. Curiously, in this case, the citation is correct (no italics for the NAC TF, NAC056). In this latter example, some other errors are only specific to PubMed, such as the lack of italics for a gene name (*NIA1*) or the absence of sub- and superscript, which are correctly represented in the original paper, so there is some overlap with type B error, i.e., Xu et al. (2022) represents a hybrid type A/B error.

An example of a type B error is Mao et al. (2022), which discusses the NAC TFs in wheat (*Triticum aestivum* L.). In this case, again referring exclusively to title and abstract metadata, PubMed does not recognize the need for (or importance of) italics, as exists for the Latin binomial scientific representation of plant names (Teixeira da Silva, 2016a), such as for *cis* or gene names, such as *TaNAC071-A* (Fig. 2A), an error that is also present in the “Cite” metadata (Fig. 2B), but that is not present on the original publisher’s page (Fig. 2C). Another, more egregious example of a type B error is Ma et al. (2022), in which words requiring italics, such as gene names or the Latin botanical name of the subject plant, *Camellia sinensis*, are misrepresented in the title, abstract, and citation metadata. Here, too, a figure is not presented for this case.

Using the titles of papers exclusively (i.e., even if errors in the abstracts were considered, they were not listed here), other cases of type A and B errors i.e., the use of italics for a NAC TR on both the original journal website and on PubMed, were discovered for *Aegilops tauschii* (Wang M et al., 2022), *Glycine max* (Yang et al., 2022), *Lilium pumilum* (Wang Y et al., 2022), and *Tamarix hispida* (Mijiti et al., 2022). In contrast, control cases, i.e., where the NAC TF was correctly represented in the paper’s title in plain font and/or where the gene encoding the TF is represented in italics, in both the original journal website and on PubMed, include: *A. thaliana* (Ailizati et al., 2022; Alshareef et al., 2022; Peng et al., 2022; Tao et al., 2022), *Brassica rapa* var. *parachinensis* (Li et al., 2022), *Camellia sinensis* (Zhang X et al., 2022), *Fragaria vesca* (Dang et al., 2022), *Haloxylon ammodendron* (Liu et al., 2022), *Lolium perenne* (Yu G et al., 2022), *Nicotiana tabacum* (Li et al., 2022), *Phalaenopsis aphrodite* (Valoroso et al., 2022), and *Tulipa × gesneriana* (Meng et al., 2022),

Young researchers with little or no experience with TFs, or even unsuspecting seasoned researchers with ample experience with TFs may unwittingly adopt the erroneous citation format, even if they have read the original paper, trusting the accuracy of PubMed metadata blindly, but in doing so, carrying forward the error(s) into the downstream literature. Even if PubMed attaches a disclaimer to every entry, that merely relieves them of direct responsibility for the accuracy of information on that database, but should not be the responsible way to address erroneous indexed literature (Teixeira da Silva et al., 2024).

In such a situation, through no fault of their own, authors’ literature may be erroneously cited in the literature.

Conclusion and Limitations

There is a risk of carrying citation-related errors that exist in PubMed into the wider plant TF literature, especially from the “how to cite” metadata. Where citations of erroneous metadata occurs, there is a risk of propagating those errors into downstream literature (Teixeira da Silva, 2016b). Despite the existence of such errors, as evidenced in Fig. 1 and 2 of this paper, such errors are rarely corrected, suggesting that the current corrective measures for scientific literature are insufficiently robust to accommodate minor errors (Teixeira da Silva, 2022), one possibly reason being the trouble associated with making such corrections each time they are made. To address this limitation, a dual-DOI-based solution has been proposed (Teixeira da Silva and Nazarovets, 2022). Finally, the cases that are noted in this paper are illustrative examples, and an in-depth bibliometric analysis would be needed to identify other nomenclatural errors in plant TFs, and more widely in TFs in other organisms. It is very important to stress that the disclosure of errors in any papers highlighted in this paper (e.g., Fig. 1, 2) is not done in any way to discredit the authors or their work, and that even with the existence of such errors, their scientific value is not being questioned. The main purpose of this exercise is to raise awareness of three issues (1, inconsistent nomenclature of plant TFs, especially newly discovered ones, despite the existence of some conventions; 2, the misrepresentation of TFs, or the genes encoding them, associated with the use, or not, of italics; 3, the existence of citation-related errors in PubMed), and stoke debate. Hopefully, with such debate, the quality of indexed metadata at PubMed would improve, thereby benefitting the authors and any researcher citing currently erroneous bibliometric data. Evidently, there are a multitude of databases or platforms where bibliometric metadata, as is used in citations, is indexed, such as Web of Science, Scopus, or Google Scholar, so it would be interesting for those with access to some of the proprietary scientific databases to appreciate whether the errors detected in this paper on PubMed are also present in other databases. In addition, only a small sample of the results listed at PubMed for “plants NAC”, limited to the first 50 of the 348 results screened in 2022, are represented. A detailed analysis of the other results to confirm how widely the issue raised in this paper exists, is needed. Finally, the plant TF database noted above appears to be privately managed, and one possible reason why some researchers of plant TFs might not know clearly how to name their TFs, or about the importance of italics, might be due to their lack of knowledge of this database. In this case, a powerful and popular database like PubMed could instill a dedicated website that offers guidance, especially for literature that is indexed in it, guiding not only authors and readers, but also editors of journals and publishers, allowing them to hyperlink such guidance into their journals’ instructions for

authors. Such a dedicated website could be established after consultation with a team of leading scientists who are highly knowledgeable in research pertaining to plant TFs, so that the guidance is accurate.

Author Contributions

The author contributed to the conceptualization, literature exploration, discussion, writing, reviews and editing.

Conflicts of interest

The author declares no conflicts of interest of relevance to this topic.

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