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Stress2TF: a manually curated database of TF regulation in plant response to stress

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ABSTRACT

Considerable studies demonstrate that plant transcription factors (TFs) play key regulatory roles in abiotic/biotic stress conditions, such as drought and pathogen attack. However, there is no effort dedicated to curate experimentally validated stress-TF regulatory relationships from these individual reports into a central database, which put an obstacle in the exploration of stress-TF regulations in plants. To address this issue, we presented a literature-curated database 'Stress2TF' that currently documented 1533 regulatory relationships between 71 abiotic/biotic stresses and 558 TFs in 47 plant species. Each entry in Stress2TF contains detailed information about a stress-TF relationship such as plant name, stress name, TF and brief description of stress-TF relationship. Stress2TF provided a user-friendly interface for entry browse, search and download. In addition, a submission page and several useful tools (e.g., BLAST, network visualization) were integrated. Stress2TF may be a valuable resource for the research of stress-TF regulatory mechanisms in plants. Stress2TF is available at http://csgenomics.ahau.edu.cn/Stress2TF.

1. Background

During the entire life circle, plants are constantly being exposed to abiotic and biotic stresses such as drought, high salinity, changing light conditions and pathogen attack (Yang et al., 2011; Long et al., 2012; Peng et al., 2012; Wang et al., 2012; Cai et al., 2014; Zhao et al., 2014; Zhang et al., 2016). These stress factors impose adverse effects on plant growth and significantly limit the productivity of crop plants (Shrivastava and Kumar, 2015). Over the long periods of evolution, the sessile lifestyle of plants has driven the adaptive stress responsive mechanisms at physiological, biochemical, and molecular levels to enable them to survive under adverse environmental conditions (Zhu, 2002; Munns and Tester, 2008; Deshmukh, 2014).

Transcription factors (TFs) are proteins (trans-acting factors) that control gene expression levels by binding to specific DNA sequences (cis-acting elements) in the promoter region of target genes, thereby enhancing or repressing their transcriptional rates (Kidokoro et al., 2015). In plant genomes, approximately 7% of the coding sequences are assigned to TFs (Ambawat et al., 2013). The identification and functional characterization of TFs is critical for the reconstruction of transcriptional regulatory networks that govern major cellular pathways in the response to abiotic and biotic stimuli (Umezawa et al., 2010; Huang et al., 2015). Therefore, genetic engineering of one or a few of these TFs may be sufficient to enhance stress tolerance in plants, making these TFs attractive targets for engineering (Golldack et al., 2011).

To date, several plant TF-related databases have been released in the public, including LegumeTFDB (Mochida et al., 2010), PlnTFDB (Pérezrodríguez et al., 2010), PlantTFDB (Jin et al., 2014), STIFDB (Shameer et al., 2009) and RiceSRTFDB (Priya and Jain, 2013). LegumeTFDB is a TF repertory of three legume species: *Glycine max*, *Lotus japonicus* and *Medicago truncatula*. PlnTFDB is an integrative plant TF database of only several typical species. Instead, PlantTFDB is a plant TF database which covering 83 plant species in the third version. STIFDB is the first stress-TF interaction database which focuses on TF regulation in plant stress conditions other than the TF-centered design in the first three databases. In the latest version STIFDB2 (Naika et al., 2013), three species (*Arabidopsis thaliana*, *Oryza sativa* subsp. *japonica*

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*Abbreviation list:*TFs, transcription factors

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and *Oryza sativa* subsp. *indica*) were included. RiceSRTFDB is a rice-specific database regarding stress-TF interactions. Both STIFDB and RiceSRTFDB use a computational pipeline to predict plant stress-TF regulatory relationships from public microarray data. There is a vast amount of scientific literature that documents experimentally validated stress-TF regulations in a wide range of plant species. Hence, collecting and integrating the information in these articles into a single database can help conceal the connections and differences of stress-TF association in different plant species and further the elucidation of stress-TF regulatory mechanisms.

In view of the above concerns, we developed a comprehensive repository named a manually curated database of TF regulation in plant response to stress (Stress2TF), by compiling data from widely scattered published articles. Stress2TF's interface allows users to retrieve stress-TF regulatory entries by keyword search using plant species, TF and abiotic/biotic stress. In addition, we presented a submission interface and several useful applications, such as BLAST and network visualization and analysis to facilitate the database use. We believe that Stress2TF can serve as a valuable bioinformatics platform in plant stress physiology research community.

2. Results

2.1. Data content

As a comprehensive database of regulatory relationships between abiotic/biotic stresses and TFs in plants, Stress2TF represents the critical regulatory cascades of the two biological entities of stresses and TFs in plant stress response. Detailed information was collected for both stress and TFs, such as plant name, stress name, stress type, TF, TF family, Entrez TF ID, TF expression pattern, detecting method for TF expression, target gene(s) of TF, brief description of stress-TF relationship and the corresponding reference. All the data were compiled from over 200 research articles, and the current release of Stress2TF documented 1533 entries between 71 abiotic/biotic stresses and 558 TFs in 47 plant species (Fig. 1, SI Table 1). The vast majority (95.4%) of the Stress2TF entries were related to regulations between TFs and abiotic stresses. Stress2TF covered a total of 16 TF families among which NAC, HSF and WRKY families tend to be up-regulated in response to Temperature stress, Hormone and Drought, waterlogging conditions, respectively, in model species *Arabidopsis thaliana* and *Oryza sativa* (SI Tables 2 and 3). In total, several typical stress-related TF families such as HSF, NAC and WRKY accounting for the 59.6% of the database entries.

2.2. Database usage and web interface

Stress2TF (http://csgenomics.ahau.edu.cn/Stress2TF) provides a simple and user friendly interactive web interface that allows for the literature-curated stress-TF regulatory relationships to be clearly browsed, searched, queried using BLAST, downloaded, and updated. The corresponding functional sections are on the site which can be accessed from the menu bar at the top of the homepage, and this page also provides general information about the database, such as stress2TF introduction, citation and entry statistics (see homepage page).

Various browsing functions are organized based on the logical categories as plant species, TF family, abiotic stress and biotic stress, which can be further expanded to their subcategories by clicking the left plus signs (+) (see browse page). For example, the category "TF family" can be expanded as AP2/EREBP, bZIP, ERF, WRKY, MYB and so on. In different subcategories, arabic numerals in the right brackets are placed to indicate the numbers of the related entries documented in Stress2TF.

In the search page, four search fields are present that may be used

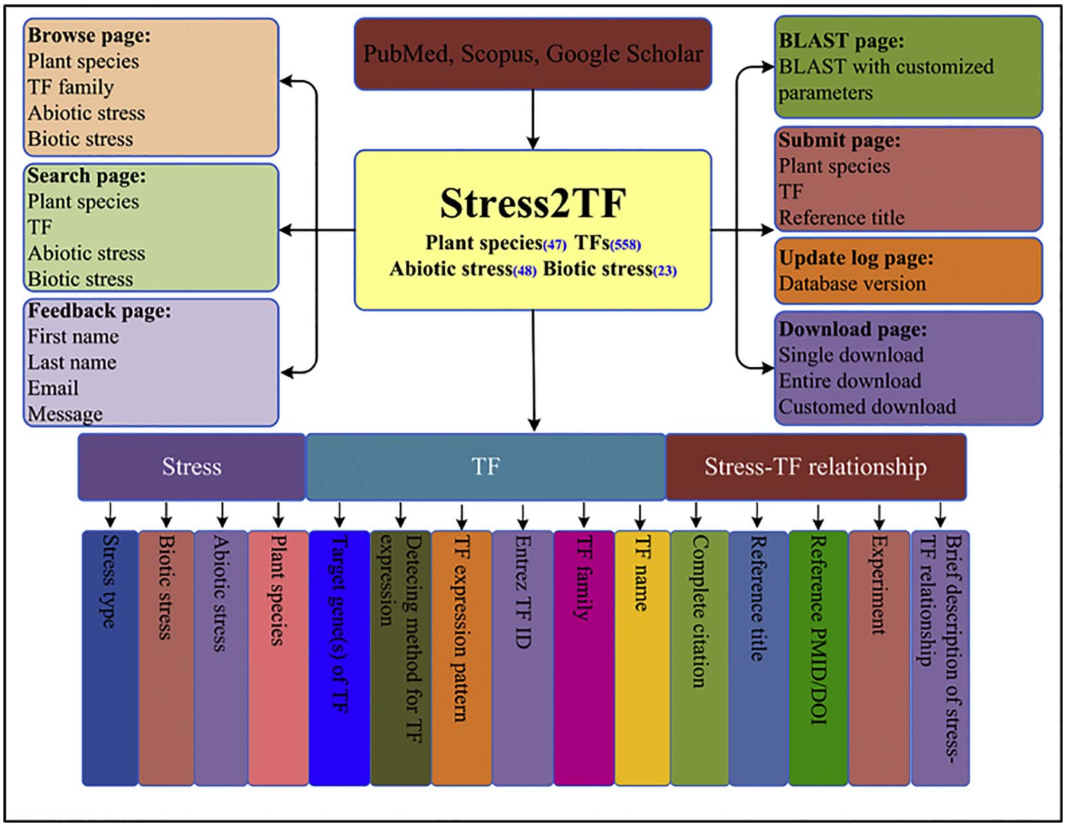

Fig. 1. An overview of the architecture of Stress2TF. The web-accessible Stress2TF allows for curated stress-TF regulatory relationships to be clearly browsed, searched, downloaded and updated, under a well-organized platform framework.