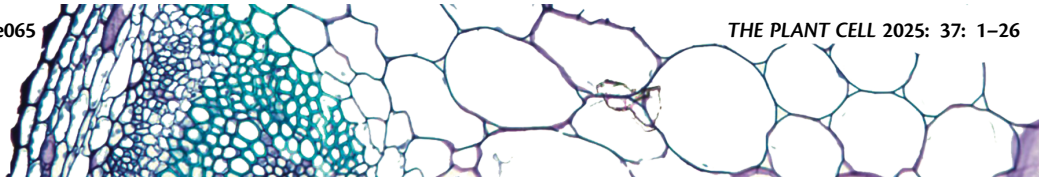
https://doi.org/10.1093/plcell/koae065 THE PLANT CELL 2025: 37: 1–26



Review

Arabidopsis as a model for translational research

Anna E. Yaschenko [1], **Jose M. Alonso** [1], **Anna N. Stepanova** [1,*]

1 Department of Plant and Microbial Biology, Genetics and Genomics Academy, North Carolina State University, Raleigh, NC 27695, USA

*Author for correspondence: atstepan@ncsu.edu (A.N.S.)
The author responsible for distribution of materials integral to the findings presented in this article in accordance with the policy described in the Instructions for Authors (https://academic.oup.com/plcell/pages/General-Instructions) is: Anna N. Stepanova (atstepan@ncsu.edu).

Abstract

Arabidopsis thaliana is currently the most-studied plant species on earth, with an unprecedented number of genetic, genomic, and molecular resources having been generated in this plant model. In the era of translating foundational discoveries to crops and beyond, we aimed to highlight the utility and challenges of using Arabidopsis as a reference for applied plant biology research, agricultural innovation, biotechnology, and medicine. We hope that this review will inspire the next generation of plant biologists to continue leveraging Arabidopsis as a robust and convenient experimental system to address fundamental and applied questions in biology. We aim to encourage laboratory and field scientists alike to take advantage of the vast Arabidopsis datasets, annotations, germplasm, constructs, methods, and molecular and computational tools in our pursuit to advance understanding of plant biology and help feed the world's growing population. We envision that the power of Arabidopsis-inspired biotechnologies and foundational discoveries will continue to fuel the development of resilient, high-yielding, nutritious plants for the betterment of plant and animal health and greater environmental sustainability.

Introduction

About 150 years ago, in the summer of 1873, in the meeting proceedings of the Society of Friends of Natural Sciences in Berlin, a report was published that described what appears to be the first documented *Arabidopsis thaliana* mutant (Braun 1873). A renowned German botanist, Alexander Braun, recounted an *agamous*-like mutant "found by Mr. Vatke in a single specimen in the field between Schoneberg and Willmersdorf" that had multiple whorls of petals replacing other flower organs. It was not until the 1980s that Arabidopsis was adopted as a model organism, largely due to its practicality for studying plant physiology and genetics. With its compact size, small 5-chromosome genome, speedy reproductive cycle, prolific seed set, and ease of genetic transformation, Arabidopsis quickly became the gold standard of plant models in the era of genomics. Classical forward and reverse genetics in Arabidopsis were leveraged to identify core molecular pathways (Arabidopsis Genome Initiative 2000; Somerville and Koornneef 2002). Natural variation was relied on to uncover key gene variants underlying quantitative traits in genome-wide association studies (Weigel 2012). Arabidopsis has quickly proven instrumental to revealing the logic of developmental mechanisms, metabolic networks, and gene regulatory pathways in plants and beyond (Meyerowitz 1999). Indeed, the broader usefulness of Arabidopsis as a model lies in the translation of scientific findings to more applied fields, from crop trait improvement to medicine.

This organism's translational potential is amplified by the ease with which researchers can screen genetic targets associated with relevant traits. This knowledge can then be applied to genetically complex, transformation-recalcitrant crops for the purpose of improving yield under a variety of environmental conditions. Given that many crop plants have higher orders of ploidy and larger genomes than Arabidopsis, gene knockouts and other types of genetic alterations are more achievable in Arabidopsis. The simple and rapid transformability of Arabidopsis enables fundamental molecular research aimed at gaining a fundamental understanding of the biological processes that underlie

Received December 05, 2023. Accepted January 26, 2024. Advance access publication February 27, 2024.

important agronomic traits. In this review, we highlight the practicality of using Arabidopsis as a model for research through an analysis of current literature. We examine the ways in which Arabidopsis discoveries have been applied to other plant species, as well as in the biomedical sciences. Biotechnology tools and methods developed in or sourced from Arabidopsis are described. Finally, we discuss how computational approaches have been employed to facilitate the translation of Arabidopsis research. This review dedicated to the 150th anniversary of Arabidopsis genetics is not meant to be comprehensive but rather aims to highlight the great potential of Arabidopsis in advancing the frontiers of our knowledge base while acknowledging the challenges of translating fundamental research into practical applications. By providing representative examples of Arabidopsis knowledge transferability, we hope to inspire the next generation of plant biologists to adopt Arabidopsis as their model of choice or leverage Arabidopsis-generated information resources in their pursuit of solving the world's most pressing issues.

Translatability of Arabidopsis discoveries to other plants

Many plant genes are first identified and characterized in Arabidopsis due to the ease of genetic screening and molecular characterization in this species, as well as public access to a wide array of genetic and germplasm resources through well-established stock centers (Arabidopsis Biological Resource Center, Nottingham Arabidopsis Stock Centre, and RIKEN BioResource Research Center). Testing the degree to which the knowledge of gene function generated in Arabidopsis can be extrapolated to crop species is of utmost importance given that one of the goals of Arabidopsis research is to cultivate foundational knowledge that can fuel the development of improved crops. In general, it is much easier to characterize or manipulate a gene from a species with a curated annotation than it is to start from scratch. Gene functional information from Arabidopsis can act as a framework or starting point for gene discoveries in other species. This allows researchers to, colloquially, play a matching game instead of searching for a needle in a haystack. In fact, a majority of Gene Ontology (GO) annotations for other plant species are based on annotations initially curated for orthologous Arabidopsis genes (Whitt et al. 2020; Wimalanathan and Lawrence-Dill 2021; Sessa et al. 2023). However, there are challenges involved with translating Arabidopsis knowledge to other species. Some genes and pathways are missing, partially missing, or not conserved in either Arabidopsis or the species of interest. Other genes may be relatively conserved based on sequence identity but diversified in their function. This could be due to species-specific gene sequence variation, a lack of pathway conservation, or the decrease in synteny between more distantly related species. For example, when infested with the two-spotted spider mite (*Tetranychus urticae*), Arabidopsis and tomato plants diverge in their transcriptional response, with only 96 differentially expressed genes shared out of 1,092 orthologous pairs (Martel et al. 2015). Another representative example is the inability of a tomato *INNER NO OUTER* (*INO*) gene to rescue the defects of an Arabidopsis *ino* mutant in spite of a significant sequence identity and similarity in expression pattern (Skinner et al. 2016). Despite these limitations, the function of many genes originally studied in Arabidopsis has been shown to be either partially or fully conserved in plants of agronomic importance (Lim et al. 2005; Sun et al. 2016; Lu et al. 2022). Even if gene function is not conserved, using Arabidopsis as a reference model for comparative genomics or to study conservation of genes across species can uncover previously unknown complex interactions between genes and the environment (Brendel et al. 2002; Hall et al. 2002; Town et al. 2006; Sharma et al. 2014).

Those studying crop genes with the goal of trait improvement often default to re-examining the function of well-characterized Arabidopsis homologs, which, thanks to streamlined transformation methods and libraries of T-DNA insertion lines, likely already have existing knockout mutants available (O'Malley et al. 2015). The putative crop orthologs can then be tested through gene complementation in the Arabidopsis mutants, confirming the ortholog's function without having to generate mutants in the crop of interest (Dubouzet et al. 2003). Gene complementation can also work the other way, where a knockout crop line is complemented with the Arabidopsis version of the gene (Yuan et al. 2005). This tends to be the less popular approach because generating knockout mutants in crops with higher orders of ploidy and transformation recalcitrance can be tedious. In some cases, Arabidopsis genes have been tested for potential roles in crop trait improvement through the creation of overexpression lines in a crop of interest (Lin et al. 2004; Yuan et al. 2005). This requires the generation of transgenic crops, which, depending on the laws governing where the crop is grown or sold, may have limited commercial application. However, there are still many ways in which Arabidopsis genes can contribute to the development of improved crops (Fig. 1).

Studies that conduct large-scale screening of genetic targets for crop improvement often leverage Arabidopsis to identify candidate genes. From 2000 to 2018, Corteva Agriscience field-tested maize transgenic events to identify genes that could be used to improve yield, drought tolerance, and other agronomic traits (Simmons et al. 2021). Among 35,000 genes pre-screened for field testing, 90% were identified from Arabidopsis transgenic and knockout lines. Arabidopsis served as a high-throughput pre-screening platform for both forward and reverse genetic screens to identify candidate genes to test in the field. Out of 1,671 genes tested in maize field trials, a total of 22 genes (3 of them associated with drought tolerance from Arabidopsis) showed promising results (Simmons et al. 2021). These methods can be employed to understand the molecular mechanisms of important pathways in plant growth and development, flowering time, disease resistance, and abiotic stress tolerance for the purpose of generating information for crop breeders on which genes to target for optimal crop performance.

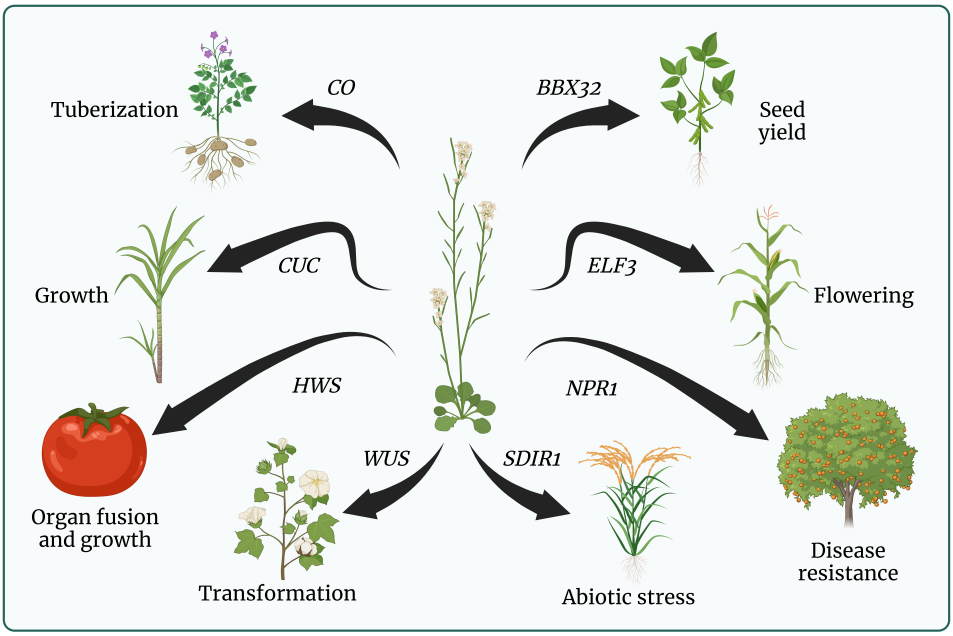


Figure 1. Graphical representation of Arabidopsis gene discoveries translated to crop traits. Examples of genes originally characterized in Arabidopsis that have contributed to elucidation of the crop traits in potato (tuberization), sugarcane (plant growth), tomato (organ fusion and plant growth), cotton (transformation), soybean (seed yield), maize (flowering), sweet orange (disease resistance), and rice (abiotic stress). Gene name abbreviations are as follows: *CONSTANS* (*CO*); *CUP-SHAPED COTYLEDON* (*CUC*); *HAWAIIAN SKIRT* (*HWS*); *WUSHEL* (*WUS*); *B-BOX DOMAIN CONTAINING PROTEIN32* (*BBX32*); *EARLY FLOWERING3* (*ELF3*); *NONEXPRESSOR OF PATHOGENESIS-RELATED GENES1* (*NPR1*); *SALT- AND DROUGHT-INDUCED RING-FINGER1* (*SDIR1*). Created with BioRender.

Plant development, growth, and yield

It is no surprise that plant growth and development are among the most common traits targeted in crop improvement. Arabidopsis has proven to be an excellent model for research in this field, especially due to the simplicity of its genome and small stature. Thus, there have been many studies that leverage Arabidopsis-generated knowledge to search for orthologs that can be targeted to increase yield and biomass, as well as understand how a particular crop progresses through development. One example is the discovery of *CUP-SHAPED COTYLEDON* (*CUC*) genes in sugarcane, a crop utilized worldwide for sugar and biofuel. In Arabidopsis, *CUC* genes are known to play an important role in plant growth, particularly in organ boundary formation, ovule development, and shoot apical meristem establishment (Hibara et al. 2006). Given that sugarcane is an octoploid with a fairly recently published genome, leveraging Arabidopsis would greatly enhance the speed at which crop improvement traits can be pinpointed in sugarcane (Zhang et al. 2018). *SsCUC2* and *SsCUC3* were identified as putative orthologs of Arabidopsis *CUC2* and *CUC3* genes, respectively (Aslam et al. 2022). *SsCUC2* was able to rescue the classic phenotype of Arabidopsis cotyledons when ectopically expressed in a *cuc2 cuc3* mutant background that had a cup-shaped cotyledon phenotype, suggesting that the known function of *CUC2* may be conserved in sugarcane. This gene complementation assay in Arabidopsis allowed for quick and easy assessment of *SsCUC2* function without the laborious process of generating a knockout mutant in the octoploid crop. This result illustrates that genetic findings in Arabidopsis can be relevant even in distantly related species. However, significant additional work would still be needed to determine the exact agronomically relevant effects of altering the activity of this gene in sugarcane.

Another way of utilizing complementation to confirm putative gene function is by expressing the curated Arabidopsis version of a gene in a mutant background of the crop of interest. This method may be preferred when studying the effects of a knockout and rescue directly in the crop of interest, especially because plant growth and development traits tend to be controlled by multiple genes and their interactions with the environment. One noteworthy study used this complementation method to evaluate the function of a tomato ortholog of an Arabidopsis gene (Nagata et al. 2021). *HAWAIIAN SKIRT* (*HWS*), an F-box containing gene, was first characterized in Arabidopsis to regulate organ fusion and growth (González-Carranza et al. 2007). A tomato knockdown mutant, *slhws-1*, shows increased Brix levels (a sugar content proxy) and displays parthenocarpy (ability to produce fruit without fertilization), establishing it as a gene of interest for crop improvement. To test for orthology in the tomato and Arabidopsis *HWS* gene function, the *slhws-1* mutant was complemented with a functional copy of *AtHWS* (Nagata et al. 2021). The complementation construct restored the wild-type (WT) phenotype to the same degree as did the *SlHWS* construct, implying conservation of *HWS*

function across species and suggesting that the wealth of knowledge in Arabidopsis could accurately inform the development of agronomically important traits in tomato.

Besides plant growth, another important agricultural trait is crop yield, which is a complex quantitative trait that is typically difficult to breed for. Sourcing genes that produce desirable traits from Arabidopsis would greatly benefit the rate at which we are able to produce high yielding crops, and this is exactly what researchers have done. For example, Arabidopsis-derived *B-BOX DOMAIN PROTEIN32* (*AtBBX32*), a putative transcription factor (TF) gene originally found to play a role in light signal transduction in Arabidopsis, was used to generate a transgenic soybean line with increased seed yield (Preuss et al. 2012). In this study, an *AtBBX32* cDNA driven by a *CaMV 35S* constitutive promoter was introduced into soybean, and the resulting transgenic lines were evaluated in a multi-year, multi-location trial. The transgenic lines exhibited increased plant height, flower number, and seed number compared with WT control and affected downstream soybean circadian clock–associated genes. This study also identified orthologous *BBX32* genes in soybean. Overexpression lines of soybean orthologs *GmBBX52* and *GmBBX53* exhibited higher yield than WT control (Preuss et al. 2012), suggesting that these genes may function in the same pathway in Arabidopsis as they do in soybean. This example of the successful introduction of an Arabidopsis gene into crops highlights yet another way Arabidopsis research benefits applied plant science.

Disease resistance and defense-related traits

Perhaps the most significant impact Arabidopsis research has had on crop breeding is the discovery of disease resistance and defense-related genes. Host-induced gene silencing is one method employed to increase disease resistance in Arabidopsis studies, which informs future applications in crop studies. In 2006, researchers were able to silence the root-knot nematode (RKN) parasitism gene, *16D10*, using RNA interference (RNAi) in Arabidopsis (Huang et al. 2006). The resulting reduction in number of root galls in *16D10* dsRNA transgenic lines demonstrated host resistance to 4 major RKN species in Arabidopsis and unveiled a mechanism by which crops could be engineered to possess broad resistance to the pathogen. The method was later employed in soybean (Ibrahim et al. 2011) and grape (Yang et al. 2013) and successfully decreased root gall number and size caused by RKN, demonstrating the translatability of disease-related methods initially tested in Arabidopsis.

Gene complementation has also been utilized in the study of disease resistance in crops. A notable recent example leverages *ETHYLENE INSENSITIVE2* (*EIN2*), a gene well known to play a role in ethylene signaling, to increase *Fusarium* head blight (FHB) resistance in barley (Low et al. 2022). This study employed CRISPR gene editing to create site-specific mutations in *AtEIN2* to generate *ein2* knockout Arabidopsis lines. Subsequently, a barley ortholog of Arabidopsis *EIN2*, *HvEIN2*, was transformed into the Arabidopsis *ein2* mutant. The knockout line displayed a higher resistance to fungal hyphal growth on inflorescences than either WT or the *ein2 HvEIN2* Arabidopsis line, indicating that *HvEIN2* was able to restore the FHB susceptibility phenotype and suggesting the functional equivalence of the barley *HvEIN2* ortholog (Low et al. 2022). The results of this paper suggest that ethylene signaling advances FHB infection, thus making *EIN2* a gene of interest to target for disease resistance.

To acquire a high level of disease resistance to a variety of pathogens, it is more efficient to target genes that increase systemic acquired resistance rather than focusing on 1 gene that grants resistance to 1 pathogen at a time. *NONEXPRESSOR OF PATHOGENESIS-RELATED GENES1* (*NPR1*) is a gene, originally cloned from Arabidopsis, that is involved in the regulation of systemic acquired resistance to microbial pathogens in plants (Zhang and Cai 2005). Many studies have shown success in increasing disease resistance against a range of different types of infections when overexpressing *AtNPR1* in horticultural crops (Wally et al. 2009; Parkhi et al. 2010b; Molla et al. 2016). For example, a study in 2015 introduced *AtNPR1* into sweet orange trees as a way to increase resistance to Huanglongbing (HLB), colloquially known as citrus greening, which is a fatal phloem-specific bacterial disease caused by *Candidatus* Liberibacter asiaticus (Dutt et al. 2015). Due to the fact that its vector, the Asian citrus psyllid (ACP), has no native predators in the United States, HLB has been able to rapidly spread and has wiped out many citrus-producing areas since its first detection in 2005 (Halbert 2005). With no cures and little to no commercially available resistance rootstock, genetic intervention is the best path to increased resistance in sweet orange. The Dutt et al. study led to the production of transgenic sweet orange trees that overexpress *AtNPR1* either in all tissues or specifically in the phloem, sourcing a phloem-specific Arabidopsis *SUCROSE-PROTON SYMPORTER2* promoter. These transgenic sweet orange trees displayed effective resistance to HLB, with the phloem-specific expression of *AtNPR1* lines conferring more relative resistance than either WT or constitutive expression lines. The successful increase in resistance to HLB by the phloem-specific lines opens the door to HLB resistant, nontransgenic sweet orange trees being grafted onto transgene-containing HLB-resistant rootstocks. *AtNPR1* has also been utilized in other species to increase resistance to a variety of different diseases, including cotton resistance to *Verticillium* wilt (Parkhi et al. 2010a), canola resistance to bacterial disease (Potlakayala et al. 2007), and tobacco resistance to root-knot nematodes (Priya et al. 2011).

Flowering-related traits

Flowering-related genes and pathways have been well researched in Arabidopsis and horticultural crops due to the important role these genes play in reproduction and fruit development. Understanding of the flowering pathway in Arabidopsis has proven instrumental to the selection of key flowering genes to be targeted by classical plant breeding in a variety of field crops (Eshed and Lippman 2019),

including soybean (Weller and Ortega 2015), tomato (Lifschitz et al. 2014), and even tree species (Flachowsky et al. 2009). A well-known, extensively studied gene involved in flowering is *FLOWERING LOCUS T* (*FT*) originally identified and characterized in Arabidopsis as a positive regulator of flowering (Koornneef et al. 1998). Orthologs of *FT* have been identified in many plant species, including apple (Blümel et al. 2015). Expression of 2 apple FT orthologs, *MdFT1* and *MdFT2*, correlates with floral initiation, and the ectopic, constitutive expression of either apple ortholog in Arabidopsis leads to early flowering (Kotoda et al. 2010), demonstrating the utility of this model plant in validating the functional conservation of flowering genes across different species. Despite Arabidopsis not producing fleshy fruits, the knowledge base generated on flowering genes in Arabidopsis can significantly aid in the elucidation of flowering mechanisms for the purpose of controlling flowering time and fruiting in horticultural crops. This utility extends to trees as well, as the use of *FT*-overexpressing lines and *FT*-based tools have revolutionized the breeding process in multiple tree species (Flachowsky et al. 2009; Zhang et al. 2010; Soares et al. 2020).

Another noteworthy flowering-related gene is *EARLY FLOWERING3* (*ELF3*), a repressor of flowering. ELF3 is a component of the evening complex (EC) in Arabidopsis along with ELF4 and LUX ARRHYTHMO (LUX) (Nusinow et al. 2011). In this complex, ELF3 acts as a bridge between ELF4 and LUX to form a transcriptional repressor complex that mediates plant circadian rhythms. These findings in Arabidopsis led to the identification of 2 *ELF3* orthologs in maize, *ZmELF3.1* and *ZmELF3.2*, as well as 2 *ELF4* orthologs, *ZmELF4.1* and *ZmELF4.2* (Zhao et al. 2023). These orthologs were found to interact in maize, mirroring the interaction of ELF3 and ELF4 in Arabidopsis. Lines with overexpressed *ZmELF3* genes in an *elf3-7* Arabidopsis knockout mutant rescued the early flowering phenotype in long-day conditions. However, *ZmELF3* genes lack a C-terminal prion-like domain that was implicated in the *AtELF3* gene's heat-responsive ability to act as a thermosensor (Jung et al. 2020). This domain is partially or fully absent in other plants, including tomato and *Brachypodium distachyon*. Interestingly, the prion domain-lacking maize genes expressed in a mutant *elf3-1* Arabidopsis background phenotypically resemble the WT under normal temperature conditions but do not rescue the thermally responsive phenotype of *AtELF3*, suggesting that the missing C-terminus is essential for thermosensing (Jung et al. 2020). This *ELF3* gene study illustrates the ways in which not only Arabidopsis genes but even Arabidopsis-specific variations of a gene can greatly contribute to improving our understanding of pathways and traits of agricultural importance.

Another important gene in flowering is the Arabidopsis-discovered *CONSTANS* (*CO*) gene that acts upstream of *FT* and plays a role in flowering during long-day conditions (Yoo et al. 2005). One study tested whether this gene affects tuberization in potatoes, despite the seemingly unrelated nature of the processes of flowering and tuberization (González-Schain et al. 2012). *StCO* was identified as a putative potato ortholog of *CO*, and its effect on flowering in potato was tested with overexpression and RNAi silencing. Under long-day conditions, *StCO* seemed to have a significant but weak effect on flowering time in potato, causing the plants to flower earlier. When tested in an Arabidopsis *co* mutant background, *StCO* was able to only partially rescue the late-flowering phenotype, as flowering time was still delayed with regards to WT. However, *StCO* was shown to have a repressive effect on tuberization under long-day conditions, unlike the *AtCO*'s promotive effect on flowering (González-Schain et al. 2012). This is congruent with the fact that potato is a short-day plant for tuberization, meaning long-day conditions inhibit the growth of tubers, whereas Arabidopsis is a long-day plant that flowers earlier in long-day conditions than in short-day. There is therefore only partial conservation of *CO* function between Arabidopsis and potato, with the divergence explainable by possible subfunctionalization in potato as there are other *CO-LIKE* genes in potato, including *St-lCOL1* and *St-sCOL1* (González-Schain et al. 2012).

Abiotic stress tolerance

Every year, abiotic stressors play a major role in loss of crop yield worldwide (Kopecká et al. 2023). With changing climates and rising temperatures, it is becoming increasingly imperative to find genes that can impart adaptability to new environmental conditions. Natural variation in Arabidopsis facilitates the discovery of novel abiotic stress-tolerant genes and underscores the potential of Arabidopsis to improve crop resistance to stresses like fluctuating temperature, heavy metals, intense UV light, flooding, high salinity, and drought. Here, we will highlight examples of this plant's contributions to elucidating drought and salt stress pathways in crops.

SALT- AND DROUGHT-INDUCED RING-FINGER1 (*SDIR1*) encodes an E3 ligase originally identified in Arabidopsis that was discovered to play a role in abscisic acid (ABA)-related stress signaling (Zhang et al. 2007). Arabidopsis overexpression lines of *SDIR1* showed significant resistance to drought, indicating that *SDIR1* may be an ideal target for improving drought tolerance in crops. To test whether this gene could increase drought tolerance in monocot and dicot crops, Zhang et al. generated transgenic tobacco (*Nicotiana tabacum*) and rice (*Oryza sativa*) that ectopically express the Arabidopsis *SDIR1* gene (Zhang et al. 2008). Upon dehydration, transgenic lines of both species showed significantly less drought-stress symptoms relative to controls. Importantly, the level of drought tolerance exhibited in the transgenic crops was comparable to that in *SDIR1*-expressing Arabidopsis (Zhang et al. 2008), suggesting that the drought-response pathways regulated by *SDIR1* are conserved across plant species.

Arabidopsis salt stress–responsive genes have also shown evidence of translatability to crops. *SALT OVERLY SENSITIVE1* (*SOS1*) codes for an Na+ efflux protein in the plasma membrane that, when mutated, renders Arabidopsis plants sensitive to salt stress (Shi et al. 2000). Overexpression of Arabidopsis *SOS1* in Arabidopsis or tobacco leads to increased salt

tolerance (Shi et al. 2003; Yue et al. 2012). Furthermore, rice *OsSOS1* can partially suppress growth defects of the Arabidopsis *sos1* mutant in the presence of NaCl, but not to the same extent as does At*SOS1* (Martínez-Atienza et al. 2007). These findings reveal that there is only partial conservation of *SOS1* between dicots and monocots. Thus, the identification of crop orthologs of candidate Arabidopsis genes of interest may maximize the benefits of gain-of-function work and avoid the need for traditional transgenic approaches if gene editing or classical breeding alone can achieve higher levels of native gene's activity.

Plant transformation

Unlike most plant species, Arabidopsis and some of its close Brassicaceae relatives are amenable to flower-dip transformation (Clough and Bent 1998; Verma et al. 2008) and are currently the only flowering plants where hundreds of independent transformants can be generated rapidly without incurring an enormous cost. This unique Arabidopsis attribute reduces the amount of effort and time it takes to test the consequences of genetic modifications or new transgene designs. In contrast, in most crop species, the process of transgenic line production involves several steps of in vitro tissue culturing to initially achieve degeneration of transformed plant explants or protoplasts into callus and subsequently regenerate whole plants (Yue et al. 2021). This process can be arduous and time-consuming, especially in species that are recalcitrant to genetic transformation (Anjanappa and Gruissem 2021). Furthermore, plant regeneration can cause unintentional genomic and epigenomic changes (Filipecki and Malepszy 2006).

To circumvent these issues, researchers have focused on using particular genes with morphogenic potential to induce pluripotency in a subset of somatic cells and speed up the rate at which newly transformed plants are produced (Chen et al. 2022). Arabidopsis has been a source for many of these genes, with 1 notable example being the well-researched *WUSHEL* (*WUS*) gene that encodes a homeobox transcription factor (Laux et al. 1996). In an attempt to increase somatic embryogenesis and calli formation, one study expressed the Arabidopsis *WUS* in coffee plants under an estradiol-inducible transcriptional control (Arroyo-Herrera et al. 2008). Transformed plants exhibited the ability to form calli and showed an increase in somatic embryo induction, confirming that *WUS* plays a critical role in embryogenesis. However, overexpression of Arabidopsis *WUS* in coffee also led to malformations in growth, impairing the ability of embryos to regenerate into full plants (Arroyo-Herrera et al. 2008). Similar results were found in cotton, with overexpression of *WUS* leading to increase in embryogenic tissue in explants without the production of regenerated plants (Bouchabké-Coussa et al. 2013). Nonetheless, Arabidopsis *WUS* and its orthologs in crop species have been instrumental in shedding light on the regulatory mechanisms of plant transformation, regeneration, and growth (Jha et al. 2020).

There are a number of other Arabidopsis genes that have been identified as developmental regulators that can be leveraged in plant transformation and regeneration work (Yan et al. 2023). A recent study focusing on organogenesis targeted *WUS*, *PLETHORA5* (*PLT5*), and *WOUND INDUCED DEDIFFERENTIATION1* (*WIND1*) genes from Arabidopsis (Lian et al. 2022). Genetic transformations were carried out in snapdragon, tomato, *Brassica rapa*, and sweet pepper, with each of these genes transformed individually and driven by a *CaMV 35S* promoter. In snapdragon and tomato transformations carried out in planta (i.e. via injection of *Agrobacterium tumefaciens* in soil-grown plants), ectopic expression of Arabidopsis *PLT5* led to the highest frequency of transgenic shoots out of all genes tested. In contrast, in *B. rapa* and sweet pepper, crops that are recalcitrant to genetic transformation, *PLT5* did not trigger shoot regeneration in planta but did promote plant and embryo regeneration in vitro (i.e. tissue culture-grown explants) (Lian et al. 2022). These studies underscore the utility of Arabidopsis-generated knowledge in plant transformation work and suggest that efficient regeneration methods for recalcitrant crops rely on a thorough understanding of a complex network of developmental genes and their regulation. These methods may differ between species but will nonetheless benefit from comparative analysis with respect to a common well-studied reference like Arabidopsis.

Comparative genomics

The thorough curation of the Arabidopsis genome and development of Arabidopsis-specific data storage platforms have enabled comparative genomics using Arabidopsis as a reference genome. Those studying plant species with less annotated genomes can search Arabidopsis databases to find characterized genes associated with particular traits, such as biotic or abiotic stress responsiveness, and identify orthologs of those genes in their species of interest (Sayers et al. 2022). On a genome-wide scale, there are tools that can elucidate the level of synteny, the conservation of gene block order, between Arabidopsis and other genomes, such as SimpleSynteny (Veltri et al. 2016), MCScan (Wang et al. 2012), and SynFind (Tang et al. 2015). An example of the Arabidopsis genome being utilized as an anchoring point for other genomes is a study in which researchers examined the domestication potential of pennycress as a new oilseed crop by referencing the Arabidopsis genome to identify domestication genes (Chopra et al. 2018). These researchers found that Arabidopsis and pennycress have similar gene duplication and display a high degree of identity in a one-to-one comparison of coding sequences. In forward genetic screens, mutants in pennycress genes related to vegetative growth that have clear Arabidopsis orthologs included *asymmetric leaf1* (*as1*) and *phytochromeB* (*phyB*) (Chopra et al. 2018). In reverse genetic screens, a pennycress line with a mutation in a *CAROTENOID CLEAVAGE DIOXYGENASE7/MORE AXILLARY BRANCHING3* (*CCD7/MAX3*) ortholog was associated with the classic bushy dwarf phenotype also observed in Arabidopsis mutants (Booker et al. 2004). These findings illustrate the general

utility of Arabidopsis in mass identification of genes in a species of interest and its potential to aid in the domestication of new crops.

The use of Arabidopsis as a reference genome for comparative genomics has led to better understanding of plant genomes and gene families outside of the model organism. For example, to generate the genome of oilseed rape (*Brassica napus*), the well-annotated Arabidopsis genome was utilized as a reference along with much less polished *Brassica rapa* and *Brassica oleracea* genome scaffolds (Bancroft et al. 2011). Genomic comparisons to Arabidopsis are also useful in the annotation and classification of much more distantly related plant genes, including that of monocots. Thus, for example, by comparing the genomes of Arabidopsis and rice, the structure of the *APETALA2* (*AP2*)/*ETHYLENE RESPONSE FACTOR* (*ERF*) gene family in plants was elucidated (Nakano et al. 2006), providing a roadmap for classifying AP2/ERF family genes in other species (Liu et al. 2023). Arabidopsis has also been used as a resource for the classification of wheat genes homologous to well-characterized Arabidopsis gene families associated with response to biotic stress enabling the mass discovery of candidate wheat genes that could be targeted in the follow-up work to develop cereal crops resistant to a wide spectrum of plant pathogens (Yang et al. 2017).

Noncoding RNAs

Although plants are at the forefront of the discovery of gene silencing mechanisms triggered by double-stranded (ds) RNA in eukaryotes (Chaudhary et al. 2024), Arabidopsis is not the first plant species where silencing was initially demonstrated (Napoli et al. 1990). Nonetheless, Arabidopsis has proven to be instrumental to identifying the molecular machinery of the RNA interference pathway (Schröder and Jullien 2019) and to characterizing different types of silencing-inducing noncoding RNAs (Hajieghrari and Farrokhi 2022). Furthermore, the artificial microRNA (amiRNA) technology to downregulate target genes was first developed in Arabidopsis (Alvarez et al. 2006; Schwab et al. 2006). Since then, amiRNAs have been broadly utilized in various species, including multiple crops, with a notable example being the recent development of a short-stature amiRNA corn (Paciorek et al. 2022). Researchers targeted 2 maize *GIBBERELLIN 20 OXIDASE* (*GA20ox*) genes involved in gibberellin biosynthesis and suppressed gene expression using a dominant, amiRNA-based construct leading to a short-stature phenotype. This compact corn line is projected to go into commercial production in 2027 and is believed to have the potential to markedly impact crop productivity under an array of suboptimal environmental conditions (Plume 2022). Overall, Arabidopsis has played a key role in the detection, characterization, and utilization of various forms of ncRNAs to silence specific genes, serving as a platform for systematic, well-controlled experiments to knockdown genes of interest for both gene function exploration and applied purposes (Schröder and Jullien 2019; Hajieghrari and Farrokhi 2022; Chaudhary et al. 2024).

Chemical screens and herbicide resistance

Arabidopsis is often leveraged as a "lab rat" in chemical genetic screens to identify compounds that interfere with or trigger molecular pathways of interest, as well as to elucidate the molecular activity of best-performing chemical effectors or inhibitors in vivo or in vitro (Serrano et al. 2015). For example, in a seedling screen of 2000 compounds, a small molecule kynurenine was identified for its ability to revert the heightened ethylene response of 2 Arabidopsis hormonal mutants, *ethylene overproducer1* and *constitutive triple response1* (He et al. 2011). This chemical was shown to partially block ethylene responses of these mutants by interfering with auxin production, with specific threshold levels of hormone auxin known to be a prerequisite of the normal ethylene response. Kynurenine was found to act as a competitive substrate for the key auxin biosynthesis enzyme, TRYPTOPHAN AMINOTRANSFERASE OF ARABIDOPSIS1 (He et al. 2011). In subsequent studies, kynurenine was successfully adopted by the plant biology community as an effective pharmacological tool to manipulate auxin production in several plant species, from rice (Guo et al. 2020) to cork oak (Carneros et al. 2023).

Not only Arabidopsis plant lines but also Arabidopsis genes expressed in heterologous systems such as yeast have been leveraged in chemical screens aimed at identifying powerful synthetic effectors (Serrano et al. 2015). One of the most illustrative examples comes from the work of Sean Cutler's group on an ABA receptor, PYRABACTIN RESISTANCE1 (PYR1) (Park et al. 2015). A small library of 15 commercially available nonherbicidal agrichemicals was screened against 475 Arabidopsis PYR1 mutant variants that harbor amino acid substitutions in its ABA-binding pocket. One specific chemical effector, mandipropamid, was able to induce the heterodimerization of mutant PYR1 with its molecular target, PROTEIN PHOSPHATASE 2C (PP2C), in a yeast 2-hybrid assay (Park et al. 2015). Repeated rounds of targeted mutagenesis of amino acid residues in the PYR1 ABA binding pocket dramatically increased the affinity of the mutant protein for mandipropamid and abolished its affinity for ABA. Critically, when the resulting $PYR1^{MANDI}$ mutant variant was stably expressed in Arabidopsis and tomato, the transgene was able to trigger ABA-like responses and drought tolerance upon application of mandipropamid (Park et al. 2015). This exiting study demonstrates how rational engineering of an Arabidopsis protein can have promising practical implications for crops.

Herbicides have long been an effective way to control weed growth in agricultural plots, but continuous herbicide use comes with a high probability of unintentionally selecting for mutations that enable weeds to overcome herbicide sensitivity, eventually rendering these agrichemicals ineffective (Damalas and Koutroubas 2024). Arabidopsis has historically been leveraged to evaluate the risk of plants developing resistance to herbicides through genetic mutations that cause single amino acid substitutions in the herbicide binding pockets of target proteins (Sathasivan et al. 1991; Jander et al. 2003; Paris et al. 2008). Furthermore, recombinantly

produced Arabidopsis proteins of interest have been used to screen chemical libraries to identify novel chemicals with herbicidal properties (Pinneh et al. 2019; Soares da Costa et al. 2021). WT or mutant versions of Arabidopsis protein structures, either experimentally determined or predicted, have been employed to interrogate the mode of herbicide action (Pang et al. 2004; Lonhienne et al. 2022). Lonhienne and colleagues investigated site-of-action mutations in ACETOHYDROXYACID SYNTHASE (AHAS), an enzyme in plants known to be targeted by over 50 commercial herbicides (Lonhienne et al. 2022). Arabidopsis AtAHAS was chosen as a model to understand how herbicide resistance develops in crops. Two main ways were identified by which herbicides can inhibit this enzyme and AtAHAS mutations can block herbicide effectiveness. If a herbicide binds to the catalytic pocket and blocks substrate access, a resistance mutation in AtAHAS alters the pocket conformation and prevents herbicide binding. Likewise, if a herbicide acts by triggering AHAS cofactor oxidation causing time-dependent accumulative enzyme inhibition, a mutation in AtAHAS alters the enzyme conformation making it more resistant to herbicide-induced accumulative inhibition due to reduced affinity of the herbicide for its binding pocket (Lonhienne et al. 2022). The study analyzed the binding of 7 herbicides to 4 AtAHAS mutant proteins. One of the herbicides, bispyribac, was found to exhibit improved accumulative AtAHAS inhibition in all mutants, as well as greater binding affinity in some mutants, compared with WT, reducing the likelihood of resistance mutations showing up relative to other herbicides tested. This work benefited from the abundance of AtAHAS crystal structures that have been solved in complex with 13 different herbicides (spanning the 5 different chemical classes of herbicides that target AHAS) and added to this data collection by resolving crystal structures of the AtAHAS mutants with 2 commercial herbicides, bispyribac and chlorimuron ethyl (Lonhienne et al. 2022). Taken together, these examples illustrate the power of Arabidopsis research to inform applied work.

Applications of Arabidopsis in biomedicine

Though Arabidopsis was intended to be a model organism for plants, it has also had significant impacts on the biomedical field. Despite the fact that Arabidopsis and humans have had 1.6 billion years to diverge, there appears to be quite a bit of conservation among the 2 species in gene function and general cellular processes. A high percentage of genes associated with human diseases, particularly neurological diseases (71%), such as Alzheimer and Parkinson, and cancer (70%), are orthologous to Arabidopsis (Xu and Møller 2011). There is actually a higher percentage of cancer-associated gene orthologs in Arabidopsis (70%) than there are in *Drosophila melanogaster* (67%) or *Saccharomyces cerevisiae* (41%), model organisms that are more closely related to humans evolutionarily than Arabidopsis. Discoveries in protein degradation, the circadian clock, and G-proteins in Arabidopsis have greatly informed different facets of cancer studies (Xu and Møller 2011). A recent report utilized cancer-hallmark (CH) genes as a framework for the mechanistic comparison of biological processes and metabolic pathways in Arabidopsis and humans (Clavijo-Buriticá et al. 2023). The number of Arabidopsis orthologs for proto-oncogenes associated with onset and progression of cancer in humans makes Arabidopsis a potentially useful model for cancer studies. This study highlighted the practicality of using Arabidopsis at the genetic, cellular, and metabolic levels to elucidate the key events in the process of oncogenesis. First, Arabidopsis CH orthologs were identified, then associated with biological processes and metabolic reactions based on gene ontology enrichment analysis. Next, protein interactomes for both human and Arabidopsis were generated and used to select for candidate genes in Arabidopsis that are associated with carcinogenesis (Clavijo-Buriticá et al. 2023). This was done by identifying highly interconnected nodes in both Arabidopsis and human interactomes, detecting CH-associated proteins from the Arabidopsis interactome, or detecting Arabidopsis orthologs of CH-associated proteins from the human interactome. These Arabidopsis candidate genes were then validated through the analysis of transcriptomic data of their human orthologs, where it was found that Arabidopsis orthologs of the most differentially expressed human genes in cancerous tissues were retrieved as potentially CH-associated in the analysis of an Arabidopsis protein interactome. Overall, the study demonstrated the potential utility of using Arabidopsis to unravel the mechanisms of CHs associated with cellular proliferation, energetics deregulation, genome instability, and programmed cell death (Clavijo-Buriticá et al. 2023).

Molecular pathways elucidated in Arabidopsis can provide valuable insights into the mechanistic underpinning of particular genetic disorders, syndromes, or autoimmune diseases in humans (Xu and Møller 2011). In Parkinson disease, a gene called *PARKINSON DISEASE PROTEIN7* (*PARK7*) that codes for the protein DJ-1 has been shown to play a role in protecting neurons from neurodegeneration and was found to have an Arabidopsis ortholog, *AtDJ-1a*. To elucidate the function of DJ-1 on a molecular level, *AtDJ-1a* loss-of-function mutants were generated and characterized (Xu et al. 2010). These mutants showed accelerated cell death in aging plants, confirming that AtDJ-1 functions in a similar capacity to DJ-1 by protecting cells from stress-related cell death. Additionally, AtDJ-1a interacts with proteins within Arabidopsis that are orthologous to DJ-1-interacting proteins in humans. An example of this is the interaction of AtDJ-1a with COPPER/ZINC SUPEROXIDE DISMUTASE 1 (CSD1), an Arabidopsis cytosolic SUPEROXIDE DISMUTASE (SOD), in plant cells, which mirrors DJ-1's interaction with SOD1 in mammalian cells. AtDJ-1a was also shown to interact with human SOD1 in plant cells (Xu et al. 2010), further solidifying the value of utilizing Arabidopsis genes to study mechanisms in human disease.

Another mechanism that Arabidopsis has helped uncover in human neurodegenerative diseases is the process of polyglutamine repeat (polyQ) aggregation in human Huntington

disease (Llamas et al. 2023). An exon from the human *Huntingtin* (*HTT*) gene was engineered to contain an expanded polyQ stretch (Q69), making the protein product prone to aggregation. When the gene was expressed in Arabidopsis, the plant was able to suppress cytosolic aggregation of Q69 through a chloroplast STROMAL PROCESSING PEPTIDASE (SPP) that interacts with Q69, preventing aggregate formation. A human cell compatible synthetic SPP was able to decrease polyQ aggregation in both human cells and *Caenorhabditis elegans* when ectopically expressed (Llamas et al. 2023), highlighting yet another example in which Arabidopsis could hold the key to unlocking new routes in the treatment of human diseases. For more information and examples of Arabidopsis's role in understanding human neurological diseases, refer to the 2011 review by Xu and Moller (Xu and Møller 2011).

Biomedical sciences have also benefited from Arabidopsis research on NUCLEOTIDE-BINDING SITE—LEUCINE-RICH REPEATS (NB-LRR) proteins, which are encoded by genes implicated in disease resistance. These proteins are associated with molecular chaperones, cytosolic HEAT SHOCK PROTEIN90 (HSP90) and SUPPRESSOR OF THE G2 ALLELE OF SKP1 (SGT1), that interact with the immune responsive NB-LRR proteins in a signal-dependent manner (Jones and Dangl 2006). Though this interaction was first identified in plants, it was quickly found that orthologs of HSP90 and SGT1 in humans also interact with NB-LRR proteins (Mayor et al. 2007). The conservation of this mechanism across species exemplifies the commonalities between plant and animal innate immune responses and further establishes that Arabidopsis can be used as a supplemental model for biomedical research. More comprehensive examples of these commonalities can be found in a 2008 review by Jones et al (Jones et al. 2008).

In addition to gene discoveries, the biomedical community has successfully leveraged genetic tools and platforms that were developed by the Arabidopsis community. The application GENEVESTIGATOR was a popular plant-focused platform that was developed for storing and analyzing Arabidopsis microarray data (Zimmermann et al. 2004). This database, along with its associated tools, allowed for the identification of genes expressed in certain organs under specific conditions, enabling users to determine which genes and gene families were coexpressed in particular types of plant tissues. The platform was later expanded to other model crops, such as soybean, rice, and maize, and eventually into the biomedical field, where human, mouse, and rat gene expression studies were incorporated. In fact, after the acquisition by the pharmaceutical company Immunai, GENEVESTIGATOR currently focuses solely on immunology-related research, providing an example of a research platform originally developed to study Arabidopsis and later adopted by the biomedical community.

Development of Arabidopsis-inspired tools

The enormous data resource pool that has accumulated in Arabidopsis research has facilitated the development of biotechnological applications and synthetic biology tools that leverage Arabidopsis genetic parts as building blocks. From signal-responsive elements to complex expression systems, Arabidopsis has been foundational for studying a variety of plant and animal processes.

Inducible expression systems

One of the tools inspired by genes characterized in Arabidopsis is the CRY2-CIB1 optogenetic system (Fig. 2A). Optogenetics is a modern approach to studying cell-signaling in live cells, leveraging light-responsive proteins that undergo a conformational change upon light exposure. CRYPTOCHROME2 (CRY2) is an example of a light-responsive protein, sourced from Arabidopsis that homo-oligomerizes and binds to CRYPTOCHROME-INTERACTING BASIC HELIX-LOOP-HELIX1 (CIB1) in response to blue light (405–488 nm) exposure (Tischer and Weiner 2014). After removal of blue light, the CRY2-CIB1 complex dissociates and resets within approximately 5 minutes. The CRY2-CIB1 system was first established in yeast by fusing a transcriptional activation domain to *CIB1* and a DNA-binding domain to *CRY2* (Kennedy et al. 2010). Seven years later, the system was adapted for mammalian cells by removing a dimerization motif from the DNA-binding domain and adding back an orthogonal domain to preserve dimerization ability in order to avoid nuclear clearing of CRY2 (Pathak et al. 2017). It is important to highlight that the system was also adapted for use in zebrafish back in 2012 as the first artificial light–inducible transcription system in vertebrates (Liu et al. 2012) and utilized in other animal systems in following years (Yamada et al. 2020).

Optogenetics in mammalian systems has also adopted Arabidopsis PHYB regulated by red and far-red light (Reed et al. 1993). Originally known for controlling stem elongation in Arabidopsis seedlings, PHYB bound to a chromophore is activated under red light conditions (650 nm). This triggers a conformational change in PHYB that allows it to bind to PHYTOCHROME INTERACTING FACTOR3 (PIF3) until exposure to far-red light at a wavelength of 750 nm reverses the association (Fig. 2B). However, this interaction is difficult to recapitulate in mammals because mammalian cells do not inherently produce the right PHYB-compatible chromophore. To use the PHYB-PIF system in mammals, Uda et al. constructed a biosynthesis system for the chromophore phycocyanobilin (PCB) in mammalian cells by genetically encoding a synthetic gene, *PHFF*, made up of the CDSs of 4 bacterial genes required for PCB synthesis separated by self-cleaving peptides (Uda et al. 2017). This allowed for the PHYB-PCB interaction to occur, which is required for phytochrome to become light sensitive. Compared with the CRY2-CIB1 system, the PHYB-PIF system is favorable in certain applications because it is more compatible with fluorescent imaging of GFP-based biosensors due to the non-overlapping light wavelengths used for activation vs imaging.

It is well known that plants and animals have different sets of hormones, enabling the cross-use of hormones as inducers for synthetic systems. Just as the plant community will often employ the animal-based dexamethasone system as an

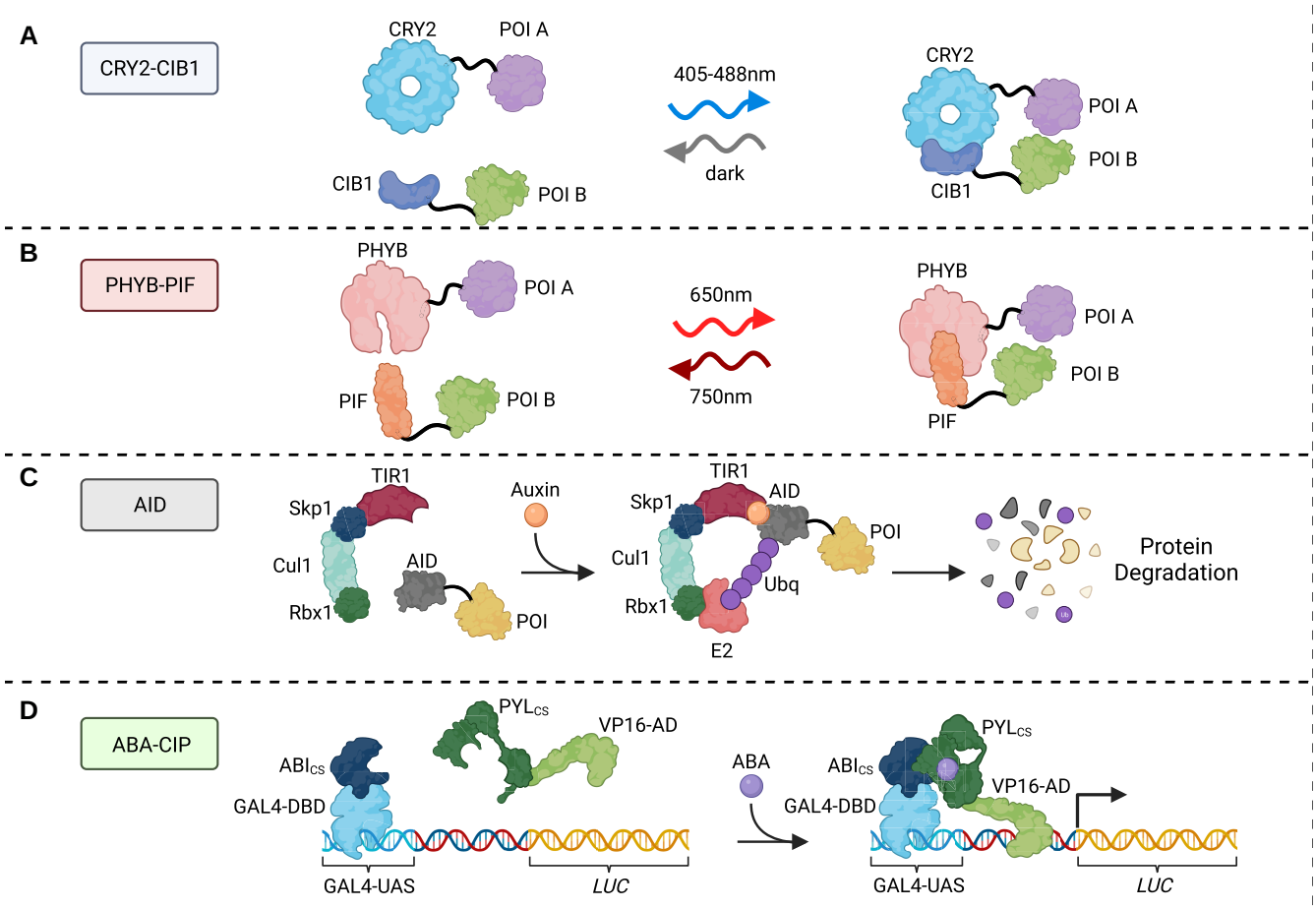


Figure 2. Schematic illustration of tools developed from genetic parts discovered in Arabidopsis. **A)** Depiction of the optogenetic CRY2-CIB1 system. Under blue light (405–488 nm), CRY2 binds to CIB1, allowing for proteins of interest (POI) A and B to interact. Dark conditions cause the CRY2-CIB1 complex to dissociate. **B)** Depiction of the optogenetic PHYB-PIF system. PHYB interacts with PIF only under red light (650 nm). The POIs fused to PHYB and PIF can then interact. The PHYB-PIF complex dissociates under far-red light conditions (750 nm). **C)** Illustration of the AID system, where an auxin-inducible degron (AID) is fused to POI. The presence of auxin allows for the interaction between the AID and an E3 ligase (SCF-TIR1) through the co-receptor roles of AID and TIR1. An E2 ligase is recruited to add ubiquitin (Ubq) to the AID, marking the AID-POI fusion for degradation. **D)** Illustration of the ABA-CIP system, utilized to induce transcription of a *LUCIFERASE* (*LUC*) reporter gene. The ABI1-GAL4 fusion binds to a GAL4 upstream activation sequence (UAS). In the presence of ABA, PYL fused to a VP16 activation domain (VP16-AD) binds to the ABI1-GAL4 fusion, allowing for the transcription of the reporter gene. Images created with BioRender.

inducer in plant synthetic systems, those working with mammalian systems have employed plant hormones to regulate transcription in mammalian cells (Cutler 2011). The plant community has extensively studied phytohormones, with many hormone pathways elucidated in Arabidopsis (Santner and Estelle 2009). Plant hormones are not found in animals, nor are they recognized by animal receptors, which makes them excellent molecules to utilize in synthetic transcriptional regulation systems. The first phytohormone that was adopted in animal research was auxin, whose role has been extensively studied in Arabidopsis. The auxin-inducible degron (AID) system was developed in 2009 to rapidly degrade proteins of interest in mammalian cells (Nishimura et al. 2009). It borrows proteins from the auxin-dependent degradation pathway in plants to generate an inducible and tunable system that can degrade target proteins in the presence of natural or synthetic auxins, such as indole-3-acetic-acid (IAA) and 1-naphthaleneacetic acid (NAA). Auxins are known to promote the interaction of AUX/IAA transcription co-repressors with the auxin-specific TRANSPORT INHIBITOR RESPONSE1 (TIR1) F-box protein that, together with the highly conserved SKP1 and CULLIN proteins, form the SCF-TIR1 E3 ligase complex. Thus, by fusing just the degron region (44–68 amino acids) of an AUX/IAA to a protein of interest, this target protein will be recruited by SCF-TIR1 and degraded by the proteasome, but only in the presence of IAA or NAA (Nishimura et al. 2009). Particularly, the study that developed the AID system leveraged the degron of the Arabidopsis INDOLE-3-ACETIC ACID INDUCIBLE17/AUXIN RESISTANT3 (IAA17/AXR3) protein to destabilize any target protein of interest (Fig. 2C). The AID system was first tested in yeast visually with a nuclear GFP as the target protein and functionally with DNA replication proteins or cell cycle

regulators as the targets. Both tests yielded positive results, where the proteins were degraded in the presence of auxin and untouched in its absence (Nishimura et al. 2009). To adapt the system to animal cells, a rice ortholog of *TIR1*, *OsTIR1*, replaced the *AtTIR1* because it conferred better thermostability to the AID system. The thermostable system was then subjected to the same tests in animal cells as in yeast, utilizing human cells for the visual depletion test and chicken cells for the functionality test. The AID system's generalizability later allowed for its use in other organisms like *Drosophila melanogaster* and *C. elegans* (Zhang et al. 2015; Trost et al. 2016; McClure et al. 2022).

Another phytohormone that has been utilized in animals is ABA. A study in mice modified ABA pathway proteins so that they could be used in a chemically induced proximity (CIP) system (Liang et al. 2011). Natively, ABA binds to a family of intracellular receptors called REGULATORY COMPONENTS OF ABA RECEPTORS (RCARs), specifically to the PYR 1-LIKE (PYL) component, which then goes on to physically interact with and inhibit PP2C activity. The study exploited this PYL-PP2C interaction by fusing a *GAL4* DNA binding domain with a coding region of the Arabidopsis *PP2C* gene *ABA INSENSITIVE1* (*ABI1*) and a *VP16* activation domain with a coding region of Arabidopsis *PYL*, ensuring that a *Luciferase* reporter gene with a GAL4-binding upstream activating sequence would only be transcribed in the presence of ABA (Fig. 2D). This system conferred transcriptional activity of the reporter gene in murine cells (NIH 3T3), human cells (HEK 293 T), and Chinese hamster ovary (CHO) cells with a linear ABA dose response (Liang et al. 2011). The ABA CIP system was found to be more stable, less toxic, and more affordable compared with using rapamycin, one of the more commonly used molecules for CIP in animals.

Promoters and promoter cis-elements

In molecular and synthetic biology, different types of biological parts have been exploited to create systems and circuits for the purpose of targeted, tunable gene expression in all types of organisms (Wang et al. 2013). A significant number of biotech applications involving transgenes have sourced DNA parts from Arabidopsis, including promoters, promoter motifs, transcriptional domains, and terminators. Due to the intricate knowledge that has been gathered on Arabidopsis signaling pathways, TFs, and their DNA binding motifs, Arabidopsis has become an essential resource for extracting well-characterized components to be employed in other organisms. Thus, for example, constitutive Arabidopsis promoters, such as that of *UBIQUITIN10* (*UBQ10*), a gene moderately active in nearly all Arabidopsis tissues, have been utilized in recombinant DNA constructs to drive genes of interest in different plant species (Norris et al. 1993). The *UBQ10* promoter was leveraged in a vector set developed in 2010 to fluorescently tag proteins to visualize their subcellular localization in transient expression assays (Grefen et al. 2010). The system, initially tested in Arabidopsis and tobacco, was successfully applied in other plants including *Medicago truncatula* (Zhang et al. 2022). The *UBQ10* promoter has also been utilized in rice to observe cytoplasmic Ca^{2+} responses in roots by driving the expression of a GFP-based Ca^{2+} sensor (Behera et al. 2015) and in apple as a stronger driver of gene expression of an array of genes than the classical *CaMV 35S* promoter (Wang et al. 2021b). Its wide range of applications gives credibility to the *UBQ10* promoter's transferability to other angiosperms.

Select promoter fragments can also be used to express genes of interest constitutively. *PD7*, a 456-base pair fragment from the Arabidopsis *SERINE CARBOXYPEPTIDASE-LIKE30* gene, was found to serve as a strong, constitutive promoter when transformed into Arabidopsis and *Nicotiana benthamiana*, with greater expression achieved than with the well-known *CaMV 35S* promoter (Jiang et al. 2018). The *PD7* promoter fused to *GUS* was subsequently evaluated in maize calli demonstrating that *PD7* was able to drive gene expression in that system at a higher level than a maize *UBQ1* promoter. These results confirmed that *PD7* is usable in both monocots and dicots for constitutive gene expression.

The ability to express a gene in a conditional, stimulus-inducible manner allows for tunable expression systems that respond to environmental signals but rests on the identification of signal-responsive DNA elements. Take for example pathogen detection, where pathogen-inducible promoter elements are leveraged to build reporters that respond either to pathogen-produced elicitors, such as chitin or flagellin, or to plant defense molecules, such as camalexins, salicylic acid (SA), or jasmonic acid (JA) (Huang et al. 2021). Arabidopsis is a reliable source of well-characterized pathogen-responsive promoters and DNA elements. A study from 2008 sourced 4 of the 10 pathogen-inducible cis-regulatory elements tested from promoter regions of Arabidopsis genes to create robust pathogen biosensors (Mazarei et al. 2008). Synthetic promoters made of a tandem of 4 copies of these defense-related cis-elements, *CaMV 35S* enhancer elements, and the *CaMV 35S* minimal promoter were fused to a β-*GLUCURONIDASE* (*GUS*) reporter gene. These biosensors were then evaluated in tobacco and Arabidopsis transgenic plants in response to plant-defense elicitor molecules or plant viruses (Mazarei et al. 2008). Several of these treatments induced the GUS activity in tobacco plants harboring reporters made with cis-elements from Arabidopsis *PATHOGENESIS-RELATED GENE1* (*PR1*) and *NONEXPRESSOR OF PR GENES1* (*NPR1*). For example, SA or chitin exposure and Alfalfa mosaic virus (AMV) inoculation all upregulated the GUS levels but ethephon application or Tobacco mosaic virus (TMV) infection did not, suggesting some level of biosensor construct specificity (Mazarei et al. 2008).

A follow-up study focused on the use of transient expression in *Agrobacterium*-infiltrated tobacco plants as a quick assay to test the inducibility of 4 plant defense cis-elements (Liu et al. 2011). Two of these elements were sourced from Arabidopsis, the aforementioned SA-responsive *PR1* motif and a JA responsive element (JAR) derived from the *VEGETATIVE STORAGE PROTEIN1* (*VSP1*) gene promoter. Synthetic promoters were created by fusing 4 copies of these

regulatory elements to a *CaMV 35S* (−46) core promoter with or without the *35S* enhancer motifs to a red fluorescent protein, *pporRFP* (Liu et al. 2011). Transient tobacco agroinfiltration assays showed that *PR1* constructs were responsive to SA, *JAR* constructs were induced by JA, and both types of reporters were upregulated by 2 different *Pseudomonas syringae* strains (Liu et al. 2011). This work demonstrates that Arabidopsis-sourced pathogen-responsive DNA cis-elements are functional in tobacco, implying the conservation of defense pathways across different plant species.

Hormone- and stress-inducible promoter fragments as well as short DNA elements derived from Arabidopsis genes have also been successfully employed in crops. For example, a synthetic promoter containing a tandem of 5 copies of the ETHYLENE INSENSITIVE3 binding site (EBS) from the native promoter of the Arabidopsis *ETHYLENE RESPONSE DNA-BINDING FACTOR1* gene fused to the *CaMV 35S* (−46) promoter (Stepanova et al. 2007) works well in tomato (Cruz et al. 2018; Althiab-Almasaud et al. 2021). Likewise, a dehydration-responsive element (DRE) from the Arabidopsis *RESPONSIVE TO DESICCATION 29A* (*RD29A*) gene functions in tobacco (Yamaguchi-Shinozaki and Shinozaki 1994) and soybean protoplasts (Kidokoro et al. 2015). Moreover, Arabidopsis stimulus-inducible promoter motifs can also be utilized to create synthetic promoters that reach expression levels similar to or higher than native promoters. Two synthetic promoters called *SAB* and *SBA* were made from DNA parts sourced from Arabidopsis cold-inducible promoters of the *COLD-REGULATED15A* (*COR15A*) and *COR15B* genes (Li et al. 2013). When tested in potato and tobacco plants, *SAB and SBA* reached levels of cold-inducible activity similar to that of the native *COR15B* promoter and higher than that of *COR15A*. The use of synthetic promoters, like in the case of *SAB* and *SBA*, can help identify important regions of native promoters for the optimization and tunability of spatio-temporal and stimuli-responsive gene expression.

Besides composite synthetic promoters, native Arabidopsis regulatory sequences that harbor full-length, stimulus-responsive promoters and adjacent regions of a gene can also function in other plant species. For example, a kilobase-long region of the Arabidopsis *HEAT SHOCK PROTEIN18.2* (*HSP18.2*) gene that includes the gene's promoter, 5′UTR, and the first 25 codons can drive heat-inducible expression in petunia (Takahashi and Komeda 1989), banana (Chong-Pérez et al. 2012), *Nicotiana plumbaginifolia* (Moriwaki et al. 1999), and *Saussurea involucrate* (Li et al. 2023a) but not in Marchantia polymorpha (Nishihama et al. 2016), suggesting that the functional conservation of the heat response pathways does not extend to non-vascular plants.

Arabidopsis-sourced promoters have also been utilized in the construction of synthetic genetic circuits that function in species beyond Arabidopsis. Czarnecka et al. developed a biosensor designed with transcriptional autofeedback loop to sense the presence of human bacterial pathogens in plants, particularly in lettuce (Czarnecka et al. 2012). This feedback loop system was engineered with a variety of flagellin- and *E. coli*–inducible Arabidopsis promoters, including that of *XYLOGLUCAN ENDOTRANSGLUCOSYLASE/HYDROLASE18* (*AtXTH18*) that was chosen based on this gene's robust induction profile in Arabidopsis upon treatment with flg22, a bacterial peptide elicitor commonly used to trigger plant immune responses (Felix et al. 1999). The inducible promoters were placed upstream of a strong synthetic transcriptional activator, *GAL4-VP16*, that gets transcribed in the presence of flg22 (Czarnecka et al. 2012). The GAL4-VP16 activator then binds to a proximal promoter that drives a firefly *Luciferase* reporter. In field applications, this reporter can be fused to or replaced by a protein that increases pathogen resistance in plants. The synthetic system was transiently expressed in Arabidopsis and lettuce protoplasts and tested with an array of promoters driving *GAL4-VP16*. In both species, the *AtXTH18* promoter had the highest transcriptional activity in response to flg22 among the promoters tested (Czarnecka et al. 2012). This pathogen-sensing system shows promise for implementation in leafy cultivars and provides a roadmap for the development of other biosensors in crops. This study underscores the utility of well-characterized Arabidopsis parts in synthetic biology applications that expand far beyond Arabidopsis.

Other DNA components

Although gene promoters are more predominantly utilized than other genetic parts by the synthetic biology community to modulate levels of gene expression, terminators have also been shown to have a significant impact on the expression of transgenes (de Felippes and Waterhouse 2022). Some studies have focused on testing a variety of terminators, as well as promoter-terminator pairs, to develop synthetic transcriptional units with optimal expression outputs (Gardiner et al. 2020). These terminators are typically sourced from plant viruses or plants themselves, with Arabidopsis being no exception. In fact, one of the most popular terminators sourced from Arabidopsis is the terminator from *HSP18.2* (*tHSP*) (Nagaya et al. 2010). In Arabidopsis, *tHSP* was shown to support gene expression of transgenes at a level about 2-fold higher than that achieved with the widely used bacterial *NOPALINE SYNTHASE* (*NOS*) terminator (Nagaya et al. 2010). The increase in expression levels caused by *tHSP* was found to be transferable when this terminator was employed in several transgenes outside of Arabidopsis, including in tomato to increase miraculin production (Hirai et al. 2011; Kurokawa et al. 2013), lettuce for the expression of a protein with potential to act as a vaccine for edema disease in pigs (Matsui et al. 2011), and chickpea to develop pest resistance against a gram pod borer (Singh et al. 2022). The Arabidopsis *tHSP* terminator is also commonly used in a promoter-terminator pair in conjunction with the previously mentioned *UBQ10* promoter (Huerta et al. 2023; Mellor et al. 2023).

Transcriptional regulation domains are another type of biological part commonly sourced from plants. Activator or repressor domains can be fused to DNA-binding domains to create new synthetic TFs that regulate transcription of a native or

synthetic gene. These factors are core to genetic circuitry, as they are part of the machinery that determines where and under what conditions a gene is expressed. There are some transcriptional regulation domains that have been isolated from Arabidopsis, with 1 notable example of an activation domain being the EDLL motif from ETHYLENE RESPONSIVE FACTOR98 (AtERF98) (Tiwari et al. 2012) and 1 prominent example of a repression domain being an ERF-associated amphiphilic repression (EAR) motif (Ohta et al. 2001). Both of these motifs have been employed in synthetic systems applied to organisms beyond Arabidopsis (Vazquez-Vilar et al. 2023). The developers of a CRISPR-based programmable activator fused an EDLL activation domain downstream of a dead/inactive version of Cas9 (dCas9) to create a synthetic transcriptional activator that provided strong, specific induction of targeted endogenous genes when tested in *N. benthamiana* (Selma et al. 2019). Arabidopsis-derived EDLL has also been utilized in an orthogonal control system in yeast, producing stronger transcriptional activation than the endogenous GAL4 activation domain when fused to TFs from the Arabidopsis NAC (NAM, ATAF1/2, and CUC2) protein family (Naseri et al. 2017). On the other hand, a modified EAR motif taken from an Arabidopsis gene *SUPERMAN* (*SUP*) was employed in the creation of a chimeric repressor silencing technology (CRES-T) that can flip a TF of interest from an activator to a repressor (Hiratsu et al. 2003). This repression domain was dubbed SRDX and was subsequently tested in *Phalaenopsis aphrodite* (Lu et al. 2021), poplar (Wang et al. 2021a), liverwort (Ishizaki et al. 2015), and *Torenia fournieri* Lind. (Sasaki et al. 2014) in various repression systems.

Biotechnology methods pioneered in Arabidopsis

The versatility and convenience of studying cellular and molecular processes in Arabidopsis has given rise to important biotechnological methods that are easily applicable to studies in other organisms. One of these methods, created for the purpose of studying cell-specific transcriptomics of ribosome-associated mRNAs, is translating ribosome affinity purification (TRAP) (Zanetti et al. 2005). TRAP was originally developed in Arabidopsis as a way to isolate ribosome-associated transcripts for the quantification of gene expression via affinity purification. The success of this methodology led to the development of BACarray, a translational profiling methodology that utilized TRAP in a cell type-specific manner, in mice (Doyle et al. 2008; Heiman et al. 2008). TRAP was also adopted for use in zebrafish and later inspired the development of Trap-TRAP, a translatomics method that combined a traditional enhancer trap approach with TRAP (Tryon et al. 2013; Corbacho et al. 2022). Furthermore, TRAP has also been adapted and optimized to detect translating RNAs from rare cell populations in *Drosophila* embryos (Bertin et al. 2015). In Arabidopsis, the method has been used in combination with RNA-seq, dubbed TRAP-seq, to study cell-type specific gene expression of early floral development in Arabidopsis at a nucleotide resolution (Jiao and Meyerowitz 2010) (Fig. 3A). In this study, ribosomal proteins tagged with His and FLAG epitope tags were driven by cell type-specific promoters from 3 different master regulators of flower development, *APETALA1* (*AP1*), *APETALA3* (*AP3*) and *AGAMOUS* (*AG*), to capture all translating cellular mRNAs in specific tissue types via immunopurification. TRAP-seq was able to isolate cell-type specific mRNAs at a high yield and avoided issues of RNA bias that results from RNA amplification steps that may be necessary in methods like laser-capture microdissection and fluorescence-activated cell sorting (Galbraith and Birnbaum 2006). The TRAP and RNA-seq combination method was then tested in mice to profile rare cell populations in vivo (Hupe et al. 2014), in frogs to translationally profile optic nerve regeneration (Whitworth et al. 2017), and in soybean to study root cortex response to rhizobial inoculation (Song et al. 2022). TRAP and TRAP-seq continue to be improved upon and utilized in many applications within and outside of Arabidopsis (Reynoso et al. 2015; Traubenik et al. 2020).

Another method, given the name INTACT, which stands for isolation of nuclei tagged in specific cell types, was developed in Arabidopsis by Deal and Henikoff in 2011 (Deal and Henikoff 2011). This method utilizes affinity purification and biotinylation of nuclear envelope proteins tagged with GFP (nuclear targeting fusion protein; NTF) to isolate nuclei in specific cell-types (Fig. 3B). The system leverages a constitutively expressed *E. coli* biotin ligase, BirA, and an NTF expressed in the cell type of interest to produce nuclei with a biotin label only in the cells of interest. INTACT boasts a 50% to 70% theoretical yield of tagged nuclei with a 90% to 98% purity, with the study that developed it declaring a 93% purity and a recovery of 1.5×10^5 of root hair cell nuclei from 3 grams of wet roots (Deal and Henikoff 2011). The method was later utilized in mice to study the neuronal epigenome as the first application of INTACT in mammals (Mo et al. 2015). In the mouse study, a nuclear membrane protein, GFP, and a Myc-tag were employed to create a constitutively expressed NTF with a *loxP-3x polyA-loxP* upstream transcriptional roadblock, which is only removed in the presence of a Cre recombinase. This recombinase is expressed in a cell-specific manner to target excitatory neurons, pavalbumin interneurons, and vasoactive intestinal peptide interneurons (Mo et al. 2015). Using anti-GFP affinity-purification, INTACT applied to this mammalian system achieved more than a 50% yield with high purity (>98%), which aligns with the original claims of INTACT's capabilities. INTACT has also been implemented in frogs (Wasson et al. 2019), rice (Reynoso et al. 2018), flies, and *C. elegans* (Steiner et al. 2012). The use of Arabidopsis for the development of INTACT exemplifies the convenience of using this model organism to determine the accuracy and efficacy of new methods.

Both of the aforementioned methods, TRAP and INTACT, involve the creation of transgenic lines, which is not a feasible approach for some species. A nontransgenic approach for the study of gene mechanisms arose in 2000 to screen chemically induced mutations in the genome using ethyl

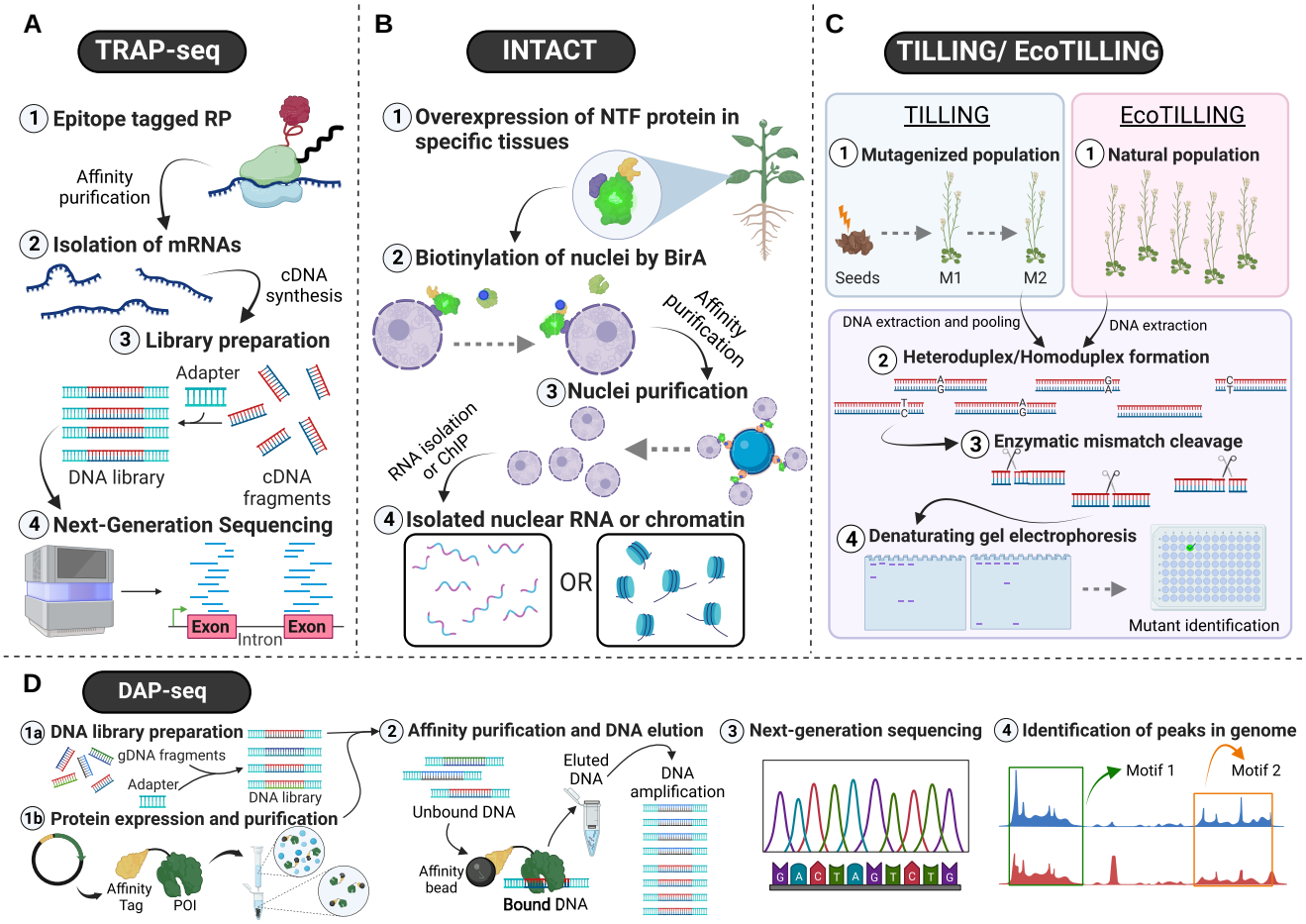


Figure 3. Biotechnology methods developed in Arabidopsis. Schematics describing the steps of each Arabidopsis-developed biotechnology discussed in this review are displayed. **A)** TRAP-seq begins with cell-type-specific promoter-driven expression of a tagged ribosomal protein (RP). Affinity purification is performed by leveraging epitope-specific antibodies to pull down tagged ribosomes along with mRNAs the ribosomes are translating. mRNAs are isolated, and reverse transcription is employed to synthesize cDNA. The cDNA library is prepped and sequenced prior to downstream computational analysis. **B)** The INTACT method starts with cell-type-specific expression of a synthetic NTF protein and constitutive expression of a bacterial biotin ligase BirA. Nuclei of cells in which NTF is expressed and bound to the nuclear envelope get biotinylated by BirA. Tagged and biotinylated nuclei are pulled down through affinity purification with streptavidin beads. Nuclear RNAs or chromatin are then extracted through RNA isolation or chromatin immunoprecipitation (ChIP), respectively, for downstream applications. **C)** TILLING utilizes a chemical mutagen (visualized as an orange lightning bolt) to induce random genomic mutations in a population of seeds. The M1 plants are selfed to produce M2 plants, DNA is extracted from M2 s, and pooled for high-throughput screening. Target genes of interest are amplified by PCR and the amplicons are denatured and re-annealed to form either heteroduplexes (containing a mismatch due to a mutation) or homoduplexes (no mismatches). The DNA products are then subjected to enzymatic cleavage by CEL1 endonuclease that preferentially cuts heteroduplexes at the mismatched sites. The products of CEL1 digestion are separated on a gel to identify mutations that show up as smaller digestion products on a gel. EcoTILLING follows a similar protocol to TILLING but uses DNA from unpooled natural populations to detect existing variation instead of generating and identifying mutants. **D)** The process of DAP-seq begins with tagged recombinant protein expression and genomic DNA isolation, fragmentation, and adapter ligation. The tagged proteins of interest (POI) are purified and immobilized on affinity beads. DNA affinity purification is performed to isolate the genomic fragments that the POI binds to in vitro. Bound DNA is eluted, amplified by PCR and subjected to next-generation sequencing. Reads are mapped to identify POI-binding motifs enriched in DAP-seq peaks. Images created with BioRender.

methanesulfonate for the mutagenesis and denaturing high-performance liquid chromatography for detection of base pair changes (McCallum et al. 2000). This approach, called targeting induced local lesions in genomes (TILLING), was developed in Arabidopsis in a pursuit to study the function of *CHROMOMETHYLASE* (*CMT*) (Fig. 3C). There was originally thought to be one *CMT* gene (*CMT1*) in the Arabidopsis genome, but after *CMT1* was found to be nonessential, 2 more *CMT* genes were identified, *CMT2* and *CMT3*, by probing an Arabidopsis genomic library (McCallum et al. 2000). Creating mutants in either of these newly discovered genes was more difficult than originally anticipated, as standard reverse genetics methods failed to either silence or knockout *CMT2* gene expression. Thus, TILLING was employed to generate *cmt2* and *cmt3* knockout mutants in the background of the natural *cmt1* null No-0 ecotype. Several mutations were

identified in both genes, with 1 *CMT3* mutation causing a truncation that presumably knocks out enzymatic function, validating the efficacy of TILLING (McCallum et al. 2000). The method was later improved with the use of a celery-derived endonuclease, CEL1, which is able to cleave at the mismatches in the heteroduplexes that are formed upon denaturation and reannealing of 2 or more chromosomes with differing sequences, allowing TILLING to become a more high-throughput method (Colbert et al. 2001). TILLING proved to be translatable to other species and was successfully adapted to maize, barley, fruit flies, nematodes, and zebrafish, to name a few (Barkley and Wang 2008). Thus, this technology originally developed in Arabidopsis is a versatile reverse genetics approach to carry out functional genomics work in a variety of species without the need for transgenesis. TILLING gave rise to EcoTILLING, which was created to study the function of genes by observing natural genetic variation instead of detecting chemically induced mutations (Comai et al. 2004) (Fig. 3C). EcoTILLING has since been utilized in multiple species, including black cottonwood, barley, mung bean, and even humans, for natural SNP detection (Barkley and Wang 2008). Several TILLING and/or EcoTILLING centers have been established across the world for many of the species that TILLING has been tested in, especially for those with an agricultural focus. Even now, TILLING is still being employed in many species, often with the help of next-generation sequencing to detect mutations (Sharma et al. 2022).

One of the more recent techniques born out of Arabidopsis research is DNA affinity purification sequencing (DAP-seq), an assay used to identify TF binding sites within genomic DNA (O'Malley et al. 2016). It combines affinity purification of tagged TFs bound to DNA and high-throughput sequencing to generate a genome-wide TF binding site map (Fig. 3D). The study that tested and developed DAP-seq leveraged Arabidopsis genomic DNA and recombinantly expressed Arabidopsis TFs to partially define the Arabidopsis cistrome, reporting data from close to 2,300 individual DAP-seq experiments (O'Malley et al. 2016). The method was also applied to maize in the same study to compare the binding landscapes of Arabidopsis and maize AUXIN RESPONSE FACTOR (ARF) family members. Since then, DAP-seq has been applied to a variety of species, from rice to bacteria to fish (Trouillon et al. 2021; Zhu et al. 2021; Wang et al. 2022). The disadvantage of this approach is that TF binding may be dependent on cofactors or other protein partners that aren't available in this in vitro method. Additionally, since DAP-seq is carried out with naked DNA and thus is independent of structural restrictions imposed by chromatin, it may capture TF-DNA interactions that do not normally occur in a native context. However, this is also an advantage, as it reveals the global binding landscape of a TF, regardless of chromatin accessibility or histone modifications. For a more accurate depiction of what occurs natively, DAP-seq is often employed in conjunction with other methods like DNase-seq and Assay for Transposase-Accessible Chromatin using sequencing (ATAC-seq) to provide a faster and cheaper way to identify in vivo TF binding sites than is currently possible with the widely used in vivo chromatin immunoprecipitation sequencing (ChIP-seq), which requires protein-specific antibodies or tagged marker lines (Park 2009; Bartlett et al. 2017). In 2023, a new method that builds on DAP-seq was published, called double DAP-seq (dDAP-seq), that allows for the mapping of heterodimer binding sites within genomic DNA and provides a new way to study the effect of TF-TF interactions on the stability and binding specificity of a particular TF (Li et al. 2023b). As an emerging technology, DAP-seq continues to be utilized in a range of applications to discover novel TF-DNA interactions to this day (Liu et al. 2021; Gomez-Cano et al. 2022; Hutin et al. 2023).

Computational approaches in the transfer of Arabidopsis knowledge

The era of next-generation sequencing and high-throughput -omics led to the creation of a vast collection of computational tools used to store, process, and analyze large amounts of data (Argueso et al. 2019). Examples of databases and warehouses created to store and analyze Arabidopsis data include The Arabidopsis Information Resource (TAIR), a database of genetic and molecular biology data (Huala et al. 2001); the Arabidopsis Gene Regulatory Information Server (AGRIS), a database server for Arabidopsis cis-regulatory elements, TFs, and TF targets (Davuluri et al. 2003); the 1001 Genomes Project, a resource for multiple types of Arabidopsis centered databases and tools (Alonso-Blanco et al. 2016); and ThaleMine, a data warehouse that integrates information from TAIR10, SwissProt, Panther, GO, and more (Krishnakumar et al. 2017) (Fig. 4). Arabidopsis, with its wealth of data generated from numerous research studies and a well-connected community of scientists, has become a hub for translating fundamental research to broader biotechnological and synthetic biology tools.

The large amount of data generated in the 2000s led to the rapid development of a wide array of databases to store and organize both raw and curated data. AraCyc was one of those databases, developed specifically for Arabidopsis metabolic pathways (Mueller et al. 2003) (Fig. 4A). Studies would then go on to use AraCyc as a resource when mining for genes involved in particular metabolic pathways. For example, a study attempting to identify sulfur-encoding biosynthetic genes in rice employed AraCyc to find *SULFUR-CONTAINING COMPOUND* (*SCC*) genes in Arabidopsis (Abdullah-Zawawi et al. 2022). These genes were then used to identify 25 orthologs of Arabidopsis *SCC* biosynthetic genes in rice that could later be putatively targeted in rice breeding. The cultivation of AraCyc led to the ability to translate Arabidopsis findings into rice and other species, highlighting the importance of Arabidopsis-focused research and data curation.

These databases also go on to fuel the creation of data analysis tools, such as MapMan (Fig. 4B). MapMan is a user-friendly tool developed to display genomics-based datasets

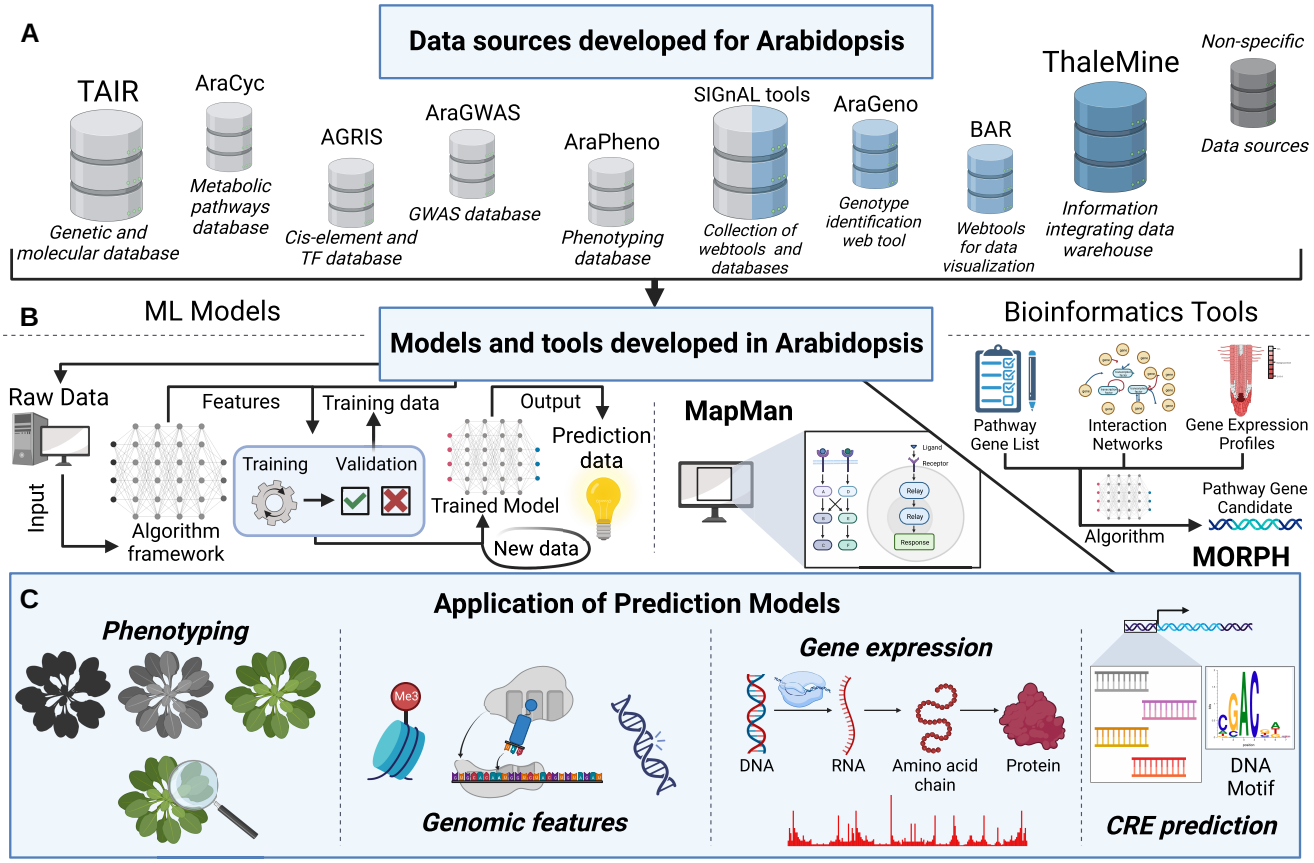


Figure 4. Relationship between data sources, machine learning models, and applications of prediction models in Arabidopsis. Panel A: A noncomprehensive compilation of existing Arabidopsis databases in light gray (TAIR (Huala et al. 2001), AraCyc (Mueller et al. 2003), AGRIS (Davuluri et al. 2003), AraGWAS (Togninalli et al. 2020), AraPheno (Togninalli et al. 2020), data warehouses in dark blue [ThaleMine (Krishnakumar et al. 2017)] and webtools in light blue [AraGeno (Pisupati et al. 2017) and the Bio-Analytic Resource for Plant Biology (BAR) (Waese and Provart 2017)]. The extensive SIGnAL tool collection contains both webtools and databases (Alonso et al. 2003). These data sources feed training or reference data into models and tools for Arabidopsis along with other, non-Arabidopsis-specific data sources (in dark gray). Font size indicates the comparative general size of the information resource. Panel B: Schematic of machine learning (ML) models and bioinformatics tools developed in Arabidopsis. Left side describes a typical ML workflow, where raw data are used to generate features of importance for the model. Features and training data are utilized as input for a training-validation process to train the model. Trained models can then take new data and make predictions based on what the model has learned from the training data. Right side shows a general overview of bioinformatic tools, MapMan and MORPH. Panel C: A graphical representation of possible prediction model applications in plants. Phenotyping applications often involve prediction of a phenotypic trait, with many models developed for plant growth predictions. Genomic features can also be predicted by ML, with some examples of features (left to right) being methylation markers, translation initiation sites, and classification of DNA mutations. Prediction models are also generated to predict gene expression patterns and cis-regulatory elements (CREs) associated with particular tissues, developmental stages, or responses to stimuli. Images created with BioRender.

in the context of metabolic and biological pathways (Thimm et al. 2004). It was developed and tested using Arabidopsis data to visually group genes, even those with limited functional information, based on function, response, or gene family. This tool was later adapted to be used for other species, such as rice, barley, and maize (Usadel et al. 2009). To showcase the utility of an Arabidopsis-inspired tool like MapMan, a case study was done to compare gene expression changes when plants were grown in a typical light/dark cycle vs a cycle with an extended dark period (Usadel et al. 2009). This experimental set-up allows for a focus on metabolism of photoassimilates. The results suggested that although some gene expression changes in Arabidopsis were similar to that in maize, there were still some key differences across species (Usadel et al. 2009). This case study underscores the ability of MapMan to be used in comparative global gene expression analysis studies to identify the degree to which we can transfer knowledge from a model species, like Arabidopsis, to more application-oriented crop species.

An algorithm for module-guided ranking of candidate pathway genes (MORPH) was developed for both Arabidopsis and tomato in 2012 by Tzfadia et al (Tzfadia et al. 2012). The model takes a list of genes from a particular pathway, gene expression profiles, and an interaction network as inputs and employs a machine learning (ML) algorithm to output a ranked list of candidate genes that may be associated with the target pathway (Fig. 4B). In the study, the list of pathway-specific genes for Arabidopsis was extracted from both MapMan and AraCyc, while for tomato, only MapMan was utilized as a resource (Tzfadia et al. 2012). The gene networks used for tomato were also created by lifting Arabidopsis networks and translating them to tomato based on sequence homology since tomato networks are far less annotated than the ones for Arabidopsis. Gene expression profiles for both species were sourced from published microarray experiments. MORPH performed better compared with other algorithms for both Arabidopsis and tomato, signifying its capability to reliably predict candidate genes associated with a specified pathway (Tzfadia et al. 2012). Its ability to maintain prediction power despite the curation of homology-based tomato gene networks underlines the transferability of Arabidopsis gene networks to genetically long-diverged species. The MORPH method was later integrated into MorphDB, a platform with the capability to perform genome-wide comparative analysis across species of candidate genes predicted by MORPH (Zwaenepoel et al. 2018).

With the rapid increase of computational power over the past few decades, it has become common to utilize ML algorithms for a variety of plant- or gene-specific analyses (Mahood et al. 2020). The sheer amount of Arabidopsis research that has been done over the years to generate raw and curated data makes Arabidopsis an ideal organism to train ML models on. However, the data used need to be translatable, at least in part, to other species. The degree to which Arabidopsis findings are transferable can be deduced by applying a model pre-trained with Arabidopsis data to another species (Magana-Mora et al. 2013; Kovalev et al. 2018; Chang et al. 2021). This allows researchers to determine accuracy and robustness of the model by comparing prediction with a known output (Jiao and Du 2016). This process will occasionally involve comparing the performance of the new model to a trusted, established model's performance, provided that such a model exists. Some ML models are generally built and trained on Arabidopsis data as a proof of concept specifically because of the large amount of information available (Koryachko et al. 2015), but may or may not be successful when applied to other species due to an inherent lack of conservation of specific pathways or genes across species. A study from 2020 using a ML model to predict specialized and general metabolism genes found that when the model was trained on Arabidopsis data and applied to tomato, the prediction accuracy dropped significantly when compared with a tomato-trained model (Moore et al. 2020). However, several noteworthy applications have successfully employed models pre-trained on Arabidopsis to predict information in other species (Fig. 4C) and some illustrative examples of these are detailed below.

Dragon TIS Spotter is a prediction tool for translation initiation sites (TIS) in plants that was intentionally built using Arabidopsis information and then tested in other species (Magana-Mora et al. 2013). This tool takes only genomic sequences as input, and outputs predicted true TIS motifs using features optimized by a genetic algorithm search. To build this model, an artificial neural network was trained on close to 19,000 genuine TIS sample sites from genes annotated as "protein coding" that were extracted from the Arabidopsis genome available at the time of the study. Arabidopsis test data results showed a sensitivity/specificity (Se/Sp) of 90.75%/92.2%, while for grape and black cottonwood, Se/Sp was 66.8%/94.4% and 81.6%/94.4%, respectively (Magana-Mora et al. 2013). This indicated that the Arabidopsis-derived model had some room for improvement when trying to identify all true TIS sites, but also that the prediction was reliable when it comes to rejecting sites that are not true TIS motifs.

Another example of using Arabidopsis to pre-train models is a pipeline developed in 2018 for the classification of deleterious mutations in the coding regions of crops (Kovalev et al. 2018). A Random Forest (RF) classifier was trained on a dataset of deleterious and neutral mutations in Arabidopsis for the purpose of identifying deleterious mutations in rice, pea, and chickpea. The RF classifier was able to predict deleterious mutations at an accuracy of 87% for rice and 93% for pea, higher than a popular ML method called PolyPhen-2 that was trained on human data (Kovalev et al. 2018). Both models were then applied to nonsynonymous SNPs from a new species, chickpea. The results revealed that the frequency of deleterious mutations is significantly lower compared with neutral and synonymous mutations, which is consistent with what is found in other species (Kovalev et al. 2018). In the future, the predictions from the RF classifier developed in this study could be used to inform plant domestication and breeding efforts, even though a non-crop model plant was used to initially train the classifier.

Pre-trained models can also be used for phenotyping applications. A deep learning (DL) model initially trained on Arabidopsis was reused to analyze images of plant growth over time to identify phenotypic differences in lettuce upon growth pattern analysis (Chang et al. 2021). The accuracy of the pre-trained model was similar to that reported in other studies using ML to identify crop segmentation where the same crop was used to both train and test the model. This DL model, originally developed for Arabidopsis, exemplifies how the short growth cycle and compact size of this model organism can be leveraged to generate generalized but accurate computational models that are easy to use for plant biologists and applied scientists working with non-model crops.

Besides phenotyping models, there has also been a multi-step DL model developed that utilized Arabidopsis cistrome datasets to predict patterns of gene expression across the

genome in tomato fruit (Akagi et al. 2022). Known Arabidopsis TF DNA binding preferences were used to infer arrays of putative cis-regulatory elements (CREs) for tomato genes, which were then relied on to predict expression patterns in the next DL step. The conservation of TF family-specific DNA-binding domains across species, as well as the extensive curation of Arabidopsis genes, allow for this kind of application. The results were experimentally validated through DAP-seq analysis on 6 tomato TFs corresponding to the Arabidopsis TFs used for CRE prediction, successfully confirming 85% to 96% of predicted CREs (Akagi et al. 2022).

One emerging field in plant sciences that greatly benefits from ML models being trained on Arabidopsis data is single-cell RNA sequencing (scRNA-seq). A study from 2022 showcases this by developing an ML pipeline called single-cell predictive marker (SPmarker) that identifies cell-specific markers in scRNA-seq data to assign cells to their respective cell types (Yan et al. 2022). Sequencing data from over 25,000 cells across 5 published scRNA-seq datasets from the Arabidopsis root were employed in the training of this pipeline. The pipeline was able to identify novel marker genes not only in Arabidopsis, but also in other species, including rice, cucumber, soybean, tomato, and maize (Yan et al. 2022). Given that scRNA-seq is currently quite expensive to perform, the ability to use Arabidopsis data to accurately predict markers in species lacking publicly available scRNA-seq datasets and well annotated genomes can greatly improve accuracy of classification and reduce the need for large species-specific training datasets.

Models trained on Arabidopsis data can also have use outside of the plant field. A neural network model called Deeplearning Explore Nanopore m^6A (DENA) trained directly on Nanopore RNA-seq data of in vivo mRNA transcripts from Arabidopsis was used to map N^6-methyladenosine (m^6A) modification sites in human transcripts (Qin et al. 2022). To train the model, the researchers used WT and mutant Arabidopsis lines, where the mutant lines were deficient in the ability to modify mRNA with m^6A. DENA proved to have an accuracy and reliability similar to a method developed using human RNA-seq data, SCARLET (Liu et al. 2013). It was the first method that attempted to directly use in vivo mRNA sequencing data to train an m^6A detection model, which circumvented noise issues that previous models had when trained on synthetic in vitro data. DENA is a prime example of how Arabidopsis mutants can inform ML models to accurately predict features in a cross-species fashion.

The examples highlighted in this review represent only a fraction of the ways in which large datasets generated from Arabidopsis research have been used to benefit crop species through computational prediction models. More examples may be found in a plant-focused ML review by Mahood *et al.* (Mahood et al. 2020).

Concluding remarks

With its short life cycle, compact size, prolific seed set, small and well-annotated genome, as well as the general conservation of molecular processes, *Arabidopsis thaliana* has proven to be an exceptional model organism for the generation of foundational knowledge and the development of biotechnological tools. The availability of information in Arabidopsis from resources like TAIR and ThaleMine has facilitated the transfer of knowledge from model plants to crops to illuminate biological mechanisms and pathways underlying plant development, general stress responses, and disease tolerance. Even when genes in Arabidopsis are not directly translatable to other species, we may still gain insight into conservation of molecular pathways in a quick and high-throughput manner. Integration of ML approaches with molecular techniques has empowered our ability to predict gene patterns, features, and expression levels in Arabidopsis and evaluate the efficiency at which Arabidopsis data can be used to pre-train prediction models. Those ML models have consequently facilitated the efficient and scalable analyses of genetic and functional conservation of genes and pathways across diverse species.

Nonetheless, there are limitations and challenges associated with leveraging Arabidopsis to draw conclusions about molecular processes and mechanisms in plants of agronomic importance or in biomedically relevant animal models. Although Arabidopsis is easy to work with, the evolutionary distance between Arabidopsis and other species affects the degree to which fundamental discoveries in Arabidopsis can be translated into practical agricultural or biomedical applications. The disparities in regulatory pathways and genetic networks may pose a challenge when attempting to utilize Arabidopsis findings to enhance crop productivity or to understand the molecular basis of a human disorder. When assessing agricultural relevance of Arabidopsis research, it is important to keep in mind that in many of the plant studies cited in this review, the effects of genes of interest on crop traits were evaluated in plants grown under environmentally controlled conditions. Traits like yield are, however, highly polygenic, with multiple contributing genes differentially responding to environmental inputs in accordance with soil and water management (Benavente and Giménez 2021). With numerous epistatic interactions occurring between these genes, the specific responses of plants become hard to predict, and thus the results of environmentally controlled studies are difficult to extrapolate to highly variable field conditions. Rigorous testing in agriculturally relevant contexts—open fields or orchards, tunnels, greenhouses, or commercial indoor farms—is still required to establish the true economic importance of identified gene variants.

To properly assess the utility of Arabidopsis-derived findings when translating knowledge into crops, 5 important criteria recently defined by Khaipho-Burch and colleagues need to be followed (Khaipho-Burch et al. 2023). These criteria are (1) outlining standard definitions of yield; (2) replication of trials across various locations and years; (3) utilization of planting practices that match those of farms; (4) use of appropriate controls; and (5) prioritization of genes not already

targeted by plant breeding. Following these important standards will expedite the identification of genetic variants with significant effects on beneficial crop traits in commercially relevant settings.

In summary, while translation of Arabidopsis findings to useful advancements in applied sciences or practical breakthroughs presents inherent challenges that must be carefully addressed, Arabidopsis remains an invaluable model system for both fundamental and applied research. Clearly, a balanced approach is necessary. Focusing solely on Arabidopsis would divert resources needed to address specific challenges faced by major crops and impede progress in meeting global food security and sustainability demands. However, diverting too many resources away from fundamental research in Arabidopsis will greatly slow the pace of critical foundational discoveries and technological developments that propel innovation. Therefore, a balance between expanding Arabidopsis knowledge and implementing existing discoveries in crops necessitates a rational -and complementary- allocation of resources to ensure that new insights continue to be generated in Arabidopsis and effectively translated into practical advancements within and beyond the agricultural world. This quandary calls for interdisciplinary, strategic approaches that combine fundamental Arabidopsis research with focused translational efforts to bridge the gap between model and applied systems, aiming for a comprehensive understanding of gene networks and biological processes that can be translated to practical solutions.

Ultimately, the historical and ongoing utilization of Arabidopsis as a translational model for agricultural systems, biomedical research, biotechnology development, and computational biology applications continues to hold great promise for deepening our comprehension of genetic interactions and regulatory networks in the realm of plant biology and beyond. Going forth, Arabidopsis-made discoveries will continue to provide answers to modern-day questions and quandaries in different fields of science that intersect with foundational plant biology (Goloubinoff et al. 2022; Roeder et al. 2022; Armstrong et al. 2023). We hope that the next 50 years of Arabidopsis research will be just as productive and exciting, with emphasis on tool development, exploration of technically challenging concepts and ideas, and new foundational discoveries. This knowledge base then needs to be translated to agricultural crops and biomedical applications to close the knowledge gap and reinforce the efficacy of employing Arabidopsis in the development of resilient, high-yielding crops, innovative research tools, and biotechnological solutions. Through joining forces, fundamental and applied plant scientists, bioinformaticians, engineers, teachers, and other professionals can continue to harness the power of this small plant for the betterment of the world we all live in.

Acknowledgments

We would like to thank Joanna Friesner, Ross Sozzani, Cranos Williams, Adrienne Roeder, Jade Lyons, Katie Vollen, and the anonymous reviewers for their constructive suggestions on this manuscript. We are also grateful to past and current members of the North American Arabidopsis Steering Committee for fruitful discussions on the utility and challenges of relying on Arabidopsis as a reference for translational work.

Author contributions

All authors contributed to writing, reviewing, and editing the article. A.E.Y. contributed to creating the figures.

Funding

The work in the Alonso-Stepanova lab is supported by the National Science Foundation grants 1444561, 1940829, and 2327912 to JMA and ANS, and 1750006 to ANS. AEY is a recipient of the Genetics and Genomics Scholars fellowship from NC State University and of Molecular Biotechnology Training Program grant from the National Institutes of Health.

Conflict of interest statement. None declared.

Data availability

No new data were generated or analysed in support of this research.

References

Abdullah-Zawawi M-R, Govender N, Muhammad NAN, Mohd-Assaad N, Zainal Z, Mohamed-Hussein Z-A. Genome-wide analysis of sulfur-encoding biosynthetic genes in rice (Oryza sativa L.) with Arabidopsis as the sulfur-dependent model plant. Sci Rep. 2022:**12**(1):13829. https://doi.org/10.1038/s41598-022-18068-0

Akagi T, Masuda K, Kuwada E, Takeshita K, Kawakatsu T, Ariizumi T, Kubo Y, Ushijima K, Uchida S. Genome-wide cis-decoding for expression design in tomato using cistrome data and explainable deep learning. Plant Cell. 2022:**34**(6):2174–2187. https://doi.org/10.1093/plcell/koac079

Alonso-Blanco C, et al. 1,135 genomes reveal the global pattern of polymorphism in Arabidopsis thaliana. Cell. 2016:**166**(2):481–491. https://doi.org/10.1016/j.cell.2016.05.063

Alonso JM, Stepanova AN, Leisse TJ, Kim CJ, Chen H, Shinn P, Stevenson DK, Zimmerman J, Barajas P, Cheuk R, et al. Genome-wide insertional mutagenesis of Arabidopsis thaliana. Science. 2003:**301**(5633):653–657. https://doi.org/10.1126/science.1086391

Althiab-Almasaud R, Sallanon H, Chang C, Chervin C. 1-Aminocyclopropane-1-carboxylic acid stimulates tomato pollen tube growth independently of ethylene receptors. Physiol Plant. 2021:**173**(4):2291–2297. https://doi.org/10.1111/ppl.13579

Alvarez JP, Pekker I, Goldshmidt A, Blum E, Amsellem Z, Eshed Y. Endogenous and synthetic MicroRNAs stimulate simultaneous, efficient, and localized regulation of multiple targets in diverse species. Plant Cell. 2006:**18**(5):1134–1151. https://doi.org/10.1105/tpc.105.040725

Anjanappa RB, Gruissem W. Current progress and challenges in crop genetic transformation. J Plant Physiol. 2021:**261**:153411. https://doi.org/10.1016/j.jplph.2021.153411

Arabidopsis Genome Initiative. Analysis of the genome sequence of the flowering plant Arabidopsis thaliana. Nature. 2000:**408**(6814):796–815. https://doi.org/10.1038/35048692

Argueso CT, Assmann SM, Birnbaum KD, Chen S, Dinneny JR, Doherty CJ, Eveland AL, Friesner J, Greenlee VR, Law JA, et al. Directions for research and training in plant omics: big questions and big data. Plant Direct. 2019:**3**(4):e00133. https://doi.org/10.1002/pld3.133

Armstrong EM, Larson ER, Harper H, Webb CR, Dohleman F, Araya Y, Meade C, Feng X, Mukoye B, Levin MJ, et al. One hundred important questions facing plant science: an international perspective. New Phytol. 2023:**238**(2):470–481. https://doi.org/10.1111/nph.18771

Arroyo-Herrera A, Ku Gonzalez A, Canche Moo R, Quiroz-Figueroa FR, Loyola-Vargas VM, Rodriguez-Zapata LC, Burgeff D′Hondt C, Suárez-Solís VM, Castaño E. Expression of WUSCHEL in Coffea canephora causes ectopic morphogenesis and increases somatic embryogenesis. Plant Cell Tiss Organ Cult. 2008:**94**(2):171–180. https://doi.org/10.1007/s11240-008-9401-1

Aslam M, She Z, Jakada BH, Fakher B, Greaves JG, Yan M, Chen Y, Zheng P, Cheng Y, Qin Y. Interspecific complementation-restoration of phenotype in Arabidopsis cuc2cuc3 mutant by sugarcane CUC2 gene. BMC Plant Biol. 2022:**22**(1):47. https://doi.org/10.1186/s12870-022-03440-z

Bancroft I, Morgan C, Fraser F, Higgins J, Wells R, Clissold L, Baker D, Long Y, Meng J, Wang X, et al. Dissecting the genome of the polyploid crop oilseed rape by transcriptome sequencing. Nat Biotechnol. 2011:**29**(8):762–766. https://doi.org/10.1038/nbt.1926

Barkley NA, Wang ML. Application of TILLING and EcoTILLING as reverse genetic approaches to elucidate the function of genes in plants and animals. Curr Genomics. 2008:**9**(4):212–226. https://doi.org/10.2174/138920208784533656

Bartlett A, O'Malley RC, Huang SC, Galli M, Nery JR, Gallavotti A, Ecker JR. Mapping genome-wide transcription-factor binding sites using DAP-seq. Nat Protoc. 2017:**12**(8):1659–1672. https://doi.org/10.1038/nprot.2017.055

Behera S, Wang N, Zhang C, Schmitz-Thom I, Strohkamp S, Schültke S, Hashimoto K, Xiong L, Kudla J. Analyses of Ca2+ dynamics using a ubiquitin-10 promoter-driven yellow cameleon 3.6 indicator reveal reliable transgene expression and differences in cytoplasmic Ca2+ responses in Arabidopsis and rice (Oryza sativa) roots. New Phytol. 2015:**206**(2):751–760. https://doi.org/10.1111/nph.13250

Benavente E, Giménez E. Modern approaches for the genetic improvement of rice, wheat and maize for abiotic constraints-related traits: a comparative overview. Agronomy. 2021:**11**(2):376. https://doi.org/10.3390/agronomy11020376

Bertin B, Renaud Y, Aradhya R, Jagla K, Junion G. TRAP-rc, translating ribosome affinity purification from rare cell populations of Drosophila embryos. J Vis Exp. 2015:**103**:52985. https://doi.org/10.3791/52985

Blümel M, Dally N, Jung C. Flowering time regulation in crops—what did we learn from Arabidopsis? Curr Opin Biotechnol. 2015:**32**:121–129. https://doi.org/10.1016/j.copbio.2014.11.023

Booker J, Auldridge M, Wills S, McCarty D, Klee H, Leyser O. MAX3/CCD7 is a carotenoid cleavage dioxygenase required for the synthesis of a novel plant signaling molecule. Curr Biol. 2004:**14**(14):1232–1238. https://doi.org/10.1016/j.cub.2004.06.061

Bouchabké-Coussa O, Obellianne M, Linderme D, Montes E, Maia-Grondard A, Vilaine F, Pannetier C. Wuschel overexpression promotes somatic embryogenesis and induces organogenesis in cotton (Gossypium hirsutum L.) tissues cultured in vitro. Plant Cell Rep. 2013:**32**(5):675–686. https://doi.org/10.1007/s00299-013-1402-9

Braun A. Sitzungsberichte der gesellschaft naturforschender freunde zu Berlin. Berlin: Gesellschaft Naturforschender Freunde; 1873.

Brendel V, Kurtz S, Walbot V. Comparative genomics of Arabidopsis and maize: prospects and limitations. Genome Biol. 2002:**3**(3):REVIEWS1005. https://doi.org/10.1186/gb-2002-3-3-reviews1005

Carneros E, Sánchez-Muñoz J, Pérez-Pérez Y, Pintos B, Gómez-Garay A, Testillano PS. Dynamics of endogenous auxin and its role in somatic embryogenesis induction and progression in cork oak. Plants (Basel). 2023:**12**(7):1542. https://doi.org/10.3390/plants12071542

Chang S, Lee U, Hong MJ, Jo YD, Kim J-B. Lettuce growth pattern analysis using U-net pre-trained with Arabidopsis. Agriculture. 2021:**11**(9):890. https://doi.org/10.3390/agriculture11090890

Chaudhary D, Jeena AS, Rohit , Gaur S, Raj R, Mishra S, Kajal , Gupta OP, Meena MR. Advances in RNA interference for plant functional genomics: unveiling traits, mechanisms, and future directions. Appl Biochem Biotechnol. 2024 Jan. 4. Online ahead of print. https://doi.org/10.1007/s12010-023-04850-x

Chen Z, Debernardi JM, Dubcovsky J, Gallavotti A. Recent advances in crop transformation technologies. Nat Plants. 2022:**8**(12):1343–1351. https://doi.org/10.1038/s41477-022-01295-8

Chong-Pérez B, Kosky RG, Reyes M, Rojas L, Ocaña B, Tejeda M, Pérez B, Angenon G. Heat shock induced excision of selectable marker genes in transgenic banana by the cre-lox site-specific recombination system. J Biotechnol. 2012:**159**(4):265–273. https://doi.org/10.1016/j.jbiotec.2011.07.031

Chopra R, Johnson EB, Daniels E, McGinn M, Dorn KM, Esfahanian M, Folstad N, Amundson K, Altendorf K, Betts K, et al. Translational genomics using Arabidopsis as a model enables the characterization of pennycress genes through forward and reverse genetics. Plant J. 2018:**96**(6):1093–1105. https://doi.org/10.1111/tpj.14147

Clavijo-Buriticá DC, Sosa CC, Heredia RC, Mosquera AJ, Álvarez A, Medina J, Quimbaya M. Use of Arabidopsis thaliana as a model to understand specific carcinogenic events: comparison of the molecular machinery associated with cancer-hallmarks in plants and humans. Heliyon. 2023:**9**(4):e15367. https://doi.org/10.1016/j.heliyon.2023.e15367

Clough SJ, Bent AF. Floral dip: a simplified method for Agrobacterium -mediated transformation of Arabidopsis thaliana. Plant J. 1998:**16**(6):735–743. https://doi.org/10.1046/j.1365-313x.1998.00343.x

Colbert T, Till BJ, Tompa R, Reynolds S, Steine MN, Yeung AT, McCallum CM, Comai L, Henikoff S. High-throughput screening for induced point mutations. Plant Physiol. 2001:**126**(2):480–484. https://doi.org/10.1104/pp.126.2.480

Comai L, Young K, Till BJ, Reynolds SH, Greene EA, Codomo CA, Enns LC, Johnson JE, Burtner C, Odden AR, et al. Efficient discovery of DNA polymorphisms in natural populations by ecotilling. Plant J. 2004:**37**(5):778–786. https://doi.org/10.1111/j.0960-7412.2003.01999.x

Corbacho J, Sanabria-Reinoso E, Buono L, Fernández-Miñan A, Martínez-Morales JR. Trap-TRAP, a versatile tool for tissue-specific translatomics in zebrafish. Front Cell Dev Biol. 2022:**9**:817191. https://doi.org/10.3389/fcell.2021.817191

Cruz AB, Bianchetti RE, Alves FRR, Purgatto E, Peres LEP, Rossi M, Freschi L. Light, ethylene and auxin signaling interaction regulates carotenoid biosynthesis during tomato fruit ripening. Front Plant Sci. 2018:**9**:1370. https://doi.org/10.3389/fpls.2018.01370

Cutler SR. Inducible gene expression in mammals: plants add to the menu. Sci Signal. 2011:**4**(164):pe13. https://doi.org/10.1126/scisignal.2001875

Czarnecka E, Verner FL, Gurley WB. A strategy for building an amplified transcriptional switch to detect bacterial contamination of plants. Plant Mol Biol. 2012:**78**(1–2):59–75. https://doi.org/10.1007/s11103-011-9845-2

Damalas CA, Koutroubas SD. Herbicide resistance evolution, fitness cost, and the fear of the superweeds. Plant Sci. 2024:**339**:111934. https://doi.org/10.1016/j.plantsci.2023.111934

Davuluri RV, Sun H, Palaniswamy SK, Matthews N, Molina C, Kurtz M, Grotewold E. AGRIS: Arabidopsis gene regulatory information server, an information resource of Arabidopsis cis-regulatory elements and transcription factors. BMC Bioinformatics. 2003:**4**(1):25. https://doi.org/10.1186/1471-2105-4-25

Deal RB, Henikoff S. The INTACT method for cell type-specific gene expression and chromatin profiling in Arabidopsis. Nat Protoc. 2011:**6**(1):56–68. https://doi.org/10.1038/nprot.2010.175

de Felippes FF, Waterhouse PM. Plant terminators: the unsung heroes of gene expression. J Exp Bot. 2022:**74**(7):2239–2250. https://doi.org/10.1093/jxb/erac467

Doyle JP, Dougherty JD, Heiman M, Schmidt EF, Stevens TR, Ma G, Bupp S, Shrestha P, Shah RD, Doughty ML, et al. Application of a translational profiling approach for the comparative analysis of CNS cell types. Cell. 2008:**135**(4):749–762. https://doi.org/10.1016/j.cell.2008.10.029

Dubouzet JG, Sakuma Y, Ito Y, Kasuga M, Dubouzet EG, Miura S, Seki M, Shinozaki K, Yamaguchi-Shinozaki K. OsDREB genes in rice, Oryza sativa L., encode transcription activators that function in drought-, high-salt- and cold-responsive gene expression. Plant J. 2003:**33**(4):751–763. https://doi.org/10.1046/j.1365-313X.2003.01661.x

Dutt M, Barthe G, Irey M, Grosser J. Transgenic citrus expressing an Arabidopsis NPR1 gene exhibit enhanced resistance against huanglongbing (HLB; Citrus greening). PLoS One. 2015:**10**(9):e0137134. https://doi.org/10.1371/journal.pone.0137134

Eshed Y, Lippman ZB. Revolutions in agriculture chart a course for targeted breeding of old and new crops. Science. 2019:**366**(6466):eaax0025. https://doi.org/10.1126/science.aax0025

Felix G, Duran JD, Volko S, Boller T. Plants have a sensitive perception system for the most conserved domain of bacterial flagellin. Plant J. 1999:**18**(3):265–276. https://doi.org/10.1046/j.1365-313X.1999.00265.x

Filipecki M, Malepszy S. Unintended consequences of plant transformation: a molecular insight. J Appl Genet. 2006:**47**(4):277–286. https://doi.org/10.1007/BF03194637

Flachowsky H, Hanke M-V, Peil A, Strauss SH, Fladung M. A review on transgenic approaches to accelerate breeding of woody plants. Plant Breed. 2009:**128**(3):217–226. https://doi.org/10.1111/j.1439-0523.2008.01591.x

Galbraith DW, Birnbaum K. Global studies of cell type-specific gene expression in plants. Annu Rev Plant Biol. 2006:**57**(1):451–475. https://doi.org/10.1146/annurev.arplant.57.032905.105302

Gardiner J, Zhao JM, Chaffin K, Jacobsen SE. Promoter and terminator optimization for DNA methylation targeting in Arabidopsis. Epigenomes. 2020:**4**(2):9. https://doi.org/10.3390/epigenomes4020009

Goloubinoff P, Woodson JD, Strader LC, Fu ZQ. Important questions and future directions in plant biochemistry. Trends Biochem Sci. 2022:**47**(10):811–813. https://doi.org/10.1016/j.tibs.2022.07.003

Gomez-Cano F, Chu Y-H, Cruz-Gomez M, Abdullah HM, Lee YS, Schnell DJ, Grotewold E. Exploring Camelina sativa lipid metabolism regulation by combining gene co-expression and DNA affinity purification analyses. Plant J. 2022:**110**(2):589–606. https://doi.org/10.1111/tpj.15682

González-Carranza ZH, Rompa U, Peters JL, Bhatt AM, Wagstaff C, Stead AD, Roberts JA. HAWAIIAN SKIRT: an F-box gene that regulates organ fusion and growth in arabidopsis. Plant Physiol. 2007:**144**(3):1370–1382. https://doi.org/10.1104/pp.106.092288

González-Schain ND, Díaz-Mendoza M, Żurczak M, Suárez-López P. Potato CONSTANS is involved in photoperiodic tuberization in a graft-transmissible manner. Plant J. 2012:**70**(4):678–690. https://doi.org/10.1111/j.1365-313X.2012.04909.x

Grefen C, Donald N, Hashimoto K, Kudla J, Schumacher K, Blatt MR. A ubiquitin-10 promoter-based vector set for fluorescent protein tagging facilitates temporal stability and native protein distribution in transient and stable expression studies. Plant J. 2010:**64**(2):355–365. https://doi.org/10.1111/j.1365-313X.2010.04322.x

Guo T, Chen K, Dong N-Q, Ye W-W, Shan J-X, Lin H-X. Tillering and small grain 1 dominates the tryptophan aminotransferase family required for local auxin biosynthesis in rice. J Integr Plant Biol. 2020:**62**(5):581–600. https://doi.org/10.1111/jipb.12820

Hajieghrari B, Farrokhi N. Plant RNA-mediated gene regulatory network. Genomics. 2022:**114**(1):409–442. https://doi.org/10.1016/j.ygeno.2021.12.020

Halbert S. The discovery of huanglongbing in Florida. Proceedings of the Second International Citrus Canker and Huanglongbing Research Workshop. Orlando (FL), November 7-11, 2005.

Hall AE, Fiebig A, Preuss D. Beyond the Arabidopsis genome: opportunities for comparative genomics. Plant Physiol. 2002:**129**(4):1439–1447. https://doi.org/10.1104/pp.004051

He W, Brumos J, Li H, Ji Y, Ke M, Gong X, Zeng Q, Li W, Zhang X, An F, et al. A small-molecule screen identifies l-kynurenine as a competitive inhibitor of TAA1/TAR activity in ethylene-directed auxin biosynthesis and root growth in Arabidopsis [C][W]. Plant Cell. 2011:**23**(11):3944–3960. https://doi.org/10.1105/tpc.111.089029

Heiman M, Schaefer A, Gong S, Peterson J, Day M, Ramsey KE, Suárez-Fariñas M, Schwarz C, Stephan DA, Surmeier DJ, et al. Development of a BACarray translational profiling approach for the molecular characterization of CNS cell types. Cell. 2008:**135**(4):738–748. https://doi.org/10.1016/j.cell.2008.10.028

Hibara K, Karim MR, Takada S, Taoka K, Furutani M, Aida M, Tasaka M. Arabidopsis CUP-SHAPED COTYLEDON3 regulates postembryonic shoot meristem and organ boundary formation. Plant Cell. 2006:**18**(11):2946–2957. https://doi.org/10.1105/tpc.106.045716

Hirai T, Kurokawa N, Duhita N, Hiwasa-Tanase K, Kato K, Kato K, Ezura H. The HSP terminator of Arabidopsis thaliana induces a high level of miraculin accumulation in transgenic tomatoes. J Agric Food Chem. 2011:**59**(18):9942–9949. https://doi.org/10.1021/jf202501e

Hiratsu K, Matsui K, Koyama T, Ohme-Takagi M. Dominant repression of target genes by chimeric repressors that include the EAR motif, a repression domain, in Arabidopsis. Plant J. 2003:**34**(5):733–739. https://doi.org/10.1046/j.1365-313X.2003.01759.x

Huala E, Dickerman AW, Garcia-Hernandez M, Weems D, Reiser L, LaFond F, Hanley D, Kiphart D, Zhuang M, Huang W, et al. The Arabidopsis information resource (TAIR): a comprehensive database and web-based information retrieval, analysis, and visualization system for a model plant. Nucleic Acids Res. 2001:**29**(1):102–105. https://doi.org/10.1093/nar/29.1.102

Huang G, Allen R, Davis EL, Baum TJ, Hussey RS. Engineering broad root-knot resistance in transgenic plants by RNAi silencing of a conserved and essential root-knot nematode parasitism gene. Proc Natl Acad Sci U S A. 2006:**103**(39):14302–14306. https://doi.org/10.1073/pnas.0604698103

Huang D, Kosentka PZ, Liu W. Synthetic biology approaches in regulation of targeted gene expression. Curr Opin Plant Biol. 2021:**63**:102036. https://doi.org/10.1016/j.pbi.2021.102036

Huerta AI, Sancho-Andrés G, Montesinos JC, Silva-Navas J, Bassard S, Pau-Roblot C, Kesten C, Schlechter R, Dora S, Ayupov T, et al. The WAK-like protein RFO1 acts as a sensor of the pectin methylation status in Arabidopsis cell walls to modulate root growth and defense. Mol Plant. 2023:**16**(5):865–881. https://doi.org/10.1016/j.molp.2023.03.015

Hupe M, Li MX, Gertow Gillner K, Adams RH, Stenman JM. Evaluation of TRAP-sequencing technology with a versatile conditional mouse model. Nucleic Acids Res. 2014:**42**(2):e14. https://doi.org/10.1093/nar/gkt995

Hutin S, Blanc-Mathieu R, Rieu P, Parcy F, Lai X, Zubieta C. Identification of plant transcription factor DNA-binding sites using seq-DAP-seq. In: **Kaufmann K, Vandepoele K**, editors. Plant gene regulatory networks: methods and protocols: Methods in Molecular Biology. New York (NY): Springer US; 2023. p. 119–145.

Ibrahim HMM, Alkharouf NW, Meyer SLF, Aly MAM, Gamal El-Din AEKY, Hussein EHA, Matthews BF. Post-transcriptional gene silencing of root-knot nematode in transformed soybean roots. Exp Parasitol. 2011:**127**(1):90–99. https://doi.org/10.1016/j.exppara.2010.06.037

Ishizaki K, Nishihama R, Ueda M, Inoue K, Ishida S, Nishimura Y, Shikanai T, Kohchi T. Development of gateway binary vector series with four different selection markers for the liverwort Marchantia polymorpha. PLoS One. 2015:**10**(9):e0138876. https://doi.org/10.1371/journal.pone.0138876

Jander G, Baerson SR, Hudak JA, Gonzalez KA, Gruys KJ, Last RL. Ethylmethanesulfonate saturation mutagenesis in Arabidopsis to determine frequency of herbicide resistance. Plant Physiol. 2003:**131**(1):139–146. https://doi.org/10.1104/pp.102.010397

Jha P, Ochatt SJ, Kumar V. WUSCHEL: a master regulator in plant growth signaling. Plant Cell Rep. 2020:**39**(4):431–444. https://doi.org/10.1007/s00299-020-02511-5

Jiang P, Zhang K, Ding Z, He Q, Li W, Zhu S, Cheng W, Zhang K, Li K. Characterization of a strong and constitutive promoter from the Arabidopsis serine carboxypeptidase-like gene AtSCPL30 as a potential tool for crop transgenic breeding. BMC Biotechnol. 2018:**18**(1):59. https://doi.org/10.1186/s12896-018-0470-x

Jiao Y, Du P. Performance measures in evaluating machine learning based bioinformatics predictors for classifications. Quant Biol. 2016:**4**(4):320–330. https://doi.org/10.1007/s40484-016-0081-2

Jiao Y, Meyerowitz EM. Cell-type specific analysis of translating RNAs in developing flowers reveals new levels of control. Mol Syst Biol. 2010:**6**(1):419. https://doi.org/10.1038/msb.2010.76

Jones AM, Chory J, Dangl JL, Estelle M, Jacobsen SE, Meyerowitz EM, Nordborg M, Weigel D. The impact of Arabidopsis on human health: diversifying our portfolio. Cell. 2008:**133**(6):939–943. https://doi.org/10.1016/j.cell.2008.05.040

Jones JDG, Dangl JL. The plant immune system. Nature. 2006:**444**(7117):323–329. https://doi.org/10.1038/nature05286

Jung J-H, Barbosa AD, Hutin S, Kumita JR, Gao M, Derwort D, Silva CS, Lai X, Pierre E, Geng F, et al. A prion-like domain in ELF3 functions as a thermosensor in Arabidopsis. Nature. 2020:**585**(7824):256–260. https://doi.org/10.1038/s41586-020-2644-7

Kennedy MJ, Hughes RM, Peteya LA, Schwartz JW, Ehlers MD, Tucker CL. Rapid blue-light–mediated induction of protein interactions in living cells. Nat Methods. 2010:**7**(12):973–975. https://doi.org/10.1038/nmeth.1524

Khaipho-Burch M, Cooper M, Crossa J, de Leon N, Holland J, Lewis R, McCouch S, Murray SC, Rabbi I, Ronald P, et al. Genetic modification can improve crop yields—but stop overselling it. Nature. 2023:**621**(7979):470–473. https://doi.org/10.1038/d41586-023-02895-w

Kidokoro S, Watanabe K, Ohori T, Moriwaki T, Maruyama K, Mizoi J, Myint Phyu Sin Htwe N, Fujita Y, Sekita S, Shinozaki K, et al. Soybean DREB1/CBF-type transcription factors function in heat and drought as well as cold stress-responsive gene expression. Plant J. 2015:**81**(3):505–518. https://doi.org/10.1111/tpj.12746

Koornneef M, Alonso-Blanco C, Peeters AJM, Soppe W. Genetic control of flowering time in arabidopsis. Annu Rev Plant Physiol Plant Mol Biol. 1998:**49**(1):345–370. https://doi.org/10.1146/annurev.arplant.49.1.345

Kopecká R, Kameniarová M, Černý M, Brzobohatý B, Novák J. Abiotic stress in crop production. Int J Mol Sci. 2023:**24**(7):6603. https://doi.org/10.3390/ijms24076603

Koryachko A, Matthiadis A, Ducoste JJ, Tuck J, Long TA, Williams C. Computational approaches to identify regulators of plant stress response using high-throughput gene expression data. Curr Plant Biol. 2015:**3–4**:20–29. https://doi.org/10.1016/j.cpb.2015.04.001

Kotoda N, Hayashi H, Suzuki M, Igarashi M, Hatsuyama Y, Kidou S, Igasaki T, Nishiguchi M, Yano K, Shimizu T, et al. Molecular characterization of FLOWERING LOCUS T-like genes of apple (Malus × domestica borkh.). Plant Cell Physiol. 2010:**51**(4):561–575. https://doi.org/10.1093/pcp/pcq021

Kovalev MS, Igolkina AA, Samsonova MG, Nuzhdin SV. A pipeline for classifying deleterious coding mutations in agricultural plants. Front Plant Sci. 2018:**9**:1734. https://doi.org/10.3389/fpls.2018.01734

Krishnakumar V, Contrino S, Cheng C-Y, Belyaeva I, Ferlanti ES, Miller JR, Vaughn MW, Micklem G, Town CD, Chan AP. ThaleMine: a warehouse for Arabidopsis data integration and discovery. Plant Cell Physiol. 2017:**58**(1):e4. https://doi.org/10.1093/pcp/pcw200

Kurokawa N, Hirai T, Takayama M, Hiwasa-Tanase K, Ezura H. An E8 promoter-HSP terminator cassette promotes the high-level accumulation of recombinant protein predominantly in transgenic tomato fruits: a case study of miraculin. Plant Cell Rep. 2013:**32**(4):529–536. https://doi.org/10.1007/s00299-013-1384-7

Laux T, Mayer KFX, Berger J, Jürgens G. The WUSCHEL gene is required for shoot and floral meristem integrity in Arabidopsis. Development. 1996:**122**(1):87–96. https://doi.org/10.1242/dev.122.1.87

Li M, Pan X, Li H. RD29A promoter constitutively drives a rice Hd3a expression to promote early-flowering in Saussurea involucrate Kar. et Kir. ex Maxim. Plant Physiol Biochem. 2023a:**195**:155–162. https://doi.org/10.1016/j.plaphy.2023.01.009

Li M, Wang X, Cao Y, Liu X, Lin Y, Ou Y, Zhang H, Liu J. Strength comparison between cold-inducible promoters of Arabidopsis cor15a and cor15b genes in potato and tobacco. Plant Physiol Biochem. 2013:**71**:77–86. https://doi.org/10.1016/j.plaphy.2013.06.021

Li M, Yao T, Lin W, Hinckley WE, Galli M, Muchero W, Gallavotti A, Chen J-G, Huang SC. Double DAP-seq uncovered synergistic DNA binding of interacting bZIP transcription factors. Nat Commun. 2023b:**14**(1):2600. https://doi.org/10.1038/s41467-023-38096-2

Lian Z, Nguyen CD, Liu L, Wang G, Chen J, Wang S, Yi G, Wilson S, Ozias-Akins P, Gong H, et al. Application of developmental regulators to improve in planta or in vitro transformation in plants. Plant Biotechnol J. 2022:**20**(8):1622–1635. https://doi.org/10.1111/pbi.13837

Liang F-S, Ho WQ, Crabtree GR. Engineering the ABA plant stress pathway for regulation of induced proximity. Sci Signal. 2011:**4**(164):rs2. https://doi.org/10.1126/scisignal.2001449

Lifschitz E, Ayre BG, Eshed Y. Florigen and anti-florigen—a systemic mechanism for coordinating growth and termination in flowering plants. Front Plant Sci. 2014:**5**:465. https://doi.org/10.3389/fpls.2014.00465

Lim J, Jung JW, Lim CE, Lee M-H, Kim BJ, Kim M, Bruce WB, Benfey PN. Conservation and diversification of SCARECROW in maize. Plant Mol Biol. 2005:**59**(4):619–630. https://doi.org/10.1007/s11103-005-0578-y

Lin W-C, Lu C-F, Wu J-W, Cheng M-L, Lin Y-M, Yang N-S, Black L, Green SK, Wang J-F, Cheng C-P. Transgenic tomato plants expressing the Arabidopsis NPR1 gene display enhanced resistance to a spectrum of fungal and bacterial diseases. Transgenic Res. 2004:**13**(6):567–581. https://doi.org/10.1007/s11248-004-2375-9

Liu Y, Chen S, Chen J, Wang J, Wei M, Tian X, Chen L, Ma J. Comprehensive analysis and expression profiles of the AP2/ERF gene family during spring bud break in tea plant (Camellia sinensis). BMC Plant Biol. 2023:**23**(1):206. https://doi.org/10.1186/s12870-023-04221-y

Liu H, Gomez G, Lin S, Lin S, Lin C. Optogenetic control of transcription in zebrafish. PLoS One. 2012:**7**(11):e50738. https://doi.org/10.1371/journal.pone.0050738

Liu W, Mazarei M, Rudis MR, Fethe MH, Stewart CN. Rapid in vivo analysis of synthetic promoters for plant pathogen phytosensing. BMC Biotechnol. 2011:**11**(1):108. https://doi.org/10.1186/1472-6750-11-108

Liu N, Parisien M, Dai Q, Zheng G, He C, Pan T. Probing N6-methyladenosine RNA modification status at single nucleotide resolution in mRNA and long noncoding RNA. RNA. 2013:**19**(12):1848–1856. https://doi.org/10.1261/rna.041178.113

Liu L, Zhang G, He S, Hu X. TSPTFBS: a Docker image for trans-species prediction of transcription factor binding sites in plants. Bioinformatics. 2021:**37**(2):260–262. https://doi.org/10.1093/bioinformatics/btaa1100

Llamas E, Koyuncu S, Lee HJ, Wehrmann M, Gutierrez-Garcia R, Dunken N, Charura N, Torres-Montilla S, Schlimgen E, Mandel AM, et al. In planta expression of human polyQ-expanded huntingtin fragment reveals mechanisms to prevent disease-related protein aggregation. Nat Aging. 2023:**3**(11):1345–1357. https://doi.org/10.1038/s43587-023-00502-1

Lonhienne T, Cheng Y, Garcia MD, Hu SH, Low YS, Schenk G, Williams CM, Guddat LW. Structural basis of resistance to herbicides that target acetohydroxyacid synthase. Nat Commun. 2022:**13**(1):3368. https://doi.org/10.1038/s41467-022-31023-x

Low YC, Lawton MA, Di R. Ethylene insensitive 2 (EIN2) as a potential target gene to enhance fusarium head blight disease resistance. Plant Sci. 2022:**322**:111361. https://doi.org/10.1016/j.plantsci.2022.111361

Lu H-C, Lam S-H, Zhang D, Hsiao Y-Y, Li B-J, Niu S-C, Li C-Y, Lan S, Tsai W-C, Liu Z-J. R2R3-MYB genes coordinate conical cell development and cuticular wax biosynthesis in Phalaenopsis aphrodite. Plant Physiol. 2021:**188**(1):318–331. https://doi.org/10.1093/plphys/kiab422

Lu S, Zhang N, Xu Y, Chen H, Huang J, Zou B. Functional conservation and divergence of MOS1 that controls flowering time and seed size in rice and Arabidopsis. Int J Mol Sci. 2022:**23**(21):13448. https://doi.org/10.3390/ijms232113448

Magana-Mora A, Ashoor H, Jankovic BR, Kamau A, Awara K, Chowdhary R, Archer JAC, Bajic VB. Dragon TIS spotter: an Arabidopsis-derived predictor of translation initiation sites in plants. Bioinformatics. 2013:**29**(1): 117–118. https://doi.org/10.1093/bioinformatics/bts638

Mahood EH, Kruse LH, Moghe GD. Machine learning: a powerful tool for gene function prediction in plants. Appl Plant Sci. 2020:**8**(7): e11376. https://doi.org/10.1002/aps3.11376

Martel C, Zhurov V, Navarro M, Martinez M, Cazaux M, Auger P, Migeon A, Santamaria ME, Wybouw N, Diaz I, et al. Tomato whole genome transcriptional response to Tetranychus urticae identifies divergence of spider mite-induced responses between tomato and Arabidopsis. MPMI. 2015:**28**(3):343–361. https://doi.org/10.1094/MPMI-09-14-0291-FI

Martínez-Atienza J, Jiang X, Garciadeblas B, Mendoza I, Zhu J-K, Pardo JM, Quintero FJ. Conservation of the salt overly sensitive pathway in rice. Plant Physiol. 2007:**143**(2):1001–1012. https://doi.org/10.1104/pp.106.092635

Matsui T, Takita E, Sato T, Aizawa M, Ki M, Kadoyama Y, Hirano K, Kinjo S, Asao H, Kawamoto K, et al. Production of double repeated B subunit of Shiga toxin 2e at high levels in transgenic lettuce plants as vaccine material for porcine edema disease. Transgenic Res. 2011:**20**(4):735–748. https://doi.org/10.1007/s11248-010-9455-9

Mayor A, Martinon F, De Smedt T, Pétrilli V, Tschopp J. A crucial function of SGT1 and HSP90 in inflammasome activity links mammalian and plant innate immune responses. Nat Immunol. 2007:**8**(5): 497–503. https://doi.org/10.1038/ni1459

Mazarei M, Teplova I, Hajimorad MR, Stewart CN. Pathogen phytosensing: plants to report plant pathogens. Sensors (Basel). 2008:**8**(4): 2628–2641. https://doi.org/10.3390/s8042628

McCallum CM, Comai L, Greene EA, Henikoff S. Targeted screening for induced mutations. Nat Biotechnol. 2000:**18**(4):455–457. https://doi.org/10.1038/74542

McClure CD, Hassan A, Aughey GN, Butt K, Estacio-Gómez A, Duggal A, Ying Sia C, Barber AF, Southall TD. An auxin-inducible, GAL4-compatible, gene expression system for Drosophila. eLife. 2022:**11**:e67598. https://doi.org/10.7554/eLife.67598

Mellor SB, Behrendorff JBYH, Ipsen JØ, Crocoll C, Laursen T, Gillam EMJ, Pribil M. Exploiting photosynthesis-driven P450 activity to produce indican in tobacco chloroplasts. Front Plant Sci. 2023:**13**: 1049177. https://doi.org/10.3389/fpls.2022.1049177

Meyerowitz EM. Plants, animals and the logic of development. Trends Cell Biol. 1999:**9**(12):M65–M68. https://doi.org/10.1016/S0962-8924(99)01649-9

Mo A, Mukamel EA, Davis FP, Luo C, Henry GL, Picard S, Urich MA, Nery JR, Sejnowski TJ, Lister R, et al. Epigenomic signatures of neuronal diversity in the mammalian brain. Neuron. 2015:**86**(6): 1369–1384. https://doi.org/10.1016/j.neuron.2015.05.018

Molla KA, Karmakar S, Chanda PK, Sarkar SN, Datta SK, Datta K. Tissue-specific expression of Arabidopsis NPR1 gene in rice for sheath blight resistance without compromising phenotypic cost. Plant Sci. 2016:**250**:105–114. https://doi.org/10.1016/j.plantsci.2016.06.005

Moore BM, Wang P, Fan P, Lee A, Leong B, Lou Y-R, Schenck CA, Sugimoto K, Last R, Lehti-Shiu MD, et al. Within- and cross-species predictions of plant specialized metabolism genes using transfer learning. In Silico Plants. 2020:**2**(1):diaa005. https://doi.org/10.1093/insilicoplants/diaa005

Moriwaki M, Yamakawa T, Washino T, Kodama T, Igarashi Y. Suppressed phenylalanine ammonia-lyase activity after heat shock in transgenic Nicotiana plumbaginifolia containing an Arabidopsis HSP18.2-parsley PAL2 chimera gene. J Biosci Bioeng. 1999:**87**(5): 588–593. https://doi.org/10.1016/S1389-1723(99)80119-4

Mueller LA, Zhang P, Rhee SY. AraCyc: a biochemical pathway database for Arabidopsis. Plant Physiol. 2003:**132**(2):453–460. https://doi.org/10.1104/pp.102.017236

Nagata T, Lombardo F, Ezura H. Complementation of the tomato HWS gene with its Arabidopsis counterpart demonstrates conservation of the gene function between both species. Plant Biotechnol (Tokyo). 2021:**38**(3):387–390. https://doi.org/10.5511/plantbiotechnology.21.0729a

Nagaya S, Kawamura K, Shinmyo A, Kato K. The HSP terminator of Arabidopsis thaliana increases gene expression in plant cells. Plant Cell Physiol. 2010:**51**(2):328–332. https://doi.org/10.1093/pcp/pcp188

Nakano T, Suzuki K, Fujimura T, Shinshi H. Genome-wide analysis of the ERF gene family in Arabidopsis and rice. Plant Physiol. 2006:**140**(2): 411–432. https://doi.org/10.1104/pp.105.073783

Napoli C, Lemieux C, Jorgensen R. Introduction of a chimeric chalcone synthase gene into petunia results in reversible co-suppression of homologous genes in trans. Plant Cell. 1990:**2**(4):279–289. https://doi.org/10.2307/3869076

Naseri G, Balazadeh S, Machens F, Kamranfar I, Messerschmidt K, Mueller-Roeber B. Plant-derived transcription factors for orthologous regulation of gene expression in the yeast Saccharomyces cerevisiae. ACS Synth Biol. 2017:**6**(9):1742–1756. https://doi.org/10.1021/acssynbio.7b00094

Nishihama R, Ishida S, Urawa H, Kamei Y, Kohchi T. Conditional gene expression/deletion systems for Marchantia polymorpha using its own heat-shock promoter and Cre/loxP-mediated site-specific recombination. Plant Cell Physiol. 2016:**57**(2):271–280. https://doi.org/10.1093/pcp/pcv102

Nishimura K, Fukagawa T, Takisawa H, Kakimoto T, Kanemaki M. An auxin-based degron system for the rapid depletion of proteins in nonplant cells. Nat Methods. 2009:**6**(12):917–922. https://doi.org/10.1038/nmeth.1401

Norris SR, Meyer SE, Callis J. The intron of Arabidopsis thaliana polyubiquitin genes is conserved in location and is a quantitative determinant of chimeric gene expression. Plant Mol Biol. 1993:**21**(5): 895–906. https://doi.org/10.1007/BF00027120

Nusinow DA, Helfer A, Hamilton EE, King JJ, Imaizumi T, Schultz TF, Farré EM, Kay SA. The ELF4–ELF3–LUX complex links the circadian clock to diurnal control of hypocotyl growth. Nature. 2011:**475**(7356): 398–402. https://doi.org/10.1038/nature10182

Ohta M, Matsui K, Hiratsu K, Shinshi H, Ohme-Takagi M. Repression domains of class II ERF transcriptional repressors share an essential motif for active repression. Plant Cell. 2001:**13**(8):1959–1968. https://doi.org/10.1105/TPC.010127

O'Malley RC, Barragan CC, Ecker JR. A user's guide to the Arabidopsis T-DNA insertional mutant collections. Methods Mol Biol. 2015:**1284**: 323–342. https://doi.org/10.1007/978-1-4939-2444-8_16

O'Malley RC, Huang SC, Song L, Lewsey MG, Bartlett A, Nery JR, Galli M, Gallavotti A, Ecker JR. Cistrome and epicistrome features shape the regulatory DNA landscape. Cell. 2016:**165**(5):1280–1292. https://doi.org/10.1016/j.cell.2016.04.038

Paciorek T, Chiapelli BJ, Wang JY, Paciorek M, Yang H, Sant A, Val DL, Boddu J, Liu K, Gu C, et al. Targeted suppression of gibberellin biosynthetic genes ZmGA20ox3 and ZmGA20ox5 produces a short stature maize ideotype. Plant Biotechnol J. 2022:**20**(6):1140–1153. https://doi.org/10.1111/pbi.13797

Pang SS, Guddat LW, Duggleby RG. Crystallization of Arabidopsis thaliana acetohydroxyacid synthase in complex with the sulfonylurea herbicide chlorimuron ethyl. Acta Crystallogr D Biol Crystallogr. 2004:**60**(1):153–155. https://doi.org/10.1107/S0907444903025423

Paris M, Roux F, Bérard A, Reboud X. The effects of the genetic background on herbicide resistance fitness cost and its associated dominance in Arabidopsis thaliana. Heredity (Edinb). 2008:**101**(6):499–506. https://doi.org/10.1038/hdy.2008.92

Park PJ. ChIP–seq: advantages and challenges of a maturing technology. Nat Rev Genet. 2009:**10**(10):669–680. https://doi.org/10.1038/nrg2641

Park S-Y, Peterson FC, Mosquna A, Yao J, Volkman BF, Cutler SR. Agrochemical control of plant water use using engineered abscisic acid receptors. Nature. 2015:**520**(7548):545–548. https://doi.org/10.1038/nature14123

Parkhi V, Kumar V, Campbell LAM, Bell AA, Rathore KS. Expression of Arabidopsis NPR1 in transgenic cotton confers resistance to

non-defoliating isolates of Verticillium dahliae but not the defoliating isolates. J Phytopathol. 2010a:**158**(11–12):822–825. https://doi.org/10.1111/j.1439-0434.2010.01714.x

Parkhi V, Kumar V, Campbell LM, Bell AA, Shah J, Rathore KS. Resistance against various fungal pathogens and reniform nematode in transgenic cotton plants expressing Arabidopsis NPR1. Transgenic Res. 2010b:**19**(6):959–975. https://doi.org/10.1007/s11248-010-9374-9

Pathak GP, Spiltoir JI, Höglund C, Polstein LR, Heine-Koskinen S, Gersbach CA, Rossi J, Tucker CL. Bidirectional approaches for optogenetic regulation of gene expression in mammalian cells using Arabidopsis cryptochrome 2. Nucleic Acids Res. 2017:**45**(20):e167. https://doi.org/10.1093/nar/gkx260

Pinneh EC, Mina JG, Stark MJR, Lindell SD, Luemmen P, Knight MR, Steel PG, Denny PW. The identification of small molecule inhibitors of the plant inositol phosphorylceramide synthase which demonstrate herbicidal activity. Sci Rep. 2019:**9**(1):8083. https://doi.org/10.1038/s41598-019-44544-1

Pisupati R, Reichardt I, Seren Ü, Korte P, Nizhynska V, Kerdaffrec E, Uzunova K, Rabanal FA, Filiault DL, Nordborg M. Verification of Arabidopsis stock collections using SNPmatch, a tool for genotyping high-plexed samples. Sci Data. 2017:**4**(1):170184. https://doi.org/10.1038/sdata.2017.184

Plume K. Bayer rolls out short corn variety tolerant of weather extremes. Reuters; 2022 [accessed 2024 Jan 22]. https://www.reuters.com/business/cop/bayer-rolls-out-short-corn-variety-tolerant-weather-extremes-2022-02-17/.

Potlakayala SD, DeLong C, Sharpe A, Fobert PR. Conservation of NON-EXPRESSOR OF PATHOGENESIS-RELATED GENES1 function between Arabidopsis thaliana and Brassica napus. Physiol Mol Plant Pathol. 2007:**71**(4–6):174–183. https://doi.org/10.1016/j.pmpp.2008.01.003

Preuss SB, Meister R, Xu Q, Urwin CP, Tripodi FA, Screen SE, Anil VS, Zhu S, Morrell JA, Liu G, et al. Expression of the Arabidopsis thaliana BBX32 gene in soybean increases grain yield. PLoS One. 2012:**7**(2):e30717. https://doi.org/10.1371/journal.pone.0030717

Priya DB, Somasekhar N, Prasad J, Kirti P. Transgenic tobacco plants constitutively expressing Arabidopsis NPR1 show enhanced resistance to root-knot nematode, Meloidogyne incognita. BMC Res Notes. 2011:**4**(1):231. https://doi.org/10.1186/1756-0500-4-231

Qin H, Ou L, Gao J, Chen L, Wang J-W, Hao P, Li X. DENA: training an authentic neural network model using nanopore sequencing data of Arabidopsis transcripts for detection and quantification of N6-methyladenosine on RNA. Genome Biol. 2022:**23**(1):25. https://doi.org/10.1186/s13059-021-02598-3

Reed JW, Nagpal P, Poole DS, Furuya M, Chory J. Mutations in the gene for the red/far-red light receptor phytochrome B alter cell elongation and physiological responses throughout Arabidopsis development. Plant Cell. 1993:**5**(2):147–157. https://doi.org/10.1105/tpc.5.2.147

Reynoso MA, Juntawong P, Lancia M, Blanco FA, Bailey-Serres J, and Zanetti ME. Translating ribosome affinity purification (TRAP) followed by RNA sequencing technology (TRAP-SEQ) for quantitative assessment of plant translatomes. In: **Alonso JM, Stepanova AN**, editors. Plant functional genomics: methods and protocols, Methods in Molecular Biology. New York (NY): Springer; 2015. p. 185–207.

Reynoso MA, Pauluzzi GC, Cabanlit S, Velasco J, Bazin J, Deal R, Brady S, Sinha N, Bailey-Serres J, Kajala K. Isolation of nuclei in tagged cell types (INTACT), RNA extraction and ribosomal RNA degradation to prepare material for RNA-Seq. Bio Protoc. 2018:**8**(7):e2458. https://doi.org/10.21769/BioProtoc.2458

Roeder AHK, Otegui MS, Dixit R, Anderson CT, Faulkner C, Zhang Y, Harrison MJ, Kirchhelle C, Goshima G, Coate JE, et al. Fifteen compelling open questions in plant cell biology. Plant Cell. 2022:**34**(1):72–102. https://doi.org/10.1093/plcell/koab225

Santner A, Estelle M. Recent advances and emerging trends in plant hormone signaling. Nature. 2009:**459**(7250):1071–1078. https://doi.org/10.1038/nature08122

Sasaki K, Yamaguchi H, Nakayama M, Aida R, Ohtsubo N. Comodification of class B genes TfDEF and TfGLO in Torenia fournieri lind. Alters both flower morphology and inflorescence architecture. Plant Mol Biol. 2014:**86**(3):319–334. https://doi.org/10.1007/s11103-014-0231-8

Sathasivan K, Haughn GW, Murai N. Molecular basis of imidazolinone herbicide resistance in Arabidopsis thaliana var Columbia 1. Plant Physiol. 1991:**97**(3):1044–1050. https://doi.org/10.1104/pp.97.3.1044

Sayers EW, Beck J, Bolton EE, Bourexis D, Brister JR, Canese K, Comeau DC, Funk K, Kim S, Klimke W, et al. Database resources of the national center for biotechnology information. Nucleic Acids Res. 2022:**50**(D1):D20–D26. https://doi.org/10.1093/nar/gkab1112

Schröder JA, Jullien PE. The diversity of plant small RNAs silencing mechanisms. Chimia (Aarau). 2019:**73**(5):362–362. https://doi.org/10.2533/chimia.2019.362

Schwab R, Ossowski S, Riester M, Warthmann N, Weigel D. Highly specific gene silencing by artificial MicroRNAs in Arabidopsis. Plant Cell. 2006:**18**(5):1121–1133. https://doi.org/10.1105/tpc.105.039834

Selma S, Bernabé-Orts JM, Vazquez-Vilar M, Diego-Martin B, Ajenjo M, Garcia-Carpintero V, Granell A, Orzaez D. Strong gene activation in plants with genome-wide specificity using a new orthogonal CRISPR/Cas9-based programmable transcriptional activator. Plant Biotechnol J. 2019:**17**(9):1703–1705. https://doi.org/10.1111/pbi.13138

Serrano M, Kombrink E, Meesters C. Considerations for designing chemical screening strategies in plant biology. Front Plant Sci. 2015:**6**:131. https://doi.org/10.3389/fpls.2015.00131

Sessa EB, Masalia RR, Arrigo N, Barker MS, Pelosi JA. GOgetter: a pipeline for summarizing and visualizing GO slim annotations for plant genetic data. Appl Plant Sci. 2023:**11**(4):e11536. https://doi.org/10.1002/aps3.11536

Sharma A, Li X, Lim YP. Comparative genomics of Brassicaceae crops. Breed Sci. 2014:**64**(1):3–13. https://doi.org/10.1270/jsbbs.64.3

Sharma V, Mishra A, Sharma H, Kumar P, Roy JK. Unraveling novel and rare mutations for alpha-amylase and key transcription factors in EMS-induced wheat mutants for amylose by TILLING. Mol Biol Rep. 2022:**49**(6):5427–5436. https://doi.org/10.1007/s11033-022-07155-0

Shi H, Ishitani M, Kim C, Zhu J-K. The Arabidopsis thaliana salt tolerance gene SOS1 encodes a putative Na+/H+ antiporter. Proc Natl Acad Sci. 2000:**97**(12):6896–6901. https://doi.org/10.1073/pnas.120170197

Shi H, Lee B, Wu S-J, Zhu J-K. Overexpression of a plasma membrane Na+/H+ antiporter gene improves salt tolerance in Arabidopsis thaliana. Nat Biotechnol. 2003:**21**(1):81–85. https://doi.org/10.1038/nbt766

Simmons CR, Lafitte HR, Reimann KS, Brugière N, Roesler K, Albertsen MC, Greene TW, Habben JE. Successes and insights of an industry biotech program to enhance maize agronomic traits. Plant Sci. 2021:**307**:110899. https://doi.org/10.1016/j.plantsci.2021.110899

Singh P, Sujayanand GK, Thakur S, Rathore M, Verma OP, Singh NP, Das A. Evaluation of transgenic chickpea harboring codon-modified Vip3Aa against gram pod borer (Helicoverpa armigera H.). PLoS One. 2022:**17**(6):e0270011. https://doi.org/10.1371/journal.pone.0270011

Skinner DJ, Brown RH, Kuzoff RK, Gasser CS. Conservation of the role of INNER NO OUTER in development of unitegmic ovules of the Solanaceae despite a divergence in protein function. BMC Plant Biol. 2016:**16**(1):143. https://doi.org/10.1186/s12870-016-0835-z

Soares JM, Weber KC, Qiu W, Stanton D, Mahmoud LM, Wu H, Huyck P, Zale J, Al Jasim K, Grosser JW, et al. The vascular targeted citrus FLOWERING LOCUS T3 gene promotes non-inductive early flowering in transgenic Carrizo rootstocks and grafted juvenile scions. Sci Rep. 2020:**10**(1):21404. https://doi.org/10.1038/s41598-020-78417-9

Soares da Costa TP, Hall CJ, Panjikar S, Wyllie JA, Christoff RM, Bayat S, Hulett MD, Abbott BM, Gendall AR, Perugini MA. Towards novel herbicide modes of action by inhibiting lysine biosynthesis in plants. eLife. 2021:**10**:e69444. https://doi.org/10.7554/eLife.69444

Somerville C, Koornneef M. A fortunate choice: the history of Arabidopsis as a model plant. Nat Rev Genet. 2002:**3**(11):883–889. https://doi.org/10.1038/nrg927

Song JH, Montes-Luz B, Tadra-Sfeir MZ, Cui Y, Su L, Xu D, Stacey G. High-resolution translatome analysis reveals cortical cell programs during early soybean nodulation. Front Plant Sci. 2022:**13**:820348. https://doi.org/10.3389/fpls.2022.820348

Steiner FA, Talbert PB, Kasinathan S, Deal RB, Henikoff S. Cell-type-specific nuclei purification from whole animals for genome-wide expression and chromatin profiling. Genome Res. 2012:**22**(4): 766–777. https://doi.org/10.1101/gr.131748.111

Stepanova AN, Yun J, Likhacheva AV, Alonso JM. Multilevel interactions between ethylene and auxin in arabidopsis roots. Plant Cell. 2007:**19**(7):2169–2185. https://doi.org/10.1105/tpc.107.052068

Sun K, Wolters A-MA, Loonen AEHM, Huibers RP, van der Vlugt R, Goverse A, Jacobsen E, Visser RGF, Bai Y. Down-regulation of Arabidopsis DND1 orthologs in potato and tomato leads to broad-spectrum resistance to late blight and powdery mildew. Transgenic Res. 2016:**25**(2):123–138. https://doi.org/10.1007/s11248-015-9921-5

Takahashi T, Komeda Y. Characterization of two genes encoding small heat-shock proteins in Arabidopsis thaliana. Mol Gen Genet. 1989:**219**(3):365–372. https://doi.org/10.1007/BF00259608

Tang H, Bomhoff MD, Briones E, Zhang L, Schnable JC, Lyons E. SynFind: compiling syntenic regions across any set of genomes on demand. Genome Biol Evol. 2015:**7**(12):3286–3298. https://doi.org/10.1093/gbe/evv219

Thimm O, Bläsing O, Gibon Y, Nagel A, Meyer S, Krüger P, Selbig J, Müller LA, Rhee SY, Stitt M. Mapman: a user-driven tool to display genomics data sets onto diagrams of metabolic pathways and other biological processes. Plant J. 2004:**37**(6):914–939. https://doi.org/10.1111/j.1365-313X.2004.02016.x

Tischer D, Weiner OD. Illuminating cell signalling with optogenetic tools. Nat Rev Mol Cell Biol. 2014:**15**(8):551–558. https://doi.org/10.1038/nrm3837

Tiwari SB, Belachew A, Ma SF, Young M, Ade J, Shen Y, Marion CM, Holtan HE, Bailey A, Stone JK, et al. The EDLL motif: a potent plant transcriptional activation domain from AP2/ERF transcription factors. Plant J. 2012:**70**(5):855–865. https://doi.org/10.1111/j.1365-313X.2012.04935.x

Togninalli M, Seren Ü, Freudenthal JA, Monroe JG, Meng D, Nordborg M, Weigel D, Borgwardt K, Korte A, Grimm DG. AraPheno and the AraGWAS catalog 2020: a major database update including RNA-Seq and knockout mutation data for Arabidopsis thaliana. Nucleic Acids Res. 2020:**48**(D1):D1063–D1068. https://doi.org/10.1093/nar/gkz925

Town CD, Cheung F, Maiti R, Crabtree J, Haas BJ, Wortman JR, Hine EE, Althoff R, Arbogast TS, Tallon LJ, et al. Comparative genomics of brassica oleracea and Arabidopsis thaliana reveal gene loss, fragmentation, and dispersal after polyploidy. Plant Cell. 2006:**18**(6): 1348–1359. https://doi.org/10.1105/tpc.106.041665

Traubenik S, Blanco F, Zanetti ME, Reynoso MA. TRAP-SEQ of eukaryotic translatomes applied to the detection of polysome-associated long noncoding RNAs. In: **Heinlein M**, editor. RNA Tagging: methods and protocols, Methods in Molecular Biology. New York (NY): Springer US; 2020. p. 451–472.

Trost M, Blattner AC, Lehner CF. Regulated protein depletion by the auxin-inducible degradation system in Drosophila melanogaster. Fly (Austin). 2016:**10**(1):35–46. https://doi.org/10.1080/19336934.2016.1168552

Trouillon J, Ragno M, Simon V, Attrée I, Elsen S. Transcription inhibitors with XRE DNA-binding and cupin signal-sensing domains drive metabolic diversification in pseudomonas. mSystems. 2021:**6**(1): e00753–e00720. https://doi.org/10.1128/mSystems.00753-20

Tryon RC, Pisat N, Johnson SL, Dougherty JD. Development of translating ribosome affinity purification for zebrafish. Genesis. 2013:**51**(3): 187–192. https://doi.org/10.1002/dvg.22363

Tzfadia O, Amar D, Bradbury LMT, Wurtzel ET, Shamir R. The MORPH algorithm: ranking candidate genes for membership in Arabidopsis and tomato pathways[C][W]. Plant Cell. 2012:**24**(11): 4389–4406. https://doi.org/10.1105/tpc.112.104513

Uda Y, Goto Y, Oda S, Kohchi T, Matsuda M, Aoki K. Efficient synthesis of phycocyanobilin in mammalian cells for optogenetic control of cell signaling. Proc Natl Acad Sci U S A. 2017:**114**(45):11962–11967. https://doi.org/10.1073/pnas.1707190114

Usadel B, Poree F, Nagel A, Lohse M, Czedik-Eysenberg A, Stitt M. A guide to using MapMan to visualize and compare omics data in plants: a case study in the crop species, maize. Plant Cell Environ. 2009:**32**(9):1211–1229. https://doi.org/10.1111/j.1365-3040.2009.01978.x

Vazquez-Vilar M, Selma S, Orzaez D. The design of synthetic gene circuits in plants: new components, old challenges. J Exp Bot. 2023:**74**(13):3791–3805. https://doi.org/10.1093/jxb/erad167

Veltri D, Wight MM, Crouch JA. SimpleSynteny: a web-based tool for visualization of microsynteny across multiple species. Nucleic Acids Res. 2016:**44**(W1):W41–W45. https://doi.org/10.1093/nar/gkw330

Verma SS, Chinnusamy V, Bansa KC. A simplified floral dip method for transformation of Brassica napus and B. carinata. J Plant Biochem Biotechnol. 2008:**17**(2):197–200. https://doi.org/10.1007/BF03263286

Waese J, Provart NJ. The bio-analytic resource for plant biology. In: **van Dijk ADJ**, editor. Plant genomics databases: methods and protocols, Methods in Molecular Biology. New York (NY): Springer; 2017. p. 119–148.

Wally O, Jayaraj J, Punja Z. Comparative resistance to foliar fungal pathogens in transgenic carrot plants expressing genes encoding for chitinase, β-1,3-glucanase and peroxidise. Eur J Plant Pathol. 2009:**123**(3):331–342. https://doi.org/10.1007/s10658-008-9370-6

Wang Q, Dai X, Pang H, Cheng Y, Huang X, Li H, Yan X, Lu F, Wei H, Sederoff RR, et al. BEL1-like homeodomain protein BLH6a is a negative regulator of CAld5H2 in sinapyl alcohol monolignol biosynthesis in poplar. Front Plant Sci. 2021a:**12**:695223. https://doi.org/10.3389/fpls.2021.695223

Wang N, Gao J, Liu Y, Shi R, Chen S. Identification of crucial factors involved in Cynoglossus semilaevis sexual size dimorphism by GWAS and demonstration of zbed1 regulatory network by DAP-seq. Genomics. 2022:**114**(3):110376. https://doi.org/10.1016/j.ygeno.2022.110376

Wang Y, Tang H, DeBarry JD, Tan X, Li J, Wang X, Lee T, Jin H, Marler B, Guo H, et al. MCScanx: a toolkit for detection and evolutionary analysis of gene synteny and collinearity. Nucleic Acids Res. 2012:**40**(7):e49. https://doi.org/10.1093/nar/gkr1293

Wang Y-H, Wei KY, Smolke CD. Synthetic biology: advancing the design of diverse genetic systems. Annu Rev Chem Biomol Eng. 2013:**4**(1): 69–102. https://doi.org/10.1146/annurev-chembioeng-061312-103351

Wang X, Xu L, Liu X, Xin L, Wu S, Chen X. Development of potent promoters that drive the efficient expression of genes in apple protoplasts. Hortic Res. 2021b:**8**(1):211. https://doi.org/10.1038/s41438-021-00646-4

Wasson L, Amin NM, Conlon FL. INTACT proteomics in xenopus. Cold Spring Harb Protoc: 2019:**2019**:(6):prot098384. https://doi.org/10.1101/pdb.prot098384.

Weigel D. Natural variation in Arabidopsis: from molecular genetics to ecological genomics1[W][OA]. Plant Physiol. 2012:**158**(1):2–22. https://doi.org/10.1104/pp.111.189845

Weller JL, Ortega R. Genetic control of flowering time in legumes. Front Plant Sci. 2015:**6**:207. https://doi.org/10.3389/fpls.2015.00207

Whitt L, Ricachenevsky FK, Ziegler GZ, Clemens S, Walker E, Maathuis FJM, Kear P, Baxter I. A curated list of genes that affect the plant ionome. Plant Direct. 2020:**4**(10):e00272. https://doi.org/10.1002/pld3.272

Whitworth GB, Misaghi B, Rosenthal D, Mills E, Heinen D, Watson A, Ives C, Ali S, Bezold K, Marsh-Armstrong N, et al. Translational profiling of retinal ganglion cell optic nerve regeneration in xenopus laevis. Dev Biol. 2017:**426**(2):360–373. https://doi.org/10.1016/j.ydbio.2016.06.003

Wimalanathan K, Lawrence-Dill CJ. Gene ontology meta annotator for plants (GOMAP). Plant Methods. 2021:**17**(1):54. https://doi.org/10.1186/s13007-021-00754-1

Xu XM, Lin H, Maple J, Björkblom B, Alves G, Larsen JP, Møller SG. The Arabidopsis DJ-1a protein confers stress protection through cytosolic SOD activation. J Cell Sci. 2010:**123**(10):1644–1651. https://doi.org/10.1242/jcs.063222

Xu XM, Møller SG. The value of Arabidopsis research in understanding human disease states. Curr Opin Biotechnol. 2011:**22**(2):300–307. https://doi.org/10.1016/j.copbio.2010.11.007

Yamada M, Nagasaki SC, Ozawa T, Imayoshi I. Light-mediated control of gene expression in mammalian cells. Neurosci Res. 2020:**152**:66–77. https://doi.org/10.1016/j.neures.2019.12.018

Yamaguchi-Shinozaki K, Shinozaki K. A novel cis-acting element in an Arabidopsis gene is involved in responsiveness to drought, low-temperature, or high-salt stress. Plant Cell. 1994:**6**(2):251–264. https://doi.org/10.1105/tpc.6.2.251

Yan T, Hou Q, Wei X, Qi Y, Pu A, Wu S, An X, Wan X. Promoting genotype-independent plant transformation by manipulating developmental regulatory genes and/or using nanoparticles. Plant Cell Rep. 2023:**42**(9):1395–1417. https://doi.org/10.1007/s00299-023-03037-2

Yan H, Lee J, Song Q, Li Q, Schiefelbein J, Zhao B, Li S. Identification of new marker genes from plant single-cell RNA-seq data using interpretable machine learning methods. New Phytol. 2022:**234**(4):1507–1520. https://doi.org/10.1111/nph.18053

Yang Y, Jittayasothorn Y, Chronis D, Wang X, Cousins P, Zhong G-Y. Molecular characteristics and efficacy of 16D10 siRNAs in inhibiting root-knot nematode infection in transgenic grape hairy roots. PLoS One. 2013:**8**(7):e69463. https://doi.org/10.1371/journal.pone.0069463

Yang R-C, Peng FY, Hu Z. Inferring defense-related gene families in Arabidopsis and wheat. BMC Genomics. 2017:**18**(1):980. https://doi.org/10.1186/s12864-017-4381-3

Yoo SK, Chung KS, Kim J, Lee JH, Hong SM, Yoo SJ, Yoo SY, Lee JS, Ahn JH. CONSTANS activates SUPPRESSOR OF OVEREXPRESSION OF CONSTANS 1 through FLOWERING LOCUS T to promote flowering in Arabidopsis. Plant Physiol. 2005:**139**(2):770–778. https://doi.org/10.1104/pp.105.066928

Yuan YX, Zhang J, Wang DW, Ling HQ. AtbHLH29 of Arabidopsis thaliana is a functional ortholog of tomato FER involved in controlling iron acquisition in strategy I plants. Cell Res. 2005:**15**(8):613–621. https://doi.org/10.1038/sj.cr.7290331

Yue J-J, Yuan J-L, Wu F-H, Yuan Y-H, Cheng Q-W, Hsu C-T, Lin C-S. Protoplasts: from isolation to CRISPR/Cas genome editing application. Front Genome Ed. 2021:**3**:717017. https://doi.org/10.3389/fgeed.2021.717017

Yue Y, Zhang M, Zhang J, Duan L, Li Z. SOS1 gene overexpression increased salt tolerance in transgenic tobacco by maintaining a higher K(+)/Na(+) ratio. J Plant Physiol. 2012:**169**(3):255–261. https://doi.org/10.1016/j.jplph.2011.10.007

Zanetti ME, Chang I-F, Gong F, Galbraith DW, Bailey-Serres J. Immunopurification of polyribosomal complexes of Arabidopsis for global analysis of gene expression. Plant Physiol. 2005:**138**(2):624–635. https://doi.org/10.1104/pp.105.059477

Zhang H-Z, Cai X-Z. [Nonexpressor of pathogenesis-related genes 1 (NPR1): a key node of plant disease resistance signaling network]. Sheng Wu Gong Cheng Xue Bao. 2005:**21**:511–515. PMID: 16176083

Zhang H, Harry DE, Ma C, Yuceer C, Hsu C-Y, Vikram V, Shevchenko O, Etherington E, Strauss SH. Precocious flowering in trees: the FLOWERING LOCUS T gene as a research and breeding tool in Populus. J Exp Bot. 2010:**61**(10):2549–2560. https://doi.org/10.1093/jxb/erq092

Zhang Y, Li Y, Gao T, Zhu H, Wang D, Zhang H, Ning Y, Liu L, Wu Y, Chu C, et al. Arabidopsis SDIR1 enhances drought tolerance in crop plants. Biosci Biotechnol Biochem. 2008:**72**(8):2251–2254. https://doi.org/10.1271/bbb.80286

Zhang X, Wang Q, Wu J, Qi M, Zhang C, Huang Y, Wang G, Wang H, Tian J, Yu Y, et al. A legume kinesin controls vacuole morphogenesis for rhizobia endosymbiosis. Nat Plants. 2022:**8**(11):1275–1288. https://doi.org/10.1038/s41477-022-01261-4

Zhang L, Ward JD, Cheng Z, Dernburg AF. The auxin-inducible degradation (AID) system enables versatile conditional protein depletion in C. elegans. Development. 2015:**142**(24):4374–4384. https://doi.org/10.1242/dev.129635

Zhang Y, Yang C, Li Y, Zheng N, Chen H, Zhao Q, Gao T, Guo H, Xie Q. SDIR1 is a RING finger E3 ligase that positively regulates stress-responsive abscisic acid signaling in Arabidopsis. Plant Cell. 2007:**19**(6):1912–1929. https://doi.org/10.1105/tpc.106.048488

Zhang J, Zhang X, Tang H, Zhang Q, Hua X, Ma X, Zhu F, Jones T, Zhu X, Bowers J, et al. Allele-defined genome of the autopolyploid sugarcane Saccharum spontaneum L. Nat Genet. 2018:**50**(11):1565–1573. https://doi.org/10.1038/s41588-018-0237-2

Zhao Y, Zhao B, Xie Y, Jia H, Li Y, Xu M, Wu G, Ma X, Li Q, Hou M, et al. The evening complex promotes maize flowering and adaptation to temperate regions. Plant Cell. 2023:**35**(1):369–389. https://doi.org/10.1093/plcell/koac296

Zhu C-C, Wang C-X, Lu C-Y, Wang J-D, Zhou Y, Xiong M, Zhang C-Q, Liu Q-Q, Li Q-F. Genome-wide identification and expression analysis of OsbZIP09 target genes in rice reveal its mechanism of controlling seed germination. Int J Mol Sci. 2021:**22**(4):1661. https://doi.org/10.3390/ijms22041661

Zimmermann P, Hirsch-Hoffmann M, Hennig L, Gruissem W. GENEVESTIGATOR. Arabidopsis microarray database and analysis toolbox. Plant Physiol. 2004:**136**(1):2621–2632. https://doi.org/10.1104/pp.104.046367

Zwaenepoel A, Diels T, Amar D, Van Parys T, Shamir R, Van de Peer Y, Tzfadia O. MorphDB: prioritizing genes for specialized metabolism pathways and gene ontology categories in plants. Front Plant Sci. 2018:**9**:352. https://doi.org/10.3389/fpls.2018.00352