



Editorial

New Horizons in Plant Cell Signaling

Aloysius Wong^{1,2,3,*} and Christoph Gehring^{4,*}

¹ Department of Biology, College of Science and Technology, Wenzhou-Kean University, 88 Daxue Road, Wenzhou 325060, China

² Zhejiang Bioinformatics International Science and Technology Cooperation Center, Wenzhou 325060, China

³ Wenzhou Municipal Key Lab for Applied Biomedical and Biopharmaceutical Informatics, Wenzhou 325060, China

⁴ Department of Chemistry, Biology & Biotechnology, University of Perugia, Borgo XX Giugno, 74, 06121 Perugia, Italy

* Correspondence: alwong@kean.edu (A.W.); christophandreas.gehring@unipg.it (C.G.)

Editorial on the Special Issue: New Horizons in Plant Cell Signaling

Responding to environmental stimuli with appropriate molecular mechanisms is essential to all life forms and particularly so in sessile organisms such as plants. To this end, plants have evolved both rapid early mechanisms such as the activation of channels and kinases directly or indirectly through protein sensors [1–6], as well as the slower systemic adaptive responses that include changes in their transcriptomes and proteomes [7–12]. To enable these processes and concomitantly tune their responses to the environment, complex cellular-signaling mechanisms have evolved, some of which have no homologues in animals [13–21]. This Special Issue aims to broaden the current understanding of plant cell signaling, specifically highlighting recent and exciting discoveries such as the identification of novel signaling molecules and mechanisms that participate across all stages of plant growth and development, and in cellular and biological processes triggered by abiotic and biotic stresses.

One such signaling molecule is the cyclic mononucleotide phosphodiesterases (PDEs), which, together with nucleotide cyclases, regulate the cellular concentrations of the second messengers, cyclic nucleotide monophosphates (cNMPs), cAMP and cGMP. While well-defined in bacteria, yeast and animals, the components of cNMP signaling pathways in plants are still poorly characterized [22–26]. The use of manually curated amino acid motifs based only on the catalytic centers of the corresponding enzymes in organisms across species have enabled the identification and concomitantly also the characterization of several novel adenylate cyclases (ACs) and guanylate cyclases (GCs) [27,28]. The latter is reviewed by Turek and Irving 2021 [29] within the context of moonlighting roles in modulating signal cascades. The authors discussed how the GC activities that moonlight within complex plant proteins, such as the receptor-like kinases and lipid kinases, can potentiate localized cGMP-enriched niches surrounding their primary domains and interactomes [30–32]. Such effects include the downregulation of kinase activity, the modulation of other components or complexes in the signaling pathway and the triggering of degradation cascades leading to signal termination [25,33]. The authors proposed that these moonlighting GCs which generate cGMP-enriched nanodomains in complex proteins form a new paradigm in homeostatic responses that enable a highly precise, spatially differentiated and stimulus-specific cellular signaling in plants [21,29,34,35].

While the generating enzymes of cyclic mononucleotides are being increasingly characterized, the degrading enzymes, the phosphodiesterases (PDEs), have remained elusive in vascular plants until recently. Previously, a novel protein harboring both AC and PDE activities known as CAPE (COMBINED AC with PDE) that may be involved in spermatogenesis and sperm motility, has been identified in the liverwort *Marchantia polymorpha* [36,37]. Adopting a motif-based approach similar to the one mentioned above, Kwiatkowski et al.,



Citation: Wong, A.; Gehring, C. New Horizons in Plant Cell Signaling. *Int. J. Mol. Sci.* **2022**, *23*, 5826. <https://doi.org/10.3390/ijms23105826>

Received: 9 May 2022

Accepted: 13 May 2022

Published: 23 May 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

2021 [38] reported that a monocot *Brachypodium distachyon* (BdPDE1) can hydrolyze cNMPs to 5'NMPs but with a preference for cAMP over cGMP. Much like the PDE activities of other systems [39], BdPDE1 activity was significantly enhanced by Ca²⁺-calmodulin. Mutagenesis studies also identified and revealed the importance of several key residues in the catalytic center. Based on the biochemical, mutagenesis and structural analyses, as well as cross-species sequence analyses, the authors have deduced an amino acid consensus sequence that can be applied in eukaryotes and prokaryotes. Identifying functional PDEs in monocots is a significant step towards crop biotechnology, e.g., enabling the design of specific inhibitors with a view to developing improved crops. Previously, a tandem motif and structural approach has identified a functional PDE moonlighting at the C-terminal of a potassium transporter from the model plant *Arabidopsis thaliana* (AtKUP5) which also harbors a functional AC at the N-terminal [40,41]. The discovery of such dual moonlighting AC-PDE architecture in complex proteins raises the exciting possibility of providing an intricate and dynamic localized spatiotemporal fine-tuning mechanism for signal intensity [30,31,42,43]. Recent discoveries of PDEs in both monocots and dicots suggest that this PDE architecture may well be a common feature in higher plants and that this motif-based strategy can be used to identify novel PDEs in model and crop plants.

The non-cyclic form of cAMP, adenosine monophosphate (AMP), is present in all life forms and is central for energy metabolism achieved through the enzyme 5' adenosine monophosphate-activated protein kinase (AMPK). As an energy sensor, AMPK is activated by decreasing ATP or increasing AMP and ADP [44–46]. AMP is a direct agonist for AMPK and its activation by AMP has been observed through allosteric regulation in various organisms [47]. In this regard, Clark et al., 2020 [48] reviewed the enzymes that generate AMP through the hydrolysis of ATP in plants. They are known as apyrases (APYs). The authors provided a historical account of plant APYs with a particular focus on the progress that has been made in their biochemistry, structures, and functions, reported between 2015 and 2020. Among the recent studies described were reports on how APY expression is linked to growth through extracellular ATP (eATP) treatments and how APY exerts a protective role in plant biotic and abiotic stress responses through the induction of gene expression changes while also appearing to crosstalk with hormones such as ethylene and auxin [49–53]. The authors noted that the initial discovery of plant eATP receptor in *Arabidopsis thaliana*, AtAPY1 [54], has encouraged research on APYs and despite several contradictory reports [55,56], recent data supported the ability of AtAPY1 to bind and hydrolyze ATP [57]. Additionally, new data on APY functions in multiple plant species such as peas, Brassica, and poplar assign the important role of APYs in plant defense responses [58–60]. These, and other major recent advances including the availability of new crystal structures, offer insights on the NTP-binding domain [57], the ability of APYs to hydrolyze ATP in the ECM and nuclei [60], and the identification of APY-binding partners [61]. The findings are summarized in a table. The authors also reviewed the prospect of using APY-specific inhibitors and their value in future research that focuses on how APY regulates cellular activities. The state of the current field is also framed in the form of outstanding major questions that serve to guide research in the field of plant APYs.

Salicylic acid (SA), a phenolic plant hormone found in many plant species, functions as a critical signaling molecule in local and systemic disease resistance pathways [62]. Responding to a broad spectrum of pathogens and abiotic stresses, SA also crosstalks with many signaling pathways ranging from reactive oxygen species, lipids, and circadian clock to other hormones such as jasmonic acid and ethylene [63–67]. Plant defense signaling by SA is initiated when it binds to target proteins such as the nonexpresser of pathogenesis-related protein 1 (NPR1) which is a well-established transcriptional regulator of SA signaling [68]. Pokotylo et al., 2020 [69] proposed that SA could bind to many other proteins, some of which are enzymes involved in primary metabolism such as the glyceraldehyde 3-phosphate dehydrogenase (GAPDH) which was previously shown to bind SA in both humans and plants [70–72]. The authors reported that GAPDH activity was inhibited by SA and showed in surface plasmon resonance studies that SA binds to

the A1 isomer of a chloroplastic glyceraldehyde 3-phosphate dehydrogenase (GAPA1) from *Arabidopsis thaliana* with a K_D of 16.7 nM. The authors further revealed two putative binding pockets through molecular docking and molecular dynamics simulations on the apoprotein and protein–ligand complex, but only one pocket around Asn35 could bind SA when simulated in an aqueous environment. This pocket is also the binding site of the NADP⁺ cofactor and the binding of SA to GAPA1 inhibited NADH in a dose–response manner. Mutagenesis simulations assigned key roles to Asn35 and Arg81 for binding of SA to GAPA1 which the authors then used as a guide for the subsequent in vitro biochemical validations. Mutations of these two residues markedly reduced the ability of GAPA1 to bind SA. Taken together, this research offers novel insights into how SA controls energy fluxes in stressed plants while also providing a new dimension to the current paradigm of SA signaling through its interaction with proteins which have not normally been associated with SA [73,74].

Another signaling molecule, Ca²⁺, has long been known to have a significant role in many cellular activities in both plant and animal systems signaling for cell division, cell movement, cell death, fertilization, and metabolism [75,76]. Ca²⁺ ions in the cytosol of a resting cell are maintained at very low levels typically about 10,000 times lower than that at the extracellular space, or in the vacuole and the lumen of intracellular stores. As such, cytosolic Ca²⁺ must be tightly regulated by the presence of various Ca²⁺ ion pumps, exchangers, and channels. Ca²⁺ entry can be activated by membrane hyperpolarization among other possible mechanisms, but unlike the more common depolarization activation, membrane hyperpolarization would mean that hyperpolarization-activated Ca²⁺ channels (HACCs) are normally kept open in the resting state of the membrane [77–79]. If not regulated, HACCs, which are also permeable to Ba²⁺ and Mg²⁺, would leak Ca²⁺ into cells. Lemtiri-Chlieh et al., 2020 [80] showed that Mg-ATP, but not ATP on its own, significantly reduces HACC activity especially at –200 mV or lower in *Vicia faba* guard cells and this effect is specifically due to Mg²⁺. It led the authors to conclude that Mg²⁺ prevents the continuous leakage of Ca²⁺ into the cells through the inactivation of HACCs and that the opening of these channels would require high negative voltages or displacement of Mg²⁺. Through structural analysis of other Mg²⁺-sensitive K⁺ channels, the authors proposed that the particular HACCs responsible for this result in the guard cell are the cyclic nucleotide-gated channel (CNGCs) which harbor a conserved Mg²⁺-binding motif within their pores [81–83]. In the guard cell, HACCs can be activated by the sesquiterpene hormone ABA and H₂O₂ [84,85]. Therefore, this study establishes an important role for Mg²⁺ in Ca²⁺ signaling and in plant physiological processes including ABA-dependent responses which might bridge existing gaps concerning Ca²⁺ homeostasis in the current literature [75].

Being immobile, plants are constantly exposed to biotic and abiotic stresses and must also respond to a changing external environment. As the boundary between the plant and the external environment, the plant epidermis is not just a barrier that protects the plant against pathogens, but it also regulates exchange of water, nutrients, and gases crucial for growth and development processes [86,87]. The mechanisms involved in transcriptional regulation of epidermal cells in processes such as shoot growth, lipid metabolism and cuticle synthesis, as well as defense responses, are largely unknown [88]. Wang et al., 2020 [89] dissected the promoter of *Triticum aestivum* lipid transfer protein 1 (TaLTP1) by generating multiple deletion constructs and studying their activities in transgenic *Arabidopsis thaliana* and *Brachypodium distachyon*. Through histochemical GUS and quantitative fluorometric analyses, the –400TaLTP1::uidA construct was able to confer full activity at the vegetative stage. A separate construct, –343TaLTP1::uidA, caused a loss of quantitative GUS activity by about 90% in transgenic plant leaves which is associated with pavement cells but not trichomes. Another construct, –297TaLTP1::uidA, resulted in a complete loss of GUS activity in true leaves but the activity was not altered in cotyledon until the promoter region was shortened to position –247 bp. Through mutagenesis studies, the authors also identified the specific *cis*-elements which they named as GC(N₄)GGCC at positions

–380 bp to –372 bp, that are responsible for pavement-cell-specific expression. Using electrophoretic mobility shift and transgenic reporter assays, the authors found a CCAacAt motif at –303 bp that regulates trichome-specific expression while a conserved CcATC motif at –268 bp was found to be involved in regulating pavement-cell-specific expression. In summary, this study identified the specific promoter regions of TaLTP1 responsible for tissue-specific expression as well as the *cis* elements responsible for epidermal-cell-specific expression in shoots, thus contributing to the broader understanding of gene transcription regulation in plant epidermis of aerial tissues [90,91].

Another exciting development related to the regulation of gene expression are the microRNAs. Present in both animals and plants, these single-stranded non-coding RNAs are involved in silencing and post-transcriptional regulation of RNAs [92,93]. Han and Zhou (2022) [94] reviewed the recent progress of one such group of RNAs, the microRNA171 (miR171) in plants. The authors described that miR171 is ancient and conserved in land plants and exerts its regulatory effects by repressing the HAIRYMERISTEM (HAM) gene family [95–98]. In *Arabidopsis thaliana*, miR171 acts as a mobile short-range signal that initiates the epidermal layer of shoot meristems and affects the patterning of apical–basal polarity of gene expression and stem cell dynamics [99]. Besides providing a brief account of miRNA171 and its targets, the authors also discussed its function as a regulatory hub in diverse plant developmental processes, as well as their expression patterns and regulations in response to abiotic stresses such as light. The authors noted that miR171 family members are conserved and have lineage-specific functions in land plants. Thus, they proposed, among other research directions, to focus on how miR171 connects environmental factors to plant development not just in seed plants but also in non-seed vascular plants such as the fern *Ceratopteris richardii*. This may well provide a better account of its evolution in land plants and could potentially make miR171 a target for crop improvement and protection [100–102].

Contributions in this Special Issue have revealed novel signaling molecules, signaling mechanisms, and regulations that broaden our view on how plants signal for growth and development, and their responses to environmental stresses. The body of research presented in this series will hopefully inspire hypothesis generation as well as encourage and guide experiments that will collectively advance our understanding in the rapidly evolving field of plant cell signaling.

Author Contributions: A.W. and C.G. wrote, edited, and approved the manuscript for publication. All authors have read and agreed to the published version of the manuscript.

Funding: A.W. is supported by grants from the National Natural Science Foundation of China (32100581) and the International Collaborative Research Program of Wenzhou-Kean University (ICRP202202).

Conflicts of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Chen, X.; Ding, Y.; Yang, Y.; Song, C.; Wang, B.; Yang, S.; Guo, Y.; Gong, Z. Protein kinases in plant responses to drought, salt, and cold stress. *J. Integr. Plant Biol.* **2021**, *63*, 53–78. [[CrossRef](#)] [[PubMed](#)]
2. Dong, Q.; Wallrad, L.; Almutairi, B.O.; Kudla, J. Ca²⁺ signaling in plant responses to abiotic stresses. *J. Integr. Plant Biol.* **2022**, *64*, 287–300. [[CrossRef](#)] [[PubMed](#)]
3. Lee, H.-J.; Seo, P.J. Ca²⁺-talyzing Initial Responses to Environmental Stresses. *Trends Plant Sci.* **2021**, *26*, 849–870. [[CrossRef](#)] [[PubMed](#)]
4. Xu, G.; Moeder, W.; Yoshioka, K.; Shan, L. A tale of many families: Calcium channels in plant immunity. *Plant Cell* **2022**, *34*, 1551–1567. [[CrossRef](#)]
5. Kleist, T.J.; Wudick, M.M. Shaping up: Recent advances in the study of plant calcium channels. *Curr. Opin. Cell Biol.* **2022**, *76*, 102080. [[CrossRef](#)]
6. Kollist, H.; Zandalinas, S.I.; Sengupta, S.; Nuhkat, M.; Kangasjärvi, J.; Mittler, R. Rapid Responses to Abiotic Stress: Priming the Landscape for the Signal Transduction Network. *Trends Plant Sci.* **2019**, *24*, 25–37. [[CrossRef](#)]

7. Huang, J.; Zhao, X.; Chory, J.; Huang, J.; Zhao, X.; Chory, J. The Arabidopsis Transcriptome Responds Specifically and Dynamically to High Light Stress. *Cell Rep.* **2019**, *29*, 4186–4199.e3. [[CrossRef](#)]
8. Nagano, A.J.; Kawagoe, T.; Sugisaka, J.; Honjo, M.N.; Iwayama, K.; Kudoh, H. Annual transcriptome dynamics in natural environments reveals plant seasonal adaptation. *Nat. Plants* **2019**, *5*, 74–83. [[CrossRef](#)]
9. Wang, P.; Hsu, C.-C.; Du, Y.; Zhu, P.; Zhao, C.; Fu, X.; Zhang, C.; Paez, J.S.; Macho, A.P.; Tao, W.A.; et al. Mapping proteome-wide targets of protein kinases in plant stress responses. *Proc. Natl. Acad. Sci. USA* **2020**, *117*, 3270–3280. [[CrossRef](#)]
10. Marondedze, C.; Thomas, L.; Gehring, C.; Lilley, K.S. Changes in the Arabidopsis RNA-binding proteome reveal novel stress response mechanisms. *BMC Plant Biol.* **2019**, *19*, 139. [[CrossRef](#)]
11. Seaton, D.D.; Graf, A.; Baerenfaller, K.; Stitt, M.; Millar, A.J.; Gruijsem, W. Photoperiodic control of the Arabidopsis proteome reveals a translational coincidence mechanism. *Mol. Syst. Biol.* **2018**, *14*, e7962. [[CrossRef](#)] [[PubMed](#)]
12. Orr, M.W.; Mao, Y.; Storz, G.; Qian, S.-B. Alternative ORFs and small ORFs: Shedding light on the dark proteome. *Nucleic Acids Res.* **2020**, *48*, 1029–1042. [[CrossRef](#)] [[PubMed](#)]
13. Toyota, M.; Spencer, D.; Sawai-Toyota, S.; Jiaqi, W.; Zhang, T.; Koo, A.J.; Howe, G.A.; Gilroy, S. Glutamate triggers long-distance, calcium-based plant defense signaling. *Science* **2018**, *361*, 1112–1115. [[CrossRef](#)]
14. Trewavas, A. Mindless mastery. *Nature* **2002**, *415*, 841. [[CrossRef](#)]
15. Bradford, W.; Buckholz, A.; Morton, J.; Price, C.; Jones, A.M.; Urano, D. Eukaryotic G Protein Signaling Evolved to Require G Protein-Coupled Receptors for Activation. *Sci. Signal.* **2013**, *6*, ra37. [[CrossRef](#)]
16. Wu, T.-Y.; Goh, H.; Azodi, C.B.; Krishnamoorthi, S.; Liu, M.-J.; Urano, D. Evolutionarily conserved hierarchical gene regulatory networks for plant salt stress response. *Nat. Plants* **2021**, *7*, 787–799. [[CrossRef](#)]
17. Maruta, N.; Trusov, Y.; Urano, D.; Chakravorty, D.; Assmann, S.M.; Jones, A.M.; Botella, J.R. GTP binding by Arabidopsis extra-large G protein 2 is not essential for its functions. *Plant Physiol.* **2021**, *186*, 1240–1253. [[CrossRef](#)]
18. Wong, A.; Hu, N.; Tian, X.; Yang, Y.; Gehring, C. Nitric oxide sensing revisited. *Trends Plant Sci.* **2021**, *26*, 885–897. [[CrossRef](#)]
19. Wong, A.; Tian, X.; Yang, Y.; Gehring, C. Identification of potential nitric oxide-sensing proteins using the H-NOX motif. *Mol. Plant* **2021**, *14*, 195–197. [[CrossRef](#)]
20. Wong, A.; Bi, C.; Pasqualini, S.; Gehring, C. Abscisic acid (ABA) signaling: Finding novel components off the beaten track. *Plant Growth Regul.* **2022**, 1–8. [[CrossRef](#)]
21. Campos, M.L. Round and round it goes: A cyclic nucleotide modulates stress responses in plants. *Plant Physiol.* **2022**, *188*, 1942–1943. [[CrossRef](#)] [[PubMed](#)]
22. Gehring, C.; Turek, I.S. Cyclic nucleotide monophosphates and their cyclases in plant signaling. *Front. Plant Sci.* **2017**, *8*, 1704. [[CrossRef](#)] [[PubMed](#)]
23. Marondedze, C.; Wong, A.; Thomas, L.; Irving, H.; Gehring, C. Cyclic nucleotide monophosphates in plants and plant signaling. *Handb. Exp. Pharmacol.* **2017**, *238*, 87–103. [[CrossRef](#)]
24. Blanco, E.; Fortunato, S.; Viggiano, L.; De Pinto, M.C. Cyclic AMP: A Polyhedral Signalling Molecule in Plants. *Int. J. Mol. Sci.* **2020**, *21*, 4862. [[CrossRef](#)]
25. Świeżawska-Boniecka, B.; Duszyn, M.; Kwiatkowski, M.; Szmidi-Jaworska, A.; Jaworski, K. Cross talk between cyclic nucleotides and calcium signaling pathways in plants-achievements and prospects. *Front. Plant Sci.* **2021**, *12*, 643560. [[CrossRef](#)]
26. Sun, J.; Ning, Y.; Wang, L.; Wilkins, K.A.; Davies, J.M. Damage signaling by extracellular nucleotides: A role for cyclic nucleotides in elevating cytosolic free calcium? *Front. Plant Sci.* **2021**, *12*, 788514. [[CrossRef](#)]
27. Zhou, W.; Chi, W.; Shen, W.; Dou, W.; Wang, J.; Tian, X.; Gehring, C.; Wong, A. Computational Identification of Functional Centers in Complex Proteins: A Step-by-Step Guide with Examples. *Front. Bioinform.* **2021**, *1*, 652286. [[CrossRef](#)]
28. Wong, A.; Tian, X.; Gehring, C.; Marondedze, C. Discovery of Novel Functional Centers with Rationally Designed Amino Acid Motifs. *Comput. Struct. Biotechnol. J.* **2018**, *16*, 70–76. [[CrossRef](#)]
29. Turek, I.; Irving, H. Moonlighting Proteins Shine New Light on Molecular Signaling Niches. *Int. J. Mol. Sci.* **2021**, *22*, 1367. [[CrossRef](#)]
30. Irving, H.R.; Cahill, D.M.; Gehring, C. Moonlighting Proteins and Their Role in the Control of Signaling Microenvironments, as Exemplified by cGMP and Phytosulfokine Receptor 1 (PSKR1). *Front. Plant Sci.* **2018**, *9*, 415. [[CrossRef](#)]
31. Su, B.; Qian, Z.; Li, T.; Zhou, Y.; Wong, A. PlantMP: A database for moonlighting plant proteins. *Database* **2019**, *2019*, baz050. [[CrossRef](#)]
32. Wong, A.; Donaldson, L.; Portes, M.T.; Eppinger, J.; Feijó, J.; Gehring, C. The Arabidopsis Diacylglycerol Kinase 4 is involved in nitric oxide-dependent pollen tube guidance and fertilization. *Development* **2020**, *147*, 183715. [[CrossRef](#)]
33. Ma, Y.; Walker, R.K.; Zhao, Y.; Berkowitz, G.A. Linking ligand perception by PEPR pattern recognition receptors to cytosolic Ca²⁺ elevation and downstream immune signaling in plants. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 19852–19857. [[CrossRef](#)]
34. Yang, H.; Zhao, Y.; Chen, N.; Liu, Y.; Yang, S.; Du, H.; Wang, W.; Wu, J.; Tai, F.; Chen, F.; et al. A new adenylyl cyclase, putative disease-resistance RPP13-like protein 3, participates in abscisic acid-mediated resistance to heat stress in maize. *J. Exp. Bot.* **2021**, *72*, 283–301. [[CrossRef](#)]
35. Rahman, H.; Wang, X.-Y.; Xu, Y.-P.; He, Y.-H.; Cai, X.-Z. Characterization of tomato protein kinases embedding guanylate cyclase catalytic center motif. *Sci. Rep.* **2020**, *10*, 4078. [[CrossRef](#)]

36. Kasahara, M.; Suetsugu, N.; Urano, Y.; Yamamoto, C.; Ohmori, M.; Takada, Y.; Okuda, S.; Nishiyama, T.; Sakayama, H.; Kohchi, T.; et al. An adenylyl cyclase with a phosphodiesterase domain in basal plants with a motile sperm system. *Sci. Rep.* **2016**, *6*, 39232. [[CrossRef](#)]
37. Yamamoto, C.; Takahashi, F.; Ooe, Y.; Shirahata, H.; Shibata, A.; Kasahara, M. Distribution of adenylyl cyclase/cAMP phosphodiesterase gene, CAPE, in streptophytes reproducing via motile sperm. *Sci. Rep.* **2021**, *11*, 10054. [[CrossRef](#)]
38. Kwiatkowski, M.; Wong, A.; Kozakiewicz-Piekarz, A.; Gehring, C.; Jaworski, K. In Search of Monocot Phosphodiesterases: Identification of a Calmodulin Stimulated Phosphodiesterase from *Brachypodium distachyon*. *Int. J. Mol. Sci.* **2021**, *22*, 9654. [[CrossRef](#)]
39. Kakkar, R.; Raju, R.V.; Sharma, R.K. Calmodulin-dependent cyclic nucleotide phosphodiesterase (PDE1). *Cell Mol. Life Sci.* **1999**, *55*, 1164–1186. [[CrossRef](#)]
40. Kwiatkowski, M.; Wong, A.; Kozakiewicz, A.; Gehring, C.; Jaworski, K. A tandem motif-based and structural approach can identify hidden functional phosphodiesterases. *Comput. Struct. Biotechnol. J.* **2021**, *19*, 970–975. [[CrossRef](#)]
41. Al-Younis, I.; Wong, A.; Lemtiri-Chlieh, F.; Schmöckel, S.; Tester, M.; Gehring, C.; Donaldson, L. The Arabidopsis thaliana K⁺-Uptake Permease 5 (AtKUP5) Contains a Functional Cytosolic Adenylate Cyclase Essential for K⁺ Transport. *Front. Plant Sci.* **2018**, *9*, 1645. [[CrossRef](#)] [[PubMed](#)]
42. Zhang, Y.; Sampathkumar, A.; Kerber, S.M.-L.; Swart, C.; Hille, C.; Seerangan, K.; Graf, A.; Sweetlove, L.; Fernie, A.R. A moonlighting role for enzymes of glycolysis in the co-localization of mitochondria and chloroplasts. *Nat. Commun.* **2020**, *11*, 4509. [[CrossRef](#)] [[PubMed](#)]
43. Allipra, S.; Anirudhan, K.; Shivanandan, S.; Raghunathan, A.; Maruthachalam, R. The kinetochore protein NNF1 has a moonlighting role in the vegetative development of *Arabidopsis thaliana*. *Plant J.* **2021**, *109*, 1064–1085. [[CrossRef](#)] [[PubMed](#)]
44. Herzig, S.; Shaw, R.J. AMPK: Guardian of metabolism and mitochondrial homeostasis. *Nat. Rev. Mol. Cell Biol.* **2018**, *19*, 121–135. [[CrossRef](#)] [[PubMed](#)]
45. Trefts, E.; Shaw, R.J. AMPK: Restoring metabolic homeostasis over space and time. *Mol. Cell* **2021**, *81*, 3677–3690. [[CrossRef](#)] [[PubMed](#)]
46. Hardie, D.G.; Ross, F.A.; Hawley, S.A. AMPK: A nutrient and energy sensor that maintains energy homeostasis. *Nat. Rev. Mol. Cell Biol.* **2012**, *13*, 251–262. [[CrossRef](#)]
47. Hardie, D.G. AMP-activated protein kinase: An energy sensor that regulates all aspects of cell function. *Genes Dev.* **2011**, *25*, 1895–1908. [[CrossRef](#)]
48. Clark, G.; Brown, K.; Tripathy, M.; Roux, S. Recent Advances Clarifying the Structure and Function of Plant Apyrases (Nucleoside Triphosphate Diphosphohydrolases). *Int. J. Mol. Sci.* **2021**, *22*, 3283. [[CrossRef](#)]
49. Lim, M.H.; Wu, J.; Yao, J.; Gallardo, I.F.; Dugger, J.; Webb, L.J.; Huang, J.; Salmi, M.; Song, J.; Clark, G.; et al. Apyrase Suppression Raises Extracellular ATP Levels and Induces Gene Expression and Cell Wall Changes Characteristic of Stress Responses. *Plant Physiol.* **2014**, *164*, 2054–2067. [[CrossRef](#)]
50. Liu, X.; Wu, J.; Clark, G.; Lundy, S.; Lim, M.; Arnold, D.; Chan, J.; Tang, W.; Muday, G.K.; Gardner, G.; et al. Role for Apyrases in Polar Auxin Transport in Arabidopsis. *Plant Physiol.* **2012**, *160*, 1985–1995. [[CrossRef](#)]
51. Clark, G.; Roux, S.J. Apyrases, extracellular ATP and the regulation of growth. *Curr. Opin. Plant Biol.* **2011**, *14*, 700–706. [[CrossRef](#)] [[PubMed](#)]
52. Lang, T.; Deng, C.; Yao, J.; Zhang, H.L.; Wang, Y.; Deng, S.R. A Salt-Signaling Network Involving Ethylene, Extracellular ATP, Hydrogen Peroxide, and Calcium Mediates K⁺/Na⁺ Homeostasis in Arabidopsis. *Int. J. Mol. Sci.* **2020**, *21*, 8683. [[CrossRef](#)] [[PubMed](#)]
53. Jewell, J.B.; Sowders, J.M.; He, R.F.; Willis, M.A.; Gang, D.R.; Tanaka, K. Extracellular ATP Shapes a Defense-Related Transcriptome Both Independently and along with Other Defense Signaling Pathways. *Plant Physiol.* **2019**, *179*, 1144–1158. [[CrossRef](#)] [[PubMed](#)]
54. Choi, J.; Tanaka, K.; Cao, Y.R.; Qi, Y.; Qiu, J.; Liang, Y.; Lee, S.Y.; Stacey, G. Identification of a Plant Receptor for Extracellular ATP. *Science* **2014**, *343*, 290–294. [[CrossRef](#)]
55. Chiu, T.Y.; Christiansen, K.; Moreno, I.; Lao, J.M.; Loque, D.; Orellana, A.; Heazlewood, J.L.; Clark, G.; Roux, S.J. AtAPY1 and AtAPY2 Function as Golgi-Localized Nucleoside Diphosphatases in Arabidopsis thaliana. *Plant Cell Physiol.* **2012**, *53*, 1913–1925. [[CrossRef](#)]
56. Chiu, T.Y.; Lao, J.; Manalansan, B.; Loque, D.; Roux, S.J.; Heazlewood, J.L. Biochemical characterization of Arabidopsis APYRASE family reveals their roles in regulating endomembrane NDP/NMP homeostasis. *Biochem. J.* **2015**, *472*, 43–54. [[CrossRef](#)]
57. Summers, E.L.; Cumming, M.H.; Oulavallickal, T.; Roberts, N.J.; Arcus, V.L. Structures and kinetics for plant nucleoside triphosphate diphosphohydrolases support a domain motion catalytic mechanism. *Protein Sci.* **2017**, *26*, 1627–1638. [[CrossRef](#)]
58. Veerappa, R.; Slocum, R.D.; Siegenthaler, A.; Wang, J.; Clark, G.; Roux, S.J. Ectopic expression of a pea apyrase enhances root system architecture and drought survival in Arabidopsis and soybean. *Plant Cell Environ.* **2019**, *42*, 337–353. [[CrossRef](#)]
59. Cao, L.W.; Liu, B.; Li, J.X.; Yu, N.N.; Zou, X.X.; Chen, L.P. Light- and temperature-regulated BjAPY2 may have a role in stem expansion of Brassica juncea. *Funct. Integr. Genom.* **2015**, *15*, 753–762. [[CrossRef](#)]
60. Deng, S.R.; Sun, J.; Zhao, R.; Ding, M.Q.; Zhang, Y.N.; Sun, Y.L.; Wang, W.; Tan, Y.Q.; Liu, D.D.; Ma, X.J.; et al. Populus euphratica APYRASE2 Enhances Cold Tolerance by Modulating Vesicular Trafficking and Extracellular ATP in Arabidopsis Plants. *Plant Physiol.* **2015**, *169*, 530–548. [[CrossRef](#)]

61. Li, H.; Hu, J.B.; Pang, J.; Zhao, L.T.; Yang, B.; Kang, X.L.; Wang, A.M.; Xu, T.D.; Yang, Z.B. Rho GTPase ROP1 Interactome Analysis Reveals Novel ROP1-Associated Pathways for Pollen Tube Polar Growth in Arabidopsis. *Int. J. Mol. Sci.* **2020**, *21*, 7033. [[CrossRef](#)] [[PubMed](#)]
62. Janda, T.; Szalai, G.; Pál, M. Salicylic Acid Signalling in Plants. *Int. J. Mol. Sci.* **2020**, *21*, 2655. [[CrossRef](#)] [[PubMed](#)]
63. Thaler, J.S.; Humphrey, P.T.; Whiteman, N.K. Evolution of jasmonate and salicylate signal crosstalk. *Trends Plant Sci.* **2012**, *17*, 260–270. [[CrossRef](#)] [[PubMed](#)]
64. Yang, J.; Duan, G.; Li, C.; Liu, L.; Han, G.; Zhang, Y.; Wang, C. The Crosstalks Between Jasmonic Acid and Other Plant Hormone Signaling Highlight the Involvement of Jasmonic Acid as a Core Component in Plant Response to Biotic and Abiotic Stresses. *Front. Plant Sci.* **2019**, *10*, 1349. [[CrossRef](#)] [[PubMed](#)]
65. Saxena, I.; Srikanth, S.; Chen, Z. Cross Talk between H₂O₂ and Interacting Signal Molecules under Plant Stress Response. *Front. Plant Sci.* **2016**, *7*, 570. [[CrossRef](#)]
66. Zhang, Q.; Xiao, S. Lipids in salicylic acid-mediated defense in plants: Focusing on the roles of phosphatidic acid and phosphatidylinositol 4-phosphate. *Front. Plant Sci.* **2015**, *6*, 387. [[CrossRef](#)]
67. Philippou, K.; Davis, A.M.; Davis, S.J.; Sánchez-Villarreal, A. Chemical Perturbation of Chloroplast-Related Processes Affects Circadian Rhythms of Gene Expression in Arabidopsis: Salicylic Acid Application Can Entrain the Clock. *Front. Physiol.* **2020**, *11*, 429. [[CrossRef](#)]
68. Liu, Y.; Sun, T.; Sun, Y.; Zhang, Y.; Radojčić, A.; Ding, Y.; Tian, H.; Huang, X.; Lan, J.; Chen, S.; et al. Diverse Roles of the Salicylic Acid Receptors NPR1 and NPR3/NPR4 in Plant Immunity. *Plant Cell* **2020**, *32*, 4002–4016. [[CrossRef](#)]
69. Pokotylo, I.; Hellal, D.; Bouceba, T.; Hernandez-Martinez, M.; Kravets, V.; Leitao, L.; Espinasse, C.; Kleiner, I.; Ruelland, E. Deciphering the Binding of Salicylic Acid to Arabidopsis thaliana Chloroplastic GAPDH-A1. *Int. J. Mol. Sci.* **2020**, *21*, 4678. [[CrossRef](#)]
70. Pokotylo, I.; Kravets, V.; Ruelland, E. Salicylic acid binding proteins (SABPs): The hidden forefront of salicylic acid signalling. *Int. J. Mol. Sci.* **2019**, *20*, 4377. [[CrossRef](#)]
71. Choi, H.W.; Wang, L.; Powell, A.F.; Strickler, S.R.; Wang, D.; Dempsey, D.A.; Schroeder, F.C.; Klessig, D.F. A genome-wide screen for human salicylic acid (SA)-binding proteins reveals targets through which SA may influence development of various diseases. *Sci. Rep.* **2019**, *9*, 13084. [[CrossRef](#)] [[PubMed](#)]
72. Klessig, D.F.; Tian, M.; Choi, H.W. Multiple Targets of Salicylic Acid and Its Derivatives in Plants and Animals. *Front. Immunol.* **2016**, *7*, 206. [[CrossRef](#)] [[PubMed](#)]
73. Nadarajah, K.; Abdul Hamid, N.W.; Abdul Rahman, N. SA-Mediated Regulation and Control of Abiotic Stress Tolerance in Rice. *Int. J. Mol. Sci.* **2021**, *22*, 5591. [[CrossRef](#)] [[PubMed](#)]
74. Dempsey, D.A.; Klessig, D.F. How does the multifaceted plant hormone salicylic acid combat disease in plants and are similar mechanisms utilized in humans? *BMC Biol.* **2017**, *15*, 23. [[CrossRef](#)]
75. Kudla, J.; Becker, D.; Grill, E.; Hedrich, R.; Hippler, M.; Kummer, U.; Parniske, M.; Romeis, T.; Schumacher, K. Advances and current challenges in calcium signaling. *New Phytol.* **2018**, *218*, 414–431. [[CrossRef](#)]
76. Luan, S.; Wang, C. Calcium Signaling Mechanisms Across Kingdoms. *Annu. Rev. Cell Dev. Biol.* **2021**, *37*, 311–340. [[CrossRef](#)]
77. Edel, K.H.; Marchadier, E.; Brownlee, C.; Kudla, J.; Hetherington, A.M. The Evolution of Calcium-Based Signalling in Plants. *Curr. Biol.* **2017**, *27*, R667–R679. [[CrossRef](#)]
78. Thor, K. Calcium-Nutrient and Messenger. *Front. Plant Sci.* **2019**, *10*, 440. [[CrossRef](#)]
79. Miedema, H.; Demidchik, V.; Véry, A.-A.; Bothwell, J.H.F.; Brownlee, C.; Davies, J.M. Two voltage-dependent calcium channels co-exist in the apical plasma membrane of Arabidopsis thaliana root hairs. *New Phytol.* **2008**, *179*, 378–385. [[CrossRef](#)]
80. Lemtiri-Chlieh, F.; Arold, S.T.; Gehring, C. Mg²⁺ Is a Missing Link in Plant Cell Ca²⁺ Signalling and Homeostasis—A Study on Vicia faba Guard Cells. *Int. J. Mol. Sci.* **2020**, *21*, 3771. [[CrossRef](#)]
81. Duszyn, M.; Świeżawska, B.; Szmidt-Jaworska, A.; Jaworski, K. Cyclic nucleotide gated channels (CNGCs) in plant signalling—Current knowledge and perspectives. *J. Plant Physiol.* **2019**, *241*, 153035. [[CrossRef](#)] [[PubMed](#)]
82. Pan, Y.; Chai, X.; Gao, Q.; Zhou, L.; Zhang, S.; Li, L.; Luan, S. Dynamic Interactions of Plant CNGC Subunits and Calmodulins Drive Oscillatory Ca²⁺ Channel Activities. *Dev. Cell* **2019**, *48*, 710–725.e5. [[CrossRef](#)] [[PubMed](#)]
83. Jarratt-Barnham, E.; Wang, L.; Ning, Y.; Davies, J.M. The Complex Story of Plant Cyclic Nucleotide-Gated Channels. *Int. J. Mol. Sci.* **2021**, *22*, 874. [[CrossRef](#)] [[PubMed](#)]
84. Wang, P.; Song, C.P. Guard-cell signalling for hydrogen peroxide and abscisic acid. *New Phytol.* **2008**, *178*, 703–718. [[CrossRef](#)]
85. Pei, Z.M.; Murata, Y.; Benning, G.; Thomine, S.; Klüsener, B.; Allen, G.J.; Grill, E.; Schroeder, J.I. Calcium channels activated by hydrogen peroxide mediate abscisic acid signalling in guard cells. *Nature* **2000**, *406*, 731–734. [[CrossRef](#)]
86. Javelle, M.; Vernoud, V.; Rogowsky, P.M.; Ingram, G.C. Epidermis: The formation and functions of a fundamental plant tissue. *New Phytol.* **2011**, *18*, 17–39. [[CrossRef](#)]
87. Zuch, D.T.; Doyle, S.M.; Majda, M.; Smith, R.S.; Robert, S.; Torii, K.U. Cell biology of the leaf epidermis: Fate specification, morphogenesis, and coordination. *Plant Cell* **2022**, *34*, 209–227. [[CrossRef](#)]
88. Bhatia, S.; Kumar, H.; Mahajan, M.; Yadav, S.; Saini, P.; Yadav, S.; Sahu, S.K.; Sundaram, J.K.; Yadav, R.K. A cellular expression map of epidermal and subepidermal cell layer-enriched transcription factor genes integrated with the regulatory network in Arabidopsis shoot apical meristem. *Plant Direct* **2021**, *5*, e00306. [[CrossRef](#)]

89. Wang, G.; Yu, G.; Hao, Y.; Cheng, X.; Zhao, J.; Sun, S.; Wang, H. Molecular Dissection of TaLTP1 Promoter Reveals Functional Cis-Elements Regulating Epidermis-Specific Expression. *Int. J. Mol. Sci.* **2020**, *21*, 2261. [[CrossRef](#)]
90. Tian, N.; Liu, F.; Wang, P.; Yan, X.; Gao, H.; Zeng, X.; Wu, G. Overexpression of BraLTP2, a Lipid Transfer Protein of Brassica napus, Results in Increased Trichome Density and Altered Concentration of Secondary Metabolites. *Int. J. Mol. Sci.* **2018**, *19*, 1733. [[CrossRef](#)]
91. Balmant, K.M.; Lawrence, S.R., 2nd; Duong, B.V.; Zhu, F.; Zhu, N.; Nicklay, J.; Chen, S. Guard cell redox proteomics reveals a role of lipid transfer protein in plant defense. *J. Proteomics* **2021**, *242*, 104247. [[CrossRef](#)] [[PubMed](#)]
92. Samad, A.F.A.; Kamaroddin, M.F.; Sajad, M. Cross-Kingdom Regulation by Plant microRNAs Provides Novel Insight into Gene Regulation. *Adv. Nutr.* **2021**, *12*, 197–211. [[CrossRef](#)] [[PubMed](#)]
93. Khraiweh, B.; Arif, M.A.; Seumel, G.I.; Ossowski, S.; Weigel, D.; Reski, R.; Frank, W. Transcriptional control of gene expression by microRNAs. *Cell* **2010**, *140*, 111–122. [[CrossRef](#)] [[PubMed](#)]
94. Han, H.; Zhou, Y. Function and Regulation of microRNA171 in Plant Stem Cell Homeostasis and Developmental Programming. *Int. J. Mol. Sci.* **2022**, *23*, 2544. [[CrossRef](#)] [[PubMed](#)]
95. Zhu, X.; Leng, X.; Sun, X.; Mu, Q.; Wang, B.; Li, X.; Wang, C.; Fang, J. Discovery of Conservation and Diversification of miR171 Genes by Phylogenetic Analysis based on Global Genomes. *Plant Genome* **2015**, *8*, plantgenome2014-10. [[CrossRef](#)]
96. Geng, Y.; Guo, L.; Han, H.; Liu, X.; Banks, J.A.; Wisecaver, J.H.; Zhou, Y. Conservation and diversification of HAIRY MERISTEM gene family in land plants. *Plant J.* **2021**, *106*, 366–378. [[CrossRef](#)]
97. Couzigou, J.M.; Combier, J.P. Plant microRNAs: Key regulators of root architecture and biotic interactions. *New Phytol.* **2016**, *212*, 22–35. [[CrossRef](#)]
98. Geng, Y.; Zhou, Y. HAM Gene Family and Shoot Meristem Development. *Front. Plant Sci.* **2021**, *12*, 800332. [[CrossRef](#)]
99. Han, H.; Yan, A.; Li, L.; Zhu, Y.; Feng, B.; Liu, X.; Zhou, Y. A signal cascade originated from epidermis defines apical-basal patterning of Arabidopsis shoot apical meristems. *Nat. Commun.* **2020**, *11*, 1214. [[CrossRef](#)]
100. Siré, C.; Moreno, A.B.; Garcia-Chapa, M.; López-Moya, J.J.; San Segundo, B. Diurnal oscillation in the accumulation of Arabidopsis microRNAs, miR167, miR168, miR171 and miR398. *FEBS Lett.* **2009**, *583*, 1039–1044. [[CrossRef](#)]
101. Wu, X.; Yan, A.; McAdam, S.A.M.; Banks, J.A.; Zhang, S.; Zhou, Y. Timing of meristem initiation and maintenance determines the morphology of fern gametophytes. *J. Exp. Bot.* **2021**, *72*, 6990–7001. [[CrossRef](#)] [[PubMed](#)]
102. Djami-Tchatchou, A.T.; Sanan-Mishra, N.; Ntushelo, K.; Dubery, I.A. Functional Roles of microRNAs in Agronomically Important Plants-Potential as Targets for Crop Improvement and Protection. *Front. Plant Sci.* **2017**, *8*, 378. [[CrossRef](#)] [[PubMed](#)]