Vegetable Research

REVIEW

Open Access

https://doi.org/10.48130/vegres-0026-0019

Vegetable Research **2026**, 6: e026

Integrated regulatory networks: coordinating glandular trichome development and terpenoid synthesis in plants

Jinfeng Zhao[1,2#], Wanjie Xue[1,2#], Jiaxu Shi[1,2], Xinyu Zhao[1,2], Yumeng Zhang[1,2] and Yang Zhang[1,2*]

[1] *Key Laboratory of Saline- alkali Vegetation Ecology Restoration, Northeast Forestry University, Ministry of Education, Harbin 150040, China*
[2] *College of Life Science, Northeast Forestry University, Harbin 150040, China*
[#] Authors contributed equally: Jinfeng Zhao, Wanjie Xue
[*] Correspondence: summerzhang@126.com (Zhang Y)

Abstract

Glandular trichomes (GTs) are specialized epidermal structures in plants, which function as sites for the biosynthesis and storage of secondary metabolites, predominantly terpenoids. Traditionally, GT development and terpenoid biosynthesis were regarded as independent processes. However, accumulating evidence indicates that these two processes are often associated. In this review, we examine this relationship across multiple regulatory levels. At the spatiotemporal level, terpenoid accumulation is temporally associated with GT maturation. At the structural level, the subcuticular cavity formed during GT development provides a compartment for terpenoid storage. At the transcriptional level, key regulators such as MYB and bHLH transcription factors (TFs) have been shown to directly regulate both GT development and terpenoid biosynthetic pathways. We describe the developmental stages of GTs alongside the accumulation patterns of terpenoids and propose an integrated regulatory framework governing both processes in model plants and economically important crop species. We also discuss how this regulatory framework may inform strategies for engineering terpenoid-producing crops and constructing plant cell factories for terpenoid production.

Keywords: Glandular trichomes, Terpenoids, Synergistic regulation, Transcriptional network, Metabolic engineering

Citation: Zhao J, Xue W, Shi J, Zhao X, Zhang Y, et al. 2026. Integrated regulatory networks: coordinating glandular trichome development and terpenoid synthesis in plants. *Vegetable Research* 6: e026 https://doi.org/10.48130/vegres-0026-0019

Introduction

Plants have evolved diverse strategies for environmental adaptation, among which trichomes serve as the primary defensive interface on plant surfaces[1]. Trichomes are classified into two categories: glandular trichomes (GTs) and non-glandular trichomes (NGTs). GTs act as major metabolic sites responsible for the biosynthesis, storage, and secretion of bioactive secondary metabolites, mediating chemical defense. NGTs mainly function in physical protection[2].

GTs exhibit multiple biological functions. In chemical defense, the secondary metabolites synthesized and stored in GTs defend the plants against herbivores. For example, the methyl ketones produced by GTs in wild *Solanum lycopersicum* are toxic to arthropods[3], and the nicotine in the GTs of *Nicotiana tabacum* repels insects[4]. The antimicrobial compounds secreted by GTs, such as sesquiterpene lactones in *Artemisia annua*, inhibit pathogenic microorganisms[5]. GTs also enhance abiotic stress tolerance by reducing water loss and reflecting ultraviolet radiation. During reproduction, the volatile compounds released by floral GTs can attract pollinators[6]. In addition, the subcuticular cavity of GTs provides a sequestered storage space for metabolites, preventing autotoxicity[7].

Increasing evidence indicates that GT development and terpenoid biosynthesis are not independent processes but are linked at multiple levels. Spatially and temporally, terpenoid accumulation is associated with GT maturation. Structurally, the subcuticular cavity enables metabolite compartmentalization and storage. At the molecular level, key transcription factors (TFs) such as AaMYC3/AaHD1 in *A. annua* and the Woolly/SlMYC1 module in *S. lycopersicum* have been shown to regulate genes involved in both GT formation and terpenoid biosynthesis[8,9]. Such multi-level association suggests that GT development and terpenoid production form an integrated system for metabolite sequestration and defense integration.

The current understanding of the regulatory logic connecting GT development and terpenoid biosynthesis is fragmented across species and experimental systems. A coherent framework is needed to integrate cell differentiation, metabolic pathways, and transcriptional control, in order to understand their potential coordinated mechanisms and support their applications in plant engineering. For the purpose of this review, GTs are defined as epidermal appendages containing secretory cells capable of producing, accumulating, or secreting specialized metabolites, including peltate and capitate GTs[10]. NGTs are not involved in metabolite synthesis or secretion and are therefore only compared morphologically[11].

In this review, we present the recent advances and propose an integrated framework for the coordinated regulation of GT development and terpenoid biosynthesis. First, we describe the developmental stages of GTs and the accumulation dynamics of terpenoids, emphasizing their spatiotemporal and structural coupling. Next, we analyze the transcriptional networks governing both processes, focusing on TFs that simultaneously regulate GT development and terpenoid biosynthesis. Finally, we discuss the implications of this regulatory logic for synthetic biology strategies aimed at crop improvement and plant-based terpenoid production systems. Through this review, we aim to systematically summarize the current knowledge, identify key research gaps, and propose future directions toward the synergy of plant development and specialized metabolism.

https://doi.org/10.48130/vegres-0026-0019

Spatiotemporal coupling of GT development and terpenoid biosynthesis

Types and distribution of GTs

GTs are specialized epidermal structures characteristic of terrestrial plants. Morphologically and functionally, they are categorized as capitate and peltate types. For comparison, NGTs are also briefly described (Fig. 1).

Peltate GTs have short stalks and discoid multicellular secretory heads. Separation of the epidermis from the outer cell wall creates a subcuticular storage cavity, in which terpenoids, flavonoids, alkaloids, and other secondary metabolites accumulate. Metabolites are released via cuticle rupture or diffusion[12,13]. In *S. lycopersicum*, Type VI peltate GTs comprise four secretory cells and a relatively small internal chamber[14]. *A. annua* peltate GTs possess large subcuticular cavities that store high concentrations of volatile terpenoids such as artemisinin[15]. *Mentha×piperita* peltate GTs exhibit multicellular secretory heads with two to eight secretory cells, synthesizing and storing essential oils[16].

Capitate GTs possess elongated stalks, topped by one or several glandular cells. Most lack a distinct subcuticular storage cavity, and secretions are released through micropores or thin cuticular regions. For example, *S. lycopersicum* Type I capitate GTs have long stalks and unicellular heads[17], while *Nicotiana spp.* produce long-stalked capitate GTs with elongated stalk cells and a swollen unicellular head[18].

NGTs are non-secretory structures devoid of secretory cells and subcuticular cavities. They exhibit diverse morphological forms, including unbranched, branched, filamentous, and hooked types. For example, the T-shaped NGTs of *A. annua* are composed of branched cells arranged in a biseriate manner[19]. In *Cucumis sativus*, fruit spines have multicellular, cuticularized structures lacking secretory cavities, which project from the fruit epidermis as broad-based cones[20]. As terpenoid biosynthesis is not associated with development of NGTs, these structures are included here solely for morphological comparison and will not be further addressed in the regulatory framework of this review.

Synthesis and release of terpenoids in GTs

Terpenoids are plant secondary metabolites composed of isoprene units. They participate in plant defense, signal transduction, and aroma formation and include monoterpenes (C10) such as camphor[21] and menthol[22]; sesquiterpenes (C15) such as farnesol and caryophyllene[23]; diterpenes (C20) such as ginkgo lactones[24]; and triterpenes (C30) such as ginsenosides[25] and oleanolic acid[26]. Terpenoid precursors are provided by the methylerythritol phosphate (MEP) pathway in plastids and the mevalonate (MVA) pathway in the cytoplasm. Geranyl diphosphate synthase (GPPS), Farnesyl diphosphate synthase (FPPS), geranylgeranyl diphosphate synthase (GGPPS), and downstream terpene synthases constitute the main-chain structure. Cytochrome P450 (CYP450) and other enzymes modify the products. Monoterpenes and most diterpenes are synthesized in plastids[27]. Sesquiterpenes and triterpenes are synthesized in the cytoplasm. Products accumulate in specialized structures such as GTs, resin ducts, and vacuoles[28].

Certain terpenoid biosynthetic pathways are spatially restricted to GT secretory cells, in which key biosynthetic genes show distinct cell-specific expression, and end products are sequestered and enriched in specialized subcuticular cavities. A typical example is menthol, a high-value compound widely used in the food, cosmetic, tobacco, and pharmaceutical industries. In peltate GTs of *M. piperita*, the menthol biosynthetic pathway operates across plastids and the endoplasmic reticulum. After synthesis, the product is transported and stored in subcuticular cavities, which directly determines the plant's organoleptic and therapeutic properties[29]. Consistent with this spatial specificity, artemisinin localization is strictly dependent on GTs. Comparative analyses show that artemisinin is undetectable in plants lacking GTs and possessing only NGTs[30]. Similarly, GTs on *N. tabacum* leaf surfaces produce sucrose esters and diterpenoids that vary by cultivar and growth environment. Z-abienol, the predominant labdane-type diterpene and a key aroma precursor in certain aromatic *N. tabacum* cultivars, is synthesized from GGPP derived from plastids. After oxidative modification by endoplasmic reticulum-associated enzymes, it accumulates in GT secretory layers[31]. GTs in female flowers of *Cannabis sativa* are responsible for the synthesis and accumulation of resins rich in terpenes. The

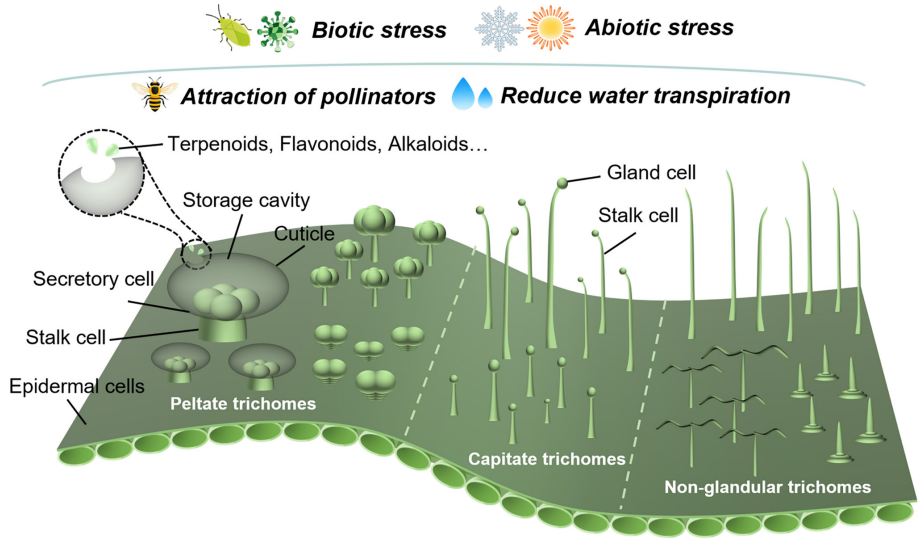

Fig. 1 Schematic comparison of different types of trichomes on the leaf surfaces of various plant species. Trichomes are classified into three categories: peltate GTs, capitate GTs, and NGTs. Examples for these are shown from *M. piperita*, *A. annua*, *S. lycopersicum*, *Nicotiana* spp., and *C. sativus*. The major biological functions of trichomes, including defense against biotic and abiotic stress, pollinator attraction, and reduced transpiration, are illustrated at the top of the figure.

diversity of monoterpenes and sesquiterpenes therein generates a unique aroma and modulates the pharmacological effects of different cultivars[32]. In female inflorescences of *Humulus lupulus*, GTs synthesize and accumulate key bitter acids related to brewing, such as humulone. The content of these acids is strongly correlated with GT density and type, traits used to distinguish aromatic and bitter hop varieties[33].

Developmental dynamics and the accumulation patterns of terpenoids in GTs

GTs develop through a coordinated multicellular differentiation process from initiation to senescence (Fig. 2). Although most current evidence relies on temporal correlations between the developmental stages of GTs and terpenoid contents rather than direct causal experimental data, GT development can be clearly divided into four stages[34–36].

In the initiation stage, most species undergo asymmetric division of protodermal cells followed by periclinal division to form an apical initial cell and a basal cell, establishing the structural foundation of GTs.

During the early secretion stage, apical cells show a meristem-like morphology with only a small number of vacuoles. The endoplasmic reticulum gradually proliferates to supply membrane structures, the Golgi apparatus is active for vesicle transport, mitochondria increase sharply in number, and leucoplasts emerge. These changes prepare the plant for terpenoid biosynthesis and conversion. Biosynthetic activity remains low at this stage. Peltate GTs of *Ocimum basilicum* display few lipophilic droplets with no essential oil accumulation. Immature GTs of *O. basilicum* at the cell division stage show no secretory products after lipophilic staining, indicating that terpenoid biosynthesis has not yet started[37]. In *Lavandula angustifolia*, immature peltate GTs at the early developmental stage lack detectable essential oil accumulation, and terpenoid production commences only after the secretory head is fully formed[38].

In the active secretion stage, the thick cuticle at the GT apex detaches to form a subcuticular cavity. Cells contain abundant mitochondria and microbodies. Mature leucoplasts are diverse in shape, contain numerous oil-like droplets, and large numbers of vesicles release terpenoids into the storage cavity via exocytosis. In *Salvia greggii*, secretory cells of peltate GTs at the active secretion stage show high leucoplast activity and abundant smooth endoplasmic reticulum, with essential oil content reaching a maximum[39]. In *Prostanthera ovalifolia*, peltate GTs reach peak secretory capacity during the active stage, with 16-celled heads producing and storing large volumes of terpenoid-rich essential oil in the subcuticular cavity[40].

In the late secretion stage, large vacuoles occupy cellular volume, and vacuolar membrane invagination leads to the formation of vesicular bodies, with the gland filled with essential oil. The terpenoid content in single *S. lycopersicum* GTs can be over 100-fold higher than that in mesophyll cells of the same leaf[41], and 10-15-fold higher in short *N. tabacum* GTs compared with controls[42]. Terpenoids may be released through two main mechanisms: either continuous diffusion of volatile components across the cuticle or rapid release when the cuticle ruptures due to mechanical damage[43].

Overall, terpenoid accumulation is low during GT initiation, increases significantly during secretory differentiation, peaks when the subcuticular cavity forms at full maturity, and may decline in some species thereafter. Finally, during strictly regulated programmed cell death, the accumulated terpenoids retain their biological activity and continue to function in plant defense.

TFs synergistically regulating trichome development and terpenoid production

Structural architecture established by glandular trichome developmental regulators supports terpenoid biosynthesis and secretion

Systematic studies on TFs regulating GT development show that many TFs drive GT formation and differentiation by regulating GT-specific genes. Although these TFs have no direct evidence of regulating terpenoid synthases, they establish and maintain the differentiated state of GT secretory cells, create specialized sites for terpenoid synthesis and storage, and, thus, indirectly but critically contribute to the yield and accumulation level of volatile terpenoids. This represents an indirect but essential component supporting potential coordination between the two processes. Here, we summarize the TFs related to GT development in model plants for GT research, including *A. annua*, *S. lycopersicum*, and *Nicotiana* spp. Given the extensive information available in this field, we have further compiled these factors into a structured table. Unlike other

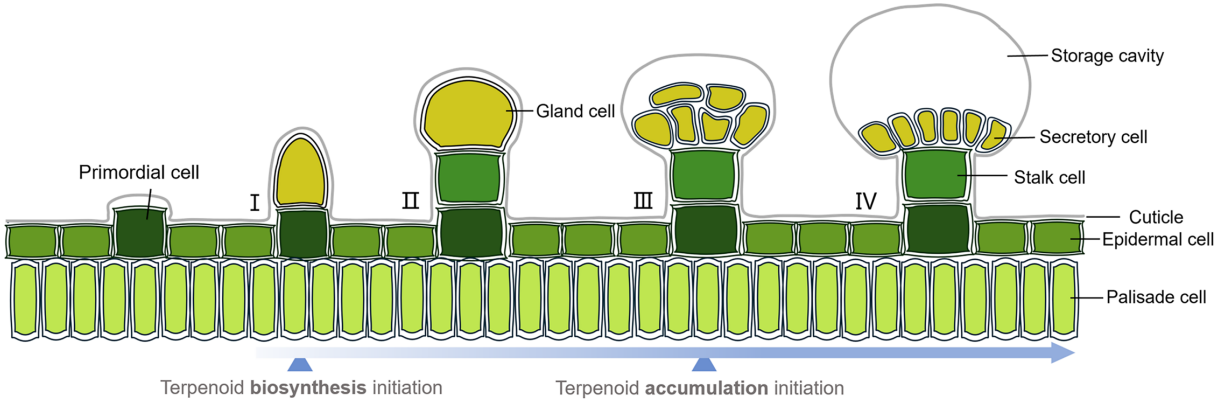

Fig. 2 Schematic diagram of the glandular trichome developmental process. GT primordial cells originate from protodermal cells of leaf primordia or young leaves. I. Epidermal cells first undergo directional differentiation and protrude outward. II. GT primordia form, followed by the differentiation of basal, stalk, and head cells. III. Head cells continue to divide and specialize into secretory cells. IV. Secretions accumulate in the subcuticular cavity, ultimately producing mature GT with swollen heads.

https://doi.org/10.48130/vegres-0026-0019

relevant reviews, we systematically integrate their interacting genes and diverse experimental verification approaches such as gene overexpression and RNAi, yielding a clearer and more comprehensive overview (Supplementary Tables S1, S2 andS3).

In *A. annua*, AaHD1 and AaHD8, members of the HD-Zip IV TF family, directly bind to the promoters of GT-specific genes such as *AaGWS2* and *AaPDF2*, and their regulatory functions have been confirmed by molecular experiments[44–46]. As a MIXTA family TF, AaMIXTA1 synergistically regulates GT development through interaction with AaHD1[47]. In *S. lycopersicum*, SlHD8 plays a core regulatory role in various GT types. It interacts with the non-specific lipid transfer protein (nsLTP) SlnsLTP33 and regulates the cell cyclin family *SlCycB2*, which then jointly participate in the regulation of typical type VI GT development[48,49]. In *N. tabacum* and *N. benthamiana*, HD-Zip IV TFs such as NtHD9 drive GT development and form a regulatory cascade through interaction with NtHD12[50,51]. Additional TFs governing GT development in these model plants are not repeated here; relevant information is provided in Supplementary Tables S1, S2 andS3.

Dual-function TFs in *Artemisia annua* and *Solanum lycopersicum*

Deeper regulatory mechanisms involve TFs with dual functions, which both bind and activate the promoters of GT development-related genes and directly regulate the expression of key terpenoid synthase genes (Table 1).

Artemisia annua

The bHLH TFs AaMYC3 and AaMYC2 identified in *A. annua* have been shown to directly regulate both processes. They bind to the promoters of key artemisinin synthase genes *AaCYP71AV1* and *AaALDH1* to activate the artemisinin biosynthetic pathway and simultaneously bind to the promoter of the GT development TF AaHD1 to coordinate GT formation[8,52]. AaWRKY9 directly activates the artemisinin biosynthetic pathway by binding to the promoter of *AaDBR2* and also regulates GT development by targeting the promoter of *AaGSW1*[53]. The dual regulation of the R2R3-MYB TF AaTLR1 is more direct. It represses *AaADS*, the rate-limiting enzyme gene for artemisinin synthesis, and also represses the GT development TF AaMIXTA1[54]. This mechanism has been verified in transgenic plants; overexpression or knockdown of *AaMYC3*, *AaMYC2*, *AaWRKY9*, and *AaTLR1* leads to synchronous changes in GT number and artemisinin content, indicating that coordinated regulation by these TFs ensures efficient artemisinin synthesis and full utilization of GT space.

Solanum lycopersicum

SlWoolly, an HD-Zip IV TF, has been shown to directly regulate the promoters of monoterpene and sesquiterpene synthase genes in type VI GTs through interaction with SlMYC1[9]. SlMYC1, a member of the bHLH family, binds to and activates the promoters of multiple monoterpene and sesquiterpene synthase genes. It also targets the promoter of *SlTOR1* and acts synergistically with this GT-specific TF through DNA–protein interaction[55,56]. The R2R3-MYB transcription factor SlMYB75 inhibits sesquiterpene biosynthesis by directly repressing the expression of key sesquiterpene synthase genes such as *SlTPS12*, *SlTPS31*, and *SlTPS35*. Meanwhile, it negatively regulates the formation of type II, V, and VI GT by activating the GT development-related gene *SlCycB2*. The significantly increased GT density and sesquiterpene content in *SlMYB75* knockdown plants further support the close coupling between GT development and sesquiterpene metabolism[57].

Cross-species conservation of dual-regulatory mechanisms controlling GTs and terpenoid metabolism

Cross-species comparative analysis shows that similar regulatory associations are common in many economic plants (Table 2). In *Chrysanthemum morifolium*, CmMYBML1 binds to the promoters of *CmTPS9* and *CmTPS12* to promote terpene biosynthesis. It interacts with CmMYC2 to form a regulatory module that coordinately controls trichome development and terpene accumulation, enhancing plant defense against herbivores[58]. In *Conyza blinii*, CbMYB108 regulates not only the expression of terpenoid synthases *CbDXS* and *CbGGPPS* but also the promoter of the GT-specific gene *CbTTG1* to control the development of capitate GTs[59]. In *M. canadensis*, the nsLTP protein McLTPII.9 interacts with the GT development-related genes *McMIXTA* and *McHD-Zip3*. Although the direct regulation of terpenoid synthases by McLTPII.9 has not been verified, quantitative polymerase chain reaction (qPCR) shows that it regulates the expression of monoterpene and sesquiterpene synthase genes[60]. Overexpression of *StMYC2* in *Schizonepeta tenuifolia* increases the number of peltate GTs and regulates the expression of terpenoid synthases *StL3OH* and *StPR*[61].

Table 1. Synergistic regulation of GT development and terpenoid biosynthesis by dual-function transcription factors.

Gene name	TF family	Key target genes of terpene biosynthesis	Terpenoid type	Evidence type	Key target genes of GT development	GT type	Evidence type	Gene function identification	Ref.
AaMYC3 (+)	bHLH	*AaCYP71AV1/ AaALDH1*	Artemisinin	Y1H/DLR/EMSA	*AaHD1* (+)	GST	Y1H/DLR/EMSA	OE/RNAi	[8]
AaMYC2 (+)	bHLH	*AaCYP71AV1/ AaALDH1*	Artemisinin	Y1H	*AaHD1*(+)/ *AaGWS2* (+)	GST	RT-qPCR	OE/RNAi	[52]
AaWRKY9 (+)	WRKY	*AaDBR2*	Artemisinin	Y1H/EMSA	*AaGSW1* (+)	GST	Y1H/EMSA	OE/RNAi	[53]
AaTLR1 (–)	R2R3-MYB	*AaADS*	Artemisinin	DLR	*AaMIXTA1* (+)	GST	DLR	OE/RNAi/ectopic expression	[54]
SlWoolly (+)	HD-Zip IV	*SlTPSs*	Monoterpenes/sesquiterpenes	Y1H/Biotin-DNA IP	SlMYC1 (+)	VI	Y2H/Pull-down/ BiFC/LCA	Mutant/CRISPR-Cas9	[9]
SlMYC1 (+)	bHLH	*SlTPSs*	Monoterpenes/sesquiterpenes	RT-qPCR	*SlTOR1* (+)	VI	Y1H/GUS	RNAi/Mutant/ VIGS	[55,56]
SlMYB75 (–)	R2R3-MYB	*SlTPS12/31/35*	Sesquiterpene	EMSA/ChIP-qPCR	*SlCycB2* (–)	II/V/VI	DLR/EMSA/ ChIP-qPCR	OE/RNAi	[57]

*(+): Positive regulation of GT development and terpenoid synthesis. (–): Negative regulation of GT development and terpenoid synthesis. Y1H: yeast one-hybrid; GST: glandular secretory trichome; DLR: dual-luciferase reporter; GUS: β-glucuronidase; EMSA: electrophoretic mobility shift assay; Biotin-DNA IP: biotin-labelled DNA IP assays; Y2H: yeast two-hybrid; pull-down: pull-down assay; LCA: luciferase complementation assay; BiFC: bimolecular fluorescence complementation; OE: overexpression; RNAi: RNA interference; VIGS: virus-induced gene silencing; ChIP-qPCR: chromatin immunoprecipitation qPCR.

Table 2. Cross-species comparison of the dual regulatory modes of transcription factors.

Gene name	TF family	Species	Key target genes of terpene biosynthesis	Terpenoid type	Evidence type	Key target genes of GT development	GT type	Evidence type	Gene function identification	Ref.
CmMYBML1 (+)	R2R3-MYB	*C. morifolium*	*CmTPS9/12*	Monoterpenes/ sesquiterpenes	Y1H/DLR/EMSA/ChIP-qPCR	CmMYC2 (+)	GST/TST	Y2H/pull-down/BiFC	OE	[58]
CbMYB108 (+)	R2R3-MYB	*C. blinii*	*CbDXS/ CbGGPPS*	Blinin	Y1H/DLR/GUS	*CbTTG1* (+)	Capitate GT	Y1H/DLR/ GUS	OE/VIGS	[59]
McLTPII.9 (+)	nsLTP	*M. canadensis*	*StL3OH/ StIPD/StGPPS*	Monoterpenes/ sesquiterpenes	RT-qPCR	*McMIXTA1* (+)*/McHD-Zip3*(+)	Peltate GT	RT-qPCR	OE	[60]
StMYC2 (+)	bHLH	*S. tenuifolia*	*StL3OH/StPR*	Monoterpenes	Y1H/DLR/EMSA	–	Peltate GT	–	OE/RNAi	[61]

*(+): Positive regulation of GT development and terpenoid synthesis. (–): Negative regulation of GT development and terpenoid synthesis.

It should be noted that the dual-function TFs reviewed here differ in the strength of evidence supporting their roles. The functions of some TFs are strongly supported by genetic data (obtained through CRISPR-Cas9 or RNAi knockdown) that showed the TFs as having caused coordinated changes in GT development and terpenoid content, by molecular confirmation (via Y1H or ChIP-qPCR) of dual promoter binding, and by phenotypic reversibility studies. The functions of other TFs stated here are based mainly on co-expression patterns and protein interactions without genetic validation. Both types of TFs are discussed here because it informs our understanding of the regulatory framework, though readers should be aware of the differences in the robustness of the evidence supporting the roles of these TFs.

Two strategies for coupling trichome development with terpenoid biosynthesis

Comparative studies across diverse plant species reveal a conserved regulatory strategy, despite diversity in the specific TFs involved. Two complementary regulatory mechanisms support potential coordination between GT development and terpenoid biosynthesis. First, a cohort of TFs regulate genes essential for GT development. These factors establish the morphological structure, including the subcuticular cavity, which provides the physical space and cellular compartments necessary for the synthesis and accumulation of terpenoids. These developmental factors indirectly support terpenoid production by establishing specialized secretory cells. Second, dual-function TFs directly couple the two pathways. These factors have two-pronged regulatory activities: on one hand, they bind to and activate the promoters of genes involved in GT development. On the other hand, they simultaneously bind to the promoters of terpenoid synthase genes to activate the terpenoid biosynthetic pathway. Genetic evidence consistently shows that overexpression or knockdown of these dual-function factors results in synchronous changes in both GT density and terpenoid content, indicating a direct regulatory link (Fig. 3).

This dual-layer regulatory architecture consists of two components. Development-specific factors establish the structural foundation for terpenoid synthesis and storage, while dual-function factors coordinately control both GT morphogenesis and terpenoid metabolism. This coordination prevents wasteful metabolic investment in NGT cells and maximizes the utilization of specialized subcuticular compartments for efficient metabolite accumulation.

Perspectives

Elucidation of the multi-level connections between GT development and terpenoid biosynthesis has advanced our current understanding of how specialized metabolism integrates with

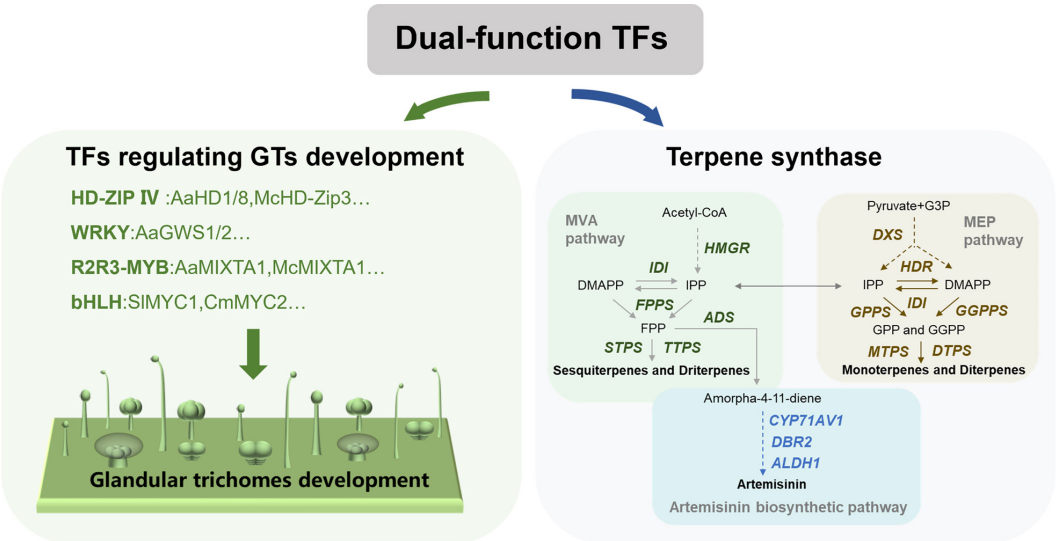

Fig. 3 Synergistic regulation of glandular trichome development and terpenoid biosynthesis by dual-function transcription factors. Dual-function TFs act as central regulators that simultaneously control GT morphogenesis and the terpenoid biosynthetic network, including MVA/MEP pathways, terpene synthases, and the artemisinin pathway, linking cellular differentiation to specialized metabolite production in plants.

epidermal differentiation. This regulatory logic, spanning spatial compartmentalization to shared transcriptional networks, provides a framework for translating mechanistic studies into synthetic biology and metabolic engineering applications. Beyond descriptive research, we outline three directions that leverage this coordination and summarize the key challenges requiring further investigation.

Deciphering the causality dilemma and physical bottlenecks via high-resolution omics

Although we have established the correlations between GT organogenesis and terpenoid biosynthesis, the fundamental causal hierarchy remains an open question. It is unclear whether a pre-determined GT developmental program activates terpenoid metabolic pathways, or whether accumulation of metabolic precursors acts as a signal to trigger GT development. The rapid advancement of single-cell multi-omics and spatial transcriptomics has allowed researchers to construct pseudotime trajectories of GT development, which helped in determining the precise temporal order of metabolic activation and cell fate commitment[62]. These technologies provide the resolution needed to define GT-specific regulons and interaction networks, and to identify shared regulatory nodes that link development and metabolism. These nodes are typically masked in traditional bulk tissue sequencing. Furthermore, these tools are essential for identifying molecular switches that link subcuticular cavity formation with terpenoid metabolic surges. Clarifying these processes is critical for overcoming the storage space limits and transport barriers of terpenoids, and for providing key breeding targets for increased secondary metabolite accumulation.

Engineering crops with coordinated GT traits and terpenoid outputs

Conventional breeding is often limited by trade-offs between GT density, plant vigor, and secondary metabolite production. Genome modification and engineering based on synergistic regulatory networks, rather than single-trait enhancement, offers a strategy to overcome this bottleneck. Future crop engineering can achieve simultaneous improvements in GT development and terpenoid synthesis by reconfiguring endogenous regulatory modules. Using multiplex CRISPR-Cas9 editing and plant transformation, core TFs can be fine-tuned to increase GT initiation and density without reducing the crop biomass. For example, GT morphogenesis can be used to generate higher-capacity peltate types by modulating HD-Zip IV/MIXTA modules. Alternatively, key TFs such as AaMYC3/AaHD1, SlMYC1/SlWoolly, and CmMYBML1/CmMYC2 can be modulated to synergistically activate downstream terpenoid synthase genes, ensuring that the proliferated GTs maintain efficient metabolic activity. Collectively, these strategies can enable the development of crop germplasm that combines high yield and tailored metabolite profiles. Examples for these include *S. lycopersicum* with elevated volatile terpenes that enhance both flavor and pest resistance, and *A. annua* lines with increased artemisinin content without yield penalties. Together, these examples achieve the simultaneous genetic improvement of GT development and terpenoid metabolism.

De novo construction of plant cell factories

Synthetic biology provides a new approach beyond traditional breeding for terpenoid accumulation in cultivable species, moving away from reliance on metabolic engineering in native plants[63,64]. Using GT or GT-like structures as a chassis to construct *de novo* plant cell factories with high yield and directed metabolic flux is a promising alternative. A primary strategy involves engineering GT-like structures in tractable heterologous host plants. By introducing minimal GT-inducing regulatory modules, GT-like structures with ectopic high density can be induced in defined tissues of tractable plants such as *N. benthamiana*. When combined with GT-preferential promoters driving a host-optimized heterologous terpenoid metabolic pathway, and precise subcellular targeting or pathway organization, this integrated design can enable the construction of *in planta* bioreactors[65]. Such systems provide spatially and metabolically insulated production compartments, ensuring the sustainable production of high-value medicinal terpenoids without reliance on cultivation of medicinal plants.

Author contributions

The authors confirm their contributions to this study as follows: collected the data from literature: Zhao J, Xue W, Shi J, Zhao X, Zhang Y; designed the models: Xue W, Zhang Y; writing – draft manuscript preparation: Zhao J, Xue W, Shi J; writing – revise: Zhao J, Zhao X, Zhang Y. All authors reviewed the results and approved the final version of the manuscript.

Data availability

Data sharing does not apply to this article, as no datasets were generated or analyzed during the current study.

Acknowledgments

We sincerely thank Xiang Gao (Northeast Normal University, China) and Xin Li (Northeast Forestry University, China) for critically reading and revising the manuscript. We extend our apologies to colleagues whose valuable work was missed or could not be cited owing to length limitations and considering the specific focus of this review. This work was supported by the National Natural Science Foundation of China under Grant Number 32371932 to Y.Z. and supported by the Postdoctoral Fellowship Program of CPSF under Grant Number GZC20251299 to W.X., and the China Postdoctoral Science Foundation under Grant Number 2025M771921 to W.X.

Conflict of interest

The authors declare that they have no conflicts of interest regarding the publication of this manuscript.

Supplementary information accompanies this paper online at: https://doi.org/10.48130/vegres-0026-0019.

Dates

Received 20 January 2026; Revised 18 April 2026; Accepted 19 May 2026; Published online 29 July 2026

References

[1] Schuurink R, Tissier A. 2020. Glandular trichomes: micro-organs with model status? *New Phytologist* 225(6):2251–2266

[2] Vimala, Hans D. 2024. Variations in epidermal trichomes of a mystic weed *Parthenium hysterophorus* L. from semi-arid regions of Barmer, Rajasthan (India). *Frontiers in Plant Science* 15:1363774

[3] Antonious GF. 2001. Production and quantification of methyl ketones in wild tomato accessions. *Journal of Environmental Science and Health, Part B* 36(6):835–848

[4] Ma L, Zheng SC, Zhang TK, Liu ZY, Wang XJ, et al. 2018. Effect of nicotine from tobacco root exudates on chemotaxis, growth, biocontrol efficiency, and colonization by *Pseudomonas aeruginosa* NXHG29. *Antonie Van Leeuwenhoek* 111(7):1237–1257

[5] Molinaro F, Tyc O, Beekwilder J, Cankar K, Bertea CM, et al. 2018. The effect of isabelin, a sesquiterpene lactone from *Ambrosia artemisiifolia* on soil microorganisms and human pathogens. *FEMS Microbiology Letters* 365(4):fny001

[6] Jermakowicz E, Leśniewska J, Stocki M, Naczk AM, Kostro-Ambroziak A, et al. 2022. The floral signals of the inconspicuous orchid *Malaxis monophyllos*: how to lure small pollinators in an abundant environment. *Biology* 11(5):640

[7] Moyano F, Cocucci A, Sérsic A. 2003. Accessory pollen adhesive from glandular trichomes on the anthers of *Leonurus sibiricus* L. (Lamiaceae). *Plant Biology* 5(4):411–418

[8] Yuan M, Sheng Y, Bao J, Wu W, Nie G, et al. 2025. AaMYC3 bridges the regulation of glandular trichome density and artemisinin biosynthesis in *Artemisia annua*. *Plant Biotechnology Journal* 23(2):315–332

[9] Hua B, Chang J, Wu M, Xu Z, Zhang F, et al. 2021. Mediation of JA signalling in glandular trichomes by the *woolly/SlMYC1* regulatory module improves pest resistance in tomato. *Plant Biotechnology Journal* 19(2):375–393

[10] Feng Z, Bartholomew ES, Liu Z, Cui Y, Dong Y, et al. 2021. Glandular trichomes: new focus on horticultural crops. *Horticulture Research* 8(1):158

[11] Karabourniotis G, Liakopoulos G, Nikolopoulos D, Bresta P. 2020. Protective and defensive roles of non-glandular trichomes against multiple stresses: structure–function coordination. *Journal of Forestry Research* 31(4):1–12

[12] Haratym W, Weryszko-Chmielewska E. 2017. Ultrastructural and histochemical analysis of glandular trichomes of *Marrubium vulgare* L. (Lamiaceae). *Flora* 231(3):11–20

[13] Zhou Y, Tang N, Huang L, Zhao Y, Tang X, et al. 2018. Effects of salt stress on plant growth, antioxidant capacity, glandular trichome density, and volatile exudates of *Schizonepeta tenuifolia* Briq. *International Journal of Molecular Sciences* 19(1):252

[14] Murungi LK, Kirwa H, Salifu D, Torto B. 2016. Opposing roles of foliar and glandular trichome volatile components in cultivated nightshade interaction with a specialist herbivore. *PLoS One* 11(8):e0160383

[15] Li Y, Yang Y, Li L, Tang K, Hao X, et al. 2024. Advanced metabolic engineering strategies for increasing artemisinin yield in *Artemisia annua* L. *Horticulture Research* 11(2):uhad292

[16] Turner GW, Gershenzon J, Croteau RB. 2000. Distribution of peltate glandular trichomes on developing leaves of peppermint. *Plant Physiology* 124(2):655–664

[17] Wang J, Yuan S, Zhao Y, Shu X, Liu Z, et al. 2025. Wo interacts with SlTCP25 to regulate type I trichome branching in tomato. *Horticulture Research* 12(5):uhaf032

[18] McDowell ET, Kapteyn J, Schmidt A, Li C, Kang JH, et al. 2011. Comparative functional genomic analysis of *Solanum* glandular trichome types. *Plant Physiology* 155(1):524–539

[19] Zhang M, Li M, An Y, Liu C, Zhao Q, et al. 2025. Single-nucleus transcriptomics reveal the morphogenesis and artemisinin biosynthesis in *Artemisia annua* glandular trichomes. *Nature Communications* 16:8646

[20] Lv D, Wang G, Zhang Q, Yu Y, Qin P-C, et al. 2022. Comparative transcriptome analysis of hard and tender fruit spines of cucumber to identify genes involved in the morphological development of fruit spines. *Frontiers in Plant Science* 13:797433

[21] Tian Z, Luo Q, Zuo Z. 2021. Seasonal emission of monoterpenes from four chemotypes of *Cinnamomum camphora*. *Industrial Crops and Products* 163:113327

[22] Kamatou GP, Vermaak I, Viljoen AM, Lawrence BM. 2013. Menthol: a simple monoterpene with remarkable biological properties. *Phytochemistry* 96:15–25

[23] Froldi G, Benetti F, Mondin A, Roverso M, Pangrazzi E, et al. 2023. *Pterodon emarginatus* seed preparations: antiradical activity, chemical characterization, and in silico ADMET parameters of β-caryophyllene and farnesol. *Molecules* 28(22):7494

[24] Hébert M, Bellavance G, Barriault L. 2025. Advanced synthetic strategies toward ginkgolide diterpenoids: total synthesis of (±)-ginkgolide C and formal syntheses of (±)-ginkgolides A and B. *The Journal of Organic Chemistry* 90(26):9147–9159

[25] Xu W, Zhang JH, Liu X, Jia AL, Liu XL, et al. 2017. Two new dammarane-type triterpenoid saponins from ginseng medicinal fungal substance. *Natural Product Research* 31(10):1107–1112

[26] Ravichandran B, Sanniyasi E, Kuppusamy SG, Perumal P. 2024. Oncotherapeutic effect of novel triterpenoid compound oleanolic acid isolated and characterized from the methanolic extract of *Coldenia procumbens* (Linn.). *Applied Biochemistry and Biotechnology* 196(11):8096–8116

[27] Frey M, Jochimsen CM, Degenhardt J. 2025. Cytochrome P450-induced backbone rearrangements in terpene biosynthesis of plants. *Molecules* 30(17):3540

[28] Ma Y, Chen Q, Wang Y, Zhang F, Wang C, Wang G. 2023. Heteromerization of short-chain *trans*-prenyltransferase controls precursor allocation within a plastidial terpenoid network. *Journal of Integrative Plant Biology* 65(5):1170–1182

[29] Bergman ME, Phillips MA. 2021. Structural diversity and biosynthesis of plant derived *p*-menthane monoterpenes. *Phytochemistry Reviews* 20(2):433–459

[30] Salehi M, Karimzadeh G, Naghavi MR, Naghdi Badi H, Rashidi Monfared S. 2018. Expression of key genes affecting artemisinin content in five *Artemisia* species. *Scientific Reports* 8(1):12659

[31] Sallaud C, Giacalone C, Töpfer R, Goepfert S, Bakaher N, et al. 2012. Characterization of two genes for the biosynthesis of the labdane diterpene Z-abienol in tobacco (*Nicotiana tabacum*) glandular trichomes. *The Plant Journal* 72(1):1–17

[32] Booth JK, Yuen MMS, Jancsik S, Madilao LL, Page JE, Bohlmann J. 2020. Terpene synthases and terpene variation in *Cannabis sativa*. *Plant Physiology* 184(1):130–147

[33] Patzak J, Henychová A, Matoušek J. 2021. Developmental regulation of lupulin gland-associated genes in aromatic and bitter hops (*Humulus lupulus* L.). *BMC Plant Biology* 21(1):534

[34] Turner GW, Gershenzon J, Croteau RB. 2000. Development of peltate glandular trichomes of peppermint. *Plant Physiology* 124(2):665–680

[35] Huchelmann A, Boutry M, Hachez C. 2017. Plant glandular trichomes: natural cell factories of high biotechnological interest. *Plant Physiology* 175(1):6–22

[36] Bergau N, Bennewitz S, Syrowatka F, Hause G, Tissier A. 2015. The development of type VI glandular trichomes in the cultivated tomato *Solanum lycopersicum* and a related wild species *S. habrochaites*. *BMC Plant Biology* 15(1):289

[37] Gang DR, Simon J, Lewinsohn E, Pichersky E. 2002. Peltate glandular trichomes of *Ocimum basilicum* L. (sweet basil) contain high levels of enzymes involved in the biosynthesis of phenylpropenes. In *Breeding Research on Aromatic and Medicinal Plants*, eds. Johnson CB, Franz C. Boca Raton: CRC Press. pp. 189–195 doi: 10.1201/9781003573227-28

[38] Zhang Y, Wang D, Li H, Bai H, Sun M, et al. 2023. Formation mechanism of glandular trichomes involved in the synthesis and storage of terpenoids in lavender. *BMC Plant Biology* 23(1):307

[39] Giuliani C, Ascrizzi R, Corrà S, Bini LM, Flamini G, et al. 2017. Ultrastructural insight into terpene-producing trichomes and essential oil profile in *Salvia greggii* A. gray. *Flora* 236-237:107–114

[40] Gersbach PV. 2002. The essential oil secretory structures of *Prostanthera ovalifolia* (Lamiaceae). *Annals of Botany* 89(3):255–260

[41] Balcke GU, Bennewitz S, Bergau N, Athmer B, Henning A, et al. 2017. Multi-omics of tomato glandular trichomes reveals distinct features of central carbon metabolism supporting high productivity of specialized metabolites. *The Plant Cell* 29(5):960–983

[42] Sallets A, Beyaert M, Boutry M, Champagne A. 2014. Comparative proteomics of short and tall glandular trichomes of *Nicotiana tabacum*

reveals differential metabolic activities. *Journal of Proteome Research* 13(7):3386−3396

[43] Holopainen JK, Gershenzon J. 2010. Multiple stress factors and the emission of plant VOCs. *Trends in Plant Science* 15(3):176−184

[44] Xie L, Yan T, Li L, Chen M, Ma Y, et al. 2021. The WRKY transcription factor AaGSW2 promotes glandular trichome initiation in *Artemisia annua*. *Journal of Experimental Botany* 72(5):1691−1701

[45] Hu X, Liu H, Chen T, Ye Y, Shao J, et al. 2025. *AaPDF2* promotes glandular trichome formation in *Artemisia annua* through jasmonic acid signaling. *Industrial Crops and Products* 234:121630

[46] Yan T, Li L, Xie L, Chen M, Shen Q, et al. 2018. A novel HD-ZIP IV/MIXTA complex promotes glandular trichome initiation and cuticle development in *Artemisia annua*. *New Phytologist* 218(2):567−578

[47] Shi P, Fu X, Shen Q, Liu M, Pan Q, et al. 2018. The roles of *AaMIXTA1* in regulating the initiation of glandular trichomes and cuticle biosynthesis in *Artemisia annua*. *New Phytologist* 217(1):261−276

[48] Gao Y, Ruan J, Wang G, Zhang Y, Wang Y, et al. 2025. SlHDZIV8-SlnsLTP33 module controls trichome density and lipid metabolism in tomato. *The Plant Journal* 123(3):e70398

[49] Gao S, Gao Y, Xiong C, Yu G, Chang J, et al. 2017. The tomato B-type cyclin gene, *SlCycB2*, plays key roles in reproductive organ development, trichome initiation, terpenoids biosynthesis and *Prodenia litura* defense. *Plant Science* 262:103−114

[50] Zhang H, Xu H, Xu M, Yan X, Wang Z, et al. 2023. Transcription factors *NtHD9* and *NtHD12* control long glandular trichome formation *via* jasmonate signaling. *Plant Physiology* 191(4):2385−2399

[51] Tian Y, Dai TW, Fan CX, Zhou J, Ren XI, et al. 2020. An HD-Zip IV transcription factor protein NbGL3 regulates glandular trichome initiation in tobacco. *Biologia Plantarum* 64(1):378−384

[52] Khan RA, Kumar A, Abbas N. 2024. A bHLH transcription factor AaMYC2-type positively regulates glandular trichome density and artemisinin biosynthesis in *Artemisia annua*. *Physiologia Plantarum* 176(5):e14581

[53] Fu X, Peng B, Hassani D, Xie L, Liu H, et al. 2021. AaWRKY9 contributes to light- and jasmonate-mediated to regulate the biosynthesis of artemisinin in *Artemisia annua*. *New Phytologist* 231(5):1858−1874

[54] Lv Z, Li J, Qiu S, Qi F, Su H, et al. 2022. The transcription factors TLR1 and TLR2 negatively regulate trichome density and artemisinin levels in *Artemisia annua*. *Journal of Integrative Plant Biology* 64(6):1212−1228

[55] Yu L, Zhang Y, Ding Q, Wang H, Meng X, et al. 2024. The SlMYC1-TOR module regulates trichome formation and terpene biosynthesis in tomatoes (*Solanum lycopersicum* L.). *Journal of Plant Growth Regulation* 43(9):3282−3294

[56] Xu J, van Herwijnen ZO, Dräger DB, Sui C, Haring MA, et al. 2018. SlMYC1 regulates type VI glandular trichome formation and terpene biosynthesis in tomato glandular cells. *The Plant Cell* 30(12):2988−3005

[57] Gong Z, Luo Y, Zhang W, Jian W, Zhang L, et al. 2021. A SlMYB75-centred transcriptional cascade regulates trichome formation and sesquiterpene accumulation in tomato. *Journal of Experimental Botany* 72(10):3806−3820

[58] Guan Y, Jiang L, Wang Y, Liu G, Wu J, et al. 2024. CmMYC2-CmMYBML1 module orchestrates the resistance to herbivory by synchronously regulating the trichome development and constitutive terpene biosynthesis in *Chrysanthemum morifolium*. *New Phytologist* 244(3):914−933

[59] Zhan J, Di T, Chen X, Zheng T, Sun W, et al. 2024. CbMYB108 integrates the regulation of diterpene biosynthesis and trichome development in *Conyza blinii* against UV-B. *Plant, Cell & Environment* 47(4):1300−1318

[60] Chen Q, Li L, Qi X, Fang H, Yu X, et al. 2023. The non-specific lipid transfer protein McLTPII. 9 of *Mentha canadensis* is involved in peltate glandular trichome density and volatile compound metabolism. *Frontiers in Plant Science* 14:1188922

[61] Shi J, Zhang J, Sun L, Tang X, Wang K. 2026. Jasmonate-responsive transcription factor StMYC2 coordinately regulates peltate glandular trichome development and monoterpenoid biosynthesis in *Schizonepeta tenuifolia*. *Plant Physiology and Biochemistry* 233:111208

[62] Yu X, Liu Z, Sun X. 2023. Single-cell and spatial multi-omics in the plant sciences: technical advances, applications, and perspectives. *Plant Communications* 4(3):100508

[63] Wang K, Liu Z. 2025. Plant synthetic biology-based biofortification, strategies and recent progresses. *Journal of Integrative Plant Biology* 67(8):1997−2004

[64] Yang JS, Reyna-Llorens I. 2023. Plant synthetic biology: exploring the frontiers of sustainable agriculture and fundamental plant biology. *Journal of Experimental Botany* 74(13):3787−3790

[65] Sun X, Wu X, Jiang X, Huang H, Yang A, et al. 2026. Heterologous production of forskolin in tobacco (*Nicotiana tabacum*) *via* glandular trichome specific engineering and metabolic flux redirection. *Plant Biotechnology Journal* 24(3):1548−1563