

Fruit quality and nutrient composition of grapevines – a review

Omid Askari-Khorasgani¹, Mohammad Pessarakli^{*2}

¹*Young Researchers and Elite Club, Department of Horticulture, College of Agriculture and Natural Resources, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran*
ORCID: <https://orcid.org/0000-0002-8956-5977>

²*Professor, School of Plant Sciences, College of Agriculture and Life Sciences, The University of Arizona, Tucson, AZ 85721, USA* ORCID: <https://orcid.org/0000-0002-7662-2258> * Corresponding Author E-mail: Mohammad Pessarakli pessarak@email.arizona.edu

ABSTRACT

Grape quality and its nutrient composition vary depending on agronomical management practices (fertilization, irrigation, weed and pest control), and agrochemicals treatments (such as, kaolin, hormones and sucrose), viticultural (grape cultivars and varieties, training, pruning, cluster thinning, and trunk girdling), and biotechnological techniques, as well as growth stage and environmental changes (soil, climate, and season). Understanding the mentioned agro-biotechnological techniques assist grape growers and geneticists in breeding grapevines to improve yield, tolerance, quality, and nutraceutical values based on their usage purposes. Thus, this review article focuses on the up-to-date approaches and incentivizes further studies on the unknown mechanisms related to engineering grape flavonoid/phenylpropanoid biosynthetic pathways to improve its health promoting effects in both grape and human. The engineering/breeding strategies and viticultural practices have been proposed based on the grape usage purposes and environmental conditions.

Key words: anthocyanin, berry, flavonoid, flavonol, phenol, grapevine, physico-chemical characteristic, viticulture

CONTACT: Mohammad Pessaraki, Professor pessarak@email.arizona.edu School of Plant Sciences, College of Agriculture & Life Sciences, The University of Arizona, Tucson, Arizona 85721, USA.

Introduction

Grapevine is a commercially valuable plant, which can be used as a rich source of nutrient in multiple industries (Xu et al. 2017; Chitarrini et al. 2017). Plant phenolic compounds possess a number of bioactive functions, such as, protective effects against cardiovascular and hepatic diseases, anticancer, anti-inflammatory, antioxidant, antimicrobial and antiviral activities, organoleptic properties, color and protection against environmental challenges, and their synthesis and distribution can be affected by climate, soil, agronomic management practices, and seasonal conditions (He et al. 2010; Han et al. 2017; Basile et al. 2018). The phenylpropanoids represent a major group of plant secondary metabolites associated with a wide range of biological functions. It mainly includes flavonoids, monolignols, phenolic acids, stilbenes, and coumarins (Deng and Lu 2017). The flavonoids including, flavanols (catechins and proanthocyanidins (PAs)), anthocyanidins, anthocyanins, chalcones, flavones, flavonols, flavanones, flavanonols, bioflavonoids, isoflavones, and other important phenolic compounds, such as tannins, stilbenes, curcuminoids, coumarins, lignans, quinones are widespread in plant kingdom and play critical roles in plant and human health (Cai et al. 2004; Petridis et al. 2016). Grapevine (*Vitis vinifera*) flavonoids are largely consisted of flavonols, anthocyanins and flavan-3-ols (monomers, oligomers and polymers), among which PAs, that is, oligomer and polymer flavan-3-ols, are the dominant flavonoids in berries (Gou et al. 2011). In plants, anthocyanins attract pollinators and seed dispersers, protect plants against multiple stresses (e.g., drought, high salinity, high light irradiation, cold and oxidative stress) and prolong life span (Chen et al. 2013; Kovinich et al. 2015; Yan et al. 2016). Anthocyanins possess multifaceted beneficial effects on human health, including

antioxidant, anti-inflammatory, anticarcinogenic (protective roles against certain cancer types), cardioprotective (Pojer et al. 2013), and antiaging properties (Liu et al. 2011), protective roles against cognitive function disorders (Pojer et al. 2013), light- and H₂O₂-induced damage in retina (Liu et al. 2011; Huang et al. 2018), and protective roles and control of metabolic syndromes or disfunctions (i.e., obesity and diabetes by modulating mitochondrial pathways related to glucose and lipid metabolism for the systematic regulation of energy balance) (Skates et al. 2018). Modification of grapevines metabolites, particularly flavonoids, through genetically engineering or conventional breeding programs and manipulation of their biosynthetic pathways have the potential to improve grape yield, tolerance/resistance (to biotic and abiotic stresses), quality (e.g., color, size), nutraceutical values (nutrition, antimicrobial, and antioxidant properties), and marketability (Xu et al. 2017; Chitarrini et al. 2017). To achieve these goals, this review article discusses the critical regulatory aspects of flavonols, anthocyanins and PAs and agro-biotechnological approaches to assist grape breeders and growers improve grape quality, yield, nutraceutical values, and stress tolerance, the latter with particular emphasize on cold and heat tolerance.

The roles of agrochemicals and biotechnological approaches in improving fruit quality and grapevine flavnoids, mainly anthocyanins, flavonols, and proanthocyanidins

Agrochemicals and biotechnological approaches differentially affect expression of genes encoding different types of anthocyanins, including glucosilated (i.e., monoglucosides and diglucosides), hydroxylated (e.g., di- and tri-hydroxylated), acetylated, and coumaroylated derivates (Olivares et al. 2017). Abscisic acid (ABA) induces gene expression by activating ABA-responsive *cis*-acting elements (ABRE; core-sequence: ACGTGG/TG) and a coupling element (CE; core-sequence: CACC), in addition to one or more ABRE-like and also CE-like sequences in their promoter regions. Sucrose, which can also be stimulated by cluster thinning

(CT), induces gene expression by activating sucrose responsive elements (SURE) and W box elements in their promoter regions (Pastore et al. 2011; Olivares et al. 2017). Accumulation of anthocyanin pigments in red grape varieties starts from *véraison* and reaches its peak at the terminal stages of fruit maturation when its synthesis halts (Figure 1) (Basile et al. 2018). Accordingly, in grapevine, the regulatory roles of environmental cues and agrochemicals on gene expression and, thereby, flavonoid biosynthetic pathways greatly vary depending on the plant genotype-environment interactions, particularly growth season. Olivares et al.'s (2017) study demonstrated that under anthocyanin inductive conditions (AICs) ABA and/or sucrose application has the potential to improve grape ripeness and quality attributes without exerting negative effects on firmness, TSS, and TA as occurs by applying ethephon. Application of sugar and/or ABA at early stages of *véraison* accelerates grape ripening, promotes moderate softening and color development by anthocyanin accumulation and chlorophyll metabolism (Olivares et al. 2017). A review of the pertinent literature indicates that the skin color of ABA-treated grapes are more attractive than untreated ones and have the higher potential to increase ripeness and the percentage of harvestable fruit at a certain time period (Olivares et al. 2017). Joint application of ABA and sucrose upregulates the expression of *VvPAL* (*V. vinifera phenylalanine ammonia-lyase*), *VvCHS* (*V. vinifera chalcone synthase*) and *VvCHI* (*V. vinifera chalcone isomerase*) genes as well as *VvMYBA1* (*V. vinifera myeloblastosis anthocyanin1*) and *VvUFGT* (*V. vinifera uridine diphosphate glucose (UDP)-flavonoid 3-O-glucosyltransferase genes*) at 26 days after *véraison* more than control treatments (Olivares et al. 2017). In *V. vinifera* 'Crimson Seedless' grape, 400 mg L⁻¹ ABA + sucrose at *véraison* had stronger effect on improving grape quality attributes than 400 g L⁻¹ ABA, activating a wider range of genes and, thereby, pigments. Tri-hydroxylated anthocyanins (malvidin, delphinidin, and petunidin) were increased by ABA not sucrose (Olivares et al. 2017). In *V. vinifera* L. 'Rubi' grape, two-step application of 400 mg L⁻¹ ABA at *Véraison* + 200 mg L⁻¹

ABA at 25 days after the first application was more effective in inducing the accumulation of anthocyanins and total carotenoids and total phenolic compounds (Neto et al. 2017).

Benzothiadiazole (BTH), jasmonic acid (JA), methyl jasmonate (MeJA), salicylic acid (SA), and chitosan can also improve grape phenolic compounds as well as responses to both biotic and abiotic stresses. Because the agrochemicals' effects vary depending on their crosstalk, combinations, concentrations, growth stage, applied tissue (leaves or berries), environmental conditions and grape species, all these factors in addition to cultivation purpose in specific grape species should be taken into accounts for viticultural management in large scales (Ruiz-Garcia et al. 2013; Prakongkha et al. 2013; Champa et al. 2015). In *V. vinifera* 'Flame Seedless', application of 1.5 mM SA at pea stage and at *véraison* promoted berry maturation, color, size, weight, yield, and produced less compact bunches during growth stage, reduced pectin methyl esterase activity, electrolyte leakage, and weight loss and promoted TSS, TA, color, phenols, organoleptic properties, firmness and shelf life during storage, while reducing rachis browning and decay incidence (Champa et al. 2015). Chitosan and BTH are also capable of inducing SA to activate defense responses against biotic stresses in grapevine (Prakongkha et al. 2013). Ruiz-García et al. (2013) reported that joint application of BTH and MeJA at *véraison* and 3 and 6 days after the first application improved *V. vinifera* 'Monastrell' anthocyanin and flavonol contents and its wine, while ABA was less effective in improving its wine chromatic characteristics.

At the onset of *véraison*, the elevated ethylene (ETH) in grape berries (*V. vinifera* L.) upregulates TRYPTOPHAN AMINOTRANSFERASE OF ARABIDOPSIS1/TRYPTOPHAN AMINOTRANSFERASE RELATED (TAA1/TAR) proteins. TAA1/TAR converts tryptophan to indole-3-pyruvate which is, then, converted to indole 3-acetic acid (IAA) by the YUCCA (YUC) family of flavin-containing monooxygenases, inducing the biosynthesis of free indole 3-acetic acid (IAA).

Synergistically, the elevated ETH, ABA, and sucrose at *véraison* induce the expression of *Gretchen Hagen 3-1 (GH3-1)* to conjugate IAA to aspartic acid (IAA-Asp) and participate in AUX homeostasis by releasing a low level of free IAA, thereby, promoting anthocyanin biosynthesis and ripening (Böttcher et al. 2010; Böttcher et al. 2013). In a dose dependent manner, application of indole 3-acetic acid (IAA), naphthaleneacetic acid (NAA) and 2,4-dichlorophenoxyacetic acid (2,4-D) inhibit or promote anthocyanin biosynthesis by differentially targeting anthocyanin biosynthetic pathways (Liu, Shi, and Xie 2014) and, thus, like the ETH inhibitors (e.g., aminoethoxyvinylglycine) (Böttcher et al. 2013) have the potential to improve the quality of red and white wine grapes by inhibiting or promoting anthocyanin production. However, because the influence of ETH and ETH inhibitors on AUX homeostasis vary depending on the concentration and crosstalk with ABA and sucrose (Böttcher et al. 2013; Liu, Shi, and Xie 2014), their influence on grape and wine quality attributes require more investigations. In a pioneer effort, Dinis and coworkers' (2018) study on Mediterranean grapevines showed that foliar exogenous application of kaolin promoted stomatal conductance, water use efficiency, net CO₂ assimilation, photosynthesis, and hormone homeostasis by slightly reducing ABA and increasing IAA levels, thereby, enhancing summer stress tolerance (Dinis et al. 2018). In this regard, studies on the influence of kaolin on other hormones and chemical composition, and regulation of TFs and genes in different grape genotypes under different environmental and viticultural conditions provides valuable information for improving grapevine quality and yield in the future. Overall, understanding the effects of separate and joint application of BTH, MeJA, ETH, AUX, chitosan, SA, ABA, and/or sucrose as well as manipulation of their signalling and metabolic pathways on both grape and wine quality require more investigations.

Plant metabolic engineering by manipulation of biosynthetic pathways through modification of transcriptional regulators, small RNAs (sRNAs) and, thereby, gene regulation

is an effective strategy to improve plant secondary metabolites and phytochemicals involved in regulating plant growth, development, tolerance, fruit quality, pigmentation and nutritional values (Gou et al. 2011; Zhang et al. 2018). Hence, the regulatory roles of TFs and genes on grapevine chemical composition (Table 1, Figures 1 and 2), fruit quality and tolerance (Table 1) is discussed. Grape internal signalling and environmental cues induce the activities of MYB-bHLH-WD40 [Repeat2Repeat3 (R2R3) myeloblastosis- basic helix-loop-helix-WD40 termed as MBW] TF complexes (Lai et al. 2016; Petridis et al. 2016) as the key regulator of flavonoid biosynthetic genes, such as *glutathione S-transferases* (GSTs) (Xu et al. 2018) and *CHS*, determining the chemical composition of berries (Harris et al. 2013). R2R3-MYB proteins involved in the transcriptional regulation of anthocyanins are PRODUCTION OF ANTHOCYANIN PIGMENTS1 (PAP1)/MYB DOMAIN PROTEIN 75 (MYB75), PAP2/MYB90, MYB113, MYB114, and MYB-like Domain (MYBD) TFs, whereas, the bHLH proteins are GLABROUS3 (GL3), ENHANCER OF GLABRA3 (EGL3), and anthocyanin transporter proteins, such as, TRANSPARENT TESTA8 (TT8) in Arabidopsis (Gou et al. 2011; Petridis et al. 2016; Wang et al. 2016). Antagonistically, MYB-LIKE 2 (MYBL2), an R3-MYB-related protein, LATERAL ORGAN BOUNDARY DOMAIN (LBD), viz. LBD37, LBD38, and LBD39, and SQUAMOSA PROMOTER BINDING PROTEIN-LIKE9 (SPL9) act as the negative regulators of anthocyanin biosynthesis in Arabidopsis (Gou et al. 2011; Petridis et al. 2016). Glutathione *S*-transferases (GSTs) (e.g., Transparent Testa 19 (TT19) and TT19-4 in Arabidopsis, anthocyanin9 (AN9) in petunia, flavonoid3 (FL3) in carnation, and *V. vinifera* GSTs) function as the anthocyanin carriers to sequester and increase water solubility of cyanidin (Cya) and cyanidin-3-*O*-glycoside (C3G) synthesized in the cytosolic surface of the endoplasmic reticulum (ER) and, then, transport them into the tonoplast and vacuole. Though the GSTs functions as anthocyanin carrier have been corroborated, its influence on anthocyanin sequestration have remained controversial

(Li et al. 2011; Sun, Li, and Huang 2012). *VvWRKY26* (Amato et al. 2016), TT19 and TT19-4 enzymes have the potential to transport anthocyanins in aerial tissues and PAs in seed coat (Li et al. 2011). The Arabidopsis Transporter TT12 acts as a flavonoid/H⁺-antiporter on tonoplast to transport flavan-3-ols, PAs and C3G, with the latter in the presence of MgATP, to vacuoles of the seed coat, energized by the proton gradient established by AHA10 (P-type H⁺-ATPase) localized in tonoplast (Marinova et al. 2007). In grapevine, anthoMATE1 (AM1) and AM3 transporters are involved in vacuolar H(+)-dependent acylated anthocyanin transportation in the presence of MgATP, but not malvidin 3-O-glucoside or cyanidin 3-O-glucoside forms (Gomez et al. 2009). Likewise, *VvWRKY26* expression regulates ATPase pump activity on the tonoplast and, thereby, promotes vascular acidification, facilitating anthocyanin and PAs accumulation as well as berry development (Amato et al. 2016). In addition to the regulation of TFs involved in flavonoid biosynthesis, regulation of flavonoid transporters has the potential to alter their biosynthetic pathways and, thereby, their types and contents (Sun, Li, and Huang 2012). Transport of anthocyanins from cytoplasm to vacuole prevents their oxidation and polymerization and, thereby, prevents their color change from bright (purple-red) to brown (brick-red) and, thereby, increases the quality of wine grapes (Mueller et al. 2000). In Arabidopsis, sucrose-treated *tt19-7* null mutant barely accumulate anthocyanins, but produces a higher level of flavonol than the wild-type (WT) as the result of upregulating *flavonol synthase (FLS)* genes, in ethyl methanesulfonate mutagenized seeds. Since TT19 has no activity of glutathionation towards Cya and C3G *in vitro* (with a stronger affinity to Cya) (Sun, Li, and Huang 2012), it can be hypothesized that additional transporters, such as, AN9-like type-I GST, might assist TT19 to transport anthocyanins from cytoplasm to vacuole. After anthocyanin glycosylation, acylation, malonylation or methylation, these transporters bind and sequester anthocyanin substrates. Anthocyanin carriers like AN9 bind to flavonoid substrate 1-chloro-2,4-dinitrobenzene (CDNB) with GSH,

which can be catalyzed by *AN9*-encoded GSTs, to prevent flavonoid oxidation and form dinitro-phenolglutathione (DNP-GS) and, thereby, facilitates flavonoid transport to vacuole (Mueller et al. 2000; Li et al. 2011) (Sun, Li, and Huang 2012; Amato et al. 2016). Following the GSTs activity, transporters of the ABC (ATP-binding cassette) and MATE (multidrug and toxin extrusion; also named anthoMATE) families assist GSTs to transfer anthocyanin molecules into the vacuolar lumen or respectively into ER lumen, vesicles and/or membrane-bound organelles and then the vacuole lumen through the autophagy (macro or micro)-related machinery (Chanoca and Kovinich 2015). In grapevine, ABC protein, ABCC1 (responsible for transferring anthocyanidin 3-*O*-glucosides and preferentially malvidin 3-*O*-glucoside) and vesicle-mediated anthoMATE transporters (responsible for transferring malonylated anthocyanins and to a lesser extent glycosylated anthocyanidins) are involved in different anthocyanin transport mechanisms depending on GSTs activities. However, the role of ABCC1 in PA transportation has not been corroborated (Gomez et al. 2011; Francisco et al. 2013). Thus, it can be hypothesized that the coexpression activities of grapevine *VvWRKY26*, *AN9*-like type-I GST, *Vv*GSTs, ABCC1 and anthoMATE transporters and likely *Arabidopsis* TT19, TT12 and *petunia AN9* might benefit color and nutraceutical values of grapes by accumulating anthocyanins, particularly acylated anthocyanins by anthocyanidin 3-*O*-glucosides transportation and/or PAs more than overexpression of a single gene, which require further studies (Mueller et al. 2000; Marinova et al. 2007; Pourcel et al. 2010; Li et al. 2011; Sun, Li, and Huang 2012; Chanoca and Kovinich 2015; Amato et al. 2016). Therefore, coexpression of these anthocyanin transporters might cooperatively exert stronger effect than a single transporter to improve anthocyanin accumulation, particularly under AICs. Their downregulation to stimulate other flavonoid biosynthetic pathway may also have a high potential for engineering grapevines by, for example, shifting anthocyanins to flavonols and scopolin to induce cold acclimation.

Inside the vacuolar lumen, anthocyanins are found either in a uniformly distributed, soluble form or in intravacuolar bodies called anthocyanoplasts or anthocyanin vacuolar inclusions (AVIs). In *Arabidopsis*, formation of AVIs, which is a rich source of acylated anthocyanins, is promoted by both an increase in C3G (which is usually absent in *Arabidopsis* under normal condition and can be stimulated by naringenin) and its derivatives and by depletion of the *TT19*-encoded GST. As a strategy to stimulate AVIs accumulation, 5-*O*-glucosyltransferase (*5gt*) mutation in *Arabidopsis*, a common attribute in non-hybrid *V. vinifera*, prevents accumulation of glycosylate anthocyanidins at the 5-O position and enhances AVIs formation in almost every epidermal cell of the cotyledons, particularly under AICs, such as vanadate treatment, whereas *Arabidopsis* WT plants accumulate AVIs in a small fraction of the cells (Janvary et al. 2009; Pourcel et al. 2010; Chanoca and Kovicich 2015). However, the AVIs in *5gt* mutants are incapable of producing sufficient anthocyanins in *Arabidopsis* (Pourcel et al. 2010), and more importantly anthocyanin diglucosides in grapevines suitable for color stabilization in red wines. The restoration of the C-terminus and the site specific of V121L would assist in regaining *5GT* catalytic activity, and perhaps enhances wine quality (Janvary et al. 2009). Additionally, *ATG* genes (sterol 3-beta-glucosyltransferase; autophagy-related protein 26) required for autophagy induction (He et al. 2017), and application of naringenin as well as vanadate (Pourcel et al. 2010) have the potential to increase the number of AVIs. Naringenin increases anthocyanins diversity and C3G and, thereby, AVIs in WT and *tt5* (Transparent Testa 5 also known as chalcone-flavonone isomerase 1 or CHI1) seedlings. Vanadate reduces C3G content with only an increase in a specific peak in specific *atg* mutants, but increases AVIs in WT or naringenin-complemented *tt5* seedlings independent of anthocyanin contents, suggesting its involvement in anthocyanin autophagy, the mechanism of which remains elusive (Pourcel et al. 2010). Since AVIs are a rich source of acylated anthocyanins, the above-mentioned strategies for

increasing the number of AVIs and its anthocyanins contents together have the potential to increase nutraceutical and therapeutic values of grapevines and quality of wine grapes.

The regulatory roles of TFs and genes in grapevine is discussed in [Table 1](#). In short, *VvMYBA1* and *VvMYBA2* regulate anthocyanins in red grapes. *VvMYBPA1* and *VvMYBPA2* regulate PA synthesis. Depending on the *VvMYB5a&b* interactions with *VvMYBA1&2* and/or *VvMYBPA1&2*, *VvMYB5a&b* regulate flavonoids, particularly PAs. *V. vinifera* myeloblastosis flavonol1 (*VvMYBF1*), *V. vinifera* flavonol synthase (*VvFLS*)1,4&5, *VvCHI*, *VvMYB12*, *V. vinifera* myelocytomatosis anthocyanin1 (*VvMYCA1*), *V. vinifera* WD-repeat proteins (*VvWDRs*), *V. vinifera* UV-B resistance8 (*VvUVR8*), *V. vinifera* elongated hypocotyls (*VvHY5*), *V. vinifera* constitutive photomorphogenic1 (*VvCOP1*), *V. vinifera* mitogen-activated protein kinase3 (*VvMAPK3*) and *VvCHS* regulate flavonols pathways (Deluc et al. 2008; Hichri et al. 2010; Czemplak et al. 2009; Liu et al. 2014). In *V. vinifera*, transcription of *VvMYC1* gene (from bHLH family) during berry development regulates the synthesis of anthocyanins by *VvMYC1-VvMYBA1* interaction and/or PAs by *VvMYC1-VvMYBPA1* interaction (Hichri et al. 2010). Hence, the interactions between TFs should be taken into account under different growth stages and environmental conditions for the correct interpretation of their regulatory roles with respect to different grape genotypes.

In Arabidopsis, increased miR156 activity downregulates SPL9 and, thereby, promotes anthocyanin biosynthesis, whereas reduced miR156 activity by plant aging increases the levels of flavonols (conversion of dihydrokaempferol to kaempferol) due to the increased SPL activity and, thereby, upregulation of *FLS* genes (Gou et al. 2011). A recent study on Sea buckthorn showed that the biosynthesis of ascorbic acid, carotenoids and flavonoids is regulated by the interaction between specific long non-coding RNAs with micro RNAs and messenger RNA (miRNA-lncRNA-mRNA). LNC1 (lncRNA TCONS_00694050)

expression increased anthocyanin biosynthesis by downregulating *SPL9*, acting like miR156a. In contrast, LNC2 (lncRNA TCONS_00438839) expression reduced anthocyanin biosynthesis by downregulating MYB114, acting like miR828a (Zhang et al. 2018). Like LNC2 and miR828a, small interfering RNA TAS4-siRNA81(-) reduces anthocyanin biosynthesis by targeting PAP1 (production of anthocyanin pigment 1), PAP2, and MYB113 in Arabidopsis (Luo et al. 2012). It can be hypothesized that LNC1-miRNA156 interaction downregulates *SPL9*, which, in turn, upregulates anthocyanin biosynthetic genes, such as, flavonoid 3' hydroxylase (*F3'H*), dihydroflavonol 4-reductase (*DFR*), etc. (Gou et al. 2011; Zhang et al. 2018). The roles of sRNAs on other negative regulators of anthocyanins remain to be investigated. The specific set of flavonoid biosynthetic genes that undergo regulation processes by lncRNA-miRNA (e.g., LNC1-miRNA156 and LNC2-miR828a) interactions remain to be demonstrated.

The roles of *VvMYBC2-L1,2&3* (R2R3 Myb transcription factor C2 repressor motif protein) in regulating anthocyanins and PAs are discussed in Table 1. In *V. vinifera* 'Syrah', also known as 'Shiraz', expression quantitative trait locus (eQTL) mapping has been performed to identify regulatory loci linked with the expression of PA biosynthetic genes and, thereby, polygenic regulatory mechanism for PA biosynthesis. While *VvMYB4a* and *VvMYB4b* negatively regulate synthesis of small weight phenolic compounds, *VvMYBC2-L1,2&3* balance the induction of flavonoid biosynthetic genes (Huang et al. 2014; Cavallini et al. 2015). The increase in *VvMYBC2-L1* expression at the lag phase (end of green stage at 35 d after anthesis) and after berry maturation correlated with reduction in PA (by downregulating *VvMYBPA1*, *VvMYBPA2*, *VvDFR*, *VvLDOX*, *VvLAR1* and *VvANR*) and phenylpropanoid (by downregulating *Vv4-CL1* and *VvC4HI*) synthesis (Huang et al. 2014). Since the metabolic flux from Cya to either anthocyanins or PAs is reciprocally regulated by expression of UDP-glucosyl transferase 78D2 (*UGT78D2*), *V. vinifera* anthocyanidin

reductase (*Vv*ANR), *V. vinifera* leucoanthocyanidin dioxygenase (*Vv*LDOX) and AHA10 (Marinova et al. 2007; Sun, Li, and Huang 2012; Huang et al. 2014), their coexpression with PA and/or anthocyanin biosynthetic genes and their transporters can be used for engineering grapevine metabolites and the associate quality characteristics.

Effects of viticultural and vineyard management practices on grape quality and nutrient composition selected based on the grape usage purposes

The influence of viticulture practices on grape and wine quality composition are strongly dependent on environmental conditions, time of application, vintages and grapevine genotypes (Table 2) (Cartechini, Palliotti, and Lungarotti 2000; Sivilotti et al. 2017; Hernandez-Orte et al. 2014). Due to the complexity of the interactions between vineyard management practices, grape genotype and age as well as environmental conditions, the most effective viticultural and vineyard management practices are discussed in this review article to assist grape growers and breeders choose the best strategies for improving grape yield, quality and tolerance.

Choosing the appropriate training and pruning systems has the high potential to improve grape quality and yield. Comparing the Guyot, Royat and Lyre training systems, Kyrleou and coworkers showed that *V. vinifera* ‘Xinomavro’ grapes trained by the Lyre system produced higher levels of total anthocyanins, total phenolic compounds and color intensity, while the Royat system was more beneficial to produce full-bodied wines with longer ageing potential by modifying tannin structure required for longer maceration periods (Kyrleou et al. 2015). Yet, more studies are required to determine the influence of training and pruning types on flavonoid composition, and fruit and wine quality attributes, particularly on white wine grapes.

Grapevine cluster thinning (CT) during berry development or at *véraison* promotes several cellular processes and metabolic pathways, including carbohydrate metabolism, sink/source balance (e.g., by 1.2 m² leaf area kg⁻¹ of berries in 50% CT compared to 0.6 m² in control), the synthesis and transport of secondary metabolites, and accelerating berry ripening (Pastore et al. 2011). Trunk girdling (TG) also known as ring-barking by removing phloem and cambium around the trunk is a common viticultural practice at berry set or *véraison* to increase the accumulation of carbohydrates above the girdled ring by blocking the translocation of photosynthate from source leaves to roots. In grapevine, TG is performed at berry set to improve berry size and at *véraison* to stimulate and improve berry maturation, grape color formation, and berry size. In addition to sink-source balance, the positive effects of TG on plant water status as the result of improving hydraulic conductance above the girdle have also been demonstrated. The increase in anthocyanin accumulation in girdled grapevines can be ascribed to the increase in ABA and sucrose concentrations (López et al. 2015; Basile et al. 2018). In *V. vinifera* “Sangiovese”, 50% cluster thinning-mediated elevated sucrose downregulated sucrose transporter genes, including *VvSUC11* and *VvSUC27* and increased sucrose transporter mRNA. Additionally, CT promoted malate metabolism and transportation after *véraison*, thereby, releasing malate from vacuole during post-*véraison*, followed by converting malate to malic acid, reducing TA during berry ripening and accelerating berry ripening. Cluster thinning indirectly upregulates anthocyanin biosynthetic genes by increasing sucrose or directly upregulating anthocyanin biosynthetic genes. Pastore et al.’s (2011) study showed that 50% CT upregulated four *phenylalanine ammonia-lyase* (*PAL*) isogenes and one *chalcone synthase* (*CHS*) (Basile et al. 2018). Upon exposure to biotic and abiotic stresses, grapevines accumulate bioactive components, such as stilbenes (resveratrol), stilbenoids, oxylipins, hormones, such as JA, fatty acids, such as, linoleic acid, linolenic acid and oleic *cis*-vaccenic acid, etc., to regulate stress responses by, for example, modulating cell

signalling, radical scavenging and restricting pathogen growth (Chitarrini et al. 2017). In this context, mechanical wounding performed as TG and/or CT can be used as a strategy to stimulate these bioactive components and consequently improve the stress responses, fruit quality and health promoting effects in grapevine (Chitarrini et al. 2017; Basile et al. 2018). In *V. vinifera* ‘Sangiovese’, CT upregulated stilbene by upregulating 19 *STSs* that were not expressed in control berries. Cluster thinning downregulated a *geranylgeranyl diphosphatase synthase (GGDPS)* and a *geranylgeranyl reductase (GGR)* genes involved in terpenoid metabolism. Cluster thinning upregulated *VvGST4*, *VvMYBA1*, *cinnamyl alcohol dehydrogenases (CAD)*, *isoflavone reductase*, *caffeic acid 3-O-methyltransferase (COMT)*, *ferulate 5-hydroxylase (F5H)*, and *5GTs* genes as well as ABA and MATE transporters to increase anthocyanins and downregulated *F3'H*, *LDOX*, *leucoanthocyanidin reductase1 (LARI)* and *UDP-glucose:flavonoid glucosyltransferase (UFGT)* genes to slow down the synthesis of non-anthocyanin flavonoid compounds such as PA. Cluster thinning enhanced the synthesis of phenolic compounds such as stilbenes and isoflavonoids possibly as the result of wounding since they usually increase in response to wounding and pathogens (Pastore et al. 2011). Cluster thinning can be combined to TG to increase its efficacy. In *V. vinifera* ‘Nebbiolo’ wine grape and *V. vinifera* ‘Sugrathirteen[®]’, table grape, cyanidin-3-*O*-monoglucoside and peonidin-3-*O*-monoglucoside were increased by 50% CT. In Sugrathirteen[®], pH increased from 3.54 in control to its peak at 3.64 by 50% CT accompanied by TG at berry set. The lowest pH was obtained by 33% CT accompanied by TG (by 3.37) and 33% CT without TG at berry set (by 3.38), while 50% CT and TG at *véraison* exhibited comparatively high pH (3.52). The highest polyphenols (543.61 mg L⁻¹) and anthocyanins contents (497.30 mg L⁻¹), high TSS (17.2 °Brix), and relatively high TA (5.26 g L⁻¹) were recorded by 50% CT and TG at *véraison*. The highest TA (5.71 g L⁻¹) was obtained by TG at berry set and was at its lowest (4.58 g L⁻¹) in control (Basile et al. 2018).

Normally, grapes are girdled at berry set to increase berry size or at *véraison* to ensure better maturation, improve berry color and stimulate maturation of grapes. Increment in berry size owing to girdling is the result of better carbohydrate nutrition above the girdle because the transport of sugars from leaves to the root system is blocked by girdling treatment (Basile et al. 2018). Basal leaf removal around the cluster zone, also referred to as basal leaf plucking or defoliation, can also be applied as an effective viticulture practice to optimize sunlight perception and ventilation, thereby, increasing photosynthetic capacity, reducing disease and pest spread, and improving yield, nutrient composition and quality of grapes, particularly for wine production. Leaf removal timing is commonly carried out between full bloom and fruit setting, but may also be applied during, pepper-corn sized and pea-sized berries, and *véraison*. Basal leaf removal increases the anthocyanin contents and, thereby, promotes skin color development, particularly in cool climate (Wurz et al. 2017). Typically, basal leaf removal increases sugar and polyphenols, while reducing total acidity in berries as a result of malic acid degradation and being exposure to sunlight and, thereby, increases pH of the wines (Wurz et al. 2017). In *V. vinifera* L. var. Sauvignon blanc, basal leaf removal, particularly at the full bloom (followed by pepper-corn sized and pea-sized berries), markedly reduced the risk of botrytis bunch rot, and increased the amount of gallic acid. The control grapes had the highest contents of catechin, rutin, relatively high contents of *p*-coumaric acid, and the lowest amounts of vanillic acid. The *p*-coumaric acid was high in control and defoliated grapes at full bloom, and was low in defoliated grape at pepper-corn size and pea-sized berries. As the prevalent flavonoid in white wines, catechins and *p*-coumaric acid (the polyphenolic compounds rich in hydroxyl groups) are highly susceptible to oxidization by the phenoloxidase enzymes in the respective quinones and, thereby, lowers the quality of the white wines by causing darkening and some bitterness (Wurz et al. 2017). Wurz et al.'s (2017) study concluded that defoliation at pepper-corn size phonological stage not only

effectively reduced botrytis bunch rot, but also preserved oenological performance of grapes and wine quality. Like defoliation, head trimming or hedging has the potential to improve grape quality (e.g., cluster weight, TSS, TA, pH), nutrient and chemical composition, aroma, and yield in red and white grapes and their products. However, because their influence varies depending on the grape age, genotypes, culture, growth stage, and environmental conditions (Cartechini, Palliotti, and Lungarotti 2000; Hernandez-Orte et al. 2014) the case-by-case studies should be conducted before applying in a large scale for commercial production. Understanding the influence of viticultural practices on chemical composition, particularly in white wine grapes, requires more investigations.

Regulated deficit irrigation (RDI) and partial root drying (PRD) can be applied as strategy to both reduce the amount of water and increase grape and wine quality. Chaves and co-workers' study showed that PRD was more effective than RDI to improve grape quality by reducing vigor and consequently improving light perception and hence synthesis of bioactive compounds such as anthocyanins and total phenols (Chaves et al. 2007). Metabolomic analysis of 279 *V. vinifera* cultivars showed that mild drought stress represses catechin and epicatechin, both as flavan-3-ol monomers and as constitutive units of PAs and total flavan-3-ols (Pinasseau et al. 2017) and, thereby, have the potential to reduce the risk of oxidization and browning (Wurz et al. 2017). Depending on grape genotypes, mild drought stress may increase the total amount of anthocyanins, stilbenes and flavonols and, thereby, have the potential to enhance their health promoting effects in plant and human (Pinasseau et al. 2017). In addition to preharvest practices, postharvest managements are also important to maintain the quality of grapevines. Recently, Bal, Kok and Torcuk's (2017) study demonstrated the effectiveness of combined treatments of putrescine and ultrasound on improving the table grape *V. vinifera* 'Michele Palieri' quality by reducing decay incidence, maintaining visual appearance, total anthocyanin and phenolic contents and increasing

antioxidant activities under the modified atmosphere packaging at 1-2 °C with 90-95% relative humidity (Bal, Kok and Torcuk 2017). Application of essential oils from basil (*Ocimum basilicum*) wild mint (*Mentha longifolia*) and ajowan (*Carum copticum*) was also effective in improving postharvest quality indices of table grape *V. vinifera* ‘Rasha’ (Siah-e-Sardasht) by reducing decay incidence and weight loss as well as increasing TSS, TA, vitamin C (Salimi et al. 2013). Application of 300 ppm β -aminobutyric acid was also effective in improving the quality of *V. vinifera* ‘Crimson Seedless’ by inhibiting the growth of *Botrytis cinerea* and *Saccharomyces cerevisiae*, and improving TSS, TA, total sugar content and anthocyanin accumulation (El-Metwally, Tarabih, and El-Eryan 2014). The combined application of these treatments together with the manipulation of biosynthetic pathways for improving resveratrol and stable anthocyanins would also be effective strategies to enhance the postharvest quality of grapevines.

Conclusions

Grapevine chemical composition, fruit quality and performance depend on broad range of internal and external cues and hence multidisciplinary approaches according to usage purposes and environmental conditions are required prior to commercial cultivation to achieve the best results. Accordingly, taking a broad range of the influential factors involved in regulation of flavonoid signalling and metabolic pathways, this review article provides some insights required for breeding/engineering grapevines and makes suggestions for future improvements.

Table 1. Roles of TFs and genes in engineering flavonoids and their influence on grape quality and stress tolerance.

TFs/genes	Identified in	Bioactive components	Grape quality	Ref.
<i>VvMYBA1</i>	<i>V. vinifera</i>	Overexpression of <i>VvMYBA1</i> results in pigmentation in white grapes such as <i>V. vinifera</i> ‘Chardonnay’.	Improves pigmentation.	(Rinaldo et al. 2015)
<i>VvVHP1; 2</i>	‘Kyoho’ (<i>V. vinifera</i> × <i>labrusca</i>)	Type I VHP and H ⁺ -ATPase are involved in vascular acidification and thereby facilitate anthocyanin accumulation. <i>VvMYBA1</i> activates <i>VvVHP1; 2</i> and thereby promotes anthocyanin accumulation.	Improves pigmentation.	(Sun et al. 2017)
<i>Vv3AT</i>	<i>V. vinifera</i> ‘Shiraz’, ‘Cabernet Sauvignon’, and to a lower extent in ‘Malian’ and ‘Pinot Noir’. (as described earlier, ‘Pinot Noir’ lacks the acetylated anthocyanins)	<i>VvMYBA1</i> and <i>VvMYC1</i> induce <i>Vv3AT</i> and thereby <i>VvUFGT</i> expression. <i>VvUFGT</i> can be activated by both <i>VvMYBA1&2</i> . <i>Vv3AT</i> encodes BAHD acyltransferase protein, thereby producing acylated anthocyanins, respectively acetylated and coumaroylated forms, and particularly by acylating monoglucoside anthocyanins. Application of naringenin and vanadate and AVIs induction are other strategies for increasing acylated anthocyanins. <i>Vv3AT</i> utilise acetyl-, coumaroyl- and caffeoyl-CoA and to a lower extent malonyl-CoA, resulting in low concentrations of malonylated anthocyanins in grapevines.	Improves pigmentation in red wine and table grapes, and color stability.	(Janvary et al. 2009; Pourcel et al. 2010; Rinaldo et al. 2015; He et al. 2017)

AM1 and AM2	<i>V. vinifera</i> 'Shiraz'	Transport acylated anthocyanins.	Improve pigmentation in red wine and table grapes, and color stability.	(Gomez et al. 2009)
<i>VvGATI</i> , <i>VvSCP31</i> and <i>VvSCP5</i>	<i>V. vinifera</i> 'Macabeu'	Encode SCPL-AT enzymes and thereby promote biosynthesis of acylated anthocyanins.	Improve pigmentation in red wine and table grapes, and color stability.	(Bontpart et al. 2018)
<i>VvCCoAOMT</i> (induced by ABA and drought); <i>VvAOMT</i> (subclass of <i>VvCCoAOMT</i> ; regulated by <i>VvMybA1</i>) <i>VvCCoAOMT</i>	<i>V. vinifera</i>	<i>VvCCoAOMT</i> induces methylation of CoA esters <i>in vitro</i> and enhances accumulation of methylated anthocyanins and C3G (with lower efficacy than <i>VvAOMT</i>), particularly under drought stress. <i>VvCCoAOMT</i> induces the biosynthesis of lignin monomers like scopolin, thereby protecting grape against cold stress and biotic stress like fungal pathogens. <i>VvAOMT</i> is involved in accumulation of methylated anthocyanins independent of drought stress.	Methylation improves health promoting effects, anthocyanin stability and color intensity in red wine grapes. Improve grape tolerance to cold stress and fungal pathogens.	(Giordano et al. 2016)
<i>VvTPSs</i>	<i>V. vinifera</i>	<i>VvTPSs</i> can be induced by JA. Regulate biosynthesis of terpenoids. <i>VvTPS</i> genes are involved in production of (3S)-linalool (<i>VvTPS-g</i>), geraniol (<i>VvTPSg</i>), and α -terpineol synthase (<i>VvTPS-b</i>).	Improve berry and wine aroma, taste and defence against insects and pathogens.	(Martin et al. 2010)
<i>VvSTO2</i>	<i>V. vinifera</i> 'Shiraz'	Transforms α -guaiene to (-)-rotundone. It can be hypothesized that <i>VvSTO2</i> overexpression has the potential to improve the quality of wine grapes.	Improves the spicy aroma of wine grapes.	(Takase et al. 2016)

<i>CYP76F14</i>	Riesling × Gewurztraminer	Oxidizes linalool to (<i>E</i>)-8-carboxylinalool, which is a precursor to wine lactone, a potent monoterpene odorant in wine. This review suggests that the coexpression of <i>VvTPS</i> genes with <i>CYP76F14</i> might be effective to enhance the amount of lactone in wines.	Improves aroma in berry and wine.	(Martin et al. 2010; Ilc et al. 2011;)
<i>VvCHS1,2&3</i>	<i>V. vinifera</i> ‘Shiraz’	<i>VvCHS1</i> and to a lesser extent <i>VvCHS2</i> regulate tannin and flavonol synthesis. <i>VvCHS2&3</i> are predominantly involved in anthocyanin biosynthesis. <i>VvMYBA1</i> activates <i>VvCHS3</i> . <i>VvMYBPA1</i> activates <i>VvCHS1</i> . <i>VvMYBPA2</i> activates <i>VvCHS2&3</i> . <i>VvMYBA1</i> - <i>VvCHS3</i> and <i>VvMYBF1</i> - <i>VvCHS1&2</i> coexpressions have high potential to improve respectively anthocyanin and flavonoid synthesis, which remains to be investigated.	Improve pigmentation. Their influence and interactions on berry and wine quality can provide more information. <i>VvMYBF1</i> - <i>VvCHS1&2</i> has the potential to induce cold acclimation.	(Harris et al. 2013)
<i>VvWRKY26</i>	<i>V. vinifera</i>	Promotes anthocyanin and PA accumulation as well as fleshy fruit development	Improves berry size and color.	(Amato et al. 2016)
<i>VqMAPKKK38</i>	Chinese wild grapevine <i>V. quinquangularis</i> accession ‘Danfeng-2’	Is induced by SA, ABA, ETH, MeJA. Is involved in redox (H ₂ O ₂ and ROS) and calcium signalling and improves STS transcription and stilbene accumulation likely by upregulating MYB14.	Stilbene accumulation promotes health promoting effects in both grape and human.	(Jiao et al. 2017)
<i>VqDUF642</i>	Chinese wild grapevine <i>V. quinquangularis</i> accession ‘Danfeng-2’	Overexpression of <i>VqDUF642</i> accelerates berry development and increase resistance against pathogens including <i>Erysiphe necator</i> and <i>B. cinerea</i> .	Improves berry development and resistance to biotic stress.	(Xie and Wang 2016)

<i>VviMYB14</i> , <i>VviMYB15</i> ,	<i>V. monticola</i> × <i>V. riparia</i>	Improve stilbene synthesis. <i>VviWRKY3</i> may synergistically improve <i>VviMYB14</i> effect on stilbene synthesis.	Stilbene accumulation promotes health promoting effects in both grape and human.	(Vannozzi et al. 2018)
<i>VvGST3,4</i> and to a lesser extent <i>VvGST1</i>	<i>V. vinifera</i>	Transport PA. Their regulation can be used for engineering flavonoids and hence anthocyanin/PA ratios to increase the quality and tolerance of grapes. The influence of <i>VvGSTs</i> on anthocyanin types and contents require more investigation.	Require more studies.	(Pérez-Díaz et al. 2016)
<i>VvGST4</i>	<i>V. vinifera</i>	Transports anthocyanins and PA.	Improves pigmentation.	(Pérez-Díaz et al. 2016)
<i>VvGST4,5</i>	<i>V. davidii</i> (Spine grape)	Transport anthocyanins.	Improve pigmentation.	(Sun et al. 2016)
<i>VvGST4,5</i> and <i>AM2</i>	<i>V. davidii</i> (Spine grape)	Transport anthocyanins. (<i>AM1</i> and <i>AM2</i> transport acylated anthocyanins in <i>V. vinifera</i> ‘Shiraz’)	Improves pigmentation.	(Gomez et al. 2009) (Sun et al. 2016)
<i>VvibZIPC22</i>	<i>V. vinifera</i> ‘Pinot Noir’ red wine grape	Promotes kaempferol and quercetin biosynthesis. Hence, its overexpression may promote cold acclimation, which remains to be studied.	May improve cold acclimation.	(Malacarne et al. 2016)
<i>VvMYBF1</i> , <i>VvFLS1</i> and <i>VvCHI</i>	<i>V. vinifera</i> ‘Shiraz’	Regulate flavonol biosynthesis and thus may improve cold acclimation, which remains to be studied.	May improve cold acclimation.	(Czermel et al. 2009)
<i>VvFLS4</i> and 5, <i>VvMYB12</i> , <i>VvMYCA1</i> , <i>VvWDRs</i> , <i>VvUVR8</i> , <i>VvHY5</i> , <i>VvCOPI</i> and <i>VvCHS</i>	<i>Vitis vinifera</i> L. var. Sauvignon blanc	Regulate flavonol biosynthesis. <i>VvMYB12</i> and <i>VvFLS4</i> were UV-B responsive. Their influence on cold acclimation remains to be investigated.	May improve cold acclimation.	(Liu et al. 2014)

<i>VvMAPK3</i>	<i>Vitis vinifera</i> L. var. Sauvignon blanc	Regulates flavonol biosynthesis under high UV-B and thus may affect cold acclimation, which remains to be studied.	May improve cold acclimation.	(Liu et al. 2014)
<i>VvMYB5a&b</i> and <i>VvMYBC2-L1&3</i>	<i>V. vinifera</i> 'Cabernet Sauvignon'	<i>VvMYB5a&b</i> are negative regulators on their own, but their interactions with positive regulators induce the biosynthesis of flavonoids. <i>VvMYB5a-VvMYBA1-VvMYBA2</i> interaction induces anthocyanin biosynthesis. <i>VvMYB5a&b-VvMYBPA1</i> interaction induces PA biosynthesis, particularly catechin synthesis in skin cells. The downregulation of <i>VvMYB5a&b</i> on flavonoids biosynthesis provides further information on improving grapevine quality. <i>VvMYB5a&b</i> interactions with <i>VvMYBC2-L1&3</i> repress both anthocyanin and PA.	Their influence on grape quality depends on the their interaction with other TFs.	(Deluc et al. 2008; Cavallini et al. 2015)
MYBA1,6.1&7	<i>V. vinifera</i> 'Corvina'	MYBA6.1&7 and to a lesser extent MYBA1 overexpression increased total anthocyanin contents without affecting PA, but reduced stilbenoid synthesis. MYBA1 mainly induced synthesis of trihydroxylated anthocyanins. Ectopic expression of MYBA1,6.1&7 differentially induced pigmentation of white grape <i>V. vinifera</i> 'Maccabeu'.	Improve pigmentation of red wine grapes and table grapes.	(Matus et al. 2017)
<i>VvMYBPAR</i>	<i>V. vinifera</i> 'Cabernet Sauvignon'	Promotes PA biosynthesis and transportation.	Requires more studies.	(Koyama et al. 2014)

VvVHP1; 2, *V. vinifera* vacuolar H⁺-PPase; AVP1, Arabidopsis vacuolar membrane proton pump 1; *Vv3AT*, *V. vinifera* ANTHOCYANIN 3-O-GLUCOSIDE-6"-O-ACYLTRANSFERASE; *VvGAT*, *V. vinifera* glucose acyltransferase; SCPL-AT, serine carboxypeptidase-like acyltransferases; BAHD, acyltransferase protein (named after the first letter of the first four characterized proteins: BEAT [for acetyl CoA:benzylalcohol acetyltransferase], AHCT [for anthocyanin O-hydroxycinnamoyltransferase], HCBT [for anthranilate N-hydroxycinnamoyl/benzoyltransferase], and DAT [for deacetylindoline 4-O-acetyltransferase]); *VvCCoAOMT*, *V. vinifera* caffeoyl-CoA O-methyltransferases; *VqDUF642*, *V. quinquangularis* domains of unknown function 642, *VvTPS*, *V. vinifera* terpenoid synthase.

Table 2. Roles of viticultural practices in improving grapevine quality.

Practice	Grapevine	Effects on berry quality and flavonoids	Effects on grape type and wine quality	Ref.
Mild drought stress between <i>véraison</i> and maturation		Promotes berry maturation. Promotes nutrients, anthocyanins, total phenolic compounds, polyphenols and sugars. Reduces catechin, epicatechin and PAs and thereby reduces the risk of browning. Induces the expression of <i>VvCCoAOMT</i> and thereby accumulation of methylated anthocyanins, increasing the health promoting effects and wine quality.	Improves the quality of red and white wine grapes.	(Chaves et al. 2007; Giordano et al. 2016; Xu et al. 2017; Pinasseau et al. 2017; Wurz et al. 2017)
50 % CT at <i>véraison</i>	<i>V. vinifera</i> 'Sangiovese'	Promote source/sink ratio and ripening. Boosts sugar, malic acid, resveratrol, anthocyanin contents and thereby maturation and color formation at harvest. May reduce acidity depending on TSS and temperature. May increase TSS.	Improves the quality of red wine grapes.	(Pastore et al. 2011)
50 % CT at <i>véraison</i>	<i>V. vinifera</i> 'Nebbiolo' red wine grape and 'Sugrathirteen®' table grape	CT increased cyanidin-3- <i>O</i> -monoglucoside and peonidin-3- <i>O</i> -monoglucoside. Studies about the effects of CT on white wine grapes can provide valuable information in future.	Improves the quality of red wine grapes and table grapes.	(Basile et al. 2018)
50 % CT + TG at <i>véraison</i>	<i>V. vinifera</i> 'Sugrathirteen®' table grape	Resulted in high pH, polyphenols, anthocyanins, TSS, TA. CT + TG on red and white wine grapes and white table grapes can provide valuable information in future.	Improves the quality of table grapes.	(Basile et al. 2018)
Defoliation at pepper-corn size	<i>V. vinifera</i> var. Sauvignon blanc	Reduces TA and botrytis risk. May induce the synthesis of thiol precursors depending on the environmental conditions and grape genotypes. Induces the expression of <i>VvGST3</i> and <i>VvGST5</i> and therefore may improve pigmentation in red wine and table grapes.	Improves the quality of white wine grapes by reducing <i>p</i> -coumaric acid, thereby reducing browning.	(Wurz et al. 2017; Sivilotti et al. 2017)

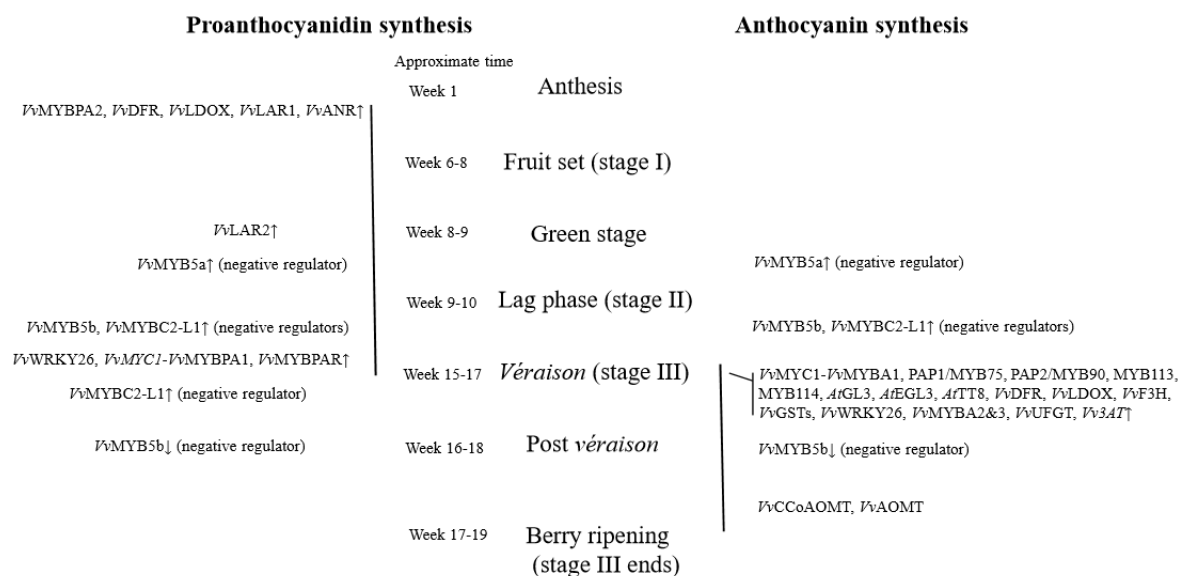


Figure 1. Simplified schematic representative of the main TFs/genes involved in the regulation of anthocyanins and/or PAs at different grape growth and development stages from anthesis to the end of berry ripening.

References

- Amato, A., E. Cavallini, S. Zenoni, L. Finezzo, M. Begheldo, B. Ruperti, and G. B. Tornielli. 2016. A grapevine TTG2-Like WRKY transcription factor is involved in regulating vacuolar transport and flavonoid biosynthesis. *Frontiers in Plant Science* 7:1979. doi:[10.3389/fpls.2016.01979](https://doi.org/10.3389/fpls.2016.01979)
- Bal, E., D. Kok D, A. L. Torcuk. 2017. Postharvest putrescine and ultrasound treatments to improve quality and postharvest life of table grapes (*Vitis vinifera* L.) cv. Michele Palieri. *Journal of Central European Agriculture* 18 (3):598-615. doi:[10.5513/JCEA01/18.3.1934](https://doi.org/10.5513/JCEA01/18.3.1934)
- Basile, T., V. Alba, G. Gentileco, M. Savino, and L. Tarricone. 2018. Anthocyanins pattern variation in relation to thinning and girdling in commercial Sugrathirteen® table grape. *Scientia Horticulturae* 227:202-206. doi:[10.1016/j.scienta.2017.09.045](https://doi.org/10.1016/j.scienta.2017.09.045)
- Bindon, K., S. Kassara, Y. Hayasaka, A. Schulkin, and P. Smith. 2014. Properties of wine polymeric pigments formed from anthocyanin and tannins differing in size distribution and subunit composition. *Journal of Agricultural and Food Chemistry* 62 (47):11582-11593. doi:[10.1021/jf503922h](https://doi.org/10.1021/jf503922h)
- Bontpart, T., M. Ferrero, F. Khater, T. Marlin, S. Vialet, A. Vallverdù-Queralt, L. Pinasseau, A. Ageorges, V. Cheynier, and N. Terrier. 2018. Focus on putative serine carboxypeptidase-like acyltransferases in grapevine. *Plant Physiology and Biochemistry* 130:356-366. doi:[10.1016/j.plaphy.2018.07.023](https://doi.org/10.1016/j.plaphy.2018.07.023)
- Böttcher, C., C. A. Burbidge, P. K. Boss, and C. Davies. 2013. Interactions between ethylene and auxin are crucial to the control of grape (*Vitis vinifera* L.) berry ripening. *BMC Plant Biology* 13 (1):222-222. doi: [10.1186/1471-2229-13-222](https://doi.org/10.1186/1471-2229-13-222)
- Böttcher, C., R. A. Keyzers, P. K. Boss, and C. Davies. 2010. Sequestration of auxin by the indole-3-acetic acid-amido synthetase GH3-1 in grape berry (*Vitis vinifera* L.) and the proposed role of auxin conjugation during ripening. *Journal of Experimental Botany* 61 (13):3615-3625. doi:[10.1093/jxb/erq174](https://doi.org/10.1093/jxb/erq174)
- Cai, Y., Q. Luo, M. Sun, and H. Corke. 2004. Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. *Life Sciences* 74 (17):2157-2184. doi:[10.1016/j.lfs.2003.09.047](https://doi.org/10.1016/j.lfs.2003.09.047)
- Cartechini, A., A. Palliotti, and C. Lungarotti. 2000. Influence of timing of summer hedging on yield and grape quality in some red and white grapevine cultivars. *Acta Horticulturae* (512): 101-110. doi:[10.17660/ActaHortic.2000.512.10](https://doi.org/10.17660/ActaHortic.2000.512.10)
- Cavallini, E., J. T. Matus, L. Finezzo, S. Zenoni, R. Loyola, F. Guzzo, R. Schlechter, A. Ageorges, P. Arce-Johnson, and G. B. Tornielli. 2015. The phenylpropanoid pathway is controlled at different branches by a set of R2R3-MYB C2 repressors in grapevine. 167 (4):1448-1470. doi:[10.1104/pp.114.256172](https://doi.org/10.1104/pp.114.256172)
- Champa, W. A. Harindra, M. I. S. Gill, B. V. C. Mahajan, and N. K. Arora. 2015. Preharvest salicylic acid treatments to improve quality and postharvest life of table grapes (*Vitis vinifera* L.) cv. Flame Seedless. *Journal of Food Science and Technology* 52 (6):3607-3616. doi:[10.1007/s13197-014-1422-7](https://doi.org/10.1007/s13197-014-1422-7)
- Chanoca, A., and N. Kovinich. 2015. Anthocyanin vacuolar inclusions form by a microautophagy mechanism. 27 (9):2545-2559. doi: [10.1105/tpc.15.00589](https://doi.org/10.1105/tpc.15.00589)
- Chaves, M. M., T. P. Santos, C. R. Souza, M. F. Ortuño, M. L. Rodrigues, C. M. Lopes, J. P. Maroco, and J. S. Pereira. 2007. Deficit irrigation in grapevine improves water-use efficiency while controlling vigour and production quality. *Annals of Applied Biology* 150 (2):237-252. doi:[10.1111/j.1744-7348.2006.00123.x](https://doi.org/10.1111/j.1744-7348.2006.00123.x)
- Chen, W., D. Muller, E. Richling, and M. Wink. 2013. Anthocyanin-rich purple wheat prolongs the life span of *Caenorhabditis elegans* probably by activating the DAF-16/FOXO transcription factor. *Journal of Agricultural and Food Chemistry* 61 (12):3047-3053. doi:[10.1021/jf3054643](https://doi.org/10.1021/jf3054643)

- Chitarrini, G., L. Zulini, D. Masuero, and U. Vrhovsek. 2017. Lipid, phenol and carotenoid changes in 'Bianca' grapevine leaves after mechanical wounding: a case study. *Protoplasma* 254 (6):2095-2106. doi: [10.1007/s00709-017-1100-5](https://doi.org/10.1007/s00709-017-1100-5)
- Czemmel, S., S. C. Heppel, and J. Bogs. 2012. R2R3 MYB transcription factors: key regulators of the flavonoid biosynthetic pathway in grapevine. *Protoplasma* 249 Suppl 2:S109-118. doi:[10.1007/s00709-012-0380-z](https://doi.org/10.1007/s00709-012-0380-z)
- Czemmel, S., R. Stracke, B. Weisshaar, N. Cordon, N. N. Harris, A. R. Walker, S. P. Robinson, and J. Bogs. 2009. The grapevine R2R3-MYB transcription factor VvMYBF1 regulates flavonol synthesis in developing grape berries. *Plant Physiology* 151 (3):1513-1530. doi:[10.1104/pp.109.142059](https://doi.org/10.1104/pp.109.142059)
- Deluc, L., Jochen B., A. R. Walker, T. Ferrier, A. Decendit, J.-M. Merillon, S. P. Robinson, and F. Barrieu. 2008. The transcription factor VvMYB5b contributes to the regulation of anthocyanin and proanthocyanidin biosynthesis in developing grape berries. *Plant Physiology* 147 (4):2041-2053. doi: [10.1104/pp.108.118919](https://doi.org/10.1104/pp.108.118919)
- Deng, Y., and S. Lu. 2017. Biosynthesis and regulation of phenylpropanoids in plants. *Critical Reviews in Plant Sciences* 36 (4):257-290. doi:[10.1080/07352689.2017.1402852](https://doi.org/10.1080/07352689.2017.1402852)
- Dinis, L. T., S. Bernardo, A. Luzio, G. Pinto, M. Meijón, M. Pintó-Marijuan, A. Cotado, C. Correia, and J. Moutinho-Pereira. 2018. Kaolin modulates ABA and IAA dynamics and physiology of grapevine under Mediterranean summer stress. *Journal of Plant Physiology* 220:181-192. doi:[10.1016/j.jplph.2017.11.007](https://doi.org/10.1016/j.jplph.2017.11.007)
- El-Metwally, M. A., M. E. Tarabih, and E. E. El-Eryan. 2014. Effect of application of β -aminobutyric acid on maintaining quality of crimson seedless grape and controlling postharvest diseases under cold storage condition. *Plant Pathology Journal* 3 (3):139-151. doi:[10.3923/ppj.2014.139.151](https://doi.org/10.3923/ppj.2014.139.151)
- Francisco, R. Maria, A. Regalado, A. Ageorges, B. J. Burla, B. Bassin, C. Eisenach, O. Zarrouk, S. Vialet, T. Marlin, M. M. Chaves, E. Martinoia, and R. Nagy. 2013. ABCC1, an ATP binding cassette protein from grape berry, transports anthocyanidin 3-O-glucosides. *The Plant Cell* 25 (5):1840-1854. doi:[10.1105/tpc.112.102152](https://doi.org/10.1105/tpc.112.102152)
- Fulcrand, H., M. Dueñas, E. Salas, and V. Cheynier. 2006. Phenolic reactions during winemaking and aging. *American Journal of Enology and Viticulture* 57 (3):289-297.
- Giordano, D., S. Provenzano, A. Ferrandino, M. Vitali, C. Pagliarani, F. Roman, F. Cardinale, S. D. Castellarin, and A. Schubert. 2016. Characterization of a multifunctional caffeoyl-CoA O-methyltransferase activated in grape berries upon drought stress. *Plant Physiology and Biochemistry* 101:23-32. doi:[10.1016/j.plaphy.2016.01.015](https://doi.org/10.1016/j.plaphy.2016.01.015)
- Gomez, C., N. Terrier, L. Torregrosa, S. Vialet, A. Fournier-Level, C. Verries, J. M. Souquet, J. P. Mazauric, M. Klein, V. Cheynier, and A. Ageorges. 2009. Grapevine MATE-type proteins act as vacuolar H⁺-dependent acylated anthocyanin transporters. *Plant Physiology* 150 (1):402-415. doi:[10.1104/pp.109.135624](https://doi.org/10.1104/pp.109.135624)
- Gomez, C., G. Conejero, L. Torregrosa, V. Cheynier, N. Terrier, and A. Ageorges. 2011. In vivo grapevine anthocyanin transport involves vesicle-mediated trafficking and the contribution of anthoMATE transporters and GST. *The Plant Journal* 67 (6):960-970. doi:[10.1111/j.1365-3113X.2011.04648.x](https://doi.org/10.1111/j.1365-3113X.2011.04648.x)
- Gou, J.-Y., F. F. Felippes, C.-J. Liu, D. Weigel, and J.-W. Wang. 2011. Negative regulation of anthocyanin biosynthesis in *Arabidopsis* by a miR156-Targeted SPL transcription factor. *The Plant Cell* 23 (4):1512-1522. doi: [10.1105/tpc.111.084525](https://doi.org/10.1105/tpc.111.084525)
- Han, F., Y. Ju, X. Ruan, X. Zhao, X. Yue, X. Zhuang, M. Qin, and Y. Fang. 2017. Color, anthocyanin, and antioxidant characteristics of young wines produced from spine grapes (*Vitis davidii* Foex) in China. *Food and Nutrition Research* 61 (1):1339552. doi:[10.1080/16546628.2017.1339552](https://doi.org/10.1080/16546628.2017.1339552)
- Harris, N. N., J. M. Luczo, S. P. Robinson, and A. R. Walker. 2013. Transcriptional regulation of the three grapevine chalcone synthase genes and their role in flavonoid synthesis in Shiraz. *Australian Journal of Grape and Wine Research* 19 (2):221-229. doi:[10.1111/ajgw.12026](https://doi.org/10.1111/ajgw.12026)
- He, F., L. Mu, G.-L. Yan, N.-N. Liang, Q.-H. Pan, J. Wang, M. J. Reeves, and C.-Q. Duan. 2010. Biosynthesis of anthocyanins and their regulation in colored grapes. *Molecules* 15 (12). doi:[10.3390/molecules15129057](https://doi.org/10.3390/molecules15129057)

- He, R., J. Peng, P. Yuan, J. Yang, X. Wu, Y. Wang, and W. Wei. 2017. Glucosyltransferase activity of clostridium difficile toxin b triggers autophagy-mediated cell growth arrest. *Scientific Reports* 7 (1):10532. doi:[10.1038/s41598-017-11336-4](https://doi.org/10.1038/s41598-017-11336-4)
- Hernandez-Orte, P., B. Concejero, J. Astrain, B. Lacau, J. Cacho, and V. Ferreira. 2014. Influence of viticulture practices on grape aroma precursors and their relation with wine aroma. *Journal of the Science of Food and Agriculture* 95 (4):688-701. doi: [10.1002/jsfa.6748](https://doi.org/10.1002/jsfa.6748)
- Hichri, I., S. C. Heppel, J. Pilet, C. Leon, S. Czernel, S. Delrot, V. Lauvergeat, and J. Bogs. 2010. The basic helix-loop-helix transcription factor MYC1 is involved in the regulation of the flavonoid biosynthesis pathway in grapevine. *Molecular Plant* 3 (3):509-523. doi:[10.1093/mp/ssp118](https://doi.org/10.1093/mp/ssp118)
- Huang, W.-Y., H. Wu, D.-J. Li, J.-F. Song, Y.-D. Xiao, C.-Q. Liu, J.-Z. Zhou, and Z.-Q. Sui. 2018. Protective effects of blueberry anthocyanins against H₂O₂-induced oxidative injuries in human retinal pigment epithelial cells. *Journal of Agricultural and Food Chemistry* 66 (7):1638-1648. doi: [10.1021/acs.jafc.7b06135](https://doi.org/10.1021/acs.jafc.7b06135)
- Huang, Y. F., S. Vialet, J. L. Guiraud, L. Torregrosa, Y. Bertrand, V. Cheynier, P. This, and N. Terrier. 2014. A negative MYB regulator of proanthocyanidin accumulation, identified through expression quantitative locus mapping in the grape berry. *New Phytologist* 201 (3):795-809. doi:[10.1111/nph.12557](https://doi.org/10.1111/nph.12557)
- Ilc, T., D. Halter, L. Miesch, F. Lauvoisard, L. Kriegshäuser, A. Ilg, R. Baltenweck, P. Huguéney, D. Werck-Reichhart, E. Duchêne, and N. Navrot. 2016. A grapevine cytochrome P450 generates the precursor of wine lactone, a key odorant in wine. *New Phytologist* 213 (1):264-274. doi:[10.1111/nph.14139](https://doi.org/10.1111/nph.14139)
- Ivanova, V., B. Vojnoski, and M. Stefova. 2012. Effect of winemaking treatment and wine aging on phenolic content in Vranec wines. *Journal of Food Science and Technology* 49 (2):161-172. doi:[10.1007/s13197-011-0279-2](https://doi.org/10.1007/s13197-011-0279-2)
- Janvary, L., T. Hoffmann, J. Pfeiffer, L. Hausmann, R. Topfer, T. C. Fischer, and W. Schwab. 2009. A double mutation in the anthocyanin 5-O-glucosyltransferase gene disrupts enzymatic activity in *Vitis vinifera* L. *Journal of Agricultural and Food Chemistry* 57 (9):3512-3518. doi:[10.1021/jf900146a](https://doi.org/10.1021/jf900146a)
- Jiao, Y., D. Wang, L. Wang, C. Jiang, and Y. Wang. 2017. VqMAPKKK38 is essential for stilbene accumulation in grapevine. *Horticulture Research* 4:17058. doi:[10.1038/hortres.2017.58](https://doi.org/10.1038/hortres.2017.58)
- Kovinich, N., G. Kayanja, A. Chanoca, M. S. Otegui, and E. Grotewold. 2015. Abiotic stresses induce different localizations of anthocyanins in Arabidopsis. *Plant Signaling & Behavior* 10 (7):e1027850. doi:[10.1080/15592324.2015.1027850](https://doi.org/10.1080/15592324.2015.1027850)
- Koyama, K., M. Numata, I. Nakajima, N. Goto-Yamamoto, H. Matsumura, and N. Tanaka. 2014. Functional characterization of a new grapevine MYB transcription factor and regulation of proanthocyanidin biosynthesis in grapes. *Journal of Experimental Botany* 65 (15):4433-4449. doi: [10.1093/jxb/eru213](https://doi.org/10.1093/jxb/eru213)
- Kyrleou, M., S. Kallithraka, S. Koundouras, K. Chira, S. Haroutounian, H. Spithiropoulou, and Y. Kotseridis. 2015. Effect of vine training system on the phenolic composition of red grapes (*Vitis vinifera* L. cv. Xinomavro). *Journal International des Sciences de la Vigne et du Vin/International Journal of Science of the Vine and Wine* 49 (1):71-84. doi:[10.20870/oenone.2015.49.2.92](https://doi.org/10.20870/oenone.2015.49.2.92)
- Lai, B., L.-N. Du, R. Liu, B. Hu, W.-B. Su, Y.-H. Qin, J.-T. Zhao, H.-C. Wang, and G.-B. Hu. 2016. Two LcbHLH transcription factors interacting with LcMYB1 in regulating late structural genes of anthocyanin biosynthesis in *Nicotiana* and *Litchi chinensis* during anthocyanin accumulation. *Frontiers in Plant Science* 7:166. doi:[10.3389/fpls.2016.00166](https://doi.org/10.3389/fpls.2016.00166)
- Li, X., P. Gao, D. Cui, L. Wu, I. Parkin, R. Saberianfar, R. Menassa, H. Pan, N. Westcott, and M. Y. Gruber. 2011. The Arabidopsis *tt19-4* mutant differentially accumulates proanthocyanidin and anthocyanin through a 3' amino acid substitution in glutathione S-transferase. *Plant Cell Environ* 34 (3):374-388. doi:[10.1111/j.1365-3040.2010.02249.x](https://doi.org/10.1111/j.1365-3040.2010.02249.x)
- Liu, L., S. Gregan, C. Winefield, and B. Jordan. 2014. From UVR8 to flavonol synthase: UV-B-induced gene expression in Sauvignon blanc grape berry. *Plant Cell Environ* 38 (5):905-919. doi:[10.1111/pce.12349](https://doi.org/10.1111/pce.12349)

- Liu, Y., X. Song, D. Zhang, F. Zhou, D. Wang, Y. Wei, F. Gao, L. Xie, G. Jia, W. Wu, and B. Ji. 2011. Blueberry anthocyanins: protection against ageing and light-induced damage in retinal pigment epithelial cells. *British Journal of Nutrition* 108 (1):16-27. doi:[10.1017/S000711451100523X](https://doi.org/10.1017/S000711451100523X)
- Liu, Z., M.-Z. Shi, and D.-Y. Xie. 2014. Regulation of anthocyanin biosynthesis in *Arabidopsis thaliana* red *pap1-D* cells metabolically programmed by auxins. *Planta* 239 (4):765-781. doi:[10.1007/s00425-013-2011-0](https://doi.org/10.1007/s00425-013-2011-0)
- López, R., R. Brossa, L. Gil, and P. Pita. 2015. Stem girdling evidences a trade-off between cambial activity and sprouting and dramatically reduces plant transpiration due to feedback inhibition of photosynthesis and hormone signaling. *Frontiers in Plant Science* 6 (285). doi:[10.3389/fpls.2015.00285](https://doi.org/10.3389/fpls.2015.00285)
- Luo, Q. J., A. Mittal, F. Jia, and C. D. Rock. 2012. An autoregulatory feedback loop involving PAP1 and TAS4 in response to sugars in Arabidopsis. *Plant Molecular Biology* 80 (1):117-129. doi:[10.1007/s11103-011-9778-9](https://doi.org/10.1007/s11103-011-9778-9)
- Malacarne, G., E. Coller, S. Czemplak, U. Vrhovsek, K. Engelen, V. Goremykin, J. Bogs, and C. Moser. 2016. The grapevine VvibZIPC22 transcription factor is involved in the regulation of flavonoid biosynthesis. *Journal of Experimental Botany* 67 (11):3509-3522. doi:[10.1093/jxb/erw181](https://doi.org/10.1093/jxb/erw181)
- Marinova, K., L. Pourcel, B. Weder, M. Schwarz, D. Barron, J. M. Routaboul, I. Debeaujon, and M. Klein. 2007. The Arabidopsis MATE transporter TT12 acts as a vacuolar flavonoid/H⁺ - antiporter active in proanthocyanidin-accumulating cells of the seed coat. *Plant Cell* 19 (6):2023-2038. doi:[10.1105/tpc.106.046029](https://doi.org/10.1105/tpc.106.046029)
- Martin, D. M., S. Aubourg, M. B. Schouwey, L. Daviet, M. Schalk, O. Toub, S. T. Lund, and J. Bohlmann. 2010. Functional annotation, genome organization and phylogeny of the grapevine (*Vitis vinifera*) terpene synthase gene family based on genome assembly, FLcDNA cloning, and enzyme assays. *BMC Plant Biology* 10 (1):226. doi:[10.1186/1471-2229-10-226](https://doi.org/10.1186/1471-2229-10-226)
- Matus, J. T., E. Cavallini, R. Loyola, J. Holl, L. Finezzo, S. Dal Santo, S. Vialet, M. Commisso, F. Roman, A. Schubert, J. A. Alcalde, J. Bogs, A. Ageorges, G. B. Tornielli, and P. Arce-Johnson. 2017. A group of grapevine MYBA transcription factors located in chromosome 14 control anthocyanin synthesis in vegetative organs with different specificities compared with the berry color locus. *Plant Journal* 91 (2):220-236. doi:[10.1111/tbj.13558](https://doi.org/10.1111/tbj.13558)
- Mueller, L. A., C. D. Goodman, R. A. Silady, and V. Walbot. 2000. AN9, a petunia glutathione-S-transferase required for anthocyanin sequestration, is a flavonoid-binding protein. *Plant Physiology* 123 (4):1561-1570. doi:[10.1104/pp.123.4.1561](https://doi.org/10.1104/pp.123.4.1561)
- Neto, F. J. D., A. P. Junior, C. V. Borges, S. R. Cunha, D. Callili, G. P. P. Lima, S. R. Roberto, S. Leonel, and M. A. Tecchio. 2017. The exogenous application of abscisic acid induce accumulation of anthocyanins and phenolic compounds of the 'Rubi' grape. *American Journal of Plant Sciences* 8 (10):2422-2432. doi:[10.4236/ajps.2017.810164](https://doi.org/10.4236/ajps.2017.810164)
- Olivares, D., C. Contreras, V. Muñoz, S. Rivera, M. González-Agüero, J. Retamales, and B. G. Defilippi. 2017. Relationship among color development, anthocyanin and pigment-related gene expression in 'Crimson Seedless' grapes treated with abscisic acid and sucrose. *Plant Physiology and Biochemistry* 115:286-297. doi:[10.1016/j.plaphy.2017.04.007](https://doi.org/10.1016/j.plaphy.2017.04.007)
- Pastore, C., S. Zenoni, G. B. Tornielli, G. Allegro, S. Dal Santo, G. Valentini, C. Inriero, M. Pezzotti, and I. Filippetti. 2011. Increasing the source/sink ratio in *Vitis vinifera* (cv Sangiovese) induces extensive transcriptome reprogramming and modifies berry ripening. *BMC Genomics* 12:631-631. doi:[10.1186/1471-2164-12-631](https://doi.org/10.1186/1471-2164-12-631)
- Pérez-Díaz, R., J. Madrid-Espinoza, J. Salinas-Cornejo, E. González-Villanueva, and S. Ruiz-Lara. 2016. Differential roles for VviGST1, VviGST3, and VviGST4 in proanthocyanidin and anthocyanin transport in *Vitis vinifera*. *Frontiers in Plant Science* 7 (1166). doi:[10.3389/fpls.2016.01166](https://doi.org/10.3389/fpls.2016.01166)
- Petridis, A., S. Döll, L. Nichelmann, W. Bilger, and H.-P. Mock. 2016. *Arabidopsis thaliana* G2-LIKE FLAVONOID REGULATOR and BRASSINOSTEROID ENHANCED EXPRESSION1 are low-temperature regulators of flavonoid accumulation. *New Phytologist* 211 (3):912-925. doi:[10.1111/nph.13986](https://doi.org/10.1111/nph.13986)

- Pinasseau, L., A. Vallverdú-Queralt, A. Verbaere, M. Roques, E. Meudec, L. Le Cunff, J.-P. Péros, A. Ageorges, N. Sommerer, J.-C. Boulet, N. Terrier, and V. Cheynier. 2017. Cultivar diversity of grape skin polyphenol composition and changes in response to drought investigated by LC-MS Based Metabolomics. *Frontiers in Plant Science* 8 (1826). doi:[10.3389/fpls.2017.01826](https://doi.org/10.3389/fpls.2017.01826)
- Pojer, E., F. Mattivi, D. Johnson, and S. S. Creina. 2013. The case for anthocyanin consumption to promote human health: A review. *Comprehensive Reviews in Food Science and Food Safety* 12 (5):483-508. doi:[10.1111/1541-4337.12024](https://doi.org/10.1111/1541-4337.12024)
- Pourcel, L., N. G. Irani, Y. Lu, K. Riedl, S. Schwartz, and E. Grotewold. 2010. The formation of anthocyanic vacuolar inclusions in *Arabidopsis thaliana* and implications for the sequestration of anthocyanin pigments. *Molecular Plant* 3 (1):78-90. doi:[10.1093/mp/ssp071](https://doi.org/10.1093/mp/ssp071)
- Prakongkha, I., M. Sompong, S. Wongkaew, D. Athinuwat, and N. Buensanteai. 2013. Changes in salicylic acid in grapevine treated with chitosan and BTH against *Sphaceloma ampelinum*, the causal agent of grapevine anthracnose. *African Journal of Microbiology Research* 7 (7):557-563. doi:[10.5897/AJMR12.1320](https://doi.org/10.5897/AJMR12.1320)
- Ruiz-Garcia, Y., R. Gil-Munoz, J. M. Lopez-Roca, A. Martinez-Cutillas, I. Romero-Cascales, and E. Gomez-Plaza. 2013. Increasing the phenolic compound content of grapes by preharvest application of abscisic acid and a combination of methyl jasmonate and benzothiadiazole. *Journal of Agricultural and Food Chemistry* 61 (16):3978-3983. doi:[10.1021/jf400631m](https://doi.org/10.1021/jf400631m)
- Salimi, L., M. Arshad, A. R. Rahimi, A. Rokhzadi, S. Amini, and M. Azizi. 2013. Effect of some essential oils on post harvest quality of grapevine (*Vitis vinifera* cv Rasha (Siah-e-Sardasht)) during cold storage. *International Journal of Biosciences (IJB)* 3 (4):75-83. doi:[10.12692/ijb/3.4.75-83](https://doi.org/10.12692/ijb/3.4.75-83)
- Sivilotti, P., R. Falchi, J. C. Herrera, B. Škvarč, L. Butinar, M. S. Lemut, M. Bubola, P. Sabbatini, K. Lisjak, and A. Vanzo. 2017. Combined effects of early season leaf removal and climatic conditions on aroma precursors in Sauvignon Blanc grapes. *Journal of Agricultural and Food Chemistry* 65 (38):8426-8434. doi:[10.1021/acs.jafc.7b03508](https://doi.org/10.1021/acs.jafc.7b03508)
- Skates, E., J. Overall, K. DeZego, M. Wilson, D. Esposito, M. A. Lila, and S. Komarnytsky. 2018. Berries containing anthocyanins with enhanced methylation profiles are more effective at ameliorating high fat diet-induced metabolic damage. *Food and Chemical Toxicology* 111:445-453. doi:[10.1016/j.fct.2017.11.032](https://doi.org/10.1016/j.fct.2017.11.032)
- Sun, L., X. Fan, Y. Zhang, J. Jiang, H. Sun, and C. Liu. 2016. Transcriptome analysis of genes involved in anthocyanins biosynthesis and transport in berries of black and white spine grapes (*Vitis davidii*). *Hereditas* 153:17. doi:[10.1186/s41065-016-0021-1](https://doi.org/10.1186/s41065-016-0021-1)
- Sun, T., Lili X., H. Sun, Q. Yue, H. Zhai, and Y. Yao. 2017. VvVHP1; 2 Is Transcriptionally activated by VvMYBA1 and promotes anthocyanin accumulation of grape berry skins via glucose signal. *Frontiers in Plant Science* 8:1811. doi:[10.3389/fpls.2017.01811](https://doi.org/10.3389/fpls.2017.01811)
- Sun, Y., H. Li, and J. R. Huang. 2012. Arabidopsis TT19 functions as a carrier to transport anthocyanin from the cytosol to tonoplasts. *Molecular Plant* 5 (2):387-400. doi:[10.1093/mp/ssp110](https://doi.org/10.1093/mp/ssp110)
- Takase, H., K. Sasaki, H. Shinmori, A. Shinohara, C. Mochizuki, H. Kobayashi, G. Ikoma, H. Saito, H. Matsuo, S. Suzuki, and R. Takata. 2016. Cytochrome P450 CYP71BE5 in grapevine (*Vitis vinifera*) catalyzes the formation of the spicy aroma compound (-)-rotundone. *Journal of Experimental Botany* 67 (3):787-798. doi:[10.1093/jxb/erv496](https://doi.org/10.1093/jxb/erv496)
- Vannozzi, A., D. C. J. Wong, J. Höll, I. Himmam, J. T. Matus, J. Bogs, T. Ziegler, I. Dry, G. Barcaccia, and M. Lucchin. 2018. Combinatorial regulation of stilbene synthase genes by WRKY and MYB transcription factors in grapevine (*Vitis vinifera* L.). *Plant and Cell Physiology* 59 (5):1043-1059. doi:[10.1093/pcp/pcy045](https://doi.org/10.1093/pcp/pcy045)
- Wang, Y., Y. Wang, Z. Song, and H. Zhang. 2016. Repression of MYBL2 by both microRNA858a and HY5 leads to the activation of anthocyanin biosynthetic pathway in Arabidopsis. *Molecular Plant* 9 (10):1395-1405. doi:[10.1016/j.molp.2016.07.003](https://doi.org/10.1016/j.molp.2016.07.003)
- Wu, B.-H., Y.-G. Cao, L. Guan, H.-P. Xin, J.-H. Li, and S.-H. Li. 2014. genome-wide transcriptional profiles of the berry skin of two red grape cultivars (*Vitis vinifera*) in which anthocyanin synthesis is sunlight-dependent or -independent. *PLOS ONE* 9 (8):e105959. doi:[10.1371/journal.pone.0105959](https://doi.org/10.1371/journal.pone.0105959)

- Wurz, D. A., B. P. de Bem, R. Allebrandt, J. L. M. Filho, A. F. Brighenti, M. Outemane, L. Rufato, and A. A. Kretzschmar. 2017. Timing of leaf removal modifies chemical and phenolic composition of Sauvignon Blanc wine. *BIO Web Conference* 9:02027. doi:[10.1051/bioconf/20170902027](https://doi.org/10.1051/bioconf/20170902027)
- Xie, X., and Y. Wang. 2016. VqDUF642, a gene isolated from the Chinese grape *Vitis quinquangularis*, is involved in berry development and pathogen resistance. *Planta* 244 (5):1075-1094. doi:[10.1007/s00425-016-2569-4](https://doi.org/10.1007/s00425-016-2569-4)
- Xu, C., Y. Yagiz, L. Zhao, A. Simonne, J. Lu, and M. R. Marshall. 2017. Fruit quality, nutraceutical and antimicrobial properties of 58 muscadine grape varieties (*Vitis rotundifolia* Michx.) grown in United States. *Food Chem* 215:149-156. doi: [10.1016/j.foodchem.2016.07.163](https://doi.org/10.1016/j.foodchem.2016.07.163)
- Xu, J., A.-Q. Zheng, X.-J. Xing, L. Chen, X.-Y. Fu, R.-H. Peng, Y.-S. Tian, and Q.-H. Yao. 2018. Transgenic arabidopsis plants expressing grape *glutathione S-transferase* gene (*VvGSTF13*) show enhanced tolerance to abiotic stress. *Biochemistry (Moscow)* 83 (6):755-765. doi:[10.1134/S0006297918060135](https://doi.org/10.1134/S0006297918060135)
- Yan, J., G. Wang, Y. Sui, M. Wang, and L. Zhang. 2016. Pollinator responses to floral colour change, nectar, and scent promote reproductive fitness in *Quisqualis indica* (Combretaceae). *Scientific Reports* 6:24408. doi:[10.1038/srep24408](https://doi.org/10.1038/srep24408)
- Zhang, G., D. Chen, T. Zhang, A. Duan, J. Zhang, and C. He. 2018. Transcriptomic and functional analyses unveil the role of long non-coding RNAs in anthocyanin biosynthesis during sea buckthorn fruit ripening. *DNA Research*:dsy017-dsy017. doi:[10.1093/dnares/dsy017](https://doi.org/10.1093/dnares/dsy017)