# The Genomics of Grape Berry Ripening

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**Abstract**

Because of their economic and cultural importance, grapes are arguably the most studied fruit crop and are considered a model system for research on non-climacteric fruits. The sequencing of the grapevine genome has led to major discoveries that have increased our understanding of the molecular regulation of fruit ripening and berry metabolism, and how the environment and viticultural practices affect berry physiology. This chapter reviews the most recent studies on the molecular and metabolic pathways associated with grape berry ripening including the pathways involved in berry growth and softening, and sugar, organic acid, phenolic, and aroma accumulation. The role of hormones and hormone crosstalk, as well as a compendium of the most recent research on transcription factors (TFs) and non-coding RNAs are presented.

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## 12.1 Introduction: General Physiological Aspects of Ripening

Grape berry growth follows a double-sigmoid pattern where two rapid phases of growth are interrupted by "lag" during which there is little or no growth (Matthews and Shackel 2005). The first growth stage (I) begins at flowering (i.e., anthesis) and continues until the lag stage (II), while the start of the final growth stage (III) is coincident with the onset of ripening, or veraison (Fig. 12.1). Stage I growth results from both cell division and cell expansion, but stage III growth results exclusively from expansion (Coombe 1976; Ojeda et al. 1999). The transition from stage II to stage III is abrupt (i.e., veraison) in


D. Cantu and M. A. Walker (eds.), *The Grape Genome*, Compendium of Plant Genomes, https://doi.org/10.1007/978-3-030-18601-2_12

**Fig. 12.1** *Zinfandel grape (Vitis vinifera L.) clusters at the onset of ripening (i.e., veraison).* The timing of veraison is heterogeneous among berries of the same cluster and clusters of the same vine. In the picture, some berries have just begun ripening (light pink), whereas others are still green

individual berries. In viticulture, veraison is regarded as a critical moment because, in addition to the resumption of growth, numerous ripening processes begin, including softening, rapid sugar accumulation, and most conspicuously a change in color in red grape varieties.

Ripening is a critical stage for determining grape and wine quality and has major implications for the economic value of the crop. The grape berry is a non-climacteric fruit, which means that ripening is not related to, or modulated by, a burst of respiration and ethylene as in climacteric fruits such as tomato or apple (Coombe 1976; Gapper et al. 2013). In fact, the onset of ripening was originally thought to be a coordinated process where a multitude of physiological changes (softening, sugar accumulation, increase in ABA, and color development) were coincident and preceded the resumption of growth by several days (Coombe and Bishop 1980; Coombe 1992). More recently, studies have delimited the earliest events at the onset of ripening: softening, the associated decreases in cell turgor, and increases in ABA concentration (Thomas et al. 2006; Wada et al. 2009; Castellarin et al. 2016). Increases in sugar concentration and color development appear to occur only later, when the firmness of the berry has already decreased dramatically and the ABA concentration has further increased (Castellarin et al. 2016). Besides ABA, other hormones such as brassinosteroids and ethylene are involved in the ripening process, as well as sugars, which affect the synthesis of anthocyanins (Symons et al. 2006; Hayes et al. 2007; Chervin et al. 2008; Davies and Böttcher 2009; Dai et al. 2013). Auxins—normally accumulated at early stages of berry development—act as negative modulators of the ripening process, and their deactivation is necessary for ripening to begin (Böttcher et al. 2010, 2012a; Gouthu and Deluc 2015).

Sugars are one of the major metabolites that accumulate in the grape berry during ripening. Other compounds that accumulate during ripening are flavonols, which protect the berry from UV light, anthocyanins which determine the pink/red/blue coloration of red grape varieties, and several volatile organic compounds (VOCs), such as norisoprenoids, monoterpenes, thiols, or their conjugated precursors (Adams 2006; Teixeira et al. 2013; Robinson et al. 2014a, b). These VOCs determine the aroma of grapes, juices, and wines, particularly when chemical changes associated with acid and enzymatic modifications of conjugated precursors occur during fermentation and wine aging.

Many key compounds for fruit and wine quality are synthesized before veraison and normally decrease in concentration during the ripening period. This is the case for organic

acids, hydroxycinnamates, tannins, and methoxypyrazines. The two major organic acids accumulated in the grape berry, tartaric and malic acid (Kliewer 1966; Kliewer et al. 1967; Shiraishi et al. 2010), strongly affect juice and wine pH and contribute to the quality (freshness and sourness notes) and longevity of wine. Phenolic compounds such as hydroxycinnamates and tannins confer bitterness and astringency to juices and wines (Teixeira et al. 2013). Finally, methoxypyrazines impart the sensory characteristics of bell pepper, asparagus, or pea to grapes and wines. These aromas can be perceived as good or bad depending on variety and wine style (Robinson et al. 2014a, b).

## 12.2 Berry Growth and Softening

### 12.2.1 Cell Division and Expansion

Final berry size dictates in large part yield, and thus genetic and molecular studies focused on understanding the mechanisms controlling rates of cell division and expansion are of agronomic interest. Transcriptomic studies highlight the transition from cell division driven growth, during early stage I, to cell expansion driven growth, later during stage I and stage III (Deluc et al. 2007). To date, very few cornerstone regulators of grape berry size have been identified. The fleshless berry (*flb*) mutation, originally a somatic variant and later used in crosses, exhibits profound effects on fruit set and/or fruit size depending on the meristem cell layers affected (Fernandez et al. 2006a, b). Follow-up studies identified that the mutation results from mis-expression of a PISTILLATA-like MADS-box transcription factor, *VviPI* (Fernandez et al. 2013). Chialva et al. (2016) identified three potential genes involved in cell division during stage I. Members of the grape AP2/ERF transcription factor family, AINTEGUMENTA (ANT) and AINTEGUMENTA-like (AIL), were differentially expressed across different genotypes that varied in ovary size and cell number. One candidate, in particular, *VviANT1*, co-localizes with previously identified QTLs for berry size in both table and wine grapes (Doligez et al. 2002; Cabezas et al. 2006; Chialva et al. 2016).

Later in stage I, and during stage III, berry growth results from cell expansion. Cell expansion is driven by cell turgor pressure, and the rate of expansion is determined by cell wall extensibility (i.e., the yield threshold; Cosgrove 2005). Therefore, expansive growth will be modulated through a combination of processes that affect turgor, such as solute accumulation, and processes that affect cell wall extensibility and involve cell wall modifying enzymes (Matthews and Shackel 2005). During stage I, there is evidence that both processes indeed contribute to growth. Water deficits reduce berry growth, resulting largely from decreases in berry turgor pressure (Thomas et al. 2006). At the same time, expression analyses during stage I across table grape genotypes with contrasting rates of growth highlighted differences in many genes encoding cell wall modifying enzymes (Muñoz-Espinoza et al. 2016).

Grape berry cell turgor is high during stage I, but decreases during stage II, and reaches very low levels at the onset of ripening (Thomas et al. 2006; Wada et al. 2009; Castellarin et al. 2016). This decrease in turgor prior to the onset of ripening is thought to contribute to softening (discussed below), but it creates a conundrum regarding the resumption of growth that occurs at the same time. Extremely low turgor requires a corresponding decrease in the cell wall yield threshold in order for rapid expansive growth to resume. In fact, numerous studies have concluded that the resumption of growth at the onset of ripening corresponds to the upregulation of many genes encoding cell wall modifying enzymes (Nunan et al. 2001; Deluc et al. 2007; Schlosser et al. 2008; Castellarin et al. 2016). Nicolas et al. (2013) identified a basic helix–loop–helix transcription factor, VviCEB1, that positively regulates grape berry size through enhanced cell expansion, and its action was confirmed through ectopic expression in *Arabidopsis* and tobacco (Lim et al. 2018). *VviCEB1* overexpression led to the induction of numerous genes encoding cell wall modification enzymes,

which suggests a possible role for these enzymes in changing the yield threshold to modulate cell expansion (Nicolas et al. 2013). During berry development, *VviCEB1* expression increases throughout stage I, peaks at the onset of ripening, and remains high during stage III, consistent with the period of expansive berry growth.

Stage III berry growth is peculiar because grape berries are largely buffered hydraulically from the parent plant (Matthews and Shackel 2005; Thomas et al. 2006). The traditional view, that this hydraulic buffering was a result of a physical disconnection of the xylem, has been refuted (Keller et al. 2006), although the buffering does involve decreases in hydraulic conductivity (Choat et al. 2009; Knipfer et al. 2015). The membrane water channel proteins, aquaporins, may contribute to these decreases in berry hydraulic conductivity; however, the regulation of this gene family during ripening is complex (Choat et al. 2009; Wong et al. 2018). The extent to which aquaporins mediate berry growth remains unknown, but it is fair to speculate that they play a role in berry growth via their effects on berry water relations (Tyerman et al. 2012).

### 12.2.2 Softening: Decreases in Turgor and Changes in Cell Wall Composition

Berry softening occurs approximately 10 days prior to the onset of ripening and represents one of the earliest detectable changes in berry physiology leading to veraison (Wada et al. 2008; Matthews et al. 2009; Castellarin et al. 2016). Softening is thought to result from the same two compatible mechanisms as growth does decreases in cell turgor (introduced above) and changes in the structure of cell walls (Brummell and Harpster 2001; Gapper et al. 2013).

Interestingly, both of these mechanisms have links with abscisic acid (ABA), one of the key hormones regulating the onset of ripening in grape (Gambetta et al. 2010; Castellarin et al. 2016; Pilati et al. 2017) and other fruits (Leng et al. 2014). The decrease in turgor associated with softening in grape corresponds to increases in ABA, and both precede the increase in sugar concentration at the onset of ripening (Castellarin et al. 2016). The decrease in turgor results from the accumulation of solutes, mostly malate and sugars, in the apoplast of the berry (Wada et al. 2008, 2009). This accumulation of solutes in the berry apoplast may result from apoplastic sucrose unloading from the phloem and an upregulation of acid invertases, which ABA stimulates (Pan et al. 2005; Zhang et al. 2006; Koyama et al. 2010).

Many genes encoding cell wall modification enzymes are up-regulated during softening in grape, including many members of the expansin and pectin methylesterase gene families, among others (Dal Santo et al. 2013; Castellarin et al. 2016; Fasoli et al. 2016). In addition, cell wall modification enzymes are thought to contribute to postharvest changes in fruit texture and quality (Brummell and Harpster 2001), and this is consistent with findings in grape where many genes encoding cell wall modification enzymes continue to be up-regulated late into ripening and throughout the postharvest period (Castellarin et al. 2016; Zenoni et al. 2016). The master regulators of these increases are still unknown, but ABA has been shown to up-regulate cell wall modification enzymes, including expansins and pectin methylesterases, in tomato (Sun et al. 2012). Increases in *VviCEB1* expression (discussed above) correspond to softening, and along with *VviCEB1*'s induction of genes encoding cell wall modification enzymes, one can speculate a role for *VviCEB1* in softening as well (Nicolas et al. 2013).

## 12.3 Berry Composition

Grape composition determines grape, juice, and wine sensorial attributes. It changes dramatically during fruit ripening and is strongly affected by the genotype, the environment, and the viticultural practices applied in the vineyard. The complex regulation of the physiological and metabolic pathways that determine grape composition, as well as the modulation of these

pathways by the environment or viticultural practices, have been intensively investigated during recent years.

### 12.3.1 Sugars

Sugars play an important role in shaping berry sensory properties, in determining alcohol concentration after fermentation, and as precursors for the synthesis of organic acids, phenolics, and aroma compounds (Dai et al. 2011). *Vitis vinifera* berries accumulate large amounts of sugars, predominantly glucose and fructose (in equal concentrations) with only a trace amount of sucrose (Hawker et al. 1976; Liu et al. 2006; Shiraishi et al. 2010). Grapevine varieties exhibit an impressively large range of sugar concentrations at maturity. For example, Kliewer et al. (1967) compared 78 table and wine grape varieties and found that total soluble solids of the berry juice—a good representation of berry sugar concentration—varied at harvest from 18.5 to 28.2 °Brix.

In plants, sugars are synthesized in the cytoplasm of the leaf mesophyll cells and transported, in the form of sucrose, via phloem into other parts of the plant (Cheng et al. 2018). In the grape berry, sucrose is then hydrolyzed by invertases and stored in the vacuole in the form of glucose and fructose. At the onset of berry ripening or just before, sugar loading into the berry from the phloem shifts from a symplastic to an apoplastic pathway (Zhang et al. 2006). The latter requires at least two transporters—one secreting sugars from sieve elements/companion cells, the other mediating reuptake into the adjacent sink cells (Lalonde et al. 2004). Sugar transport across membranes is mainly mediated by the proton-coupled sucrose transporters (SUTs, the disaccharide transporters) and hexose transporters (HTs, the monosaccharide transporters), together with several other subfamilies of monosaccharide transporters. Acidic invertases (AI), located in the vacuole or cell wall, and neutral invertases (NI), located in the cytoplasm, are the two major classes of sucrose metabolic enzymes contributing to hexose accumulation in grape berry. Although the vacuolar invertases are considered important for sugar accumulation, the expression of the genes encoding these enzymes precedes the onset of hexose accumulation by some weeks; therefore, the synthesis of these enzymes cannot be considered a trigger for sugar accumulation in grape berry (Davies and Robinson 1996).

SUTs are essential for sucrose translocation in plants (Lalonde et al. 2004). Four genes encoding sucrose transporters have been identified in grapevine, namely *VviSUC11/VviSUT1*, *VviSUC12*, *VviSUC27*, and *VviSUT2*. *VviSUC11* and *VviSUC12* are high affinity sucrose transporters (Ageorges et al. 2000; Manning et al. 2001; Afoufa-Bastien et al. 2010), and *VviSUC27* is a low affinity sucrose transporter that has a very similar structure to *VviSUT2* (Zhang et al. 2007). *VviSUC11* and *VviSUC12* expressions have been detected in all organs. The weakest expression for both genes was observed in berries at fruit set (Afoufa-Bastien et al. 2010), but a significant upregulation was observed during ripening (Lecourieux et al. 2014). Afoufa-Bastien et al. (2010) suggest that *VviSUC12* either might be involved in phloem unloading or in sucrose import into the berry, and that *VviSUC11* might control sucrose uptake into berry vacuoles. In contrast, *VviSUT27* transcript amounts significantly decrease during ripening (Davies et al. 1999), which suggests a different physiological function for this transporter. On the other hand, *VviSUC27* transcripts have been detected at a high level in petioles, stems, and tendrils, and less abundantly in young leaves, mature leaves, and roots (Afoufa-Bastien et al. 2010). The "Sugars Will Eventually be Exported Transporter" (SWEET) proteins are a newly identified family of sugar efflux transporters (Chen 2014). SWEETs are integral membrane proteins and function as a prerequisite for *SUT1*-mediated phloem loading (Chen et al. 2012). There are 17 *SWEET* genes, with different expression levels among vegetative and reproductive organs, identified in grapevine. Generally, most *VviSWEET* genes are more highly expressed in the berry, and their expression level increases throughout berry ripening (Chong et al. 2014).

HTs in grapevine are encoded by a multigene family, of which five members (*VviHT1-5*) are well studied (Tanner and Caspari 1996; Zhang et al. 2007; Agasse et al. 2009), and 17 were identified more recently (*VvHT8-24*) (Afoufa-Bastien et al. 2010). *VviHT1* is expressed mainly in grape berry (Fillion et al. 1999), and its transcription greatly increases during leaf development. *VviHT3* and *VviHT5* are expressed in both mature leaves and grape berries, though *VviHT5* has a much lower expression level than *VviHT3*. *VviHT4*, whose function is restricted to glucose, is also expressed in grape berries (Hayes et al. 2007). *VvHT1*, *VvHT2*, and particularly *VvHT3* are highly expressed at all stages of berry development, with transcriptional patterns consistent with the shift from a symplastic to an apoplastic phloem unloading pathway that occurs prior to veraison (Lecourieux et al. 2014). A gene named *VviHT8*, which has a high similarity to *VviHT1*, was identified as a molecular target for the selection of grapes with improved sugar accumulation (Xin et al. 2013).

Other monosaccharide transporters present in the grapevine genome include tonoplast monosaccharide transporters (*VviTMTs*), polyol/monosaccharide transporters (*VviPMTs*), glucose transporters (*VviGlcTs*), and ERD6-like transporters (Afoufa-Bastien et al. 2010).

### 12.3.2 Organic Acids

Tartaric acid and malic acid are the major organic acids in grapevine. Most of the tartrate and malate in immature berries originate from glucose and fructose (Hardy 1968). Tartaric and malic acid accumulate in berry cell vacuoles before veraison. Unlike many other fruits, grape berries do not contain large amounts of citrate. During ripening, the concentration of tartaric acid remains stable, but the concentration decreases through a dilution effect determined by cell expansion (Dai et al. 2011; Regalado et al. 2013). Malic acid also decreases in concentration during ripening, but in contrast to tartrate, most of this decrease is due to degradation, use in respiration, and conversion into sugars (Sweetman et al. 2009).

Tartaric acid is synthesized from L-ascorbic acid (vitamin C). L-idonate dehydrogenase (L-IdnDH) is responsible for catalyzing the proposed rate-limiting step, the oxidization of L-idonic acid to 5-keto-gluconic acid (DeBolt et al. 2006; Cholet et al. 2016), and is the only known enzyme to be involved in tartaric acid accumulation (DeBolt et al. 2006). The sudden increase of tartaric acid during stage I is paralleled by *VviL-IdnDH* gene expression and translation (Grimplet et al. 2007; Wen et al. 2010; Cholet et al. 2016). There are three different isoforms of *VviL-IdnDH* genes: two of them are specifically expressed in young berries, and the third increases during berry ripening (Sweetman et al. 2012).

The accumulation of malate before the onset of ripening is thought to be mainly due to its de novo synthesis in berries (Sweetman et al. 2009). Malic acid is produced from phosphoenolpyruvate (PEP) through the activity of different enzymes: phosphoenolpyruvate carboxylase (PEPC), malate dehydrogenase (MDH) (Givan 1999; Sweetman et al. 2012), malic enzyme (ME) (Sweetman et al. 2012), and fumarase (FUM) (Shangguan et al. 2015). There are two *VviPEPC*s, one *VviMDH*s, and two *VviFUM*s identified in grapevine (Shangguan et al. 2015).

The cytoplasmic MDH and the mitochondrial ME appear to be key enzymes for malic acid synthesis, since the decrease in expression of their codifying genes correlates to decreases in malate concentration during ripening (Sweetman et al. 2012).

MDH enzymes catalyze the reversible conversion of oxaloacetate into malate; therefore, the possible decrease of oxaloacetate in mature berries caused by altered expression of *VviPEPC* and *VviPEPCK* could influence malate degradation by shifting the function of MDH enzymes towards malate catabolism (Sweetman et al. 2012). Since the catabolism of malate can only occur when the acid is accessible to metabolic enzymes outside the vacuole, the compartmentation of malate may also influence the rates of its degradation during berry development. For this reason, the decrease of malate could also be attributed partly to the down-regulation of the genes encoding the tonoplast dicarboxylate

transporters (*VviTDT*s) (Sweetman et al. 2009, 2012), which are responsible for the transport of malate into vacuoles. Moreover, the decrease in acid content during grape ripening has been mainly associated with mitochondrial malate oxidation (Regalado et al. 2013). Three mitochondrial dicarboxylate/tricarboxylate carriers (*VviDTC1–VviDTC3*) have been characterized in *Vitis vinifera*. *VviDTC1* is able to transport all the dicarboxylates/tricarboxylates of the TCA cycle, with the exception of fumarate, and exhibits high specificity for malate. The expression of *VviDTC2* and *VviDTC3* transcripts is strongly enhanced in the mesocarp at the onset of ripening, which suggests that their role in the transport of malate into mitochondria might be critical (Regalado et al. 2013).

### 12.3.3 Phenolics

Phenolics are synthesized from phenylalanine via the phenylpropanoid, flavonoid, and stilbenoid pathways. The phenylpropanoid pathway leads to the production of *p*-coumaryl-CoA from phenylalanine, which involves enzymes such as phenylalanine ammonia lyase (PAL), cinnamate-4-hydroxylase (C4H), and 4-coumarate-CoA ligase (4CL). *p*-Coumaryl-CoA and malonyl-CoA are the substrates of both chalcone synthase (CHS) and stilbene synthase (STS), which catalyze the first steps of the flavonoid and stilbenoid pathway, respectively.

Hydroxycinnamic acids, such as *p*-coumaric, caffeic, and ferulic acid and their esterified forms coutaric, caftaric, and fertaric acid are the major phenolic acids in the berry. Their synthesis occurs before veraison via modifications of the intermediates of the phenylpropanoid pathway catalyzed by caffeic acid 3-*O*-metyltransferase (COMT) and caffeoyl-CoA 3-*O*-methyltransferase (CCoAOMT). Recently, two TFs, VviMYB4a and VviMYB4b, have been characterized as negative regulators of phenylpropanoid genes and hydrocinnamic acid synthesis (Cavallini et al. 2015).

Stilbenoids (e.g., *cis*- and *trans*-resveratrol, piceatannol, *cis*- and *trans*-piceid, astringin, pallidol, and α-, β-, γ-, δ-, ε-viniferin) are mostly accumulated from veraison onward (Gatto et al. 2008) and are strongly modulated by both biotic and abiotic factors (Vannozzi et al. 2012; Savoi et al. 2017). Forty-five stilbene synthases are found in the grapevine genome, with at least 33 encoding full-length proteins. This gene family arose from multiple events of tandem and segmental duplications (Vannozzi et al. 2012). Recent large-scale transcriptomic analysis has shown that the expression of many *VviSTSs* changes during fruit development and ripening (Massonnet et al. 2017). In red berry varieties, induction of *VviSTSs* is particularly pronounced during the late stages of ripening. The two R2R3 MYB transcription factors, VviMYB14 and VviMYB15 (Höll et al. 2013), which are known to regulate stilbene biosynthesis, also share similar expression profiles. Nonetheless, among the many TFs proposed to regulate this pathway (Wong et al. 2016b; Vannozzi et al. 2018), two WRKY TFs, VviWRKY24 and VviWRKY03, participate at different levels of *VviSTS* regulation—via direct activation of *VviSTSs* or synergistic action with MYB TFs to regulate *VviSTS*s.

The flavonoid pathway leads to the production of flavonols, flavan-3-ols, and anthocyanins. The modulation of the pathway during berry development and under environmental stresses has been largely investigated in grapevine (Teixeira et al. 2013; Kuhn et al. 2013). Most of the genes of the flavonoid pathway are present in low copy numbers except for those encoding the flavonoid-3′,5′-hydroxylases (F3′5′H s). Flavonoid-3′-hydroxylases (F3′Hs) and F3′5′Hs divide the pathway into two major branches, whose compounds are either di-hydroxylated or tri-hydroxylated. In most plants, F3′5′H genes are present in low copy numbers, but a proliferation of the F3′5′Hs has occurred in the grapevine genome and given rise to 15 paralogs within 650 kb (Falginella et al. 2010). Most *VviF3′5′Hs* are predominantly expressed in berries, and differences in cis-regulatory sequences of promoter regions are paralleled by temporal specialization of gene transcription during fruit ripening and in berry tissues (Falginella et al. 2010, 2012).

Flavonol synthases (*FLSs*) are key enzymes for the synthesis of berry flavonols such as kaempferol, quercetin, myricetin, isorhamnetin, laricitrin, and syringetin (Downey et al. 2004). The expression of the FLSs is well known to be under the control of a light-induced transcription factor (VviMYBF1/VviMYB12) (Czemmel et al. 2009). Two recent studies now show that three additional bZIP TFs, VviHY5, VviHYH, and VvibZIPC22 (Malacarne et al. 2015; Loyola et al. 2016), are involved in the regulation of flavonol synthases and flavonol accumulation in the berry. VviMYBF1 was shown to be part of a regulatory cascade of VviHY5/HYH that potentially involves positive feedback regulation (Loyola et al. 2016; Czemmel et al. 2017). Flavonols are normally glycosylated (as glucosides, galactosides, rhamnosides, rutinosides, and glucuronides) and the flavonol-3-*O*-glycosyltransferases (VviGT3-5-6) and flavonol-3-*O*-rhamnosyltransferase (VviRhaT1) responsible for this glycosylation have been recently characterized in grapevine (Ono et al. 2010; Czemmel et al. 2017).

Flavan-3-ols are produced via the activity of leucoanthocyanidin reductases (LAR1-2) or an anthocyanidin reductase (ANR) (Bogs et al. 2005). Their synthesis is promoted from anthesis to veraison and is regulated by transcription factors of the MYB family. In particular, *VviLAR1* and *VviANR* are under the control of VviMYBPA1 and VviMYBPA2 (Bogs et al. 2007; Terrier et al. 2009), whereas *VviLAR2* is under the control of VviMYBPAR (Koyama et al. 2014). The monomeric flavan-3-ols accumulated in grape, (+)-catechin, (−)-epicatechin, (−)-epicatechin-3-*O*-gallate, (+)-gallocatechin and (−)-epigallocatechin, differ according to stereochemistry, level of hydroxylation, and acylation by gallic acid (Mattivi et al. 2009). Until now, the mechanisms involved in either polymerization into tannins, galloylation, and transport into the vacuoles have not yet been well understood (Zhao et al. 2010). However, a QTL study revealed different genetic determinisms for PA composition in seeds and skin, including PA total content, PA building blocks, degree of polymerization, and ratio between building blocks (Huang et al. 2012). Three annotated glycosyltransferases (VviGT1-3) were described to be putatively involved in the galloylation of proanthocyanidins and the production of hydroxycinnamic esters (Khater et al. 2012), and two specific transporters of proanthocyanidin were identified (VviPAMATE1-2) (Pérez-Díaz et al. 2014).

Anthocyanins are responsible for the pigmentation of the grape berries. They are synthetized in the epidermis and hypodermis cells from veraison onward and then stored in the vacuole. *Teinturier* varieties, such as Alicante Bouschet, also accumulate anthocyanin in the flesh (Castellarin et al. 2011; Falginella et al. 2012). In *Vitis vinifera*, anthocyanins are glycosylated at the 3′ position by the addition of a glucose moiety through the activity of the enzyme UDP-glucose, flavonoid-3-*O*-glucosyltransferase (UFGT). Both di-hydroxylated and tri-hydroxylated anthocyanins are synthetized by VviUFGT. The *O*-methyltransferases (VviAOMT1-3) methylate cyanidin-3-*O*-glucoside and delphinidin-3-*O*-glucoside into peonidin-3-*O*-glucoside, petunidin-3-*O*-glucoside, and malvidin-3-*O*-glucoside (Fournier-Level et al. 2011). Moreover, anthocyanins can also be acylated at the 6″ position of the glucose, which produces 3-*O*-6″-acetyl-, 3-*O*-6″-coumaroyl- and 3-*O*-6″-caffeoyl-monoglucosides and, recently, an anthocyanin-3-*O*-glucoside-6″-*O*-acyltransferase was characterized (Vvi3AT) (Rinaldo et al. 2015).

The MYBA1-A2 TFs are crucial genetic determinants of berry color (Walker et al. 2007). Recent studies show that additional members of the MYBA cluster, VviMYBA6 and VviMYBA7, have the capacity to influence fruit anthocyanin pigmentation and composition under severe environmental conditions (i.e., UV-B) during veraison (Czemmel et al. 2017). Anthocyanin-acylglucosides are translocated into the vacuole by MATE-type transporters localized in the tonoplast (VviAnthoMATE1-3) (Gomez et al. 2009), whereas the glycosylated anthocyanins are translocated via a glutathione-dependent, ATP-binding cassette (ABC) protein (VviABCC1) (Francisco et al. 2013).

Furthermore, a recent QTL study identified a set of new candidate genes for the regulation of anthocyanin variation among cultivars (Costantini et al. 2015).

Overall, the synthesis of hydroxycinnamic acids, stilbenes, flavonols, flavan-3-ols, and anthocyanins is spatiotemporally separated during grape berry development and ripening and tightly regulated by positive and/or negative regulators. Besides the TFs described above, two (VviMYB5a-b) are general regulators of the flavonoid pathway and, in particular, modulate the expression profile of several flavonoid genes (*VviCHI*, *VviF3'5'H*, *VviLDOX*, *VviLAR*, and *VviANR*) during berry development and ripening (Lauvergeat et al. 2006; Cavallini et al. 2015). Recently, two TFs (VviMYBC2-L1 and L3) were characterized as repressors of both proanthocyanidin and anthocyanin biosynthesis (Huang et al. 2014; Cavallini et al. 2015). Moreover, a bHLH (VviMYC1) interacts with VviMYB5a-b, VviMYBPA1, and VviMYBA1-A2 in the transcriptional control of proanthocyanidin and anthocyanins biosynthesis in grapevine (Hichri et al. 2010).

### 12.3.4 Volatile Organic Compounds

Terpenes are a major class of volatiles in grapes and strongly affect the aroma of grapes and wines of several varieties. The sesquiterpenes and monoterpenes accumulate in the berry before and after veraison, respectively. Two independent pathways produce terpenes in plants: (1) the plastidial 2C-methyl-erythritol-4-phosphate (MEP) pathway, which is the predominant pathway for monoterpenes ($C_{10}$) and diterpenes ($C_{20}$), and (2) the cytosolic mevalonate (MVA) pathway, which is the primary pathway for sesquiterpenes ($C_{15}$) (Bohlmann and Keeling 2008).

The major monoterpenes produced in grapes are linalool, geraniol, nerol, citronellol, hotrienol, α-terpineol, and rose oxides (Matarese et al. 2014); these compounds confer flowery and fruity notes to wines (Robinson et al. 2014a; Siebert et al. 2018). Sesquiterpenes have a minor impact on grape and wine aroma because usually their concentrations are below the olfactory threshold. The most studied sesquiterpene is rotundone, which gives peppery character in some red and white varieties (Siebert et al. 2008; Wood et al. 2008; Mattivi et al. 2011; Caputi et al. 2011). Recently, key genes (*VviGuaS*, *VviTPS24*, *VviSTO2*) involved in rotundone biosynthesis were identified (Drew et al. 2015; Takase et al. 2015).

Among the several structural genes of the MEP pathway, 1-deoxy-xylulose 5-phosphate synthase (*VviDXS*) was identified as a key modulator of total monoterpene content in grapevine (Battilana et al. 2009, 2011). Terpene synthases (TPSs) control monoterpene or sesquiterpene production (Martin et al. 2010; Matarese et al. 2013, 2014). Interestingly, in the genome of *Vitis vinifera* there are 69 putative terpene synthases, 39 of them functionally characterized (Martin et al. 2010). Generally, TPSs are divided into seven clades: TPS-a, TPS-b, TPS-c, TPS-d, TPS-e/f, TPS-g, and TPS-h (Chen et al. 2011). The TPS-a clade (30 genes) contains mostly sesquiterpene and possibly diterpene synthases, whereas the TPS-b clade (19 genes) and TPS-g clade (17 genes) consist mostly of monoterpene synthases. TPS-c (2 genes) and TPS-e/f (1 gene) clades contain plant hormone metabolism genes that are typically represented with a single gene copy in plant genomes. No full-length TPS-d and TPS-h were found in grapevine (Martin et al. 2010). Recently, several genes, such as nudix hydroxylase, vesicle-associated proteins, ABCG transporters, glutathione S-transferases, and amino acid permeases have been proposed as candidate genes for regulating the monoterpene biosynthesis and accumulation in the berry (Costantini et al. 2017). Moreover, positive correlation between aroma production and ERF TFs indicates that ethylene signaling could be a factor in affecting the final terpene content (Cramer et al. 2014). In addition, a major role of jasmonic acid and methyljasmonate has been hypothesized for the regulation of terpene biosynthesis in grapes (Savoi et al. 2016; D'Onofrio et al. 2018).

Most monoterpenes and sesquiterpenes are present in grapevine as non-volatile terpene glycosides. In grapevine, only three

monoterpenol glycosyltransferases have been characterized, *VviGT7-14-15* (Bönisch et al. 2014a, b; Li et al. 2017) and the cytochrome P450 CYP76F14, which catalyzes the conversion of linalool to (E)-8-carboxylinalool, which, during wine fermentation, generates a wine lactone, a key odorant of Gewurztraminer wines (Ilc et al. 2017).

Other terpenoids synthesized in the berry before ripening are the carotenoids, which are pigments contributing to light harvesting and to protecting the photosynthetic apparatus from photooxidation (Rodríguez-Concepción and Boronat 2002). The genes involved in their biosynthetic pathway were recently identified in grapevine (Young et al. 2012). Carotenoids can be cleaved via other carotenoid cleavage dioxygenases (VviCCD1a/b, VvCCD4a/b/c) (Lashbrooke et al. 2013) to form volatile flavor and aroma-related compounds, such as the $C_{13}$-norisoprenoids β-ionone and β-damascenone, which contribute to floral and fruity aromas. The majority of them are glycosylated in grape (Robinson et al. 2014a).

The unsaturated $C_{18}$ fatty acids linoleic acid and linolenic acid are the precursors of other volatile organic compounds such as $C_6$-aldehydes and alcohols like hexanal and hexanol (Kalua and Boss 2009). They are formed by the activity of lipoxygenases (*VviLOX*) (Podolyan et al. 2010), hydroperoxide lyase (*VviHPL1-2*) (Zhu et al. 2012), and *(3Z)-(2E)* enal isomerase and alcohol dehydrogenase (VviADH) (Kalua and Boss 2009). Their synthesis occurs mainly pre-veraison (Kalua and Boss 2009), and they are responsible of green-grassy aromas even though, considering their detection threshold, they rarely contribute to the herbaceous character of juices and wines (Robinson et al. 2014a).

Methoxypyrazines like 3-isobutyl-2-methoxypyrazineare (IBMP), 3-isopropyl-2-methoxypyrazine (IPMP) are extremely volatile compounds accumulated before veraison. They contribute to the specific green-herbaceous aroma of some wines such as Sauvignon blanc, Cabernet Sauvignon, Cabernet Franc, and Merlot. Their biosynthesis starts with an adicarbonyl addition to the amino acid leucine or valine for IBMP and IPMP, respectively, followed by methoxylation reactions to form the final methoxypyrazines. Four O-methyltransferases (VviOMT1-4) have been identified in grape, with VviOMT3 having a major role in IBMP production (Dunlevy et al. 2010; Guillaumie et al. 2013).

Finally, thiols confer typical aromatic features to some varieties such as Sauvignon blanc. The thiols in grape are normally accumulated during ripening in a non-volatile form, bounded to S-cysteine or S-glutathione via the VviGST3 and VviGST4 activity (Kobayashi et al. 2011). These compounds are released during and after fermentation, conferring to wines many desired properties and sometimes off-flavors, depending on the concentration (Peña-Gallego et al. 2012).

## 12.4 Hormonal Regulation of Berry Ripening

Several hormones participate in the control of grape ripening. Genomic and high throughput technologies have been essential in characterizing the crosstalk between hormones and the expression of associated downstream genes (McAtee et al. 2013; Fortes et al. 2015) (Fig. 12.2).

### 12.4.1 Auxins

Several studies have established that IAA decline is associated with the initiation of ripening, both in climacteric fruit and in non-climacteric fruit such as grapes (Böttcher et al. 2011; Fortes et al. 2015). Auxin treatments retard sugar and anthocyanin accumulation and prevent the decrease in acidity and chlorophyll concentration, but also cause a delay in the usual ripening-associated increase in the levels of abscisic acid (ABA), by altering gene expression in grape berry (Davies et al. 1997; Ziliotto et al. 2012).

Gouthu and Deluc (2015) showed that the timing of ripening initiation is related to an auxin

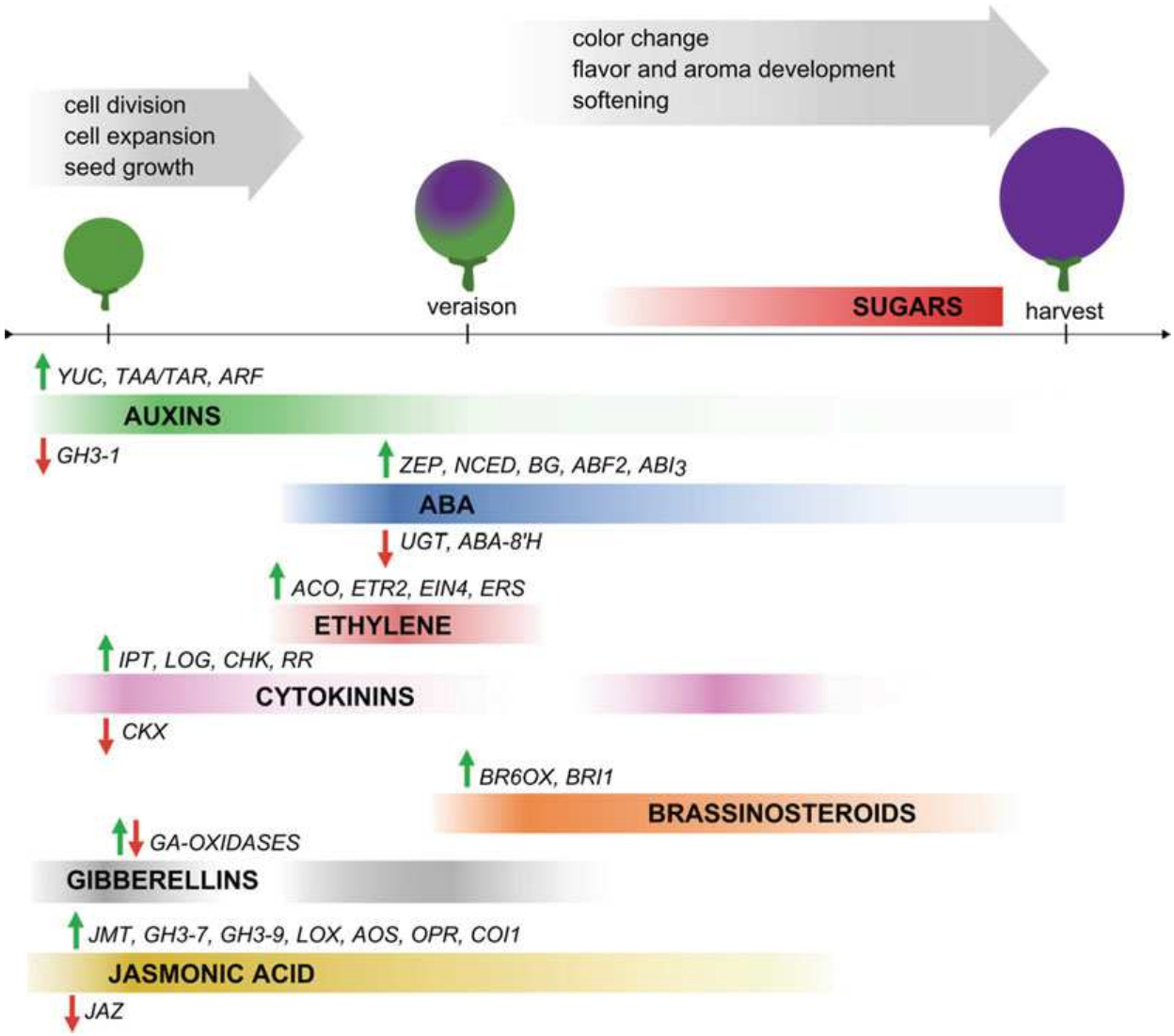


**Fig. 12.2** *Hormone dynamics during berry development and ripening*. Several studies have shown that increases in auxin, cytokinin, gibberellin, and jasmonic acid occur during the first phases of fruit growth (Stage I); brassinosteroids, ethylene, and ABA are mainly involved in physiological changes related to berry ripening (Stage III). The up- and down-regulation of the main biosynthetic/catabolic and associated downstream signaling genes are reported for each different hormone. In detail, gene names are abbreviated as follows: TRYPTOPHAN AMINOTRANSFERASE OF ARABIDOPSIS1/TRYPTOPHAN AMINOTRANSFERASE RELATED (*TAA/TAR*); YUCCA (*YUC*); auxin response factors (*ARF*); IAA-amido synthetase (*GH3-1*); 9-cis-epoxy-carotenoid dioxygenase (*NCED*); zeaxanthin epoxidase (*ZEP*); β-glucosidases (*BG*); transcription factors ABA insensitive (*ABI3*); ABRE-binding factors (*ABF*); UDP-glucosyltransferases (*UGT*); ABA 8'-hydroxylase (*ABA-8'H*); ACC oxidase (*ACO*); ethylene receptors (*ETR2*, *EIN4*, *ERS*); Adenosine phosphate-isopentenyltransferase (*IPT*); phosphoribohydrolase "Lonely guy" (*LOG*); cytokinin histidine kinase (*CHK*) receptors; response regulators (*RR*); cytokinin oxidase/dehydrogenase (*CKX*); brassinosteroid 6-oxidase gene (*BR6OX*); BR receptors (*BRI1*); GA-oxidases; *S*-adenosyl-L-methionine:jasmonic acid carboxyl methyltransferase (*JMT*); JA-amido synthetases (*GH3-7* and *GH3-9*); lipoxygenase (*LOX*); allene oxide synthase (*AOS*); 12-oxophytodienoate reductase (*OPR*), CORONATINE INSENSITIVE 1 (*COI1*) jasmonate receptor; jasmonate ZIM domain (*JAZ*)

signal and is linked to the relative seed content in berries. In a recent study that compared the berry physiology and composition to the whole genome gene expression analyzed by RNA-seq, a potential role of auxin and its conjugates in determining asynchrony between berries of different sizes was suggested (Wong et al. 2016a). Moreover, it was shown that the tight control of

the hormone concentration derives from the coordinated interplay of biosynthesis, transport, degradation, and conversion pathways (Normanly et al. 2010; Zhao 2010), in association with the fine regulation of the pool of IAA conjugates during grape ripening (Fortes et al. 2015).

The conjugation of IAA to amino acids is catalyzed by auxin-inducible GH3 proteins and provides a negative feedback loop to control auxin homoeostasis (Böttcher et al. 2010). A putative IAA-amido synthetase gene, *VviGH3-1*, was identified in grape berries. This gene displays a developmental expression pattern consistent with the increase of IAA-conjugates, which in turn is coupled to several ripening-associated processes in the berry. Indeed, the increasing levels of IAA-aspartate in grapes might be linked to the low levels of active IAA that were observed during ripening, and provide evidence for a possible mechanism for the maintenance of low auxin levels during ripening (Böttcher et al. 2012b). Members of both the TRYPTOPHAN AMINOTRANSFERASE OF ARABIDOPSIS1/TRYPTOPHAN AMINOTRANSFERASE RELATED (*TAA1/TAR*) and YUCCA (*YUC*) gene families (Won et al. 2011), involved in the two-step pathway of auxin biosynthesis, are also expressed in developing berries. Recent transcriptomic analyses revealed a consistency between TAA/TAR and YUC transcripts' evolution and auxin accumulation during berry development and ripening (Wong et al. 2016a).

Auxins' effects are mediated by early response genes, such as Aux/IAA, GH3, and SAUR family members. Several putative auxin response elements (AuxREs) have been identified, and it has been demonstrated that the conserved motif TGTCTG is responsible for the binding of the auxin response factors (ARFs) that confer specificity to auxin response through the selection of target genes, i.e., transcription factors (Hayashi 2012; Li et al. 2016). Nineteen *VviARF* genes, categorized into four groups (Classes 1, 2, 3 and 4) have been identified. Most *VviARFs* display the highest transcript levels in the berry, suggesting that they may play important roles in the regulation of grape berry maturation processes (Wan et al. 2014).

### 12.4.2 ABA

An increase in free ABA levels around veraison accompanies sugar accumulation, pigmentation, and softening (Deluc et al. 2007; Wheeler et al. 2009; Sun et al. 2010; Gambetta et al. 2010; Pilati et al. 2017), which suggests a major role for the hormone in controlling several ripening-associated processes in grape berry (Kuhn et al. 2013; Fortes et al. 2015). A decrease in fruit firmness was observed by transforming tomato with the *Vitis* transcription factor *VvABF2*, involved in ABA and abiotic stress signaling and expressed in the berry at the onset of ripening (Nicolas et al. 2014). Moreover, the upregulation of a gene encoding a glycine-rich protein, possibly involved in cell wall biogenesis and degradation, confirms a role for the hormone in fruit softening (Rattanakon et al. 2016).

The effect of ABA on the transcription of genes involved in its own biosynthesis, degradation, conjugation, transport, and signaling pathways has been extensively studied in different organs of grapevine (Rattanakon et al. 2016; Pilati et al. 2017). These studies highlighted that a small amount of ABA can trigger a positive feedback regulation of genes involved in ABA biosynthesis, including a significant up-regulation of *VviABI3* (transcription factor involved in ABA responsiveness) during the lag phase, which further supports the regulatory role of ABA in grape ripening (Rattanakon et al. 2016).

ABA biosynthesis comprises crucial steps catalyzed by 9-cis-epoxy-carotenoid dioxygenase (VviNCED) and zeaxanthin epoxidase (VviZEP). The genes codifying for those proteins are up-regulated around veraison. Conversely, *ABA 8'-hydroxylase* (*VviABA-8'H*), which regulates ABA catabolism, is down-regulated at the same stage (Deluc et al. 2007; Fortes et al. 2015). Moreover, the activity of cytosolic UDP-glucosyltransferases (VviUGTs), which conjugate ABA to form the ABA-glucose ester, and

the activity of β-glucosidases (VviBGs), which release ABA from the above conjugated form, further control ABA levels in the berry tissues (Owen et al. 2009).

Higher accumulation of anthocyanins has been observed in the skin of berries treated with ABA (Wheeler et al. 2009; Gambetta et al. 2010). This is consistent with the increased expression of anthocyanins' biosynthetic genes *VviCHI*, *VviF3H*, *VviDFR*, and *VviUFGT*, and of the related transcription factors *VviMYBA1* and *VviMYBA2* (Koyama et al. 2010). ABA is also a key modulator of water stress responses, and water deficit promotes ripening and color accumulation in grape berries (Castellarin and Di Gaspero 2007; Herrera and Castellarin 2016; Savoi et al. 2017); however, several studies have shown that under water deficit, ABA is not the only signal for color development, and sugars and other stimuli may co-regulate the metabolic response of the berry (Gambetta et al. 2010; Ferrandino and Lovisolo 2014; Pilati et al. 2017). Supporting this hypothesis, Pilati et al. (2017) analyzed berry skin transcriptional modulation by RNA-seq, and observed that ABA treatment by itself did not induce anthocyanins' biosynthetic genes.

In addition to the regulation of secondary metabolism, ABA may be able to hasten the initiation of sugar accumulation when applied before veraison by stimulating the uptake and storage of sugars in berries (Davies and Böttcher 2009; Fortes et al. 2015). The link between ABA and sugar metabolism is also supported by a study demonstrating that ABA increased the activity of both soluble and cell wall acid invertases in berry discs (Pan et al. 2005).

### 12.4.3 Other Hormones

#### 12.4.3.1 Ethylene

The role of ethylene in regulating berry ripening was usually considered negligible (Sun et al. 2010; Muñoz-Robredo et al. 2013). However, ethylene can alter the progression of ripening. For example, the application of an ethylene-releasing compound (2-chloroethylphosphonic acid, 2-CEPA) delayed ripening when applied early in berry development, and treatments with an inhibitor of ethylene biosynthesis, aminoethoxyvinylglycine (AVG), advanced ripening (Böttcher et al. 2013). However, the response to CEPA and AVG clearly changed during berry development, and this was speculated to be due to the different sensitivity of the ethylene biosynthesis and perception pathways to exogenous ethylene at different times (Böttcher et al. 2013). Interestingly, CEPA application at veraison generated an increase in the concentration of anthocyanin in Cabernet Sauvignon berries, with a concomitant increase in expression of genes such as *VviCHS*, *VviF3H*, and *VviUFGT* (El-Kereamy et al. 2003).

Ethylene also promotes berry size, stimulating the expression of several genes encoding aquaporins, polygalacturonases, xyloglucan endotransglycosylase, cellulose synthases, and expansins (Chervin et al. 2008). Ethylene is perceived by transmembrane-receptor proteins, belonging to the EThylene Receptor (ETR) family, localized in the endoplasmic reticulum. Chervin and Deluc (2010) analyzed the transcript abundance of several ethylene receptors (*VviETR2*, *VviEIN4*, *VviERS*) and transcription factors (*VviEIN3* and *VviMADS4*) across berry development and the impact of the ethylene inhibitor 1-MCP on their expression. Recently, a phylogenetic analysis performed on ETRs and related proteins, in both climacteric and non-climacteric fruits, pointed out that both classes share many aspects of ethylene perception and signaling during fruit ripening. Moreover, grape, as non-climacteric fruit, exhibits an earlier expression peak of four ETRs, concomitant with the onset of sugar accumulation (Chen et al. 2018). One gene coding for ACC oxidase (*VviACO*) was found to increase its expression at the early stages of berry development (Deluc et al. 2007), with a peak around veraison; a similar observation, together with the increase of ethylene levels, was related to the beginning of fruitlet abscission in Chardonnay berries (Hilt and Bessis 2003). Recently, the expression of genes involved in the ethylene signaling pathway, as well as ethylene transcription factors

with recognized roles in leaf senescence, were found to increase during the late stages of ripening of Cabernet Sauvignon, which suggests that ethylene may play a bigger role than expected in regulating grape berry ripening (Cramer et al. 2014).

#### 12.4.3.2 Cytokinins

Although previous studies reported that cytokinins do not participate in ripening in grapevine (Inaba et al. 1976), more recently some studies have highlighted the importance of this hormone both at the pre- and post-veraison stages (Böttcher et al. 2015; Pilati et al. 2017). Grapevine orthologues of five *Arabidopsis* gene families involved in cytokinin metabolism and signaling were identified, and their expression patterns were analyzed in developing berries. Genes regulating cytokinin biosynthesis (*VviIPTs*), activation (*VviLOGs*), perception (*VviCHKs*), and signaling (*VviRRs*) were found to be expressed in all stages of berry development and most significantly just before and after veraison, and during this time the expression of genes involved in cytokinin degradation (*VviCKXs*) progressively decrease (Böttcher et al. 2015).

#### 12.4.3.3 Brassinosteroids

Expression analysis of genes encoding brassinosteroid (BR) biosynthetic enzymes or BR receptors (i.e., *VviBRI1*) during berry development revealed transcript accumulation patterns consistent with the dramatic increase in endogenous BR levels observed at the onset of fruit ripening (Symons et al. 2006). It has been shown that levels of castasterone, the bioactive BR, and its precursor 6-deoxo-castasterone increase at veraison and remain high during ripening in Cabernet Sauvignon berries due to the upregulation of a brassinosteroid 6-oxidase gene *(VviBR6OX)* (Symons et al. 2006). The application of exogenous brassinosteroid increases the total anthocyanin content in berries, and the full coloration of grapes occurred earlier in BR-treated samples, with increased expression of anthocyanin biosynthetic genes (i.e., *VviF3H*, *VviF3'5' H*, *VviDFR*, *VviANS*, *VviUFGT*) (Luan et al. 2013; Serrano et al. 2017). In addition, the involvement of BR in sugar unloading into the berry has been recently demonstrated. Exogenous treatment of Cabernet Sauvignon berries with BR (24-epibrassinolide) increases the soluble sugar content by enhancing the activities of enzymes related to sugar unloading, including neutral and acidic invertases and sucrose synthase, and up-regulating the expression of sucrose transporter genes (Xu et al. 2015).

#### 12.4.3.4 Gibberellins

The involvement of gibberellins (GAs), produced in the seeds, in grape berry development and size determination is well known (Coombe 1960). GAs peak early during stage I (Davies and Böttcher 2009), and increase again at the initiation of stage III (Pérez et al. 2000).

A comprehensive annotation and characterization of GA-oxidases (GAox)—involved in GAs biosynthesis and deactivation—has been performed in grapevine (Giacomelli et al. 2013). The authors propose that the pool of bioactive GAs is controlled by the stage- and tissue-specific regulation of GA oxidase, and *VviGA3ox1* and *VviGA2ox4* transcripts are significantly up-regulated at fruit set.

RNA-seq analysis of "Centennial Seedless" berries treated with GAs after flowering showed an increased expression of xyloglucan endotransglycosylase (*VviXET*) genes, which participate in cell wall expansion. A crosstalk between GAs, ABA, and ethylene during berry enlargement period has also been reported, and GA3-application induces gene expression changes in plant hormone metabolism and signaling pathways (Chai et al. 2014). Moreover, GAs' soaking of cv. Kyoho clusters strongly hastens berry coloration, which allows the hypothesis of a role for the hormone in regulating anthocyanin biosynthesis (Cheng et al. 2015). In the same study, a large number of the identified differentially expressed genes were involved in GA biosynthetic and signaling pathways. Zhang et al. (2014) provided new insights into the crosstalk mechanism of GAs and glucose hexokinase-dependent signaling during grape berry sugar accumulation, and hypothesized that GAs might

regulate the expression of invertase and sucrose synthase genes in order to maintain intracellular sugar levels and normal cell metabolism.

#### 12.4.3.5 Sugars

Notably, besides their role as a metabolic substrate, sugars directly or indirectly control a wide range of processes, including photosynthesis, sugar transport itself, phenylpropanoid metabolism, cell wall metabolism, auxin homeostasis, and ultimately berry growth and ripening (Smeekens et al. 2010). The sugar-dependent regulation of anthocyanin pathway and of biotic/abiotic stress responses has been extensively reviewed by Lecourieux et al. (2014). Interaction between sugar and ABA signaling pathways likely plays a pivotal role in ripening, which is suggested by the parallel increase of sugars and ABA in the berries at veraison (Gambetta et al. 2010; Lecourieux et al. 2014). Interestingly, both sucrose and ABA were able to increase *VviSK1*—a gene encoding a protein kinase with sugar signaling function—expression in grape cell suspensions, which underlines the tight interaction between sugars and hormone signaling pathways (Smeekens 2000; Finkelstein and Gibson 2002; León and Sheen 2003).

#### 12.4.3.6 Jasmonic Acid

The plant hormone jasmonic acid (JA) is crucial for stress responses in plants, but its role in fruit development and ripening is becoming increasingly clear. In non-climacteric fruits such as grape, the jasmonate levels are high at early developmental stages, decreasing to lower values at the onset of ripening (Kondo and Fukuda 2001; Fortes et al. 2011, 2015). Conjugation of JA to isoleucine (JA-Ile) is a critical step in the JA signaling pathway since only JA-Ile is recognized by the jasmonate receptor. The conjugation reaction is catalyzed by JA-amido synthetases, belonging to the family of GH3 proteins. Böttcher et al. (2015) report that the transcriptional profiles of two grapevine GH3 genes, *VviGH3-7* and *VviGH3-9*, support a primary role for JA signaling in fruit set and cell division, but do not justify JA's involvement in the ripening process.

Methyl jasmonate (MeJA) also plays an important role in signal transduction processes that regulate the synthesis of secondary metabolites (Pauwels et al. 2009); grapevine plants and cell cultures respond to MeJA with an increase in aroma compounds or stilbene levels (D'Onofrio et al. 2009; Almagro et al. 2014; D'Onofrio et al. 2018; Portu et al. 2018). The gene coding for S-adenosyl-L-methionine:jasmonic acid carboxyl methyltransferase (JMT), putatively involved in volatile methyl jasmonate synthesis, was down-regulated in ripe fruits of three grape varieties. On the other hand, the gene coding for the jasmonate ZIM domain (JAZ) containing protein 8, a repressor of jasmonic acid signaling, has been identified as a putative positive marker of ripening (Agudelo-Romero et al. 2013). Treatments with MeJA increase the transcription levels of several ripening-related genes, such as color-related genes (i.e., *VviPAL1*, *VviDFR*, *VviCHI*, *VviF3H*, *VviGST*, *VviCHS*, and *VviUFGT*), softening-related genes (i.e., *VviPG*, *VviPL*, *VviPE*, *VviCell*, *VviEG1*, and *VviXTH1*), and aroma-related genes (i.e.,*VviEcar*, *VviQR*, and *VviEGS*). Moreover, jasmonic acid positively regulated its biosynthesis pathway genes such as lipoxygenase (*LOX*), allene oxide synthase (*AOS*), 12-oxophytodienoate reductase (*OPR*), and signal pathway genes such as *VviCOI1* and *VviJMT*. In addition, the overexpression of grape jasmonic acid receptor *VviCOI1* in strawberry fruit accelerated the fruit ripening process (Jia et al. 2016).

## 12.5 Molecular Regulators of Fruit Ripening

Transcription factors (TFs) regulate the spatial and temporal expression of genes by specific binding to cis-regulatory elements (CREs or "motifs") present in the promoter region of genes. In plants, as many as 58 TF families have been described (Jin et al. 2016), of which many play essential roles in biological processes, including fleshy fruit development, ripening, and regulation of fruit quality/composition (Karlova et al. 2014). A plethora of TFs involved in

ripening have been discovered using tomato, a climacteric fruit species, as the model species for understanding fruit ripening. For example, the MADS-box (e.g., RIPENING-INHIBITOR, RIN; FRUITFULL, FUL1 and FUL2), SBP (e.g., COLORLESS NON-RIPENING, CNR; TOMATO AGAMOUS-LIKE1, TAGL1), NAC (e.g., NON-RIPENING, NOR; NAC4), HD-Zip homeobox (HB1), and AP2/ERF (e.g., APETALA2a) TFs are among the many widely known regulators of ripening. Moreover, TFs involved in hormone response and signaling such as AP2/ERFs (e.g., ERF1, ERF6) and ARF (e.g., ARF2) are also implicated in fruit ripening and participate in the regulation of ripening-associated phenotypic traits such as flavonoid/anthocyanin biosynthesis, sugar accumulation, and softening.

While much is known about the regulation of climacteric fruit ripening, our understanding of the TFs involved in ripening remains limited for non-climacteric fruit. The roles of some TFs involved in tomato development and ripening have been elucidated also in grapevine. For example, the MADS-box TF SEPALLATA (VviSEP4) may fulfil similar functions to RIN in grapes, as revealed by its ability to partially complement the non-ripening phenotype of *RIN* mutants (Mellway and Lund 2013).

A grapevine bZIP TF, namely, ABSCISIC ACID RESPONSE ELEMENT-BINDING FACTOR2 (VviABF2), was shown to play a direct role in the ABA-dependent berry ripening processes (Nicolas et al. 2014). Regulatory networks encompassing ABA responses were either enhanced and/or altered by VviABF2, which led to enhanced sensitivity to ABA. In addition, the role of VviABF2 in the regulation of ripening-associated processes such as the biosynthesis of phenolic metabolites was also demonstrated in tomato and grapevine. The lack of MADS-box TF participation together with the enrichment of TFs (i.e., bZIP, AP2/ERF, R2R3-MYB, and NAC) in the ABA signaling network during berry ripening (Pilati et al. 2017) suggest that grapevine MADS-box TFs do not play a key role in overall ripening regulation in grapevine. This is also supported by a strong enrichment of cis-regulatory motifs bound by bZIP and NAC TFs and the lack of MADS-box TF motifs in the promoters of ABA-modulated genes in the berry (Pilati et al. 2017). Nonetheless, other TFs such as VviERF045 (AP2/ERF) (Leida et al. 2016) and VviCEB1 (bHLH) (Nicolas et al. 2013) have been implicated in the control of ripening. For example, genes involved in wax metabolism, cell expansion, defense, and phenylpropanoid/flavonoid metabolism are potential targets of VviERF045, while VviCEB1 may stimulate cell expansion through the activation of auxin metabolism, auxin signaling, and multiple cell expansion related genes.

Beyond these few cases, the function of the vast majority of TFs remains to be elucidated. To facilitate the discovery of fruit-associated TF functions, adoption of multi-omics approaches (i.e., transcriptome, metabolome), the application of network-based approaches to analyze the omics data, and subsequent network integration across different domains could be particularly useful (reviewed in Wong and Matus 2017). For example, gene co-expression network analysis of a large accession of berry cultivars during fruit development and ripening has been performed to identify putative regulators of berry developmental and ripening (Palumbo et al. 2014; Massonnet et al. 2017). Not surprisingly, many of these putative genes encode TFs that belong to AP2/ERF, MYB, NAC, and WRKY families. Independent studies were also able to link several of these ripening-related TFs to their potential roles during berry ripening using gene-metabolite co-response networks (Savoi et al. 2017). For example, VviERF1 and VviNAC33, two common berry TFs (Massonnet et al. 2017), are potentially related to the regulation of proline biosynthesis in the berry, given their strong coordinated regulation with pyrroline-5-carboxylate synthase (P5CS), the gene encoding enzyme involved in proline biosynthesis, and with proline content in the berry. Similarly, NACs such as VviNAC13 and VviNAC33 are potentially new candidate regulators for anthocyanin compounds that exhibit tight association with several anthocyanin biosynthetic gene and metabolite profiles (Savoi et al. 2017).

Such approaches can also be used to infer the regulatory candidates involved in the regulation of fruit-associated volatiles (e.g., terpenes), one of the least understood components of berry ripening. For example, Savoi et al. (2016) highlighted one promising regulatory candidate (VviMYB24) for monoterpene biosynthesis, given its strong gene-metabolite co-response profile with several TPS and monoterpene (e.g., linalool, nerol, α-terpineol) abundance in the fruit during ripening and under an abiotic stress such as drought (Fig. 12.3).

Notwithstanding the crucial roles fulfilled by various TFs during ripening, new evidence supporting the involvement of regulatory non-coding RNA classes, especially micro RNA (miRNA) and long non-coding RNA (lncRNA), in the regulation of fruit ripening and composition have been described. Although it is possible to infer the function of miRNAs in fruits through comprehensive miRNA expression profiling during development and ripening and performing in silico target prediction analysis (Gao et al. 2015; Xin et al. 2015; Zeng et al. 2015; Belli Kullan et al. 2015), the first and only study to date demonstrating a direct role for miRNAs in overall ripening regulation and fruit softening investigated the tomato miR157 and miRNA156 (Chen et al. 2015). Tomato miR156 impacts fruit softening especially at the late stages of ripening but contributes little to overall ripening regulation (Chen et al. 2015). Interestingly, miR156 sequences are highly conserved in plants, including grapevine (Belli Kullan et al. 2015). Like its tomato counterpart, grapevine miR156 also exhibits ripening-associated expression, and it has been postulated to induce ripening via the regulation of multiple SPL (Squamosa Promoter binding Like protein) and anthocyanin pathway genes (Belli Kullan et al. 2015).

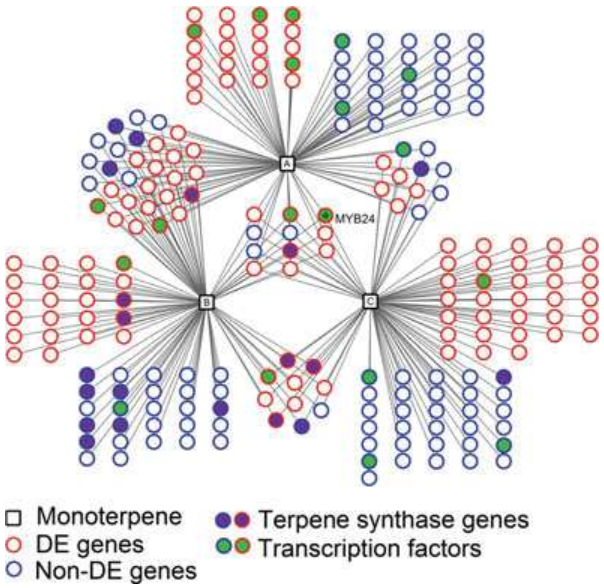


**Fig. 12.3** *Predicted gene-metabolite networks related to nerol (A), α-terpineol (B), and linalool (C) accumulation in grape berries during development.* Genes and metabolites are represented by circle and square nodes, respectively. Edges represent associations ($P < 0.001$) between transcripts and metabolites. Node borders in red represent genes that are modulated (differentially expressed, DE) under drought. Purple and green nodes identify terpene synthase genes and transcription factors, respectively. The network was re-designed from Savoi et al. (2016)

Compared to miRNAs, lncRNAs are an emerging class of RNA species that are operationally defined as non-coding transcripts, greater than 200nt in length. The advent of sequencing technologies has led to the discovery of thousands of lncRNAs in both model (Liu et al. 2015) and non-model fruit crops such as tomato (Wang et al. 2018), grapevine (Vitulo et al. 2014; Harris et al. 2017), kiwi (Tang et al. 2016), and sea buckthorn (Zhang et al. 2018); however, for the vast majority of these crops, the functions of lncRNAs remain unknown. Only a small fraction of these have been validated experimentally (Liu et al. 2015). lncRNAs are known to possess tissue- and developmental stage-specific expression in plants and these properties also manifests in the fruit (Tang et al. 2016; Zhang et al. 2018; Wang et al. 2018). Only recently their role in the regulation of fruit ripening and composition was confirmed. For example, using a combination of lncRNA-miRNA-mRNA network and functional analysis, LNC1 and LNC2 were shown to be negative and positive regulators, respectively, of anthocyanin in sea buckhorn fruits.

While novel lncRNAs continue to be discovered in grapevines (Vitulo et al. 2014; Harris et al. 2017), very little work has been done to profile their expression during ripening and/or to infer their potential regulatory role in the fruit. To date, this was done only to understand the

complex regulation of phenylpropanoid and flavonoid biosynthesis in the grape berry (Wong and Matus 2017). Using integrated lncRNA-miRNA-mRNA network analysis (as in Zhang et al. 2018), several lncRNAs identified showed strong co-regulated expression and co-location with key structural pathway genes. Notable examples include one lncRNA (VIT_210s0042n00100) that is situated within close proximity of nine *VviSTSs*. The expression pattern of the lncRNA closely mirrored the ripening-associated expression of the nine *VviSTSs*. Similarly, one predicted lncRNA (VIT_203s0180n00020) was co-located and closely mirrored the expression of *VviGT2*, a gene potentially involved in the production of hydroxycinnamic esters and proanthocyanidins galloylation (Khater et al. 2012). Such initiatives have provided a glimpse into the potential large-scale regulatory function of lncRNAs on the regulation of fruit composition during development and ripening.

## 12.6 Conclusion

Taken together, all these studies and information indicate the complex feedback and multifaceted regulation of grape berry ripening. The long-standing interest in grapevine production has led to a good knowledge in this field, but a large number of research questions, many of which have crucial practical implications, still need to be answered. New insights about the control of berry metabolism and ripening will be gained by clearly assigning functions to key regulators of these processes. This is challenging and will require innovative functional genomic approaches; in this regard, new-generation sequencing and emerging genome editing technologies, currently being developed for grapevine, could provide important contributions to our understanding.

## References

Adams DO (2006) Phenolics and ripening in grape berries. Am J Enol Vitic 57:249–256

Afoufa-Bastien D, Medici A, Jeauffre J, Coutos-Thévenot P, Lemoine R, Atanassova R et al (2010) The Vitis vinifera sugar transporter gene family: phylogenetic overview and macroarray expression profiling. BMC Plant Biol 10:245. https://doi.org/10.1186/1471-2229-10-245

Agasse A, Vignault C, Kappel C, Conde C, Gerós H, Delrot S. (2009) Sugar transport & sugar sensing in grape. In: Grapevine molecular physiology & biotechnology. Springer, Dordrecht, pp 105–139

Ageorges A, Issaly N, Picaud S, Delrot S, Romieu C (2000) Identification and functional expression in yeast of a grape berry sucrose carrier. Plant Physiol Biochem 38:177–185. https://doi.org/10.1016/S0981-9428(00)00730-0

Agudelo-Romero P, Erban A, Sousa L, Pais MS, Kopka J, Fortes AM (2013) Search for transcriptional and metabolic markers of grape pre-ripening and ripening and insights into specific aroma development in three portuguese cultivars. PLoS ONE 8:e60422. https://doi.org/10.1371/journal.pone.0060422

Almagro L, Carbonell-Bejerano P, Belchí-Navarro S, Bru R, Martínez-Zapater JM, Lijavetzky D, Pedreño MA (2014) Dissecting the transcriptional response to elicitors in *Vitis vinifera* cells. PLoS ONE 9:e109777. https://doi.org/10.1371/journal.pone.0109777

Battilana J, Costantini L, Emanuelli F, Sevini F, Segala C, Moser S, Velasco R, Versini G, Grando MS (2009) The 1-deoxy-D-xylulose 5-phosphate synthase gene co-localizes with a major QTL affecting monoterpene content in grapevine. Theor Appl Genet 118:653–669. https://doi.org/10.1007/s00122-008-0927-8

Battilana J, Emanuelli F, Gambino G, Gribaudo I, Gasperi F, Boss PK, Grando MS (2011) Functional effect of grapevine 1-deoxy-D-xylulose 5-phosphate synthase substitution K284 N on Muscat flavour formation. J Exp Bot 62:5497–5508. https://doi.org/10.1093/jxb/err231

Belli Kullan J, Lopes Paim Pinto D, Bertolini E, Fasoli M, Zenoni S, Tornielli GB, Pezzotti M, Meyers BC, Farina L, Pè ME, Mica E (2015) miRVine: a microRNA expression atlas of grapevine based on small RNA sequencing. BMC Genom 16:393. https://doi.org/10.1186/s12864-015-1610-5

Bogs J, Downey MO, Harvey JS, Ashton AR, Tanner GJ, Robinson SP (2005) Proanthocyanidin synthesis and expression of genes encoding leucoanthocyanidin reductase and anthocyanidin reductase in developing grape berries and grapevine leaves. Plant Physiol 139:652–663. https://doi.org/10.1104/pp.105.064238

Bogs J, Jaffé FW, Takos AM, Walker AR, Robinson SP (2007) The grapevine transcription factor VvMYBPA1 regulates proanthocyanidin synthesis during fruit development. Plant Physiol 143:1347–1361. https://doi.org/10.1104/pp.106.093203

Bohlmann J, Keeling CI (2008) Terpenoid biomaterials. Plant J 54:656–669. https://doi.org/10.1111/j.1365-313X.2008.03449.x

Bönisch F, Frotscher J, Stanitzek S, Rühl E, Wüst M, Bitz O, Schwab W (2014a) Activity-based profiling of

a physiologic aglycone library reveals sugar acceptor promiscuity of family 1 UDP-glucosyltransferases from grape. Plant Physiol 166:23–39. https://doi.org/10.1104/pp.114.242578

Bönisch F, Frotscher J, Stanitzek S, Rühl E, Wüst M, Bitz O, Schwab W (2014b) A UDP-glucose: monoterpenol glucosyltransferase adds to the chemical diversity of the grapevine metabolome. Plant Physiol 165:561–581. https://doi.org/10.1104/pp.113.232470

Böttcher C, Boss PK, Davies C (2012a) Delaying Riesling grape berry ripening with a synthetic auxin affects malic acid metabolism and sugar accumulation, and alters wine sensory characters. Funct Plant Biol 39:745. https://doi.org/10.1071/FP12132

Böttcher C, Boss PK, Davies C (2011) Acyl substrate preferences of an IAA-amido synthetase account for variations in grape (*Vitis vinifera* L.) berry ripening caused by different auxinic compounds indicating the importance of auxin conjugation in plant development. J Exp Bot 62:4267–4280. https://doi.org/10.1093/jxb/err134

Böttcher C, Burbidge CA, Boss PK, Davies C (2015) Changes in transcription of cytokinin metabolism and signalling genes in grape (*Vitis vinifera* L.) berries are associated with the ripening-related increase in isopentenyladenine. BMC Plant Biol 15:223. https://doi.org/10.1186/s12870-015-0611-5

Böttcher C, Dennis EG, Booker GW, Polyak SW, Boss PK, Davies C (2012b) A novel tool for studying auxin-metabolism: the inhibition of grapevine indole-3-acetic acid-amido synthetases by a reaction intermediate analogue. PLoS ONE 7:e37632. https://doi.org/10.1371/journal.pone.0037632

Böttcher C, Harvey KE, Boss PK, Davies C (2013) Ripening of grape berries can be advanced or delayed by reagents that either reduce or increase ethylene levels. Funct Plant Biol 40:566. https://doi.org/10.1071/FP12347

Böttcher C, Keyzers RA, Boss PK, Davies C (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. J Exp Bot 61:3615–3625. https://doi.org/10.1093/jxb/erq174

Brummell DA, Harpster MH (2001) Cell wall metabolism in fruit softening and quality and its manipulation in transgenic plants. Plant Mol Biol 47:311–340

Cabezas JA, Cervera MT, Ruiz-García L, Carreño J, Martínez-Zapater JM (2006) A genetic analysis of seed and berry weight in grapevine. Genome 49:1572–1585. https://doi.org/10.1139/g06-122

Caputi L, Carlin S, Ghiglieno I, Stefanini M, Valenti L, Vrhovsek U, Mattivi F (2011) Relationship of changes in rotundone content during grape ripening and winemaking to manipulation of the 'peppery' character of wine. J Agric Food Chem 59:5565–5571. https://doi.org/10.1021/jf200786u

Castellarin SD, Di Gaspero G (2007) Transcriptional control of anthocyanin biosynthetic genes in extreme phenotypes for berry pigmentation of naturally occurring grapevines. BMC Plant Biol 7:46. https://doi.org/10.1186/1471-2229-7-46

Castellarin SD, Gambetta GA, Wada H, Krasnow MN, Cramer GR, Peterlunger E, Shackel KA, Matthews MA (2016) Characterization of major ripening events during softening in grape: turgor, sugar accumulation, abscisic acid metabolism, colour development, and their relationship with growth. J Exp Bot 67:709–722. https://doi.org/10.1093/jxb/erv483

Castellarin SD, Gambetta GA, Wada H, Shackel KA, Matthews MA (2011) Fruit ripening in *Vitis vinifera*: spatiotemporal relationships among turgor, sugar accumulation, and anthocyanin biosynthesis. J Exp Bot 62:4345–4354. https://doi.org/10.1093/jxb/err150

Cavallini E, Matus JT, Finezzo L, Zenoni S, Loyola R, Guzzo F, Schlechter R, Ageorges A, Arce-Johnson P, Tornielli GB (2015) The phenylpropanoid pathway is controlled at different branches by a set of R2R3-MYB C2 repressors in grapevine. Plant Physiol 167:1448–1470. https://doi.org/10.1104/pp.114.256172

Chai L, Li Y, Chen S, Perl A, Zhao F, Ma H (2014) RNA sequencing reveals high resolution expression change of major plant hormone pathway genes after young seedless grape berries treated with gibberellin. Plant Sci 229:215–224. https://doi.org/10.1016/j.plantsci.2014.09.010

Chen F, Tholl D, Bohlmann J, Pichersky E (2011) The family of terpene synthases in plants: a mid-size family of genes for specialized metabolism that is highly diversified throughout the kingdom. Plant J 66:212–229. https://doi.org/10.1111/j.1365-313X.2011.04520.x

Chen L-Q (2014) SWEET sugar transporters for phloem transport and pathogen nutrition. New Phytol 201:1150–1155

Chen L-Q, Qu X-Q, Hou B-H, Sosso D, Osorio S, Fernie AR et al (2012) Sucrose efflux mediated by SWEET proteins as a key step for phloem transport. Science (80-) 335:207–211. https://doi.org/10.1126/science.1213351

Chen W, Kong J, Lai T, Manning K, Wu C, Wang Y, Qin C, Li B, Yu Z, Zhang X, He M, Zhang P, Gu M, Yang X, Mahammed A, Li C, Osman T, Shi N, Wang H, Jackson S, Liu Y, Gallusci P (2015) Tuning LeSPL-CNR expression by SlymiR157 affects tomato fruit ripening. Sci Rep 5:7852. https://doi.org/10.1038/srep07852

Chen Y, Grimplet J, David K, Castellarin SD, Terol J, Wong DCJ, Luo Z, Schaffer R, Celton J-M, Talon M, Gambetta GA, Chervin C (2018) Ethylene receptors and related proteins in climacteric and non-climacteric fruits. Plant Sci 276:63–72. https://doi.org/10.1016/J.PLANTSCI.2018.07.012

Cheng C, Jiao C, Singer SD, Gao M, Xu X, Zhou Y, Li Z, Fei Z, Wang Y, Wang X (2015) Gibberellin-induced changes in the transcriptome of grapevine (*Vitis labrusca* × *V. vinifera*) cv. Kyoho flowers. BMC Genom 16:128. https://doi.org/10.1186/s12864-015-1324-8

Cheng J, Wen S, Xiao S, Lu B, Ma M, Bie Z (2018) Overexpression of the tonoplast sugar transporter CmTST2 in melon fruit increases sugar accumulation. J Exp Bot 69:511–523. https://doi.org/10.1093/jxb/erx440

Chervin C, Deluc L (2010) Ethylene signalling receptors and transcription factors over the grape berry development: Gene expression profiling. Vitis J Grapevine Res 49:129–136. https://doi.org/10.1016/j.ssi.2010.01.014

Chervin C, Tira-umphon A, Terrier N, Zouine M, Severac D, Roustan J-P (2008) Stimulation of the grape berry expansion by ethylene and effects on related gene transcripts, over the ripening phase. Physiol Plant 134:534–546. https://doi.org/10.1111/j.1399-3054.2008.01158.x

Chialva C, Eichler E, Grissi C, Muñoz C, Gomez-Talquenca S, Martínez-Zapater JM, Lijavetzky D (2016) Expression of grapevine AINTEGUMENTA-like genes is associated with variation in ovary and berry size. Plant Mol Biol 91:67–80. https://doi.org/10.1007/s11103-016-0443-1

Choat B, Gambetta GA, Shackel KA, Matthews MA (2009) Vascular function in grape berries across development and its relevance to apparent hydraulic isolation. Plant Physiol 151:1677–1687. https://doi.org/10.1104/pp.109.143172

Cholet C, Claverol S, Claisse O, Rabot A, Osowsky A, Dumot V, Ferrari G, Gény L (2016) Tartaric acid pathways in *Vitis vinifera* L. (cv. Ugni blanc): a comparative study of two vintages with contrasted climatic conditions. BMC Plant Biol 16:144. https://doi.org/10.1186/s12870-016-0833-1

Chong J, Piron M-C, Meyer S, Merdinoglu D, Bertsch C, Mestre P (2014) The SWEET family of sugar transporters in grapevine: VvSWEET4 is involved in the interaction with *Botrytis cinerea*. J Exp Bot 65:6589–6601. https://doi.org/10.1093/jxb/eru375

Coombe B, Bishop G (1980) Development of the grape berry. II Changes in diameter and deformability during veraison. Aust J Agric Res 31:499–509

Coombe BG (1976) The development of fleshy fruit. Ann Rev Plant Physiol 27:507–528

Coombe BG (1992) Research on development and ripening of the grape berry. Am J Enol Vitic 43:101–110

Coombe BG (1960) Relationship of growth and development to changes in sugars, auxins, and gibberellins in fruit of seeded and seedless varieties of *Vitis vinifera*. Plant Physiol 35:241–250

Cosgrove DJ (2005) Growth of the plant cell wall. Nat Rev Mol Cell Biol 6:850–861. https://doi.org/10.1038/nrm1746

Costantini L, Kappel CD, Trenti M, Battilana J, Emanuelli F, Sordo M, Moretto M, Camps C, Larcher R, Delrot S, Grando MS (2017) Drawing links from transcriptome to metabolites: the evolution of aroma in the ripening berry of Moscato Bianco (*Vitis vinifera* L.). Front Plant Sci. https://doi.org/10.3389/fpls.2017.00780

Costantini L, Malacarne G, Lorenzi S, Troggio M, Mattivi F, Moser C, Grando MS (2015) New candidate genes for the fine regulation of the colour of grapes. J Exp Bot 66:4427–4440. https://doi.org/10.1093/jxb/erv159

Cramer GR, Ghan R, Schlauch KA, Tillett RL, Heymann H, Ferrarini A, Delledonne M, Zenoni S, Fasoli M, Pezzotti M (2014) Transcriptomic analysis of the late stages of grapevine (*Vitis vinifera* cv. Cabernet Sauvignon) berry ripening reveals significant induction of ethylene signaling and flavor pathways in the skin. BMC Plant Biol 14:370. https://doi.org/10.1186/s12870-014-0370-8

Czemmel S, Höll J, Loyola R, Arce-Johnson P, Alcalde JA, Matus JT, Bogs J (2017) Transcriptome-wide identification of novel uv-b- and light modulated flavonol pathway genes controlled by VviMYBF1. Front Plant Sci 8:1084. https://doi.org/10.3389/fpls.2017.01084

Czemmel S, Stracke R, Weisshaar B, Cordon N, Harris NN, Walker AR, Robinson SP, Bogs J (2009) The grapevine R2R3-MYB transcription factor VvMYBF1 regulates flavonol synthesis in developing grape berries. Plant Physiol 151:1513–1530. https://doi.org/10.1104/pp.109.142059

D'Onofrio C, Matarese F, Cuzzola A (2018) Effect of methyl jasmonate on the aroma of Sangiovese grapes and wines. Food Chem 242:352–361. https://doi.org/10.1016/J.FOODCHEM.2017.09.084

D'Onofrio C, Cox A, Davies C, Boss PK (2009) Induction of secondary metabolism in grape cell cultures by jasmonates. Funct Plant Biol 36:323. https://doi.org/10.1071/FP08280

Dai ZW, Leon C, Feil R et al (2013) Metabolic profiling reveals coordinated switches in primary carbohydrate metabolism in grape berry (*Vitis vinifera* L.), a non-climacteric fleshy fruit. J Exp Bot 64:1345–1355. https://doi.org/10.1093/jxb/ers396

Dai ZW, Ollat N, Gomes E, Decroocq S, Tandonnet J-P, Bordenave L, Pieri P, Hilbert G, Kappel C, van Leeuwen C, Vivin P, Delrot S (2011) Ecophysiological, genetic, and molecular causes of variation in grape berry weight and composition: a review. Ann Rev Plant Physiol 62:413–425. https://doi.org/10.5344/ajev.2011.10116

Dal Santo S, Vannozzi A, Tornielli GB, Fasoli M, Venturini L, Pezzotti M, Zenoni S (2013) Genome-wide analysis of the expansin gene superfamily reveals grapevine-specific structural and functional characteristics. PLoS ONE 8:e62206. https://doi.org/10.1371/journal.pone.0062206

Davies C, Boss PK, Robinson SP (1997) Treatment of Grape Berries, a Nonclimacteric Fruit with a Synthetic Auxin, Retards Ripening and Alters the Expression of Developmentally Regulated Genes. Plant Physiol 115:1155–1161. https://doi.org/10.1104/PP.115.3.1155

Davies C, Böttcher C (2009) Hormonal control of grape berry ripening. In: Roubelakis-Angelakis KA (ed) Grapevine molecular physiology & biotechnology. Springer, Dordrecht, pp 229–261

Davies C, Robinson SP (1996) Sugar accumulation in grape berries. Cloning of two putative vacuolar invertase cDNAs and their expression in grapevine tissues. Plant Physiol 111:275–283

Davies C, Wolf T, Robinson SP (1999) Three putative sucrose transporters are differentially expressed in grapevine tissues. Plant Sci 147:93–100. https://doi.org/10.1016/S0168-9452(99)00059-X

DeBolt S, Cook DR, Ford CM (2006) L-Tartaric acid synthesis from vitamin C in higher plants. Proc Natl Acad Sci 103:5608–5613. https://doi.org/10.1073/pnas.0510864103

Deluc LG, Grimplet J, Wheatley MD, Tillett RL, Quilici DR, Osborne C, Schooley DA, Schlauch KA, Cushman JC, Cramer GR (2007) Transcriptomic and metabolite analyses of Cabernet Sauvignon grape berry development. BMC Genom 8:429. https://doi.org/10.1186/1471-2164-8-429

Doligez A, Bouquet A, Danglot Y, Lahogue F, Riaz S, Meredith C, Edwards K, This P (2002) Genetic mapping of grapevine (*Vitis vinifera* L.) applied to the detection of QTLs for seedlessness and berry weight. Theor Appl Genet 105:780–795. https://doi.org/10.1007/s00122-002-0951-z

Downey MO, Harvey JS, Robinson SP (2004) The effect of bunch shading on berry development and flavonoid accumulation in Shiraz grapes. Aust J Grape Wine Res 10:55–73. https://doi.org/10.1111/j.1755-0238.2004.tb00008.x

Drew DP, Andersen TB, Sweetman C, Møller BL, Ford C, Simonsen HT (2015) Two key polymorphisms in a newly discovered allele of the *Vitis vinifera* TPS24 gene are responsible for the production of the rotundone precursor α-guaiene. J Exp Bot. https://doi.org/10.1093/jxb/erv491

Dunlevy JD, Soole KL, Perkins MV, Dennis EG, Keyzers RA, Kalua CM, Boss PK (2010) Two O-methyltransferases involved in the biosynthesis of methoxypyrazines: grape-derived aroma compounds important to wine flavour. Plant Mol Biol 74:77–89. https://doi.org/10.1007/s11103-010-9655-y

El-Kereamy A, Chervin C, Roustan J-P, Cheynier V, Souquet J-M, Moutounet M, Raynal J, Ford C, Latche A, Pech J-C, Bouzayen M (2003) Exogenous ethylene stimulates the long-term expression of genes related to anthocyanin biosynthesis in grape berries. Physiol Plant 119:175–182. https://doi.org/10.1034/j.1399-3054.2003.00165.x

Falginella L, Castellarin SD, Testolin R, Gambetta GA, Morgante M, Di Gaspero G (2010) Expansion and subfunctionalisation of flavonoid 3′,5′-hydroxylases in the grapevine lineage. BMC Genom 11:562. https://doi.org/10.1186/1471-2164-11-562

Falginella L, Di Gaspero G, Castellarin SD (2012) Expression of flavonoid genes in the red grape berry of "Alicante Bouschet" varies with the histological distribution of anthocyanins and their chemical composition. Planta 236:1037–1051. https://doi.org/10.1007/s00425-012-1658-2

Fasoli M, Dell'Anna R, Dal Santo S, Balestrini R, Sanson A, Pezzotti M, Monti F, Zenoni S (2016) Pectins, hemicelluloses and celluloses show specific dynamics in the internal and external surfaces of grape berry skin during ripening. Plant Cell Physiol 57:1332–1349. https://doi.org/10.1093/pcp/pcw080

Fernandez L, Chaïb J, Martinez-Zapater J-M, Thomas MR, Torregrosa L (2013) Mis-expression of a *PISTILLATA*- like MADS box gene prevents fruit development in grapevine. Plant J 73:918–928. https://doi.org/10.1111/tpj.12083

Fernandez L, Doligez A, Lopez G, Thomas MR, Bouquet A, Torregrosa L (2006a) Somatic chimerism, genetic inheritance, and mapping of the *fleshless berry* ( *flb* ) mutation in grapevine (*Vitis vinifera* L.). Genome 49:721–728. https://doi.org/10.1139/g06-034

Fernandez L, Romieu C, Moing A, Bouquet A, Maucourt M, Thomas MR, Torregrosa L (2006b) The grapevine fleshless berry mutation. A unique genotype to investigate differences between fleshy and nonfleshy fruit. Plant Physiol 140:537–547. https://doi.org/10.1104/pp.105.067488

Ferrandino A, Lovisolo C (2014) Abiotic stress effects on grapevine (*Vitis vinifera* L.): focus on abscisic acid-mediated consequences on secondary metabolism and berry quality. Environ Exp Bot 103:138–147. https://doi.org/10.1016/J.ENVEXPBOT.2013.10.012

Fillion L, Ageorges A, Picaud S et al (1999) Cloning and expression of a hexose transporter gene expressed during the ripening of grape berry. Plant Physiol 120:1083–1094. https://doi.org/10.1104/pp.120.4.1083

Finkelstein RR, Gibson SI (2002) ABA and sugar interactions regulating development: cross-talk or voices in a crowd? Curr Opin Plant Biol 5:26–32

Fortes A, Teixeira R, Agudelo-Romero P (2015) Complex interplay of hormonal signals during grape berry ripening. Molecules 20:9326–9343. https://doi.org/10.3390/molecules20059326

Fortes AM, Agudelo-Romero P, Silva MS, Ali K, Sousa L, Maltese F, Choi YH, Grimplet J, Martinez-Zapater JM, Verpoorte R (2011) Transcript and metabolite analysis in Trincadeira cultivar reveals novel information regarding the dynamics of grape ripening. BMC Plant Biol 11:149–183

Fournier-Level A, Hugueney P, Verriès C et al (2011) Genetic mechanisms underlying the methylation level of anthocyanins in grape (*Vitis vinifera* L.). BMC Plant Biol 11:179. https://doi.org/10.1186/1471-2229-11-179

Francisco RM, Regalado A, Ageorges A, Burla BJ, Bassin B, Eisenach C, Zarrouk O, Vialet S, Marlin T, Chaves MM, Martinoia E, Nagy R (2013) ABCC1, an ATP binding cassette protein from grape berry, transports anthocyanidin 3-*O*-glucosides. Plant Cell 25:1840–1854. https://doi.org/10.1105/tpc.112.102152

Gambetta GA, Matthews MA, Shaghasi TH, McElrone AJ, Castellarin SD (2010) Sugar and abscisic acid signaling orthologs are activated at the

onset of ripening in grape. Planta 232:219–234. https://doi.org/10.1007/s00425-010-1165-2

Gao C, Ju Z, Cao D, Zhai B, Qin G, Zhu H, Fu D, Luo Y, Zhu B (2015) MicroRNA profiling analysis throughout tomato fruit development and ripening reveals potential regulatory role of RIN on microRNAs accumulation. Plant Biotechnol J 13:370–382. https://doi.org/10.1111/pbi.12297

Gapper NE, McQuinn RP, Giovannoni JJ (2013) Molecular and genetic regulation of fruit ripening. Plant Mol Biol 82:575–591. https://doi.org/10.1007/s11103-013-0050-3

Gatto P, Vrhovsek U, Muth J, Segala C, Romualdi C, Fontana P, Pruefer D, Stefanini M, Moser C, Mattivi F, Velasco R (2008) Ripening and genotype control stilbene accumulation in healthy grapes. J Agric Food Chem 56:11773–11785. https://doi.org/10.1021/jf8017707

Giacomelli L, Rota-Stabelli O, Masuero D, Acheampong AK, Moretto M, Caputi L, Vrhovsek U, Moser C (2013) Gibberellin metabolism in *Vitis vinifera* L. during bloom and fruit-set: functional characterization and evolution of grapevine gibberellin oxidases. J Exp Bot 64:4403–4419. https://doi.org/10.1093/jxb/ert251

Givan CV (1999) Evolving concepts in plant glcolysis: two centuries of progress. Biol Rev 74:277–309

Gomez C, Terrier N, Torregrosa L, Vialet S, Fournier-Level A, Verriès C, Souquet JM, Mazauric JP, Klein M, Cheynier V, Ageorges A (2009) Grapevine MATE-type proteins act as vacuolar H + -dependent acylated anthocyanin transporters. Plant Physiol 150:402–415. https://doi.org/10.1104/pp.109.135624

Gouthu S, Deluc LG (2015) Timing of ripening initiation in grape berries and its relationship to seed content and pericarp auxin levels. BMC Plant Biol 15:46. https://doi.org/10.1186/s12870-015-0440-6

Grimplet J, Deluc L, Tillett R, Wheatley M, Schlauch K, Cramer G, Cushman J (2007) Tissue-specific mRNA expression profiling in grape berry tissues. BMC Genom 8:187

Guillaumie S, Ilg A, Rety S, Brette M, Trossat-Magnin C, Decroocq S, Leon C, Keime C, Ye T, Baltenweck-Guyot R, Claudel P, Bordenave L, Vanbrabant S, Duchene E, Delrot S, Darriet P, Hugueney P, Gomes E (2013) Genetic analysis of the biosynthesis of 2-methoxy-3-isobutylpyrazine, a major grape-derived aroma compound impacting wine quality. Plant Physiol 162:604–615. https://doi.org/10.1104/pp.113.218313

Hardy PJ (1968) Metabolism of sugars and organic acids in immature grape berries. Plant Physiol 43:224–228. https://doi.org/10.1104/pp.43.2.224

Harris ZN, Kovacs LG, Londo JP (2017) RNA-seq-based genome annotation and identification of long-noncoding RNAs in the grapevine cultivar 'Riesling'. BMC Genom 18:937. https://doi.org/10.1186/s12864-017-4346-6

Hawker JS, Ruffner HP, Walker RR (1976) The sucrose content of some Australian grapes. Am J Enol Vitic 27:125–129

Hayashi K (2012) The interaction and integration of auxin signaling components. Plant Cell Physiol 53:965–975. https://doi.org/10.1093/pcp/pcs035

Hayes MA, Davies C, Dry IB (2007) Isolation, functional characterization, and expression analysis of grapevine (*Vitis vinifera* L.) hexose transporters: differential roles in sink and source tissues. J Exp Bot 58:1985–1997. https://doi.org/10.1093/jxb/erm061

Herrera JC, Castellarin SD (2016) Preveraison water deficit accelerates berry color change in merlot grapevines. Am J Enol Vitic 67:356–360. https://doi.org/10.5344/ajev.2016.15083

Hichri I, Heppel SC, Pillet J, Léon C, Czemmel S, Delrot S, Lauvergeat V, Bogs J (2010) The basic helix-loop-helix transcription factor MYC1 is involved in the regulation of the flavonoid biosynthesis pathway in grapevine. Mol Plant 3:509–523. https://doi.org/10.1093/mp/ssp118

Hilt C, Bessis R (2003) Abscission of grapevine fruitlets in relation to ethylene biosynthesis. Vitis 42:1–3

Höll J, Vannozzi A, Czemmel S, D'Onofrio C, Walker AR, Rausch T, Lucchin M, Boss PK, Dry IB, Bogs J (2013) The R2R3-MYB transcription factors MYB14 and MYB15 regulate stilbene biosynthesis in *Vitis vinifera*. Plant Cell 25:4135–4149. https://doi.org/10.1105/tpc.113.117127

Huang Y-F, Doligez A, Fournier-Level A et al (2012) Dissecting genetic architecture of grape proanthocyanidin composition through quantitative trait locus mapping. BMC Plant Biol 12:30. https://doi.org/10.1186/1471-2229-12-30

Huang Y-F, Doligez A, Fournier-Level A, Le Cunff L, Bertrand Y, Canaguier A, Morel C, Miralles V, Veran F, Souquet J-M, Cheynier V, Terrier N, This P (2014) A negative MYB regulator of proanthocyanidin accumulation, identified through expression quantitative locus mapping in the grape berry. New Phytol 201:795–809. https://doi.org/10.1111/nph.12557

Ilc T, Halter D, Miesch L, Lauvoisard F, Kriegshauser L, Ilg A, Baltenweck R, Hugueney P, Werck-Reichhart D, Duchêne E, Navrot N (2017) A grapevine cytochrome P450 generates the precursor of wine lactone, a key odorant in wine. New Phytol 213:264–274. https://doi.org/10.1111/nph.14139

Inaba A, Ishida M, Sobajima Y (1976) Changes in endogenous hormone concentrations during berry development in relation to the ripening of delaware grapes. J Jpn Soc Hortic Sci 45:245–252. https://doi.org/10.2503/jjshs.45.245

Jia H, Zhang C, Pervaiz T, Zhao P, Liu Z, Wang B, Wang C, Zhang L, Fang J, Qian J (2016) Jasmonic acid involves in grape fruit ripening and resistant against *Botrytis cinerea*. Funct Integr Genomics 16:79–94. https://doi.org/10.1007/s10142-015-0468-6

Jin J, Tian F, Yang D-C, Meng Y-Q, Kong L, Luo J, Gao G (2016) PlantTFDB 4.0: toward a central hub for transcription factors and regulatory interactions in plants. Nucleic Acids Res 45:gkw982. https://doi.org/10.1093/nar/gkw982

Kalua CM, Boss PK (2009) Evolution of volatile compounds during the development of cabernet sauvignon grapes (*Vitis vinifera* L.). J Agric Food Chem 57:3818–3830. https://doi.org/10.1021/jf803471n

Karlova R, Chapman N, David K, Angenent GC, Seymour GB, De Maagd RA (2014) Transcriptional control of fleshy fruit development and ripening. J Exp Bot 65:4527–4541. https://doi.org/10.1093/jxb/eru316

Keller M, Smith JP, Bondada BR (2006) Ripening grape berries remain hydraulically connected to the shoot. J Exp Bot 57:2577–2587. https://doi.org/10.1093/jxb/erl020

Khater F, Fournand D, Vialet S, Meudec E, Cheynier V, Terrier N (2012) Identification and functional characterization of cDNAs coding for hydroxybenzoate/hydroxycinnamate glucosyltransferases co-expressed with genes related to proanthocyanidin biosynthesis. J Exp Bot 63:1201–1214. https://doi.org/10.1093/jxb/err340

Kliewer WM (1966) Sugars and organic acids of *Vitis vinifera*. Plant Physiol 41:923–931

Kliewer WM, Howarth L, Omori M (1967) Concentrations of tartaric acid and malic acids and their salts in *Vitis vinifera* grapes. Am J Enol Vitic 18:42–54

Knipfer T, Fei J, Gambetta GA, McElrone AJ, Shackel KA, Matthews MA (2015) Water transport properties of the grape pedicel during fruit development: insights into xylem anatomy and function using microtomography. Plant Physiol 168:1590–1602. https://doi.org/10.1104/pp.15.00031

Kobayashi H, Takase H, Suzuki Y, Tanzawa F, Takata R, Fujita K, Kohno M, Mochizuki M, Suzuki S, Konno T (2011) Environmental stress enhances biosynthesis of flavor precursors, *S*-3-(hexan-1-ol)-glutathione and *S*-3-(hexan-1-ol)-L-cysteine, in grapevine through glutathione *S*-transferase activation. J Exp Bot 62:1325–1336. https://doi.org/10.1093/jxb/erq376

Kondo S, Fukuda K (2001) Changes of jasmonates in grape berries and their possible roles in fruit development. Sci Hortic (Amsterdam) 91:275–288. https://doi.org/10.1016/S0304-4238(01)00271-0

Koyama K, Numata M, Nakajima I, Goto-Yamamoto N, Matsumura H, Tanaka N (2014) Functional characterization of a new grapevine MYB transcription factor and regulation of proanthocyanidin biosynthesis in grapes. J Exp Bot 65:4433–4449. https://doi.org/10.1093/jxb/eru213

Koyama K, Sadamatsu K, Goto-Yamamoto N (2010) Abscisic acid stimulated ripening and gene expression in berry skins of the Cabernet Sauvignon grape. Funct Integr Genomics 10:367–381. https://doi.org/10.1007/s10142-009-0145-8

Kuhn N, Guan L, Dai ZW, Wu B-H, Lauvergeat V, Gomès E, Li S-H, Godoy F, Arce-Johnson P, Delrot S (2013) Berry ripening: recently heard through the grapevine. J Exp Bot 65:4543–4559. https://doi.org/10.1093/jxb/ert395

Lalonde S, Wipf D, Frommer WB (2004) Transport mechanisms for organic forms of carbon and nitrogen between source and sink. Ann Rev Plant Biol 55:341–372. https://doi.org/10.1146/annurev.arplant.55.031903.141758

Lashbrooke JG, Young PR, Dockrall SJ, Vasanth K, Vivier MA (2013) Functional characterisation of three members of the *Vitis vinifera* L. carotenoid cleavage dioxygenase gene family. BMC Plant Biol 13:156. https://doi.org/10.1186/1471-2229-13-156

Lauvergeat V, Decendit A, Richard T, Deluc L (2006) Characterization of a grapevine R2R3-MYB transcription factor that regulates the phenylpropanoid pathway. Plant Physiol 140:499–511. https://doi.org/10.1104/pp.105.067231.ered

Lecourieux F, Kappel C, Lecourieux D, Serrano A, Torres E, Arce-Johnson P, Delrot S (2014) An update on sugar transport and signalling in grapevine. J Exp Bot 65:821–832. https://doi.org/10.1093/jxb/ert394

Leida C, Rì AD, Costa LD, Gómez MD, Pompili V, Sonego P, Engelen K, Masuero D, Ríos G, Moser C (2016) Insights into the Role of the Berry-Specific Ethylene Responsive Factor VviERF045. Frontiers in Plant Science 7:1793. https://doi.org/10.3389/fpls.2016.01793

Leng P, Yuan B, Guo Y (2014) The role of abscisic acid in fruit ripening and responses to abiotic stress. J Exp Bot 65:4577–4588

León P, Sheen J (2003) Sugar and hormone connections. Trends Plant Sci 8:110–116. https://doi.org/10.1016/S1360-1385(03)00011-6

Li S-B, Xie Z-Z, Hu C-G, Zhang J-Z (2016) A review of auxin response factors (ARFs) in plants. Front Plant Sci 7:47. https://doi.org/10.3389/fpls.2016.00047

Li X-Y, Wen Y-Q, Meng N, Qian X, Pan Q-H (2017) Monoterpenyl glycosyltransferases differentially contribute to production of monoterpenyl glycosides in two aromatic *Vitis vinifera* varieties. Front Plant Sci 8:1–13. https://doi.org/10.3389/fpls.2017.01226

Lim SD, Yim WC, Liu D, Hu R, Yang X, Cushman JC (2018) A *Vitis vinifera* basic helix-loop-helix transcription factor enhances plant cell size, vegetative biomass and reproductive yield. Plant Biotechnol J 1:15. https://doi.org/10.1111/pbi.12898

Liu H-F, Wu B-H, Fan P-G, Li S-H, Li L-S (2006) Sugar and acid concentrations in 98 grape cultivars analyzed by principal component analysis. J Sci Food Agric 86:1526–1536. https://doi.org/10.1002/jsfa.2541

Liu J, Wang H, Chua N-H (2015) Long noncoding RNA transcriptome of plants. Plant Biotechnol J 13:319–328. https://doi.org/10.1111/pbi.12336

Loyola R, Herrera D, Mas A, Wong DCJ, Höll J, Cavallini E, Amato A, Azuma A, Ziegler T, Aquea F, Castellarin SD, Bogs J, Tornielli GB, Peña-Neira A, Czemmel S, Alcalde JA, Matus JT, Arce-Johnson P (2016) The photomorphogenic factors UV-B RECEPTOR 1, ELONGATED HYPOCOTYL 5, and

HY5 HOMOLOGUE are part of the UV-B signalling pathway in grapevine and mediate flavonol accumulation in response to the environment. J Exp Bot 67:5429–5445. https://doi.org/10.1093/jxb/erw307

Luan LY, Zhang ZW, Xi ZM, Huo SS, Ma LN (2013) Brassinosteroids regulate anthocyanin biosynthesis in the ripening of grape berries. S Afr J Enol Vitic 34:196–203

Malacarne G, Costantini L, Coller E, Battilana J, Velasco R, Vrhovsek U, Grando MS, Moser C (2015) Regulation of flavonol content and composition in (Syrah × Pinot Noir) mature grapes: integration of transcriptional profiling and metabolic quantitative trait locus analyses. J Exp Bot 66:4441–4453. https://doi.org/10.1093/jxb/erv243

Manning K, Davies C, Bowen HC, White PJ (2001) Functional characterization of two ripening-related sucrose transporters from grape berries. Ann Bot 87:125–129. https://doi.org/10.1006/anbo.2000.1316

Martin DM, Aubourg S, Schouwey MB, Daviet L, Schalk M, Toub O, Lund ST, Bohlmann J (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 Biol 10:226. https://doi.org/10.1186/1471-2229-10-226

Massonnet M, Fasoli M, Tornielli GB, Altieri M, Sandri M, Zuccolotto P, Paci P, Gardiman M, Zenoni S, Pezzotti M (2017) Ripening transcriptomic program in red and white grapevine varieties correlates with berry skin anthocyanin accumulation. Plant Physiol 174:2376–2396. https://doi.org/10.1104/pp.17.00311

Matarese F, Cuzzola A, Scalabrelli G, D'Onofrio C (2014) Expression of terpene synthase genes associated with the formation of volatiles in different organs of *Vitis vinifera*. Phytochemistry 105:12–24. https://doi.org/10.1016/j.phytochem.2014.06.007

Matarese F, Scalabrelli G, Onofrio CD (2013) Analysis of the expression of terpene synthase genes in relation to aroma content in *Vitis vinifera* L. flowers, developing berries and other tissues and implications for viticultural practices. Funct Plant Biol 40:552–565

Matthews MA, Thomas TR, Shackel KA (2009) Fruit ripening in *Vitis vinifera* L.: possible relation of veraison to turgor and berry softening. Aust J Grape Wine Res 15:278–283. https://doi.org/10.1111/j.1755-0238.2009.00060.x

Matthews MA, Shackel KA (2005) Growth and water transport in fleshy fruit. In: Holbrook NM, Zwieniecki MA (eds) Vascular transport in plants. Elsevier, pp 181–197

Mattivi F, Caputi L, Carlin S, Lanza T, Minozzi M, Nanni D, Valenti L, Vrhovsek U (2011) Effective analysis of rotundone at below-threshold levels in red and white wines using solid-phase microextraction gas chromatography/tandem mass spectrometry. Rapid Commun Mass Spectrom 25:483–488. https://doi.org/10.1002/rcm.4881

Mattivi F, Vrhovsek U, Masuero D, Trainotti D (2009) Differences in the amount and structure of extractable skin and seed tannins amongst red grape varieties. Aust J Grape Wine Res 15:27–35. https://doi.org/10.1111/j.1755-0238.2008.00027.x

McAtee P, Karim S, Schaffer R, David K (2013) A dynamic interplay between phytohormones is required for fruit development, maturation, and ripening. Front Plant Sci 4:79. https://doi.org/10.3389/fpls.2013.00079

Mellway RD, Lund ST (2013) Interaction analysis of grapevine MIKCc-type MADS transcription factors and heterologous expression of putative véraison regulators in tomato. J Plant Physiol 170:1424–1433. https://doi.org/10.1016/j.jplph.2013.05.010

Muñoz-Espinoza C, Di Genova A, Correa J, Silva R, Maass A, González-Agüero M, Orellana A, Hinrichsen P (2016) Transcriptome profiling of grapevine seedless segregants during berry development reveals candidate genes associated with berry weight. BMC Plant Biol 16:104. https://doi.org/10.1186/s12870-016-0789-1

Muñoz-Robredo P, Gudenschwager O, Chervin C, Campos-Vargas R, González-Agüero M, Defilippi BG (2013) Study on differential expression of 1-aminocyclopropane-1-carboxylic acid oxidase genes in table grape cv. Thompson Seedless. Postharvest Biol Technol 76:163–169. https://doi.org/10.1016/J.POSTHARVBIO.2012.10.006

Nicolas P, Lecourieux D, Gomès E, Delrot S, Lecourieux F (2013) The grape berry-specific basic helix-loop-helix transcription factor VvCEB1 affects cell size. J Exp Bot 64:991–1003. https://doi.org/10.1093/jxb/ers374

Nicolas P, Lecourieux D, Kappel C, Cluzet S, Cramer G, Delrot S, Lecourieux F (2014) The basic leucine zipper transcription factor ABSCISIC ACID RESPONSE ELEMENT-BINDING FACTOR2 is an important transcriptional regulator of abscisic acid-dependent grape berry ripening processes. Plant Physiol 164:365–383. https://doi.org/10.1104/pp.113.231977

Normanly J, Slovin JP, Cohen JD (2010) Auxin biosynthesis and metabolism. In: Davies PJ (ed) Plant hormones. Springer, Dordrecht, pp 36–62

Nunan KJ, Davies C, Robinson SP, Fincher GB (2001) Expression patterns of cell wall-modifying enzymes during grape berry development. Planta 214:257–264

Ojeda H, Deloire A, Carbonneau A, Ageorges A, Romieu C (1999) Berry development of grapevines: Relations between the growth of berries and their DNA content indicate cell multiplication and enlargement. Vitis 38:145–150

Ono E, Homma Y, Horikawa M, Kunikane-Doi S, Imai H, Takahashi S, Kawai Y, Ishiguro M, Fukui Y, Nakayama T (2010) Functional differentiation of the glycosyltransferases that contribute to the chemical diversity of bioactive flavonol glycosides in grapevines (Vitis vinifera). Plant Cell 22:2856–2871. https://doi.org/10.1105/tpc.110.074625

Owen SJ, Lafond MD, Bowen P, Bogdanoff C, Usher K, Abrams SR (2009) Profiles of abscisic acid and its

catabolites in developing Merlot grape (*Vitis vinifera*) berries. Am J Enol Vitic 60:277–284

Palumbo MC, Zenoni S, Fasoli M, Massonnet M, Farina L, Castiglione F, Pezzotti M, Paci P (2014) Integrated network analysis identifies fight-club nodes as a class of hubs encompassing key putative switch genes that induce major transcriptome reprogramming during grapevine development. Plant Cell 26:4617–4635. https://doi.org/10.1105/tpc.114.133710

Pan Q-H, Li M-J, Peng C-C, Zhang N, Zou X, Zou K-Q, Wang X-L, Yu X-C, Wang X-F, Zhang D-P (2005) Abscisic acid activates acid invertases in developing grape berry. Physiol Plant 125:157–170. https://doi.org/10.1111/j.1399-3054.2005.00552.x

Pauwels L, Inzé D, Goossens A (2009) Jasmonate-inducible gene: what does it mean? Trends Plant Sci 14:87–91. https://doi.org/10.1016/J.TPLANTS.2008.11.005

Peña-Gallego A, Hernández-Orte P, Cacho J, Ferreira V (2012) S-Cysteinylated and S-glutathionylated thiol precursors in grapes. A review. Food Chem 131:1–13. https://doi.org/10.1016/j.foodchem.2011.07.079

Pérez-Díaz R, Ryngajllo M, Pérez-Díaz J, Peña-Cortés H, Casaretto JA, González-Villanueva E, Ruiz-Lara S (2014) VvMATE1 and VvMATE2 encode putative proanthocyanidin transporters expressed during berry development in *Vitis vinifera* L. Plant Cell Rep 33:1147–1159. https://doi.org/10.1007/s00299-014-1604-9

Pérez FJ, Viani C, Retamales J (2000) Bioactive gibberellins in seeded and seedless grapes: identification and changes in content during berry development. Am J Enol Vitic 51:315–318

Pilati S, Bagagli G, Sonego P, Moretto M, Brazzale D, Castorina G, Simoni L, Tonelli C, Guella G, Engelen K, Galbiati M, Moser C (2017) Abscisic acid is a major regulator of grape berry ripening onset: new insights into ABA signaling network. Front Plant Sci 8:1093. https://doi.org/10.3389/fpls.2017.01093

Podolyan A, White J, Jordan B, Winefield C (2010) Identification of the lipoxygenase gene family from *Vitis vinifera* and biochemical characterisation of two 13-lipoxygenases expressed in grape berries of Sauvignon Blanc. Funct Plant Biol 37:767–784

Portu J, López R, Santamaría P, Garde-Cerdán T (2018) Methyl jasmonate treatment to increase grape and wine phenolic content in Tempranillo and Graciano varieties during two growing seasons. Sci Hortic (Amsterdam) 240:378–386. https://doi.org/10.1016/J.SCIENTA.2018.06.019

Rattanakon S, Ghan R, Gambetta GA, Deluc LG, Schlauch KA, Cramer GR (2016) Abscisic acid transcriptomic signaling varies with grapevine organ. BMC Plant Biol 16:72. https://doi.org/10.1186/s12870-016-0763-y

Regalado A, Pierri CL, Bitetto M, Laera VL, Pimentel C, Francisco R, Passarinho J, Chaves MM, Agrimi G (2013) Characterization of mitochondrial dicarboxylate/tricarboxylate transporters from grape berries. Planta 237:693–703. https://doi.org/10.1007/s00425-012-1786-8

Rinaldo A, Cavallini E, Jia Y, Moss SMA, McDavid DAJ, Hooper LC, Robinson SP, Tornielli GB, Zenoni S, Ford CM, Boss PK, Walker AR (2015) A grapevine anthocyanin acyltransferase, transcriptionally regulated by VvMYBA, can produce most acylated anthocyanins present in grape skins. Plant Physiol 169:1897–1916. https://doi.org/10.1104/pp.15.01255

Robinson AL, Boss PK, Solomon PS, Trengove RD, Heymann H, Ebeler SE (2014a) Origins of grape and wine aroma. Part 1". Chemical components and viticultural impacts. Am J Enol Vitic 65:1–24. https://doi.org/10.5344/ajev.2013.12070

Robinson AL, Boss PK, Solomon PS, Trengove RD, Heymann H, Ebeler SE (2014b) "Origins of grape and wine aroma. Part 2". Chemical and sensory analysis. Am J Enol Vitic 65:25–42. https://doi.org/10.5344/ajev.2013.13106

Rodríguez-Concepción M, Boronat A (2002) Elucidation of the methylerythritol phosphate pathway for isoprenoid biosynthesis in bacteria and plastids. a metabolic milestone achieved through genomics. Plant Physiol 130:1079–1089. https://doi.org/10.1104/pp.007138

Savoi S, Wong DCJ, Arapitsas P, Miculan M, Bucchetti B, Peterlunger E, Fait A, Mattivi F, Castellarin SD (2016) Transcriptome and metabolite profiling reveals that prolonged drought modulates the phenylpropanoid and terpenoid pathway in white grapes (*Vitis vinifera* L.). BMC Plant Biol 16:67. https://doi.org/10.1186/s12870-016-0760-1

Savoi S, Wong DCJ, Degu A, Herrera JC, Bucchetti B, Peterlunger E, Fait A, Mattivi F, Castellarin SD (2017) Multi-omics and integrated network analyses reveal new insights into the systems relationships between metabolites, structural genes, and transcriptional regulators in developing grape berries (*Vitis vinifera* L.) exposed to water deficit. Front Plant Sci 8:1–19. https://doi.org/10.3389/fpls.2017.01124

Schlosser J, Olsson N, Weis M, Reid K, Peng F, Lund S, Bowen P (2008) Cellular expansion and gene expression in the developing grape (*Vitis vinifera* L.). Protoplasma 232:255–265. https://doi.org/10.1007/s00709-008-0280-9

Serrano A, Espinoza C, Armijo G, Inostroza-Blancheteau C, Poblete E, Meyer-Regueiro C, Arce A, Parada F, Santibáñez C, Arce-Johnson P (2017) Omics approaches for understanding grapevine berry development: regulatory networks associated with endogenous processes and environmental responses. Front Plant Sci 8:1486. https://doi.org/10.3389/fpls.2017.01486

Shangguan L, Sun X, Zhang C, Mu Q, Leng X, Fang J (2015) Genome identification and analysis of genes encoding the key enzymes involved in organic acid biosynthesis pathway in apple, grape, and sweet orange. Sci Hortic (Amsterdam) 185:22–28. https://doi.org/10.1016/J.SCIENTA.2015.01.012

Shiraishi M, Fujishima H, Chijiwa H (2010) Evaluation of table grape genetic resources for sugar, organic acid, and amino acid composition of berries. Euphytica 174:1–13. https://doi.org/10.1007/s10681-009-0084-4

Siebert TE, Barter SR, de Barros Lopes MA, Herderich MJ, Francis IL (2018) Investigation of 'stone fruit' aroma in Chardonnay, Viognier and botrytis Semillon wines. Food Chem 256:286–296. https://doi.org/10.1016/j.foodchem.2018.02.115

Siebert TE, Wood C, Elsey GM, Pollnitz AP (2008) Determination of rotundone, the pepper aroma impact compound, in grapes and wine. J Agric Food Chem 56:3745–3748. https://doi.org/10.1021/jf800184t

Smeekens S (2000) Sugar-induced signal transduction in plants. Ann Rev Plant Physiol Plant Mol Biol 51:49–81. https://doi.org/10.1146/annurev.arplant.51.1.49

Smeekens S, Ma J, Hanson J, Rolland F (2010) Sugar signals and molecular networks controlling plant growth. Curr Opin Plant Biol 13:273–278. https://doi.org/10.1016/j.pbi.2009.12.002

Sun L, Sun Y, Zhang M, Wang L, Ren J, Cui M, Wang Y, Ji K, Li P, Li Q, Chen P, Dai S, Duan C, Wu Y, Leng P (2012) Suppression of 9-cis-epoxycarotenoid dioxygenase, which encodes a key enzyme in abscisic acid biosynthesis, alters fruit texture in transgenic tomato. Plant Physiol 158:283–298. https://doi.org/10.1104/pp.111.186866

Sun L, Zhang M, Ren J, Qi J, Zhang G, Leng P (2010) Reciprocity between abscisic acid and ethylene at the onset of berry ripening and after harvest. BMC Plant Biol 10:257–268

Sweetman C, Deluc LG, Cramer GR, Ford CM, Soole KL (2009) Regulation of malate metabolism in grape berry and other developing fruits. Phytochemistry 70:1329–1344. https://doi.org/10.1016/j.phytochem.2009.08.006

Sweetman C, Wong DC, Ford CM, Drew DP (2012) Transcriptome analysis at four developmental stages of grape berry (*Vitis vinifera* cv. Shiraz) provides insights into regulated and coordinated gene expression. BMC Genom 13:691. https://doi.org/10.1186/1471-2164-13-691

Symons GM, Davies C, Shavrukov Y, Dry IB, Reid JB, Thomas MR (2006) Grapes on steroids. Brassinosteroids are involved in grape berry ripening. Plant Physiol 140:150–158. https://doi.org/10.1104/pp.105.070706

Takase H, Sasaki K, Shinmori H, Shinohara A, Mochizuki C, Kobayashi H, Ikoma G, Saito H, Matsuo H, Suzuki S, Takata R (2015) Cytochrome P450 CYP71BE5 in grapevine (*Vitis vinifera*) catalyzes the formation of the spicy aroma compound (−)-rotundone. J Exp Bot 67:787–798. https://doi.org/10.1093/jxb/erv496

Tang W, Zheng Y, Dong J, Yu J, Yue J, Liu F, Guo X, Huang S, Wisniewski M, Sun J, Niu X, Ding J, Liu J, Fei Z, Liu Y (2016) Comprehensive transcriptome profiling reveals long noncoding rna expression and alternative splicing regulation during fruit development and ripening in kiwifruit (*Actinidia chinensis*). Front Plant Sci 7:335. https://doi.org/10.3389/fpls.2016.00335

Tanner W, Caspari T (1996) MEMBRANE TRANSPORT CARRIERS. Ann Rev Plant Physiol Plant Mol Biol 47:595–626. https://doi.org/10.1146/annurev.arplant.47.1.595

Teixeira A, Eiras-Dias J, Castellarin SD, Gerós H (2013) Berry phenolics of grapevine under challenging environments. Int J Mol Sci 14:18711–18739. https://doi.org/10.3390/ijms140918711

Terrier N, Torregrosa L, Ageorges A, Vialet S, Verriès C, Cheynier V, Romieu C (2009) Ectopic expression of VvMybPA2 promotes proanthocyanidin biosynthesis in grapevine and suggests additional targets in the pathway. Plant Physiol 149:1028–1041. https://doi.org/10.1104/pp.108.131862

Thomas TR, Matthews MA, Shackel KA (2006) Direct in situ measurement of cell turgor in grape (*Vitis vinifera* L.) berries during development and in response to plant water deficits. Plant, Cell Environ 29:993–1001. https://doi.org/10.1111/j.1365-3040.2006.01496.x

Tyerman SD, Chaves MM, Barrieu F (2012) Water relations of the grape berry and aquaporins. In: Gerós H, Chaves MM, Delrot S (eds) The biochemistry of the grape berry. Bentham Science, Bussum, pp 3–22

Vannozzi A, Chern D, Wong J, Ho J, Hmmam I, Bogs J, Ziegler T, Dry I, Barcaccia G, Lucchin M (2018) Combinatorial regulation of stilbene synthase genes by WRKY and MYB transcription factors in grapevine (*Vitis vinifera* L.). Plant Cell Physiol 59:1043–1059. https://doi.org/10.1093/pcp/pcy045

Vannozzi A, Dry IB, Fasoli M, Zenoni S, Lucchin M (2012) Genome-wide analysis of the grapevine stilbene synthase multigenic family: genomic organization and expression profiles upon biotic and abiotic stresses. BMC Plant Biol 12:130. https://doi.org/10.1186/1471-2229-12-130

Vitulo N, Forcato C, Carpinelli E, Telatin A, Campagna D, D'Angelo M, Zimbello R, Corso M, Vannozzi A, Bonghi C, Lucchin M, Valle G (2014) A deep survey of alternative splicing in grape reveals changes in the splicing machinery related to tissue, stress condition and genotype. BMC Plant Biol 14:99. https://doi.org/10.1186/1471-2229-14-99

Wada H, Matthews MA, Shackel KA (2009) Seasonal pattern of apoplastic solute accumulation and loss of cell turgor during ripening of *Vitis vinifera* fruit under field conditions. J Exp Bot 60:1773–1781. https://doi.org/10.1093/jxb/erp050

Wada H, Shackel KA, Matthews MA (2008) Fruit ripening in *Vitis vinifera*: apoplastic solute accumulation accounts for pre-veraison turgor loss in berries. Planta 227:1351–1361. https://doi.org/10.1007/s00425-008-0707-3

Walker AR, Lee E, Bogs J, McDavid DAJ, Thomas MR, Robinson SP (2007) White grapes arose through the

mutation of two similar and adjacent regulatory genes. Plant Journal 49:772–785. https://doi.org/10.1111/j.1365-313X.2006.02997.x

Wan S, Li W, Zhu Y, Liu Z, Huang W, Zhan J (2014) Genome-wide identification, characterization and expression analysis of the auxin response factor gene family in *Vitis vinifera*. Plant Cell Rep 33:1365–1375. https://doi.org/10.1007/s00299-014-1622-7

Wang M, Zhao W, Gao L, Zhao L (2018) Genome-wide profiling of long non-coding RNAs from tomato and a comparison with mRNAs associated with the regulation of fruit ripening. BMC Plant Biol 18:75. https://doi.org/10.1186/s12870-018-1300-y

Wen Y-Q, Li J-M, Zhang Z-Z, Zhang Y-F, Pan Q-H (2010) Antibody preparation, gene expression and subcellular localization of L-idonate dehydrogenase in grape berry. Biosci Biotechnol Biochem 74:2413–2417. https://doi.org/10.1271/bbb.100448

Wheeler S, Loveys B, Ford C, Davies C (2009) The relationship between the expression of abscisic acid biosynthesis genes, accumulation of abscisic acid and the promotion of *Vitis vinifera* L. berry ripening by abscisic acid. Aust J Grape Wine Res 15:195–204

Won C, Shen X, Mashiguchi K, Zheng Z, Dai X, Cheng Y, Kasahara H, Kamiya Y, Chory J, Zhao Y (2011) Conversion of tryptophan to indole-3-acetic acid by TRYPTOPHAN AMINOTRANSFERASES OF ARABIDOPSIS and YUCCAs in arabidopsis. Proc Natl Acad Sci 108:18518–18523. https://doi.org/10.1073/pnas.1108436108

Wong DCJ, Lopez Gutierrez R, Dimopoulos N, Gambetta GA, Castellarin SD (2016a) Combined physiological, transcriptome, and cis-regulatory element analyses indicate that key aspects of ripening, metabolism, and transcriptional program in grapes (*Vitis vinifera* L.) are differentially modulated accordingly to fruit size. BMC Genom 17:416. https://doi.org/10.1186/s12864-016-2660-z

Wong DCJ, Matus JT (2017) Constructing integrated networks for identifying new secondary metabolic pathway regulators in grapevine: recent applications and future opportunities. Front Plant Sci 8:505. https://doi.org/10.3389/fpls.2017.00505

Wong DCJ, Schlechter R, Vannozzi A, Höll J, Hmmam I, Bogs J, Tornielli GB, Castellarin SD, Matus JT (2016b) A systems-oriented analysis of the grapevine R2R3-MYB transcription factor family uncovers new insights into the regulation of stilbene accumulation. DNA Res 23:451–466. https://doi.org/10.1093/dnares/dsw028

Wong DCJ, Zhang L, Merlin I, Castellarin SD, Gambetta GA (2018) Structure and transcriptional regulation of the major intrinsic protein gene family in grapevine. BMC Genom 19:248. https://doi.org/10.1186/s12864-018-4638-5

Wood C, Siebert TE, Parker M, Capone DL, Elsey GM, Pollnitz AP, Eggers M, Meier M, Vössing T, Widder S, Krammer G, Sefton MA, Herderich MJ (2008) From wine to pepper: rotundone, an obscure sesquiterpene, is a potent spicy aroma compound. J Agric Food Chem 56:3738–3744. https://doi.org/10.1021/jf800183k

Xin C, Liu W, Lin Q, Zhang X, Cui P, Li F, Zhang G, Pan L, Al-Amer A, Mei H, Al-Mssallem IS, Hu S, Al-Johi HA, Yu J (2015) Profiling microRNA expression during multi-staged date palm (*Phoenix dactylifera* L.) fruit development. Genomics 105:242–251. https://doi.org/10.1016/J.YGENO.2015.01.004

Xin H, Zhang J, Zhu W, Wang N, Fang P, Han Y, Ming R, Li S (2013) The effects of artificial selection on sugar metabolism and transporter genes in grape. Tree Genet Genomes 9:1343–1349. https://doi.org/10.1007/s11295-013-0643-7

Xu F, Xi Z, Zhang H, Zhang C, Zhang Z (2015) Brassinosteroids are involved in controlling sugar unloading in *Vitis vinifera* 'Cabernet Sauvignon' berries during véraison. Plant Physiol Biochem 94:197–208. https://doi.org/10.1016/j.plaphy.2015.06.005

Young P, Lashbrooke J, Alexandersson E, Jacobson D, Moser C, Velasco R, Vivier M (2012) The genes and enzymes of the carotenoid metabolic pathway in *Vitis vinifera* L. BMC Genom 13:243

Zeng S, Liu Y, Pan L, Hayward A, Wang Y (2015) Identification and characterization of miRNAs in ripening fruit of *Lycium barbarum* L. using high-throughput sequencing. Front Plant Sci 6:778. https://doi.org/10.3389/fpls.2015.00778

Zenoni S, Fasoli M, Guzzo F, Dal Santo S, Amato A, Anesi A, Commisso M, Herderich M, Ceoldo S, Avesani L, Pezzotti M, Tornielli GB (2016) Disclosing the molecular basis of the postharvest life of berry in different grapevine genotypes. Plant Physiol 172:1821–1843. https://doi.org/10.1104/pp.16.00865

Zhang G, Chen D, Zhang T, Duan A, Zhang J, He C (2018) Transcriptomic and functional analyses unveil the role of long non-coding RNAs in anthocyanin biosynthesis during sea buckthorn fruit ripening. DNA Res. https://doi.org/10.1093/dnares/dsy017

Zhang XY, Wang XL, Wang XF, Xia GH, Pan QH, Fan RC, Wu FQ, Yu XC, Zhang DP (2006) A shift of phloem unloading from symplasmic to apoplasmic pathway is involved in developmental onset of ripening in grape berry. Plant Physiol 142:220–232. https://doi.org/10.1104/pp.106.081430

Zhang YL, Meng QY, Zhu HL, Guo Y, Gao HY, Luo YB, Lu J (2007) Functional characterization of a LAHC sucrose transporter isolated from grape berries in yeast. Plant Growth Regul 54:71–79. https://doi.org/10.1007/s10725-007-9226-7

Zhang Y, Zhen L, Tan X et al (2014) The involvement of hexokinase in the coordinated regulation of glucose and gibberellin on cell wall invertase and sucrose synthesis in grape berry. Mol Biol Rep 41:7899–7910. https://doi.org/10.1007/s11033-014-3683-7

Zhao J, Pang Y, Dixon RA (2010) The mysteries of proanthocyanidin transport and polymerization. Plant Physiol 153:437–443. https://doi.org/10.1104/pp.110.155432

Zhao Y (2010) Auxin biosynthesis and its role in plant development. Ann Rev Plant Biol 61:49–64. https://doi.org/10.1146/annurev-arplant-042809-112308

Zhu BQ, Xu XQ, Wu YW, Duan CQ, Pan QH (2012) Isolation and characterization of two hydroperoxide lyase genes from grape berries. Mol Biol Rep 39:7443–7455. https://doi.org/10.1007/s11033-012-1577-0

Ziliotto F, Corso M, Rizzini FM, Rasori A, Botton A, Bonghi C (2012) Grape berry ripening delay induced by a pre-véraison NAA treatment is paralleled by a shift in the expression pattern of auxin- and ethylene-related genes. BMC Plant Biol 12:185. https://doi.org/10.1186/1471-2229-12-185