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Genetic regulation and the impact of omics in fruit ripening

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Abstract

Fruits are highly consumed products, especially due to their colorful appearance, sweet taste and healthy appeal. Some of these qualitative aspects such as size, color, acidity, flavor, sweetness and juiciness, which have great influence upon consumer, are dependent of specific physiological processes that occur during ripening. After a certain point, new physiological changes take place, which result in unsuitable characteristics for consumption and large losses for both farmers and consumers, the understanding of ripening regulation is of crucial economic importance. The new technologies that are currently becoming available are contributing tremendously for a better understanding of fruit growth and ripening. In this report, we focus on discussing the knowledge obtained mainly through the study of ripening mutants. We also point some future directions taking into account the impact of new technologies on the understanding of postharvest biology, also showing that phylogenetic analysis of ripening related loci from different species can reveal interesting differences between climacteric and non-climacteric fruits, helping to understand and to take control over ripening regulation.

Keywords: maturation; fruit development; gene regulation; phylogeny; ethylene.

Abbreviation list: ABA_abscisic acid; ALC_ALCATRAZ; AP2_APETALA2; ACC_1-aminocyclopropane-1-carboxylic acid; ACO_ACC oxidase; ACS_ACC synthase; bHLH_basic helix-loop-helix; CArG-box motif_ArG-box motif [C(C/T)(A/T)6(A/G)G]; *Cnr_colorless non-ripening*; CTR1_Constitutive Triple Response1; *CRC_CRABS CLAW*; ChIP_chromatin immunoprecipitation; DGE_digital gene expression; EF-Ts_translation elongation factor Ts; ERFAPETALA2 (AP2)/ETHYLENE RESPONSE FACTOR; *FUL_FRUITFULL*; GA_gibberellic acid; IND_INDEHISCENT; *KAN_KANADI*; MCP_1-methylcyclopropene; miRNA_micro RNA; NAC_NAM, ATAF1,2, CUC2; *nor_nonripening*; *NTT_NO TRANSMITTING TRACT*; *rin_ripening inhibitor*; RNA_ribonucleic acid; RNAseq_ribonucleic acid sequencing; SAM_S-adenosylmethionine; *SBP/SPL_SQUAMOSA PROMOTER-BINDING*; *STK_SEEDSTICK*; *SEP_SEPALLATA*; *SHP_ SHATTERPROOF*; sRNA_small RNA; TFs_transcription factors.

Introduction

Fruits are highly perishable products due to their cellular architecture and intense metabolic activity. Deterioration processes have caused farmers to lose up to 40% of the value of their fruits and vegetables before they reach the consumer (Kitinoja et al., 2011). Knowing that the application of appropriate technologies to maintain quality depends on the understanding of fruit structure, physiology and metabolic transformations (Pech et al., 2013), studies have been conducted in order to better understand floral organ and fruit development (Bao et al., 2010; Seymour et al., 2013), the role of hormones and related genes in maturation and ripening (Alexander and Grierson, 2002; Cara and Giovannoni, 2008; Kumar et al., 2014), as well as physiological disorders (Pegoraro et al., 2010) and epigenetic alterations associated with ripening (Manning et al., 2006; Zhong et al., 2013).

Molecular biology has contributed significantly to the elucidation of how fruit growth and development occurs (Gapper et al., 2013; McAtee et al., 2013; Osorio et al., 2013; Pech et al., 2013; Seymour et al., 2013; Gapper et al., 2014; Kumar et al., 2014). In this report, we focus on summarizing some of the most important topics in postharvest molecular biology, pointing future trends in this field.

From ovule fecundation to physiological maturation

Fruit development begins shortly after fertilization of the female gamete (egg) by the male gamete (pollen). From this point to maturation several genes are involved and among these genes are the transcription factors (TFs) which have great importance in modulating the expression of several genes and metabolic processes (O'Neill 1997; Giovannoni, 2001). Different steps take place between the onset of fruit development and its senescence (Figure 1). In the early stages of development, tissue growth is a phenomenon that occurs mainly by cell division. After this period growth occurs due to cell enlargement, when vacuoles appear. This expansion extends into maturation, a stage that leads the fruit to be capable of normal ripening of the plant. An upsurge in respiratory activity may be observed in some fruits at the end of this phase, the climacteric. The climacteric pattern is a phenomenon in which ethylene production and cellular respiration increase, with profound impacts on ripening. This has been used to distinguishing fruits, being divided in climacteric and non-climacteric, as discussed later. The climacteric phase extends to part of senescence and fruit decay. Fruit can also be classified as dry or fleshy. Fleshy are indehiscent fruits, while dry can be both dehiscent and indehiscent. The dehiscent fruits comprise mostly nuts, in which the dispersion of seeds occurs through fruit opening in the dehiscence zone. As an example of this kind of fruits we have *Arabidopsis thaliana* (L.) Heynh, which is the main model for studies in plant and fruit development (Roeder and Yanofsky, 2006; Koornneef and Meinke, 2010). Indehiscent fruits, conversely, do not form the dehiscence zone for seed dispersion and are usually characterized by their fleshiness and complex changes in biochemical composition, which comprise the late stage of cell expansion until complete maturation. After reaching the mature stage, these fruits attract herbivores, which are then in charge of seed dispersion. Tomato (*Solanun lycopersicum* L.) is a classical example of fleshy indehiscent fruit and the main model of climacteric maturation (Klee and Giovannoni, 2011; Pesaresi et al., 2014). Here however, to better describe known pathways involved in fruit development, Arabidopsis will be used most of the time. Plant hormones play key roles in tissue differentiation, becoming the target of many studies. Gibberellic acid (GA) has been reported as an important player in the events that occur just after fertilization, as it has the ability to promote a cascade of biochemical signals both in ovule and valves, playing a major role in fruit growth (van Huizen et al., 1995; Serrani et al., 2008; Dorcey et al., 2009; Ozga et al., 2009). This GA growth promotion occurs through the degradation of DELLA proteins (Fuentes et al., 2012). It is also known that in *della* mutants, fruits develop by parthenocarpy, another evidence of their role on the regulation of fruit growth (Dorcey et al., 2009). Another group of genes, the MADS-box family, are key transcriptional regulators for a variety of developmental processes. TFs containing MADS domains are present in the majority of eukaryotic organisms, but the number of MADS-box genes is much higher in land plants than in any other group of eukaryotes (Dreni and Kater, 2013). The *FRUITFULL* (*FUL*) MADS-box gene, for example, plays an important role in mediating the growth and differentiation of valves after fertilization in *Arabidopsis thaliana* and their homologues in tomato (*S. lycopersicum*) have recently been linked to fruit ripening (Gu et al., 1998; Shima et al., 2013; Fujisawa et al., 2014). *SHATTERPROOF* (*SHP*) genes have been reported as having a primary role in the stage of ripening and in dehiscence zone formation, while *SEEDSTICK* (*STK*) has been related to fruit development, formation of the cord, and seed dispersal in the abscission process (Pinyopich et al., 2003). Recently, a better understanding of the role of TFs such as the basic helix-loop-helix (bHLH) proteins INDEHISCENT (IND) and ALCATRAZ (ALC) on gibberellin synthesis and signaling in fruit opening has been achieved (Arnaud et al., 2010). A relation between *AtNAP*, a NAC family TF gene, and fruit senescence in Arabidopsis has been established (Kou et al., 2012) and new information on how the zinc-finger transcription factor *NO TRANSMITTING TRACT* (*NTT*) acts in replum development has been reported (Marsch-Martínez et al., 2014). Regarding color development, anthocyanin biosynthesis in leaves and fruits are also classical molecular events highly regulated at the transcriptional level. bHLH proteins and WD-repeat families of TFs are two important regulators involved in anthocyanin biosynthesis (Sompornpailin et al., 2002; Butelli et al., 2008). The overexpression of these TFs increased the hydrophilic antioxidant capacity and resulted in fruit with purple coloration in skin and flesh. In addition, this strategy increased fruit functional properties (Martin et al., 2013) and doubled its shelf-life, despite the increase in ethylene biosynthesis (Bassolino et al., 2013).

The ripening process

What we call maturation occurs before the complete development of the fruit which after harvested should survive from its own accumulated substrates. This is an intermediate step between the end of development and the beginning of senescence, a delayable but irreversible event. After fertilization, the fruit goes through a period of high cell division activity, followed by a rapid period of cell enlargement. During the final stages of growth and development, the fruit reaches full size and is physiologically mature. The ripening stage is the final stage of the maturation process when the fruit changes taste, texture, color of flesh, and flavor, getting ready to be consumed. Therefore, the maturation stage includes two steps: physiological maturation, when maximum seed vigor is reached, and ripening, when eating quality is the best (Biale, 1964; Seymour et al., 2013). The discovery of climacteric patterns began in 1925, when Kidd and West demonstrated that apple (*Malus* × *domestica* Borkh.), at a certain time, increases respiration and that it was associated with maturation and ripening. Later it was discovered that some, but not all fruits undergo the same increase in respiration. These differences in respiration led to the classification of fruits as climacteric and non-climacteric (Biale and Young, 1981). It is known today that climacteric fruits are those that can ripen not only on the plant but even after harvest, when harvested at pre-climacteric stage, as tomato (*S. lycopersicum*) and banana (*Musa* spp.), and reach senescence sooner (Fernández-Trujillo et al., 2007; Fernández-Trujillo, 2008). Non-climacteric fruits such as strawberries (*Fragaria* spp.) and grapes (*Vitis vinifera* L.), only complete maturation when attached to the plant, since they do not have increased ethylene production after harvest (Biale, 1964; Given et al., 1988; Chervin et al., 2004). The non-climacteric fruits do not develop the dogmatic climacteric patterns, including increasing of respiration, ethylene biosyntheses and autocatalytic ethylene response, but showed some typical responses to ethylene (degreening, softening, and others). Interestingly, there are also species that have both climacteric and non-climacteric varieties (Obando-Ulloa et al., 2009), being good models to study the genetic differences responsible for the different types of ripening. Ethylene was only identified and began to be studied after its effects on plants had already been noted (Abeles et al., 1992; Lin et al., 2009). Since then studies on fruit ripening usually focus on this compound, but what is it exactly?

Ethylene and its mighty power

Ethylene (C_2H_4), the simplest existing alkene (unsaturated hydrocarbon, with formula C_nH_{2n}), is a plant hormone with important roles in ripening and other processes. Today the pathway of ethylene biosynthesis is well defined, starting with the conversion of methionine to S-adenosylmethionine (SAM), which is subsequently transformed by ACC synthase (ACS), in 1-aminocyclopropane-1-carboxylic acid (ACC) and then converted by ACC oxidase (ACO) in ethylene (Kende, 1989). Ethylene is one major endogenous factor that stimulates the respiratory activity and, consequently, anticipates ripening and senescence of tissues, triggering climacteric reactions. More recently a compound called 1-methylcyclopropene (MCP) proved to be a powerful antagonist of ethylene action and is now being used as a

Table 1. Fruit genomes that have been sequenced to date.

Common name	Scientific name	Reference/year
Grape	*Vitis vinifera* L.	(Jaillon et al., 2007; Velasco et al., 2007)
Papaya	*Carica papaya* L.	(Ming et al., 2008)
Cucumber	*Cucumis sativus* L.	(Huang et al., 2009; Wóycicki et al., 2011)
Apple	*Malus x domestica* Borkh.	(Velasco et al., 2010)
Strawberry	*Fragaria vesca* L.	(Shulaev et al., 2011)
Date palm	*Phoenix dactylifera* L.	(Al-Dous et al., 2011)
Tomato	*Solanum lycopersicum* L.	(Tomato Genome Consortium, 2012)
Melon	*Cucumis melo* L.	(Garcia-Mas et al., 2012)
Banana	*Musa acuminata* L.	(D'Hont et al., 2012)
Chinese plum	*Prunus mume* Sieb & Zucc.	(Zhang et al., 2012)
Pear	*Pyrus bretschneideri* Rehd and *Pyrus communis* L.	(Wu et al., 2013; Chagné et al., 2014)
Watermelon	*Citrullus lanatus* L.	(Guo et al., 2013)
Peach	*Prunus persica* (L.) Batsch	(International Peach Genome Initiative, 2013)
Kiwifruit	*Actinidia chinensis* L.	(Huang et al., 2013)
Pepper	*Capsicum annuum* L.	(Kim et al., 2014; Qin et al., 2014)

Fig 1. Steps between the onset of fruit development and final senescence.

research tool in order to reach a better understanding of ethylene-regulated processes and for extension of the shelf life of fruits and vegetables (Blankenship and Dole, 2003). This understanding of the mode of action of ethylene has been advancing in recent years also trough studies dedicated to the identification of TFs capable of binding to the promoter region of genes related to ethylene biosynthesis and action, like the transcriptional regulators belonging to the APETALA2 (AP2)/ETHYLENE RESPONSE FACTOR (ERF) type (Klee and Giovannoni, 2011; Pech et al., 2012; Grierson, 2013; Pech et al., 2013). Other important genes induced by ethylene in fruit ripening are: Ethylene receptors, SlEB1 and SlEB2, Constitutive Triple Response1 (CTR1); ER49 (translation elongation factor Ts EF-Ts); Chlorophyllase, Phytoene synthase 1; Alcohol acyl-transferase 1,2,3,4, Lipoxygenase; Cellulase, Expansin, β-galactosidase, Endo-(1,4)-β-mannanase, Pectin methylesterase, Polygalacturonase, Rab GTPase, Xyloglucan endotransglucosidase/hydrolases, β-D-Xylosidase. More information about these genes can be found in literature and new technologies are being applied in order to discover more important loci involved in ethylene response and fruit ripening (Alexander and Grierson, 2002; Cara and Giovannoni, 2008; Osorio and Fernie, 2013; Pech et al., 2008; Pech et al., 2012; Grierson, 2013; Pech et al., 2013).

RipenOMICs

The new high throughput technologies for genome analysis are now deeply impacting plant research. Today genomics, methylomics, transcriptomics, proteomics, interactomics, metabolomics and phenomics as well as integrative analyses (Figure 2) are helping in the understanding of plant physiology not only during the stages comprised between early development and the reproductive stage, but also during fruit maturation and ripening (Mochida and Shinozaki, 2011; Fujisawa et al., 2012; Osorio et al., 2013; Ruiz-May et al., 2013; Zhong et al., 2013; Gapper et al., 2014). Transcriptome-wide analyses are now showing that the number of differentially expressed genes during ripening stages varies between species. In the Chinese jujube (*Ziziphus jujuba* Mill.) a total of 154 differentially expressed genes were identified when comparing fruits at the half-red and at the complete red stage (Lin et al., 2013). Nonetheless, an integrative analysis of the transcriptome and proteome comparing a spontaneous late-ripening mutant orange ('Fengwan' orange, *Citrus sinensis* L. Osbeck) and its wild type ('Fengjie 72-1') showed that at the transcript level (RNA sequencing - RNAseq), 628 genes had a 2-fold or more expression difference between the mutant and wild type, while at the protein level, 130 proteins differed by 1.5-fold or more in their relative abundance (Wu et al., 2014). High throughput technologies and Digital Gene Expression (DGE) used for transcriptome profiling are also proving to be a rapid and cost effective method for *de novo* transcriptome analysis of non model plant species that lack of prior genome annotation, such as Chinese white pear (*Pyrus bretschneideri* Rehd.), where a total of 90,227 unigenes were assembled and 62,077 unigenes were annotated through this method (Xie et al., 2013). Furthermore, many fruit genomes are now becoming available for wide-range analysis (Table 1) and may show interesting evolutionary changes in gene sequences over the years. Phylogenetic approaches, which have also become more robust with the advance of computing power, which enabled the use of Bayesian statistical analyses, can contribute greatly to a better understanding on the differences between climacteric and non-climacteric fruits. These are powerful new weapons in the war against fruit senescence and its consequent losses, but which should be our first targets for further studies on

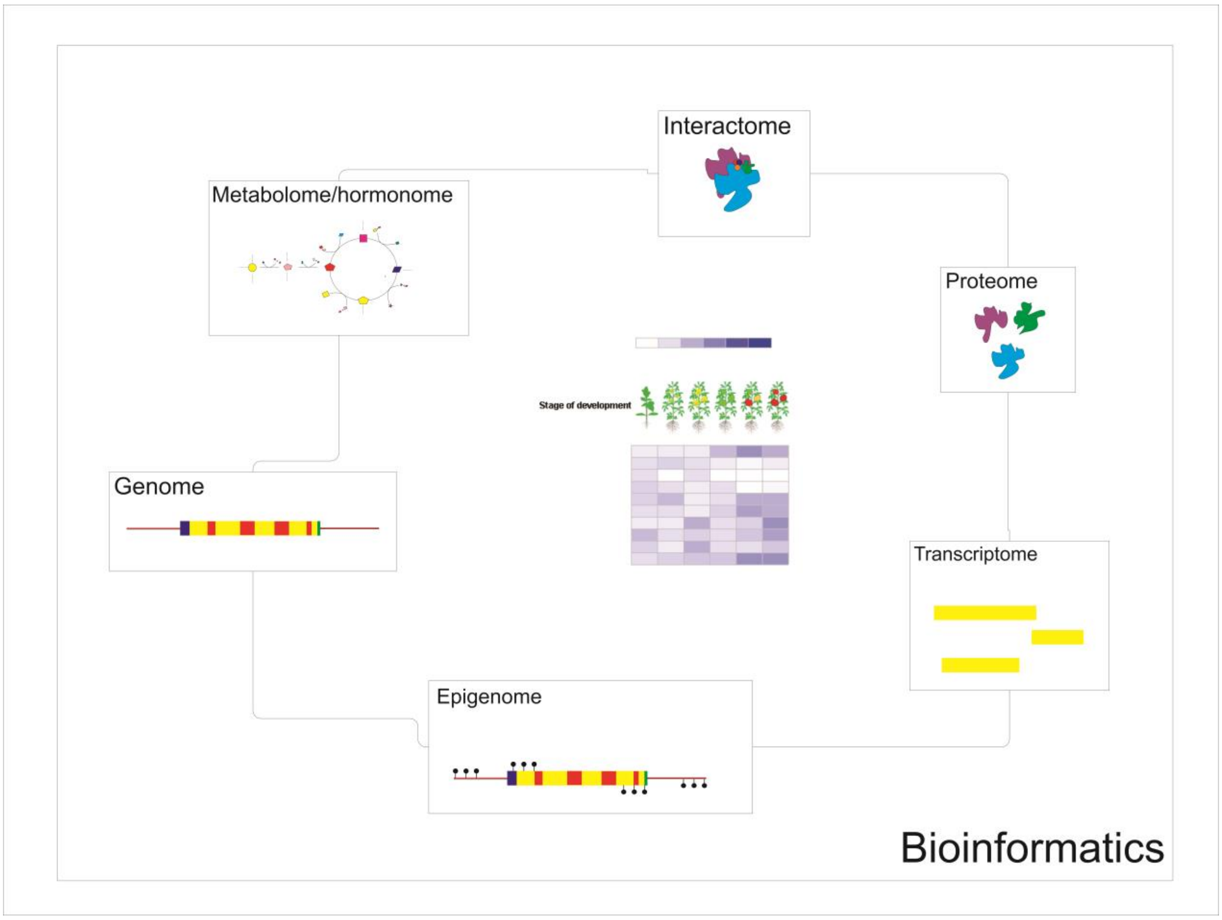

Fig 2. Systems biology and omics tools in the understanding of the fruit ripening process.

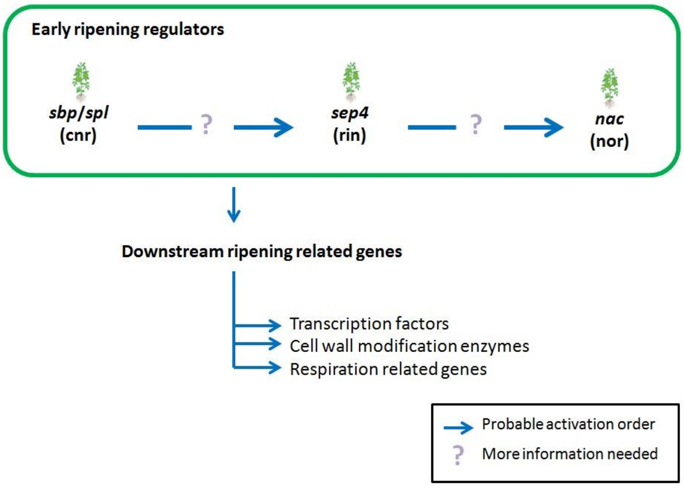

Fig 3. Network of early ripening regulators.

ripening and related events? Probably the earliest ripening regulators.

Where should we attack first? - The role of transcription factors

Transcription factors are key regulators of many cellular pathways. The study of ripening mutants showed that different TF *loci* such as *ripening inhibitor* (*rin*) *nonripening* (*nor*), *colorless non-ripening* (*cnr*) and many others (Figure 3) are involved in this event (Martel et al., 2011; Osorio et al., 2013). In this section we will focus on the role of these three TFs and some genes related to them. Fruits obtained from *rin* plants fail to ripen and display enlarged sepals as well as loss of inflorescence determinacy. Further studies of *rin* locus revealed a MADS-box gene which was called at first as *LeMADS-RIN* (Vrebalov et al., 2002). It is now known that this gene is actually a member of the MADS-box family from the *SEPALLATA4 (SEP4)* class which was partially deleted. It is also known that it is one of the earliest-acting ripening regulators for ethylene-dependent and ethylene-independent pathways. The identification of novel

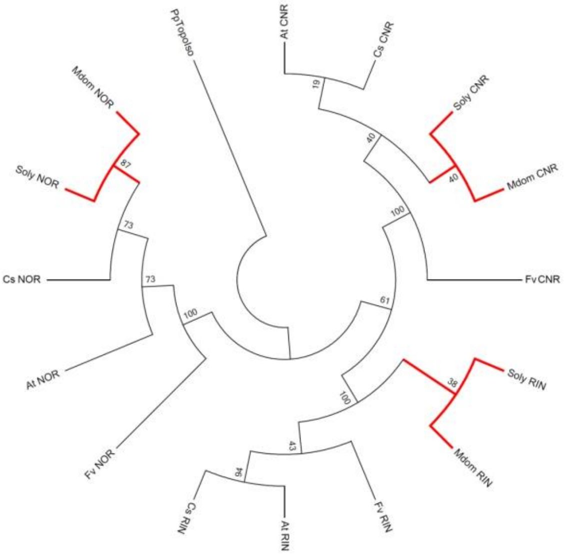

Fig 4. Protein based phylogenetic analysis of the loci of *rin*, *nor* and *Cnr* in Arabidopsis, orange, wild strawberry, apple and tomato. A putative topoisomerase (NCBI - XP_001769043.1) of *Physcomitrella patens* (Hedw.) B.S.G. was used as outgroup. Branches grouping the two fleshy climacteric fruit species are highlighted in red. Gene identifiers are available on Supplementary Table 1.

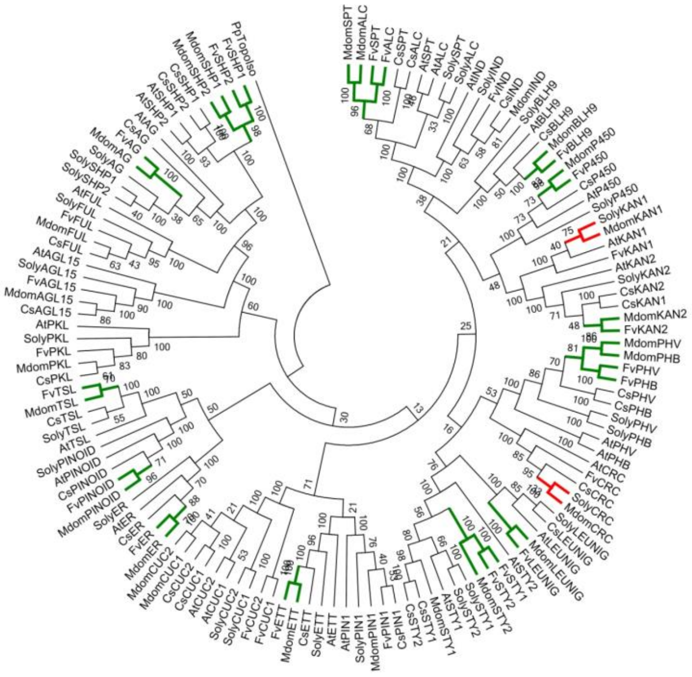

Fig 5. Protein based phylogenetic analysis of fruit development related loci (Roeder and Yanofsky, 2006) in arabidopsis, orange, wild strawberry, apple and tomato. A putative topoisomerase (NCBI - XP_001769043.1) of *Physcomitrella patens* was used as outgroup. Branches grouping homolog genes of the two fleshy climacteric fruit species are highlighted in red, while branches grouping homolog genes of the two Rosaceae species are highlighted in green. Gene identifiers are available on Supplementary Table 2.

RIN targets by transcriptome and chromatin immunoprecipitation (ChIP) analyses, detected 342 positively and 473 negatively regulated genes in which most of the positively regulated genes contained possible RIN-binding sites (CArG-box motif), constituting promising targets for further studies (Fujisawa et al., 2012). *RIN* also seems to be important for the expression of *NOR* (Martel et al., 2011), another important TF involved in ripening. *NOR* is a member of the NAC (NAM, ATAF1,2, CUC2) family, in which mutation, similar to the ones occuring in *rin*, leads to a nonripening phenotype (Giovannoni, 2007). Another phenotype conferred by the malfunction of a gene in another important locus, the *Cnr*, is due to a mutation that promotes epigenetic changes in the promoter of the *SQUAMOSA PROMOTER-BINDING* (*SBP/SPL*) gene. This epimutation represses this gene, blocking the activation of downstream genes and consequently fruit ripening (Thompson et al., 1999; Eriksson et al., 2004; Manning et al., 2006; Pech et al., 2008). The first *SBP* genes (*SBP1* and *SBP2)* were isolated from *Antirrhinum majus* L. and were found to control early flower development by regulating the MADS-box gene *SQUAMOSA* (Klein et al., 1996). Later, *SQUAMOSA PROMOTER-BINDING PROTEIN-LIKE* genes have been extensively discovered in many terrestrial plants, playing numerous important roles during plant growth and development (Chen et al., 2010) and also being pointed as necessary for *rin* induction of ripening-related genes (Martel et al., 2011). Similarly to what happens in *Cnr locus*, the possibility of epigenetic changes in ERFs has also been described (Santos et al., 2013). The ERF superfamily is not only involved in ripening, but also in several growth, development and stress related processes. These make the identification of ERF family members in several species an important step in the understanding of fruit maturation processes (Nakano et al., 2006; Pirrello et al., 2012; Girardi et al., 2013). Suppression of AP2/ERF genes, such as *SlP2a*, act downstream of *rin*, *nor*, and *Cnr* and may result in rapid softening and earlier ripening. *SlP2a* seems to be a negative regulator of ripening, promoting a negative-feedback with *Cnr* (Chung et al., 2010). In addition, it has been demonstrated that *Cnr* can bind to the promoter of *AP2a in vitro* (Karlova et al., 2011). A phylogenetic analysis (Figure 4) of proteins encoded by *rin*, *nor* and *Cnr* homologous *loci* in Arabidopsis (*A. thaliana*), orange (*C. sinensis*), wild strawberry (*F. vesca*), apple (*M.* x *domestica*) and tomato (*S. lycopersicon*), show an interesting result, a higher similarity between genes of climacteric fleshy fruits such as tomato and apple than between genes of species from the same family (i.e., Rosaceae, for strawberry and apple). A similar phylogenetic analysis including other genes associated with flower and initial fruit development was also performed (Figure 5). This analysis, which aimed to assess whether these genes also maintain a greater proximity between climacteric and non-climacteric fruits, showed, however, a higher phylogenetic proximity between the two Rosaceae (*F. vesca* and *M.* x *domestica*) species inside each group of homologous genes, as expected. The only two genes of apple and tomato (climacteric species) that grouped again were *KANADI 1* (*KAN1*) and *CRABS CLAW* (*CRC*). *KAN* and *CRC* are two closely related genes with roles in polar differentiation and development of the carpel, an organ that seems to be specially dependant of ethylene during development and senescence (Eshed et al., 1999; Kerstetter et al., 2001; Pascual et al., 2009). The *KAN1* gene regulates genes involved in response to different hormones including ethylene, while *CRC* still needs more studies related to the identification of TF binding sites (Merelo et al., 2013). More studies on these transcription factors (*Cnr*, *rin*, *nor*) are in order to understand the genetic differences responsible for climacteric and non-climacteric metabolism.

Conclusions and future directions

Transcription factors showed to have great importance not only during early development but also in the regulatory control of ripening and senescence. Much progress in the identification of these regulators has been made so far, but much remains to be investigated. High throughput technologies are contributing greatly to the elucidation of development and ripening physiology. Newly sequenced genomes will provide a good overview on the evolution of these proteins over time and physiological differences between climacteric and non-climacteric fruits will be understood in details that will assist both post-harvest techniques and crop breeding. The transcriptional regulatory pathways involved in fruit ripening and the direct interactions between ripening-related TFs are still largely unknown. The possibility to predict the most likely functions of TFs based on phylogenetic and expression analysis has been already considered in this context (Hileman et al., 2006). Still, more efforts to systematically carry out comparative genomic or functional analyses of these genes across flowering plants are needed. Possibilities are expanding with the new technologies available and systems biology approaches that can provide a large amount of data to be explored in more efficient ways (Hertog et al., 2011). The brief phylogenetic analysis of genes involved in fruit ripening and development in Arabidopsis and their putative homologs in orange (*C. sinensis*), wild strawberry (*F. vesca*), apple (*M.* x *domestica*) and tomato (*S. lycopersicon*) shown in Figure 4 demonstrates that apparently the emergence of genes and alleles responsible for fruit climacteric and/or non-climacteric behavior occurred before the divergence of these species and, for some reason, were held only in some species and/or varieties. Further studies are needed and should demonstrate how and why the climacteric behavior was important for the continuity of certain genotypes, but not for others. Species with dry fruits are probably the ancestors of fleshy fruit species, sharing common developmental mechanisms (Knapp, 2002). Arabidopsis contributed tremendously to the understanding of fruit development in dehiscent fruits, however a model species for studies of indehiscent fruits is needed. Tomato has the genome available at good quality (http://solgenomics.net/), and was also one of the first species to be genetically transformed by *Agrobacterium tumefaciens* (Filatti et al., 1987). As previously shown here, studies on this species have been contributing greatly to the understanding of ethylene induced modifications on flavor, sugar and acid contents, color, volatiles and texture during ripening of fleshy indehiscent fruits (Klee and Giovannoni, 2011; Pesaresi et al., 2014). The role of small RNAs (sRNAs) in ripening is also poorly understood. The *CNR* 3’ untranslated region has a micro RNA (miRNA) binding site that is complementary to miR156/157 but more studies about their interaction are needed (Dalmay, 2010). sRNAome sequencing of developing tomato fruits revealed that thousands of non-coding RNAs are differentially expressed during fruit development and ripening (Mohorianu et al., 2011). The role of these RNAs in fruit ripening may bring interesting findings in the understanding of ripening regulation and should be explored. Although fruit development and seed dispersal is a well understood process in Arabidopsis (Roeder and Yanofsky, 2006), several studies are still needed in order to fill gaps that currently exist in this first plant model species. It is not yet known exactly how GA and auxin pathways interact to form the valve margin (Arnaud et al., 2010) and it is still needed to find out if the levels of abscisic acid (ABA) increase during silique development and senescence in order to validate the stomatal model proposed for *AtNAP* action in silique senescence (Kou et al., 2012). It is also needed to understand if the modified phenotypes obtained due to altered *NTT* expression in Arabidopsis are caused by deregulation of the cell cycle (Marsch-Martínez et al., 2014). Currently wide-range analyses combined with bioinformatics are enabling a broader view of the transcriptional behavior of very specific tissues at key stages of reproductive development (Mantegazza et al., 2014). The formation of reproductive organs and fruits is regulated by a complex combination of genes. Also, multiple lineages of certain families of TFs controlling these phenomena have been maintained in plants (Nakano et al., 2006; Dreni and Kater, 2014), being the reasons for this high redundancy still unknown. The cost reduction and the improvement of sequencing technologies keep constant (Hamilton and Buell, 2012) and such improvements made possible the sequencing of several fruit plant genomes obtained so far. On proteomics a wide range of proteome resources are becoming available to assist the diversity of proteomic-based applications in plant sciences and these studies are already helping to elucidate physiological processes involved in fruit development and ripening (Carroll et al., 2013; Molassiotis et al., 2013). Regarding bioinformatics applied to systems biology, software and algorithm development is lagging behind from sequencing data generation. In genomics, new algorithms and software are needed in order to handle large, repetitive genomes (Hamilton and Buell, 2012). In the field of proteomic analyzes, false negatives due to environmental contamination, problems in database matching and curation of protein identifications are some of the major sources of problems (Marcotte, 2007; Bell et al., 2009). Finding alternatives to these problems is an important step for the advance in the knowledge about how maturation and ripening occur at the molecular level. However, the advances that are being made in this field points to a bright future on ripening research.

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