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Review

Genetics, Genomics, and Breeding in Melon

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Abstract: Melon is an important horticultural crop worldwide. The high diversity of melon makes it a model plant for various different properties. Some quantitative trait loci or candidates have been discovered, but few were verified as limiting genetic transformation and genome editing systems. Identifying new genetic resources with resistance and special fruit quality traits is imperative to develop effective and useful breeding technologies in melon. This review describes the advances in genetics, genomics, and the breeding of melon and puts forward some recommendations in these areas.

Keywords: melon; genetics; genomics; breeding

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1. Introduction

Melon (*Cucumis melo* L.), an important crop in the Cucurbitaceae family, is cultivated worldwide, with more than 28 million tons produced in 2020 (United Nations Food and Agriculture Organization (FAO) statistics). It is highly diverse in fruit type and other properties, such as fruit size, peel and flesh color, and flavor [1]. Based on ovary pubescence, melon has been classified into two subspecies, *C. melo* subsp. *melo* (hereafter as *melo*) and *C. melo* subsp. *agrestis* (hereafter as *agrestis*). The two subspecies can be further divided into 16 groups or varieties, five in *agrestis* and eleven in *melo* [2]. Recently, the melon was described as 19 groups of wild, feral, and domesticated melons, and some of them of sub-groups [3]. The diversity in phenotype and genetics of melon make it feasible as a model cucurbit for studying sex expression [1,4] and flower and fruit development [4–6].

The previous researchers have identified a few accessions with resistance or special characters, and several elite varieties developed using these accessions. In addition, some quantitative trait loci or candidates for important characters in melon have been discovered. Furthermore, next-generation sequencing technologies in the past years have allowed unprecedented access to draft genome sequences for the main crops and plants. Since the first melon genome sequence was released [7], more and more data from divergent genotypes by de novo sequencing and re-sequencing have become available. The advances in genetics and genomics in melon have accelerated the development of melon breeding. This paper will review the advances in genetics, genomics, and breeding in melon.

2. The Genetic Maps and Genetics of Related Characters in Melon

Dissecting the genetic base of characters is the foundation for utilizing germplasm innovation and breeding. In previous studies, several genetic and physical maps were conducted, and considerable genetic research on agronomic characteristics of melon was performed, including sex determination, fruit quality, fruit development, and resistance. The main QTLs and genes for melon reported in previous research are discussed in detail below (Table 1).

2.1. Genetic Map

Considerable melon genetic maps have been reported since the first melon genetic linkage map constructed in 1991 [8] based on relatively few markers as amplified fragment length polymorphisms (AFLPs) [9], random amplified polymorphic DNA (RAPD) [10] and simple sequence repeats (SSRs) [11]. Then, the first consensus linkage map for melon was integrated under the International Cucurbit Genomics Initiative (ICuGI) framework, including the position of QTLs related to important agronomic traits [12]. However, due to the position of ICuGI markers in the genome remaining unknown and different marker sets used, it is essential to develop an integrated genetic map with the physical position of different makers after the melon genome was released in 2012 [7]. Diaz et al. [13] integrated a total of 1850 previously reported markers in the genome sequence, which has been used as a reference genetic map for research. In recent years, with the development of next-generation sequencing (NGS), high-resolution genetic maps have been constructed using single nucleotide polymorphisms (SNPs) from genotyping-by-sequencing (GBS) and re-sequencing data for melon [7,14–18].

2.2. Genetics of Related Characters in Melon

2.2.1. Sex Expression

Melon is considered the model plant for studying sex determination [1,4]. The flowers of melon can be divided into male flowers, female flowers, and bisexual flowers. Based on the distribution and ratio of different flowers on the same plant, gynoecy, androecy, hermaphrodite, monoecy, and andromonoecy were classified as melon [19]. In melon, sex determination is governed by two major genes, *andromonoecious* (*a*) and *gynoecious* (*g*), which correspond to *CmACS-7* and *CmWIP1* [20,21], respectively. The dominant *G* allele governs the production of a separate male flower by suppressing carpel development [19,21]. In contrast, *a* gene encoding an ACC synthase inhibits the development of the male organs in female flowers [20]. The transition between monoecy and andromonoecy is conferred by a single substitution in *CmACS-7*, which leads to an inactive form of this key enzyme (1-aminocyclopropane-1-carboxylic acid synthase) in the ethylene biosynthesis [20]. Monoecious (*A-G-*) and andromonoecious (*aaG-*) individuals bear male flowers on the main stem and female or hermaphrodite flowers on axillary branches, respectively, whereas gynoecious (*AAgg*) and hermaphrodite (*aagg*) individuals only bear female and hermaphrodite flowers, respectively [20]. Additionally, a third locus having the recessive *m* allele (*CmACS11*) is essential for the production of stable gynoecious phenotypes [22]. However, sex expression in melon is quite plastic and collectively determined through mutual interaction of the hormonal, environmental, and development aspects [19].

This plasticity requires signal perception/integration, changing gene expression in response to those signals, and then the maintenance of that response until conditions change again [23]. Epigenetic mechanisms provide a molecular memory that underpins the maintenance phase of these responses. The perception of the sex-determinative signals and their translation at the product level in flowers or plants might have been regulated by some epigenetic mechanisms [4] and have been described previously [24]. In the gynoecious genotype, the transition from male to female flowers results from epigenetic changes in the *CmWIP1* promoter caused by the insertion of a transposon, Gyno-hAT [21,24]. The female-promoting gene, *CmACS11*, represses the expression of the male-promoting gene *CmWIP1* via the deposition of H3K27me3 [4]. The genes of *ACS7*, *ACS11*, and *WIP1*, in an epistatic or hypostatic manner, along with the recruitment of H3K9ac and H3K27me3, determine sex expression epigenetically [19].

2.2.2. Sugar Content

The sensory quality of fruit is largely determined by its sugar and organic acid levels, in addition to the volatile aromatic components. Sugar content is not only the major determinant of both fruit quality and consumer acceptance. Still, it is also a primary target for crop improvement in melon [25], mainly comprised of sucrose, glucose, and fructose.

Significantly, the increase in total sugar content in mature melon fruit is particularly due to sucrose accumulation during the final stages of fruit development. As sucrose is the dominant factor in sugar content, understanding the molecular mechanisms involved in the process of sucrose accumulation is essential for possible genetic improvements.

The metabolic pathway of sucrose accumulation was involved in nearly 20 enzymes, especially invertases (INV), sucrose synthase (SS), and sucrose phosphate synthase (SPS), and the balance between sucrose breakdown and sucrose synthesis activities was considered the crucial factor in final sucrose accumulation. Forty-two genes encoding the enzymatic reactions of the sugar metabolism pathway in melon were reported [26]. There has been some progress in studying the genetic control of sugar accumulation. Burger et al. [27] considered that a single major gene, *suc*, controls sucrose accumulation. However, Harel-Beja et al. [28] reported six significant QTLs on chromosomes 2, 3, 5, and 8 for sugar content. Diaz et al. [12] further developed a consensus linkage map of melon combining the previously reported QTLs from 18 mapping experiments, which consisted of more than 10 QTLs for Brix, sugars, and sucrose. Though many QTLs have been reported, few candidate genes have been identified. Recently, three important clusters related to sugar content have been identified, of which a major QTL, *SUCQSC5.1*, reducing soluble solids content (SSC) and sucrose content was detected, and *MELO3C014519* was considered as the candidate gene [25]. Additionally, some new different-expression genes responsible for the sucrose content were detected for melon, such as *CmINH3*, *CmTPP1,* and *CmTPS5*, *CmTPS7*, *CmTPS9* [29]. Sugars are synthesized in mesophyll cells and translated into the other parts of the plant, particularly sink organs in plants. Therefore, sugar accumulation in melon fruit depends not only on sugar synthesis but also on sugar transport. Three tonoplast sugar transporters (TSTs), *CmTST1*, *CmTST2*, and *CmTST3*, were isolated from melon, but only *CmTST2* plays an important role in sugar accumulation in melon fruit [30]. The considerable QTLs for sugar content detected in melon fruit is probably due to the diverse backgrounds in these research or the complex metabolic pathways in sugar. It is a challenge to discover and functionally validate the major QTLs or crucial genes for sugar accumulation and transportation.

2.2.3. Acidity

Acidity is a major determinant of the taste and quality of most fruits, in combination with sugars and flavor volatiles. Melon is fairly unique among fleshy fruit in that they have very low acidity besides a few varieties [31]. Fruit acidity is due to the presence of organic acids, and malic and citric acids are the main acids found in most ripe fruits, measured by titratable acidity and PH. In melon, citric acid is the predominant organic acid present throughout fruit development and is positively correlated with titratable acidity [32].

A single dominant locus for the sourness or acidity of melon flesh was identified based on different populations and termed *So* or *PH* [28,31,33,34], which encodes a transmembrane transporter [35]. Surprisingly, the nucleosides adenosine and the major organic acids citrate and malate in melon fruits were detected. The PH protein harboring in the endoplasmic reticulum may indirectly play a role via modification of a proton gradient or nucleoside and acid metabolism [35]. A 12-bp insertion was detected occurring in non-acidic melon accessions of the *melo* group but not consistent in the *agrestis* group. Intriguingly, *MELO3C011482*, which encodes ATP-citrate synthase, was identified on chromosome 3 in the *agrestis* group [36]. The results also support the hypothesis that the *melo* and *agrestis* groups were domesticated independently.

2.2.4. Peel Color

Peel color is an important fruit quality trait that influences the choice of the consumer and the acceptability of the melon [37]. The primary peel colors of commercial melons are green, white, or yellow, which are conferred by distinct pigments accumulation, mainly by switching from green rind containing chlorophyll to various peel colors possessing kinds of combinations of chlorophylls, carotenoids, and flavonoids [38,39].

Green peel is a dominant epistatic to non-green (white and yellow) peel by analyzing an F_2 segregating population from a cross between green peel and yellow peel lines [36]. The candidate gene *MELO3C003375* on chromosome 4 was detected associating with green peel formation of melon and fruit pigment accumulation in watermelon [40]. In fact, besides the primary color, the secondary color of the mature fruit is also present in some special melon accessions, such as speckles, stripes, and spots. Recently, two dominant epistatic genes (*CmMt1* and *CmMt2*) for mottled peel and one gene (*st3*) for striped peel were reported. *CmMt1* and *CmMt2* could control the content of chlorophyll and the different ratios in chlorophyll accumulation conjointly. Interestingly, *CmMt1* has been confirmed as *MELO3C003375* [41], and the position of *st3* harboring on the chromosome is close to *MELO3C003375* [42], which was suggested that *MELO3C003375* plays a central role on regulating the accumulation of pigment. We also detected a gene (*MELO3C003097*) encoding the protein SLOW GREEN 1, which is required for chloroplast development on chromosome 8 and is associated with the green peel trait and maybe a minor gene involved in the formation of rind color [36]. Naringenin chalcone, a kind of yellow flavonoid pigment, was found to be one of the major pigments infecting the melon rind color in 'canary yellow' type melons [37], which is independent of carotenoids and chlorophyll pigments [38]. Additionally, *CmKFB*, a kelch domain-containing F-box protein-coding gene located on chromosome 10, has been identified to be a negative regulator for naringenin chalcone accumulation [37].

Many genes controlling the rind color have been identified, and the genetic mechanism is complex. The functional verification of these genes and their application in breeding remains to be developed.

2.2.5. Flesh Color

Flesh color is one of the most important traits of melon. The different flesh colors not only affect the preference of consumers but also mean different nutrients. The primary flesh colors in commercial varieties contain orange, white and green, largely governed by two major genes, white flesh (*wf*) and green flesh (*gf*). Orange flesh is determined by *Gf* and is dominant to green flesh (*gf*). Fruit with the genotype of *gfgf* has either green (*Wf*-) or white flesh (*wfwf*) [43]. Recently, the two major genes for flesh color in melon were identified. The candidate gene *CmOr* associated with carotenoid accumulation in melon fruit flesh was discovered, which is identical to the previously described *gf* locus [44]. Combining the QTL with GWAS results, a 96-kb overlapping interval containing 11 protein-coding genes was detected [36]. However, a previously reported candidate gene *MELO3C003069* for *Wf* is 202 kb away from the 96-kb interval, and thus *MELO3C003097* was considered a strong candidate for the *Wf* locus [35,45].

2.2.6. Resistance to Abiotic and Biotic Stresses in Melon

Plants suffer from abiotic and biotic stresses frequently during their development. The occurrence of powdery mildew, downy mildew, fusarium wilt, gummy stem blight, virus, and *aphis gossypii* reduce melon yield and quality worldwide [46]. Much research has been conducted on the genetics of resistance to abiotic and biotic stresses in melon.

Powdery Mildew

Powdery mildew (PM) caused by *Podosphaera xanthii* and *Golovinomyces cichoracearum* is an important foliar disease in melon, which includes seven races of *Podosphaera xanthii* and two of *Golovinomyces cichoracearum* [47–52]. The diverse climatic conditions result in differentiation in the dominant physiological race of powdery mildew around the world. Several QTLs associating resistance to different races of powdery mildew have been identified from the different resistant accessions in previous research, including *Pm-1* from PMR 45 [53], *Pm-2* from PMR 5 and PMR 6 [54], *Pm-3* and *Pm-6* from PI 124111F [55], *Pm-4* and *Pm-5* from PI 124112 [55,56], *Pm-w* from WMR 29 [57], *Pm-x* from PI 414723 and *Pm-y* from VA 435 [8], *Pm-R* from TGR-1551 [57], *PmV.1* and *PmXII.1* from PI 124112 [47], *BPm12.1*

from MR-1 [58], *PmEdisto47–1* from Edisto47 [52], *Pm-2F* from K7–1 [59]. The different results obtained in inheritance patterns and QTL mapping may be due to the diverse physiological races of powdery mildew and resistant accessions used. Unfortunately, there are not so many functional genes reported so far.

Gummy Stem Blight

Gummy stem blight (GSB) is one of the most serious diseases causing enormous losses to melon production worldwide [60]. In previous studies, genetic analyses have explored several independent GSB resistance loci from diverse cultigens of melon. The first resistant gene for GSB, *Gsb-1*, was reported to be a monogenic dominant locus in PI 140471 [61]. The other four resistant genes, *Gsb-2*, *Gsb-3*, *Gsb-4*, and *Gsb-5,* were considered to govern the resistance of PI 157082, PI 511890, PI 482398, PI 482399 to GSB, respectively [62]. Globally, the previous studies suggested GBS is governed by a single gene in each of the resistant melon accessions. *Gsb-1*, *Gsb-2*, *Gsb-3*, *Gsb-4* and *Gsb-6* are dominant loci, except for *Gsb-5* [63–65]. In addition to *MELO03C012987*, few candidates were identified through several loci reported [66].

Fusarium Wilt

Fusarium wilt (FW) caused by *Fusarium oxysporum* (*Fom*) is one of the destructive soil-borne diseases resulting in economic damage in a large number of melon-producing countries [67]. Four races of *Fom* have been described in melon: 0, 1, 2, and 1, 2 based on resistance genes. Genetic studies on the inheritance of resistance to the different races of *Fom* have been described in previous studies [68,69]. *Fom-2* was identified and considered as the locus conferring resistance to *Fom* races 0 and 1 [70]. *Fom-1* locus was mapped and conferred as resistance to race 2 [71]. *Fom-4* conferred resistance to races 0 and 2 and was found to be a recessive gene closely linked to *Fom-1* [72]. Interestingly, *Fom-3* was found to control resistance to races 0 and 2, and it is possible allelism with *Fom-1* [73]. Recently, another single dominant gene for FW resistance and defined as *Fom-5* [74]. *Fom-1*, *Fom-2*, *Fom-3* and *Fom-5* are four single dominant genes associated with FW resistance besides *Fom-4*.

Virus Disease

Cucumber mosaic virus (CMV), *Zucchini yellow mosaic virus* (ZYMV), *Cucumber green mottle virus* (CGMV), and *Melon necrotic spot virus* (MNSV) is the main virus diseases in melon [75–77]. To date, around 200 viral-resistant genes have been found, of which more than half are recessive genes, part of the recessive genes encoding eukaryotic translation initiation factors (*eIF*) that control the viral resistance in melon [78–80]. The *Cm-eIF4E* knockdown melon plants possess resistance to MNSV, ZYMV, *Cucumber vein yellowing virus* (CVYV), and *Moroccan watermelon mosaic virus* (MWMV) [77]. The resistance to CMV in melon accession PI 161375 is governed by one gene and at least two quantitative trait loci [81]. The major gene *CmVPS41* was reported as a general gatekeeper for resistance to CMV phloem entry in melon [82]. ZYMV resistance in melon PI 414723 is controlled by a dominant allele at the *Zym* locus [83]. Nucleotide-binding leucine-rich-repeat (NB–LRR) genes are one vital resistance (R) gene in melon and have been found to resist many diseases and insect pests [84]. *Vat* belonging to an NBS-LRR gene is considered the aphid resistance gene [85]. Most NB-LRR genes are specialized in resistance. However, plant disease resistance is easily lost with the mutation of pathogenic bacteria [85]. Therefore, exploring and cloning disease resistance genes with a broad spectrum will be an important part of the research of NBS disease resistance genes.

Abiotic Stress

Salinity, drought, and temperature extremes are the main abiotic in melon. Abiotic stress tolerance is complex because the sensitivity of many crops to a particular abiotic stress varies depending on their developmental stage. Therefore, the mechanisms of

resistance or tolerance to abiotic stress are poorly understood. Compared to biotic stresses, the genetics of abiotic stress tolerance have been paid little attention in melon. The genetics of abiotic stresses in melon potassium is a major factor in resistance to salinity. Shaker-like K^+ outward rectifying channel (SKOR) is participated in the long-distance distribution of K^+ from roots to the upper parts of the plant [86]. The previous study indicated that *CmSKOR* might play a role in distributing K^+ to the shoot in melon and improving saline tolerance in *Arabidopsis* [87]. *CmLOX10* is crucial in regulating tolerance to drought in melon seedlings by promoting JA accumulation and stomatal closure [88]. Both *CmLOX08* and *CmCADs* were considered the key players in abiotic stress responses, including drought and salt [89,90]. *CmNCED3* plays a crucial role in low-temperature stress response, besides drought and salt stresses [91].

Table 1. The main QTLs and genes for melon were reported in previous research.

Traits	QTLs or Gene	Chromosome	Function of QTLs and Genes	Reference
Sex expression	*CmACS-7* (*a*)	2	Inhibiting stamen development of female flowers	[20]
	CmWIP1 (*g*)	10	Suppressing female	[21]
	CmACS11	3	Negatively regulating expression of *CmWIP1*	[22]
Sugar content	*SUCQSC5.1*	5	Sucrose metabolism	[25]
	suc		Sucrose metabolism	[27]
Acidity	*PH*	8	Flesh acidity	[35]
Peel color	*MELO3C003375*	4	Green peel	[40]
	CmKFB	10	Yellow peel color	[37]
Flesh color	*CmOr*	9	Orange flesh color	[44]
	MELO3C003097	8	White and green flesh color	[36]
Powdery mildew	*Pm-1*	9	Resistance to *P. xanthii* race 1	[53]
	Pm-2	-	Conferring resistance to PMR 5 and PMR 6	[54]
	Pm-3	-	Conferring resistance to PI 124111F	[55]
	Pm-4	5	Conferring resistance to PI 124112	[55]
	Pm-5	5	Conferring resistance to PI 124112	[56]
	Pm-w	5	Resistant to races 1 and 2	[57]
	Pm-x	-	Resistant to race 2F	[8]
	Pm-y	12	Resistant to *P. xanthii* race 2	[8]
	Pm-R	5	Resistant to races 1, 2, and 5	[57]
	PmV.1 and PmXII.1	12	Conferring resistance to PI 124112	[47]
	BPm12.1	12	Resistant to *P. xanthii* race 1	[58]
	PmEdisto47–1	2	resistance to P. xanthii race 1	[52]
	Pm-2F	2	Resistant to *P. xanthii* race 2F	[59]
Gummy stem blight	*Gsb-1*	1	Conferring resistance to PI 1401471	[61]
	Gsb-2	-	Conferring resistance to PI 157082	[62]
	Gsb-3	-	Conferring resistance to PI 511890	[62]
	Gsb-4	-	Conferring resistance to PI 482398	[62]
	Gsb-5	-	Conferring resistance to PI 482399	[62]
Fusarium wilt	*Fom-1*	9	Resistance to race 2	[71]
	Fom-2	11	Resistance to race 0 and 1	[70]
	Fom-3	-	Resistance to races 0 and 2	[73]
	Fom-4	-	Resistance to race 0 and 2	[72]
Virus disease	*Cm-eIF4E*	12	Resistance to virus	[77]
	CmVPS41	12	Resistance to CMV	[82]
Aphis gossypii	*Vat*	5	Resistance to aphid	[85]
Abiotic stress	*CmSKOR*	9	Tolerance to salt	[87]
	CmLOX10	5	Tolerance to drought	[88]
	CmLOX08	10	Tolerance to drought and salt	[89]
	CmCADs	-	Tolerance to drought and salt	[90]
	CmNCED3	7	Tolerance to drought, salt, and low temperature	[91]

3. Genomics of Melon

The reference genome containing the whole genome sequence is the premise for genomics research and the utilization of plants. The first reference genome (Version 3.5) of melon with 375 Mb total length and 27,427 protein-coding genes was released in 2012, which was derived from a double-haploid line by crossing two phylogenetically distant melon cultivars from *melo* and *agrestis* [7]. However, the ratio of oriented scaffold assembly of just 80.8% in the first released melon genome limits its application. Subsequently, the quantity of anchored and oriented melon scaffold genome assembly was significantly improved by targeted SNP selection and defined as version 3.5.1 [92]. In order to update the previous annotation version 3.5.1, an improved assembly (Version 3.6.1) of the melon genome and new genome annotation (Version 4.0) were reported, which corrected the order and the orientation of 21 previous scaffolds and identified 8000 new genes [93]. Further, Castanera et al. [94] improved the melon genome assembly (version 4.0) with the PacBio single-molecule real-time (SMRT) sequencing technology, reduced the unassigned sequences substantially, made a great effort to distinguish new gene or transposon variants related to important phenotypes. Recently, several melon genome assemblies by de novo sequencing were published based on genetically diverse individuals, which provide insights into genome structures, genome evolution, diversification, and identified candidate genes for several agronomic traits of melon [95–97]. Structural variation (SV), including copy number variation (CNV) and presence/absence variation (PAV), has been shown to be frequent in plant species [98]. Transposons may be at the origin of an important fraction of the variability in melon besides SV [99]. Melon research has entered into post-genomic generation since the genome sequences were released. The analysis of genome variability using re-sequencing data has been used to shed light on the domestication history. Based on the re-sequencing of the melon genome, a comprehensive variation map of melon was constructed, and the domestication history and loci influencing agronomic traits were identified [36,100–103].

4. Breeding of Melon

Melon breeding has been around for hundred years. The breeding objectives in melons have developed from enhanced yield, shelf life, disease resistance, and resistance to abiotic stress to improve fruit quality.

Crop plants encounter various biotic and abiotic stresses that hinder life throughout their growth and development. Therefore, resistance is a major objective in crop breeding. Several varieties with resistance to powdery mildew in the USA have developed by using exotic accessions from India. From the previous reports related to resistance evaluation, most accessions with resistance to powdery mildew and downy mildew derive from the *momordica* group and *acidulus* group. Additionally, there are some Turkish melon accessions for resistance to ZYMV and WMV [104]. PI 161375 from the *conomon* group was identified as a resistant accession to CMV and aphids [81]. Most accessions with resistance in melon come from the primary and secondary diversity centers and could be considered important germplasm reservoirs for melon breeders. Therefore, exploiting the accessions for resistance improvement in melon is imperative. In the future, there will be more and more challenges from diseases, pests, and potentially extreme weather for us. Developing cultivars with high resistance to biotic and abiotic stresses is necessary.

With the improvement of people's living standards, fruit quality has become one of the major objectives in breeding programs as it influences fruit marketability. Fruit quality consists of many attributes, including internal quality, such as sugar and acid contents, flesh texture, and flavor, and external features, such as size, shape, and rind color. The candidates and molecular markers have been identified for the traits of rind color, flesh color, and acid content, which will benefit early selection in breeding. However, it is complex for the genetic basis of most traits related to fruit quality, especially flavor. It is an efficient strategy to dissect the genetic basis and discover the candidates of fruit flavor traits by using the

comprehensive analysis of genetics, transcriptomics, and metabolomics, which has been reported in tomatoes in recent years [105,106].

Heterosis results in the phenotypic superiority of a hybrid over its parents with respect to traits such as growth rate, reproductive success, and yield [107]. The accessions of different horticultural groups in *melo* had high nucleotide diversity. Therefore, it is an alternative strategy to cross the melon accessions from the divergent horticultural group for germplasm innovation. Conversely, though *agrestis* accessions are morphological variables in fruit, it is observed that they had quite a low nucleotide diversity [36]. This is consistent with the fact that there was no obvious heterosis in hybrid by crossing two cultivated *agrestis* accessions. However, there is an obvious differentiation in the two melon subspecies, *melo*, and *agrestis*, not only for morphological characteristics, but also for ecological adaptation. It indicates that we can acquire high heterosis and diversity by inter-subspecies crossing in melon breeding, especially for the *agrestis* population.

Traditional breeding based on crossing and selection remains important for crop improvement. Although the efficiency of crossing and selection has been improved using marker-assisted selection, it faces limitations in crops with complex genetics. With the increase of re-sequencing data in melon, more and more polymorphic SNPs have been identified. It is feasible to construct the platform based on whole genome selection. Genome editing is expected to be a powerful tool to create desirable variation using molecular scissors and artificially engineered nucleases. The utilization of CRISPR/Cas editing can accelerate melon improvement through the introduction of genetic variation in a targeted manner [108]. The application of genome editing is based on an effective and stable genetic transformation system. Nevertheless, though some research related to melon genetic transformation has been reported, the efficiency and universality of distinct genotypes is the limiting factor. Fortunately, the breakthrough of genetic transformation assisted by genes encoding developmental regulators in watermelons could provide a good reference for melons [109].

5. Concluding Remarks

Melon is an important horticultural crop worldwide with high diversity. In the future, resistance to biotic and abiotic stresses and fruit quality will be the most important traits for melon breeding. Identifying new genetic resources with horizontal resistance or special quality traits of melon fruit is needed. However, the genetics of the traits associated with resistance and fruit quality are always complex and are controlled by multiple loci. Though several QTLs have been identified, few candidate genes were reported. It is becoming a challenge for us to discover the causative genes and pivotal variations for these complex traits. This might be facilitated by a comprehensive analysis of genomics, transcriptomics, metabonomics, and bioinformatics.

Most modern elite varieties were developed by conventional breeding, which may not be able to meet current demands. The new strategies, such as whole genome selection, genetic transformation, and genome editing, need to be actively utilized in current breeding programs, which will provide powerful opportunities for genetic improvement of fruit quality and accelerate the process of future breeding of melon (Figure 1).

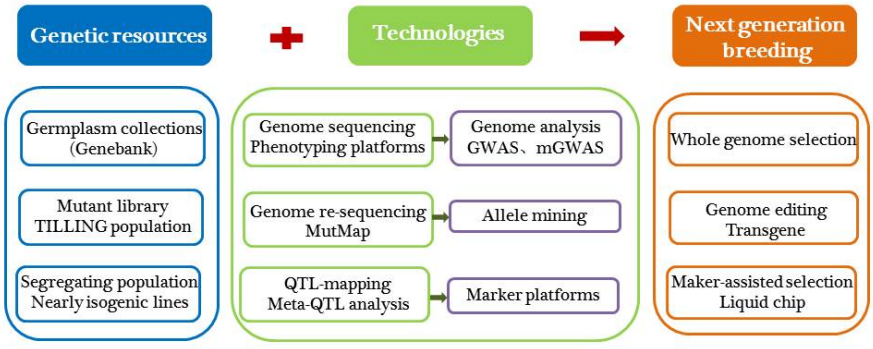

Figure 1. The key elements of 'Next generation breeding'.

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