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Report

The Chemical Interactions Underlying Tomato Flavor Preferences

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Summary

Although human perception of food flavors involves integration of multiple sensory inputs, the most salient sensations are taste and olfaction [1]. Ortho- and retronasal olfaction are particularly crucial to flavor because they provide the qualitative diversity so important to identify safe versus dangerous foods [2]. Historically, flavor research has prioritized aroma volatiles present at levels exceeding the orthonasally measured odor threshold [3], ignoring the variation in the rate at which odor intensities grow above threshold. Furthermore, the chemical composition of a food in itself tells us very little about whether or not that food will be liked. Clearly, alternative approaches are needed to elucidate flavor chemistry. Here we use targeted metabolomics and natural variation in flavor-associated sugars, acids, and aroma volatiles to evaluate the chemistry of tomato fruits, creating a predictive and testable model of liking. This nontraditional approach provides novel insights into flavor chemistry, the interactions between taste and retronasal olfaction, and a paradigm for enhancing liking of natural products. Some of the most abundant volatiles do not contribute to consumer liking, whereas other less abundant ones do. Aroma volatiles make contributions to perceived sweetness independent of sugar concentration, suggesting a novel way to increase perception of sweetness without adding sugar.

Results and Discussion

The Chemical Diversity within Tomato Varieties

Tomato flavors are primarily generated by a diverse set of chemicals including sugars (glucose and fructose), acids (citrate, malate, and glutamate), and multiple, less well-defined volatiles [4]. Of the more than 400 volatiles that are detectable in fruits, only 16 were predicted to contribute to tomato flavor based on their concentrations in fruit and odor thresholds (odor units) [3]. To bring focus on which chemicals truly drive liking and to establish a molecular blueprint of tomato flavor, we assembled a chemical profile of 278 samples representing 152 heirloom varieties. These varieties mostly predate intensive breeding of modern commercial tomatoes [5]. Levels of glucose, fructose, citrate, malate, and 28 volatiles were determined, most over multiple seasons (see Table S1 available online). Molecular studies indicate that there is a relatively low rate of DNA sequence diversity within the cultivated tomato, *Solanum lycopersicum* [6], consistent with a genetic bottleneck associated with two periods of domestication in Central America and Europe [5]. It was therefore somewhat surprising that we observed variation in volatile contents of as much as 3,000-fold across the cultivars (Table 1).

This unexpectedly large chemical diversity within the heirloom population provided an unprecedented opportunity to examine the interactions between sugars, acids, and volatiles with taste and olfaction. We conducted sensory analyses with a consumer panel on a subset of the cultivars exhibiting the most chemical diversity. Panelists rated overall liking of each variety as well as the overall tomato flavor intensity, sweetness, and sourness on sensory and hedonic versions of the general labeled magnitude scale (gLMS) [7, 8]. Thirteen panels rated 66 different cultivars as well as supermarket-purchased varieties over three seasons (Figure 1; Table S2). Several cultivars were repeated in multiple seasons. Random samples of each set were removed for chemical analysis with the number of measured chemical attributes expanded to 68 (Table S2).

Despite its popularity and important contribution to human nutrition, the commercially produced tomato is widely viewed as having poor taste, and its flavor is a major source of consumer dissatisfaction. In contrast, there is a public perception that the term “heirloom” indicates great taste. Our results indicate that this is not always the case. Some heirlooms received liking scores well below those of supermarket-purchased tomatoes (Table S2). Our results with respect to supermarket tomatoes present an interesting contrast. They were highly variable even within a single season, possibly reflecting the variation in harvest, handling, and storage among different lots.

The Relationship between Chemistry and Preferences

Close genetic relationship among highly liked or disliked varieties could potentially bias any effort to associate chemical composition with consumer preferences. To address this concern, we examined the genetic relationships of 19 varieties that were grown and subjected to consumer evaluations in a single season. A set of 27 biomarkers that are polymorphic within cultivated tomato were used to genotype each variety

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[9]Deceased

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Table 1. Observed Variation in Flavor Volatiles within *S. lycopersicum* Heirloom Varieties

	High	Low	Fold Difference	Median
1-penten-3-one	9.37	0.17	55	1.18
isovaleronitrile	68.45	0.58	117	7.63
trans-2-pentenal	5.16	0.31	17	1.23
trans-2-heptenal	2.71	0.09	30	0.42
isovaleraldehyde	51.08	1.55	33	8.59
3-methyl-1-butanol	184.46	3.20	58	27.26
methional	1.616	0.012	137	0.07
isovaleric acid	0.953	0.004	262	0.09
2-isobutylthiazole	63.61	0.37	174	8.34
6-methyl-5-hepten-2-one	20.07	0.17	120	3.38
β-ionone	0.396	0.008	47	0.05
phenylacetaldehyde	1.90	0.00	654	0.24
geranylacetone	28.96	0.03	1,095	1.22
2-phenylethanol	5.269	0.002	3,142	0.05
isobutyl acetate	11.93	0.14	85	1.67
cis-3-hexen-1-ol	124.15	10.00	12	40.00
1-nitro-2-phenylethane	2.59	0.02	149	0.25
trans,*trans*-2,4-decadienal	0.30	0.00	211	0.02
2-methylbutanal	14.66	1.14	13	3.47
hexyl alcohol	84.03	0.99	85	13.86
guaiacol	8.09	0.03	290	0.77
hexanal	381.05	15.55	25	88.65
1-octen-3-one	0.312	0.017	18	0.07
cis-3-hexenal	399.66	8.29	48	71.09
methylsalicylate	14.16	0.00	3,354	0.40
trans-2-hexenal	48.01	0.39	123	3.54
β-damascenone	0.1733	0.0020	86	0.01
2-methyl-1-butanol	115.69	1.93	60	15.08

Volatile emissions were measured as ng/g fresh weight/hr.

(Figure S1). Based on these data, we found no obvious genetic subgroups that could explain liking, sweetness, or tomato flavor intensity. There was no obvious genetic clustering of good versus bad taste when varieties were sorted by chemical composition (Figure 1). These latter data also indicate the chemical complexity of liking, as there is no simple pattern of chemical content that separates high from low consumer liking scores.

Due to the large number of chemicals potentially influencing liking, we performed a multivariate analysis of the data. The attributes were initially partitioned into six groups based on chemical properties and biosynthetic pathways: sugars, branched-chain amino acids, fatty acids, carotenoids, phenolics, and acids. Compounds for which biosynthetic pathways are not established were assigned to one of the six classes based on their correlations with other classified compounds [9]. Groups of structurally related chemicals with known metabolic links were examined for compounds within each module that were highly colinear, and compounds that were upstream in relevant metabolic pathways were preferentially selected. The selection process reduced the set to 27 compounds (Table S3). Flavor intensity was associated with twelve different compounds, seven of which were independently significant after accounting for fructose: 2-butylacetate, *cis*-3-hexen-1-ol, citric acid, 3-methyl-1-butanol, 2-methylbutanal, 1-octen-3-one, and *trans*,*trans*-2,4-decadienal. Sweetness was associated with twelve compounds, eight of which overlapped with those important for flavor and three of which were independent predictors of sweetness after accounting for fructose: geranial, 2-methylbutanal, and 3-methyl-1-butanol.

Interactions between taste (sweetness) and retronasal olfaction are of considerable interest in the chemical senses [10]. Here we present evidence for these interactions in a natural food product, the tomato. Although sweetness of tomatoes is widely thought to result from sugars, volatiles proved to be important contributors to sweetness. Volatiles are perceived in two ways. They can be sniffed through the nostrils (orthonasal olfaction), or, when foods containing volatiles are chewed and swallowed, volatiles are forced up behind the palate into the nasal cavity from the back (retronasal olfaction). Orthonasal olfaction is commonly called “smell”; retronasal olfaction contributes to “flavor.” Retronasal olfaction and taste interact in the brain. Commonly paired taste and retronasal olfactory sensations can become associated such that either sensation can induce the other centrally. Although instances of volatile-induced tastes of sweet, sour, bitter, and salty have been observed, sweet is the most common [11]. Multiple regression with sweetness as the dependent variable showed that the perception of tomato flavor (retronasal olfaction) made a significant contribution to sweetness after accounting for fructose ($p < 0.0001$).

The contributions, or lack thereof, of certain volatiles were somewhat unexpected. Prior lists of important tomato flavor volatiles were compiled based largely on odor unit values [3]. Our data indicate that some of the volatiles with high odor unit values, such as β-damascenone and phenylacetaldehyde, are not associated with tomato flavor intensity, although they have historically been considered to be important contributors to flavor [3]. Damascenone in particular was considered to be important to tomato flavor because of its extremely low reported odor threshold. Our results indicate that these volatiles should not be considered high-priority targets for genetic manipulations.

Testing the Model: Transgenic Fruits with Altered Volatile Content

The models of flavor and sweetness and the contributions of individual chemicals to liking were tested empirically. We used transgenic plants that were specifically modified to no longer express a gene, 13-lipoxygenase (*LoxC*). This enzyme catalyzes the first step in the metabolic pathway that converts 18:2 and 18:3 fatty acids to C6 volatiles (*cis*-3-hexenal, hexanal, *cis*-3-hexen-1-ol, hexyl alcohol, and hexylacetate) [12]. These genetically modified lines have vastly reduced levels of the C6 volatiles due to a 95% reduction in *LoxC* RNA levels (Table 2). Fruits from these plants are otherwise unaffected in their sugars, acids, and volatiles. Thus, they provided the means to directly test the contributions of the C6 volatiles to flavor and liking. Consumers were able to distinguish the transgenic from control fruits ($p = 0.009$) via a triangle test for differences, confirming the correlation between *cis*-3-hexen-1-ol and flavor intensity. However, there was no significant difference in preference between the two tomatoes. Even though the C6 volatiles are by far the most abundant class of volatiles in the fruit, their precise, near complete removal in the transgenic line did not impact liking. This result indicates that volatiles previously predicted to be the most important contributors to tomato flavor based on odor units have no significant impact on consumer liking.

Given the growing understanding of interactions between taste and retronasal olfaction, it was not unexpected that the correlations between certain volatiles and sugars contribute to the perceived sweetness of tomato fruits. Notably, the apocarotenoid geranial was positively correlated with sweetness. We have independently validated this aspect of the model; tomato mutants specifically deficient in carotenoid

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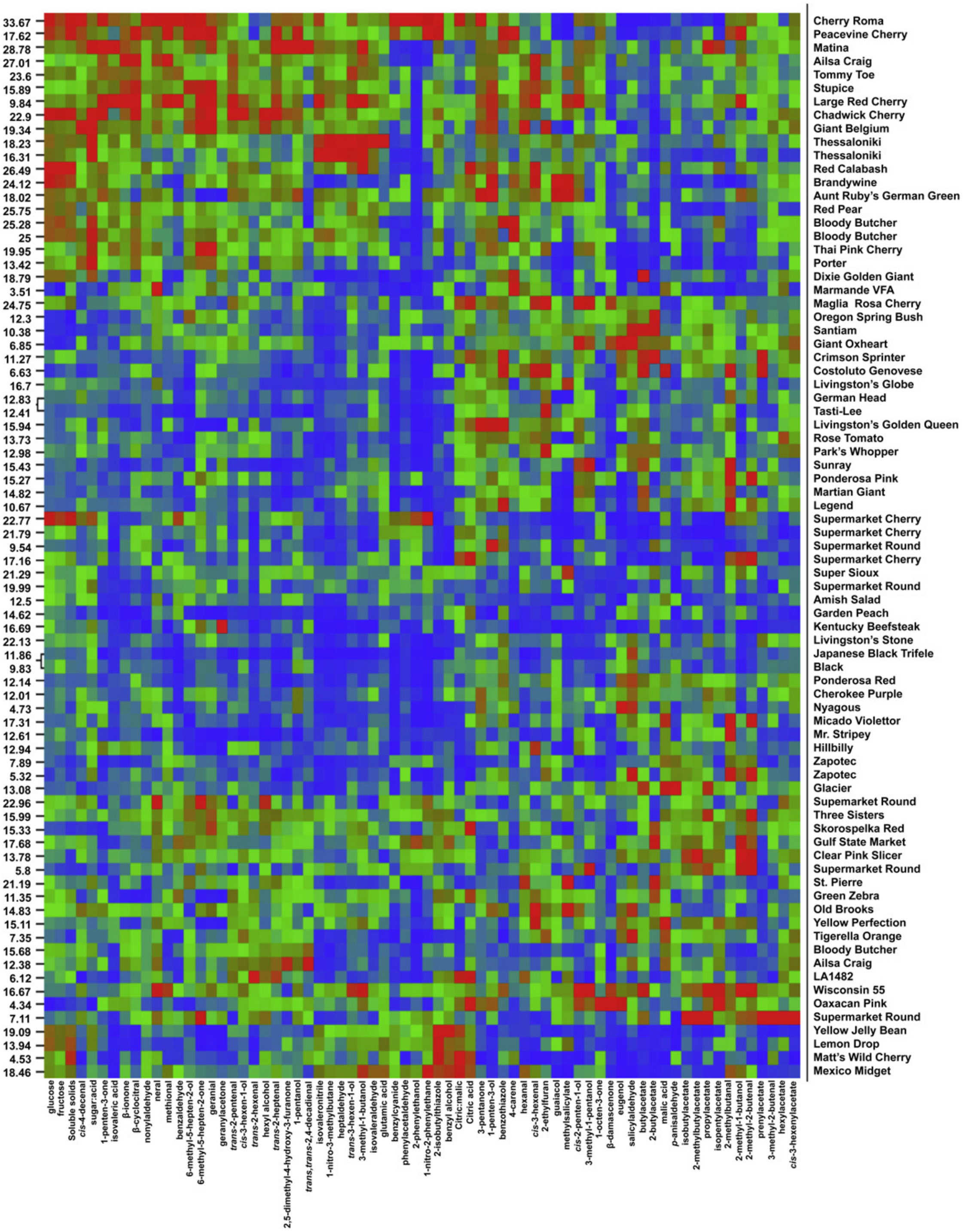

Figure 1. Cluster Analysis of Tomato Varieties Sorted by Flavor Chemical Composition

Varieties were sorted using JMP software (http://www.jmp.com/) on the basis of the 70 measured chemical attributes shown across the bottom. The names of varieties (right) and their consumer liking scores (left) are shown. Several varieties were tested in multiple seasons.

biosynthesis are deficient in apocarotenoid volatiles, including geranial, 6-methyl-5-hepten-2-one, and β-ionone, but unaltered in sugars, acids, and nonapocarotenoid volatiles. They are perceived as less sweet by consumers, validating the contribution of geranial to sweetness [13]. Consistent with a model in which liking is a function of sweetness and flavor, apocarotenoid-deficient fruits are also significantly less liked by consumers. In a complementary experiment, Baldwin et al. [14] have shown that adding sugars or acids can alter the perception of tomato aroma volatiles.

The positive association of sweet perception with volatiles such as geranial suggests that consumer liking of tomatoes could be enhanced by increasing the concentrations of certain volatiles such as geranial in the fruit. The results more broadly

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Table 2. C6 Volatile Emission in Fruit of Control M82 and *LoxC* Antisense Plants

	cis-3-hexenal	hexanal	*cis*-3-hexen-1-ol	hexyl alcohol	hexyl acetate
M82	139 ± 55	202 ± 43	59.0 ± 14.6	38.7 ± 11.2	2.61 ± 0.85
LoxCAS	0.6 ± 0.1	1.9 ± 0.3	0.07 ± 0.01	0.08 ± 0.01	0.014 ± 0.002

Volatile emissions (ng/g fresh weight/hr) from ripe control (M82) and transgenic (LoxCAS) fruits were measured as described in Experimental Procedures.

suggest that these volatiles could be used as a replacement for a portion of the sugars used in processed foods, thus reducing caloric content.

Conclusions

We exploited the natural chemical variation within tomato to determine the chemical interactions that drive consumer liking. Our data illustrate the challenge of understanding flavor, and consumer preferences in particular, in a natural product. Starting with a large set of chemically distinct volatiles, we can now focus our efforts at genetic improvement on a smaller set than previously thought possible. Despite the large number of quantitative trait loci that impact flavor chemicals [15–17], it should be possible with molecular-assisted breeding techniques to exploit the natural variation present within the heirloom population, combining desirable alleles of multiple genes to significantly improve flavor quality. It must be noted that not everyone will agree on the "best"-tasting tomato. Although we have averaged consumer liking across the entire population, the data permit us to separate out preferences by age, sex, body mass, and genetics [18]. The collected data permit us to define the parameters of a consensus best tomato in the United States, with the future possibility of optimization for specific groups. Taken together, the results provide new insights into flavor and liking and illustrate the flaws in a traditional approach based on odor units. The presence of a molecule, even at a relatively high level, does not mean that it significantly contributes to either flavor or liking. Models based on concentration and odor thresholds of individual volatiles cannot account for synergistic and antagonistic interactions that occur in complex foods such as tomato. Previous concepts of the most important volatile contributors to human food preferences based on odor units must be reevaluated.

Experimental Procedures

Plant Material

Commercial tomato seeds were obtained from Seeds of Change (Santa Fe, NM, USA), Totally Tomatoes (Randolph, WI, USA), or Victory Seed Co. (Molalla, OR, USA). Most varieties selected were described as heirloom, open-pollinated varieties. Plants were grown in the field at the University of Florida North Florida Research and Education Center–Suwannee Valley in the spring or fall seasons or in Horticultural Sciences greenhouses on the University of Florida campus in Gainesville, FL. Supermarket tomatoes were obtained from a local supermarket in Gainesville, FL.

Biochemical Analysis

Volatile collection was performed as described previously [16]. Volatile compound identification was determined by gas chromatography-mass spectrometry and coelution with known standards (Sigma-Aldrich). Sugars, acids, and soluble solids were determined as described in [13].

Sensory Analysis

All consumer panels were approved by the University of Florida Institutional Review Board. Fully ripe fruit were harvested and used for taste panels. A random subset of fruits were used for biochemical analysis. Three biological replicates, each consisting of 2–20 fruits (depending on fruit size), were assayed for each variety. A group of 170 tomato consumers (64 male, 106 female) were recruited to evaluate all of the varieties. Panelists were between the ages of 18 and 78, with a median age of 22. Panelists self-classified themselves as 101 White/Caucasian, 14 Black/African American, 32 Asian/Pacific, and 25 Other. An average of 85 (range of 66–95) of these panelists evaluated between four and six varieties in a session. All panelists went through a training session to familiarize them with the scaling and procedures. Tomatoes were sliced into wedges (or in halves, for grape/cherry types), and each panelist was given two pieces for evaluation. Panelists took a bite of each sample, chewed and swallowed it, and rated overall liking and liking for texture. They then rated the perceived intensities of sweetness, sourness, saltiness, umami sensation, bitterness, and overall tomato flavor. They were free to take as many bites as necessary to complete the assessments and were instructed to take a bite of an unsalted cracker and a sip of water between samples. Samples were presented to the panelists in a randomized order. Hedonic ratings used the hedonic general labeled magnitude scale (gLMS) [7, 8, 19]. This scale assesses the liking for tomatoes in the context of all pleasure/displeasure experiences: 0 = neutral; −100 = strongest disliking of any kind experienced; +100 = strongest liking of any kind experienced. Sensory intensity ratings used the sensory gLMS. This scale assesses taste and flavor sensations in the context of all sensory experiences [7]: 0 = no sensation; 100 = strongest sensation of any kind experienced. Both scales were devised to provide valid comparisons across subjects.

Molecular Marker Analysis

A standard protocol was used to isolate genomic DNA from young leaves of each variety. From a total of 36 markers, the following 27 were polymorphic within the set of 19 tomato varieties with liking scores: CosOH51, LEOH1.1, LEOH16.2, LEOH18, LEOH36, LEOH19, LEOH70, Rx3-L1, SP, SSR20, SSR43, SSR47, SSR63, SSR111, SSR115, SSR128, SSR134, SSR318, SSR306, TOM144, SL10126-1067i, SL10184-480i, SL10615-428i, SL20210-883i, *OVATE*, *FAS*, and *LC* [20, 21]. The cleaved amplified polymorphism sequence markers were scored on 2%–4% agarose gels, whereas the simple sequence repeat (SSR) and indels were scored on a LI-COR IR2 4200 (LI-COR Biosciences). There was 1.6% missing marker data. The missing data were imputed by replacing the missing value with the most frequent allele for that marker in the entire data set. Principal component analysis (PCA) was performed with Minitab 15.1.0.0 software. To combine SSR with SNP data, we used the allele sizes. To avoid bias due to allele size difference, we performed the PCA with the covariance matrix.

Statistical Analysis

The 68 chemical compounds measured in this experiment were divided into six groups based upon biochemical properties: sugars, branched-chain amino acids, lipids, carotenoids, phenolics, and acids. A small number of compounds for which biosynthetic pathways are not established were assigned to one of the six classes based on their correlations with other classified compounds. All pairwise correlations among the set of 68 compounds were calculated. Correlation coefficients were sorted using modulated modularity clustering (MMC) [9] as a visual aid for identifying compounds that are closely related in this sample (Figure S1; Table S3). Biochemical groups were examined for compounds within the group that were highly correlated, and compounds that were upstream in the relevant metabolic pathways were preferentially selected. The selection process resulted in 27 compounds (Figure S2) that were representative of each of the six biochemical groups and limited the amount of correlation between compounds. The set of 27 was examined using MMC, and the result confirmed that the pairwise correlation had been reduced (Figure S1). An exploratory factor analysis did not reveal obvious structure among the remaining compounds. For example, the lipids did not all load together on a single factor.

Benzothiazole, butylacetate, *cis*-3-hexen-1-ol, citric acid, fructose, geranial, methional, 3-methyl-1-butenol, 2-methylbutanal, 1-octen-3-one, phenylacetaldehyde, and *trans*,*trans*-2,4,decadienal were associated with flavor intensity in univariate models. 2-butylacetate, *cis*-3-hexen-1-ol, citric acid, 3-methyl-1-butanol, 2-methylbutanal, 1-octen-3-one, and *trans*,*trans*-2,4-decadienal were significant after accounting for fructose. Butylacetate, 4-carene, *cis*-3-hexen-1-ol, eugenol, fructose, geranial, guaiacol, heptaldehyde, methional, 3-methyl-1-butanol, 2-methylbutanal, and phenylacetaldehyde all showed evidence for association with sweetness in univariate models, and geranial, 3-methyl-1-butanol, and 2-methylbutanal were significant after accounting for fructose. All analyses were performed in SAS v9.2.

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LoxC Transgenic Tomatoes

A transformation vector containing the constitutive FMV *35S* promoter [22] and a full-length antisense tomato 13-lipoxygenase *LoxC* [12] open reading frame was introduced into *S. lycopersicum* var. M82 [23]. Total RNA from fruit tissue was extracted with a QIAGEN RNeasy Plant Mini Kit followed by DNase treatment to remove contaminating DNA. RNA levels from 200 ng total RNA were measured using an Applied Biosystems Power SYBR Green RNA-to-C_T 1-Step Kit with forward primer 5′-GCAATGCATCATGTGTGCTA-3′ and reverse primer 5′-GTAAATGTCGAATTCCCTTCG-3′. *LoxC* antisense tomato fruit RNA levels were 5% of control M82 fruit. Levels of the C6 volatiles hexyl alcohol, *cis*-3-hexenal, and *cis*-3-hexen-1-ol in *LoxC* antisense ripe fruit were less than 1% of control M82 fruit, whereas hexanal levels were less than 2% of control. Homozygous T2 plants were used for sensory analysis. Transgenic and M82 control fruits were harvested at the ripe stage. Seeds and locular material were removed from the fruits, and the remainder was used for taste panels. Random fruits were used for biochemical analysis. Seventy panelists (27 male, 43 female) were given two tomato samples (one control and one transgenic) and asked to evaluate the texture and flavor and to describe how much they liked the samples using a nine-point hedonic scale. They were subsequently asked to identify the one that they preferred. No sample was preferred over the other in any of these evaluations ($\alpha = 0.05$). In a triangle test setup, 59 panelists (25 male, 34 female) were given three samples (a triple combination of control and transgenic samples) and asked to identify the nonmatching sample. The number of correct responses (29) was significant at $\alpha = 0.01$.

Supplemental Information

Supplemental Information includes two figures and three tables and can be found with this article online at doi:10.1016/j.cub.2012.04.016.

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