

# Genetic variations associated with the soapy flavor perception in Gorgonzola PDO cheese

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## ABSTRACT

Food preferences are influenced by several factors including individual differences in the physiological perception of the sensory properties and genetic factors. This study was aimed to investigate the genetic bases underlying the perception of the soapy flavor, a sensory attribute identified as a driver of disliking for blue-veined cheese. Responses on soapy flavor perception (SFP) in six Gorgonzola Protected Designation of Origin (PDO) cheese samples were collected from 219 genotyped Italians (age 18–77 y) applying a Rate-All-That-Apply (RATA) test combined with a liking test.

Genome-Wide Association Studies (GWAS) were performed on three phenotypic traits: the SFP in at least one cheese (SFP\_1), the number of cheese samples in which each individual perceived the soapy flavor (SFP\_N) and the SFP in the cheese in which the highest number of individuals perceived the soapy flavor (SFP\_P95).

Results showed that 144 individuals (65.8%) perceived the soapy flavor in at least one cheese. Our analysis allowed identifying four loci that resulted shared in all the three GWAS and have been confirmed by the SFP in at least other two Gorgonzola cheese samples. Particularly, we highlighted four genes (*SYT9*, *PDE4B*, *AVL9* and *HTR1B*) that are involved in olfactory or taste processes, suggesting that they could play a relevant role in determining the individual differences in the SFP. In addition, a SNP near the *HTR1B* gene affected also the liking for Gorgonzola PDO cheese.

Overall, our work suggests possible candidate genes associated with the perception of soapy flavor, providing a starting point to better understand the individual differences in blue-veined cheese perception and expanding the current scientific knowledge in the emerging research area linking genetic individual differences to food perception and preferences.

## 1. Introduction

### 1.1. Relationship between genetics and chemosensory perception of food

Food liking and preferences have a multidimensional and complex nature since they are influenced by the interaction among several factors, including biological, genetic, physiological, psychological and personality-related, health, sociodemographic, lifestyle, and cultural variables (Monteleone et al., 2017). Considering the contribution of genetics, the human genetic revolution enabled the identification of the genetic determinants of sensory perception and opened to the possibility to investigate to which degree food liking has genetic foundations

(Newcomb, McRae, Ingram, Elborough, & Jaeger, 2010). Indeed, the genetic variation plays a crucial role in determining individual differences in food preferences, which ultimately influence food selection, and finally health, through food intake (see (Diószegi, Llanaj, & Ádány, 2019; Feeney, McGuinness, Hayes, & Nolden, 2021; Robino & Catamo, & Gasparini, 2019; Chamoun et al., 2018) for updated reviews). Studies investigating the relationship between chemosensory perception and genetic variations mainly examined the single nucleotide polymorphisms (SNPs) as the most common type of genetic variants within the human genome (Sherry, 2001), that occur when a single nucleotide is substituted with another in the genetic code (Running & Hayes, 2016). Polymorphism in genes codifying for specific receptors implies a

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difference in sensory receptors that affects the sensitivity across individuals for specific chemical compounds characterizing the food matrix, translating into a different liking for the considered food. This is the case for the well-known 6-n-propylthiouracil (PROP) and the related variants of the *TAS2R38* gene (Keller & Adise, 2016; Pawellek et al., 2016), which is responsible for notable individual different phenotypic responses to PROP (Bartoshuk, 2000). Besides taste, the genetic variation interests all sensory modalities, including olfaction and chemesis (Feeney et al., 2021).

### 1.2. Genetic variations associated with individual differences in odor and flavor perception

The sensitivity to many odors and flavors can strongly vary among individuals, from subjects able to perceive a specific odorous compound at a very low concentration to subjects with the inability to perceive the same odor stimulus even at a very high concentration since affected by a specific anosmia (Ulla, Antti, Oskar, & Mari, 2016). Moreover, individual differences occur among subjects also in terms of odor- and flavor-quality perception (Ayabe-Kanamura et al., 1998; Torri, Jeon, Piochi, Morini, & Kim, 2017). The perception of odor is definitely more complex to understand than the perception of taste since olfactory receptor genes represent the largest gene family (including around 400 intact/functional loci) present in the entire genome and have a high level of genetic variation relative to other proteins (nearly 30% of olfactory receptor alleles will differ functionally between two people) (Hasin-Brumshtein, Lancet, & Olender, 2009; Mainland et al., 2014). Several of these variants may interfere with the receptor functionality (e.g. in terms of expression, interaction with odorants, or signal transduction) and subsequently could alter the physiological response to a particular odor (Jimenez et al., 2021). It was pointed out that differences in smell perception may also influence food preferences and that they should be taken into account, especially where the volatile composition is relevant for the flavor profile of a food product. However, studies conducted on the genetic effect on food odor and flavor perception is still limited (Hayes, Feeney, & Allen, 2013).

Research aimed to highlight the genetic variables underlying phenotypic or behavioral variability in responses to food-related odors and flavors are based on the candidate gene approach and on the genome-wide association study (GWAS) approach. GWAS assume no hypothesis of the associated genetic variant, facilitating novel findings when investigating the relationship between genetic variants along the biological pathway and taste phenotypes or behavioral outcomes (i.e. liking/intake) (Hayes et al., 2013; Ulla et al., 2016). Literature provides some evidence of genetic variants explaining the different responsiveness of humans towards crucial volatile molecules contained in food. For instance, GWAS was effective in revealing the genetic association of human sensitivity for several food-related compounds responsible for odors, like 2-heptanone, isobutyraldehyde,  $\beta$ -damascenone, and  $\beta$ -ionone (McRae et al., 2013). Later, research has identified rs6591536, a SNP located in the coding region of the odorant receptor *OR5A1*, as responsible for major differences in ability to detect  $\beta$ -ionone odour (Jaeger et al., 2014), finding 'sensitive' (GG/AG) and insensitive (AA rs6591536) individuals. Other molecules, for which genetic variants were observed, are isovaleric acid and *cis*-3-hexen-1-ol. Indeed, a strong association signal was observed between the single nucleotide polymorphism variants in *OR11H7P* and sensitivity to the odorant isovaleric acid (Menashe et al., 2007). A group of significant SNPs on chromosome 6 around the SNP rs9295791 was identified and these localize with a cluster of olfactory receptor genes which could potentially be involved in the perception of *cis*-3-hexen-1-ol (Jaeger, McRae, Salzman, Williams, & Newcomb, 2010).

Moreover, an association between cinnamon odorant recognition and the rs317787 polymorphism, located in a cluster of olfactory receptor genes, was also recently described (Gisladottir et al., 2020), and a significant correlation of the same SNP with the liking for red wines

(normally also described by 'cinnamon' flavor, among others descriptors) was also found (Concas, Morgan, Pelliccione, Gasparini, & Girotto, 2021).

Likely the most studied odorous compound in human smell genetics is androstenone, which is often present in the skin of boars, leading to a pork defect known as 'boar taint', being the androstenone's odour described as 'sweaty', 'ammonia', 'dirty', 'silage' and 'acid'. The genetic variation of the odorant receptor *OR7D4* is known to affect the sensory perception of cooked pork meat containing androstenone (produced by male pigs) (Lunde et al., 2012). Interestingly, androstenone-containing meat is less acceptable to subjects with two copies of the RT variant of the *OR7D4* receptor, indicating that this genetic variation affects food preferences.

### 1.3. Soapy flavor perception in food

Most of the research reported in literature focused on genetic variants found in relation to single molecules dissolved in water or referring to stated liking for food products. On the contrary, scarce knowledge is available regarding the genetic variants associated to phenotypic traits based on sensory evaluation of real food and beverages, thus more research in that direction is desirable.

A relevant case of diversity in liking for specific food is that for the cilantro or coriander (*Coriandrum sativum* plant). Cilantro leaf is widely consumed globally and has purported health benefits ranging from antibacterial to anticancer activities. Interestingly, some individuals report an extreme dislike for cilantro, and the prevalence of cilantro dislike varies between different ethnocultural groups (Mauer & El-Sohemy, 2012). The polarizing disliking of cilantro is linked to the fact of perceiving it as 'soapy', and/or 'pungent'. The cilantro dislike was found to have a genetic component, being a SNP (rs72921001, lying within a cluster of olfactory receptor genes on chromosome 11) significantly associated with the 'soapy' detection (Eriksson et al., 2012).

The 'soapy' flavor was used to describe also other different foods and beverages, and it was associated to a wide diversity of molecules. Examples of products in which 'soapy' flavor was perceived were traditional Moroccan fermented butter "Smen" (Sarhir, Amanpour, Bouseta, & Sellì, 2021), lamb meat (Karamichou, Richardson, Nute, Wood, & Bishop, 2007), beef strip loins injected with a solution containing sodium tripolyphosphate (Vote et al., 2000), beers in which 'soapy' represented an off-flavor (Dietz, Cook, Wilson, Oliveira, & Ford, 2021), whisky (Lee, Paterson, Piggott, & Richardson, 2000), Turkish olive oils (Kesen, Kelebek, Sen, Ulas, & Sellì, 2013), and soluble coffee beverage powder in which the combination of phosphates and citrates may be used without generation of soapy notes (Maier & Bachtler, 2005).

The descriptor 'soapy' has been used to describe the sensory properties of some cheese types and defined as 'A detergent-like taste. Similar to when a food is tainted with a cleansing agent' (Murray & Delahunty, 2000; Kilcawley et al., 2007). Moreover, it was observed that the intensity of the soapy perception in Cheddar cheese was influenced by the milk source (Murtaza, Rehman, Anjum, & Huma, 2013) and cheese aging time (Kheadr, Vuilleumard, & El-Deeb, 2002). The term 'soapy' was also used in a previous study (Moio, Piombino, & Addeo, 2000) to describe the Italian blue-veined Gorgonzola Protected Designation of Origin (PDO) cheese odor. However, only very recently it was demonstrated that a great phenotypic variability in Gorgonzola cheese liking exists and that differences in preferences for Gorgonzola cheese were mainly linked to the perception of 'soapy' flavor (Torri et al., 2021).

### 1.4. Aims of the study

Based on the very recent findings mentioned above identifying the 'soapy flavor' as main driver of disliking for Gorgonzola cheese, the following was hypothesized: I. The perception of 'soapy' flavor in Gorgonzola cheese is associated to a genetic variation (as previously observed in other foods, like cilantro); II. Potential existing genetic

variants may partially explain the variability in Gorgonzola cheese liking experienced among consumers. Thus, the aim of this study was to investigate the genetic bases of phenotypic traits of soapy flavor perception in a real food product with a group of consumers for which genetic data and information about soapy flavor perception in six different Gorgonzola PDO cheese samples were collected.

## 2. Materials and methods

### 2.1. Gorgonzola PDO cheese samples

Six samples of Gorgonzola PDO cheese varying according to style (Sweet vs Piquant), aging time (70–95 days) and production process (Artisanal vs Industrial) were analyzed. The same samples were used in a previously published paper on Gorgonzola Cheese (Torri et al., 2021). Samples are identified with a letter indicating the cheese style followed by a number referring to the aging time expressed in days. Thus, codes S70, S75 and S80 identify Sweet style cheese samples aged for 70, 75 and 80 days, respectively, while codes P95, P85 and P80 identify Piquant style cheese samples aged for 95, 85 and 80 days, respectively. S75 and P80 were made using an industrial production process whereas the other four samples were obtained with an artisanal production process. The cheese wheels had an approximate weight of 11–12 kg each. For each cheese sample, six pieces of 1.5 kg (corresponding to 1/8 of the cheese wheel) from six different cheese wheels of the same production batch were tested (9 kg in total for each cheese sample; overall, 54 kg of cheese). All the cheese products were made with whole cow's milk (98.26%), selected milk enzymes (1.5%), selected *Penicillium* molds (0.01%; different strains of *Penicillium roquefortii* used for the different cheese products), dehydrated sea salt (0.21%) and animal rennet (0.02%). Prior to the analysis, all the products were stored at 4 °C. Before the sensory test, the outer rind (1 cm) of each 1/8 of a cheese wheel was discarded, and the products were cut into 15 g parallelepipeds. At the same time, three different portions were sampled from each 1/8 of a cheese wheel and placed (no headspace left) in a 96 mL plastic cup that was then hermetically sealed and stored at – 20 °C until the volatile compound determination.

### 2.2. Participants

Data presented here are part of a broader study on Gorgonzola cheese involving 358 subjects (Torri et al., 2021). In the present work, genetic analysis was performed on a subset of 219 subjects (43% males; age range: 18–77 years, average age: 43.4, standard deviation: 15.1; nationality: 71.7% Italian, 15.1 European different from Italian, 13.2% extra-European (all of the Caucasian ancestries)). Participants were recruited by email, websites, Facebook and articles published in local newspapers. The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of the University of Gastronomic Sciences (Ethics Committee Proceeding n. 2019.02). All participants signed an informed consent.

### 2.3. Sensory evaluations

Firstly, participants evaluated their overall liking for the cheese samples on the Labeled Affective Magnitude scale, ranging from 0 (the greatest imaginable dis-like) to 100 (the greatest imaginable like) (Schutz & Cardello, 2001). Secondly, they performed a Rate-All-That-Apply (RATA) test (Ares et al., 2014) with a list of 12 sensory attributes related to taste (salty, sweet), flavor (ammonia, cooked vegetables, floral, moldy, nutty, soapy, toasted), and mouthfeel (creamy, grainy, pungent) and using a generalized Labelled Magnitude Scale (0 = no sensation, 100 = the strongest imaginable sensation of any kind) (Bartoshuk et al., 2004). Finally, participants answered a short questionnaire on socio-demographic data (age, gender, nationality). More information on sensory evaluations are described in a previous paper

(Torri et al., 2021).

### 2.4. Saliva collection

Saliva collection was performed according to the procedure used in the Italian Taste project (Monteleone et al., 2017; Robino et al., 2022) in individual booths before the sensory evaluations. Subjects were instructed to remove their lipstick if they wore it, rinse their mouth with water, wait 10 min, and then to spit saliva into a graduated test tube until a volume of 2 mL, free of bubbles, was reached. One square (3\*3 cm) of Parafilm® M (Pechiney Plastic Packaging, USA) was provided to facilitate saliva production when required. Saliva was stored at ambient temperature using the GeneFix™ Saliva DNA collection and stabilization devices (Isohelix, Cell Projects Ltd, Kent, UK) until the DNA was extracted.

### 2.5. Genotyping and imputation

Individuals for which DNA was available have been genotyped with the GSAMD-24v1-0\_20011747\_A1 Illumina array (Illumina Inc., San Diego, CA, USA). Genotype imputation was conducted after standard quality control using IMPUTE2 software (Howie, Donnelly, & Marchini, 2009), considering as reference a custom panel generated merging the 1000 Genomes phase 3 (The 1000 Genomes Project Consortium, 2012) and Whole Genome Sequences of the Italian Network of Genetic Isolates (INGI) samples (Cocca et al., 2020). After imputation, SNPs with minor allele frequency (MAF) < 0.03 and Info Score < 0.6 were discarded from the statistical analyses.

### 2.6. Genome-wide association studies (GWAS)

GWAS were performed on three phenotypic traits:

1. The soapy flavor perception in at least one cheese (SFP\_1); this first analysis considered all soapy taster (ST) individuals versus all non-soapy taster (NST) subjects.
2. The number of cheese samples in which each individual perceived the soapy flavor (SFP\_N); this second analysis represented an individual quantitative measure of the perception of soapy flavor and its value was 0 for NSTs and a number ranging from 1 to 6 for STs.
3. The soapy flavor perception in cheese P95 (SFP\_P95); this third analysis considered only the cheese in which the highest number of individuals perceived the soapy flavor that is also the cheese in which the mean intensity of soapy perception was higher. In this case, we analyzed the P95 ST individuals versus the P95 NSTs.

For the analysis SFP\_1 and SFP\_95, we used a variable coded as 0 if the individual was NST and 1 otherwise.

GWAS were conducted using SNPTEST software (Marchini, Howie, Myers, McVean, & Donnelly, 2007). Logistic (for SFP\_1 and SFP\_P95) or linear (for SFP\_N) regressions were performed considering additive models, adjusted by gender, age and the first 10 principal components (PCs). Because SFP\_N was not normally distributed, the quantile normal transformation was applied, as available in SNPTEST. For each GWAS, all the SNPs with p-value < 1x10<sup>-5</sup> were annotated with the Variant Effect Predictor tool (VEP) (Ensembl, 2021; McLaren et al., 2016) to determine: i) their distance from the closest genes; ii) their functional characteristics (i.e., whether they were contained within an intronic, exonic, or intergenic region); iii) the genes biotype. For each SNP, the closest coding gene in a range of 250 kb was annotated. We considered the coding genes identified by at least one SNP with p-value < 1x10<sup>-6</sup> or, if no SNPs with p-value < 1x10<sup>-6</sup> were detected, coding genes identified by at least two SNPs with p-value < 1x10<sup>-5</sup>. All data are aligned to the Human genome reference build 37 (GRCh37).

## 2.7. Confirmation of the detected SNPs

For each gene identified in the GWAS, we checked the association of the relative SNP/SNPs in the other two GWAS. In addition, we verified the effect of the SNP analyzing ST individuals versus NSTs for each of the five remaining cheese samples (analysis SFP\_P85, SFP\_P80, SFP\_S80, SFP\_S75 and SFP\_S70). We considered “confirmed” the SNPs that showed an association with a p-value < 0.05 with all the SFP\_1, SFP\_N, SFP\_P95 analysis and in additional analysis for two cheese samples. In the analysis SFP\_P85, SFP\_P80, SFP\_S80, SFP\_S75 and SFP\_S70, we checked the SNPs using logistic regression and additive models with gender, age and the first 10 PCs in SNPTEST.

## 2.8. Effect of the confirmed SNPs on intensity for soapy perception

The effect of the confirmed SNPs on intensity for soapy perception was verified for each cheese. A linear regression was performed for each cheese using an additive model and considering the intensity as dependent variable (normalized by means of the quantile normal transformation), and each tagged SNP as an independent variable with gender, age and the first 10 PCs (SNPTEST software). We considered significant the effect of SNPs with p-value < 0.05.

## 2.9. Effect of the confirmed SNPs on liking for cheese

The effect of the confirmed SNPs on liking for each cheese was verified. Indeed, for each cheese and for each SNP, a linear regression was performed. Exactly, an additive model with gender, age and the first 10 PCs was carried out using SNPTEST and considering the liking as dependent variable and each tagged SNP as independent variable. When a significant result (p-value < 0.05) was found, we verified if the effect of the SNP on liking was direct or mediated by the soapy flavor

perception. To assess the significance of the mediated model, Sobel test was used (Sobel, 1982), using the function *mediation.test* available on *bda* R library ([www.r-project.org](http://www.r-project.org)) v.3.3.0.

## 2.10. Replication of already published variants associated with soapy flavor perception

Finally, the effect of the SNP rs72921001, already found associated with soapy flavor perception in cilantro (Eriksson et al., 2012), on SFP, the intensity of soapy flavor and liking for cheese samples was checked, using SNPTEST and considering a significance threshold of 5%.

The workflow of the study is shown in Fig. 1.

## 3. Results

### 3.1. Soapy flavor perception in Gorgonzola cheese

Overall, the individuals who perceived the soapy flavor in at least one cheese (soapy tasters, STs) were 144 out of 219 (65.8%), while the individuals never perceiving the soapy flavor (non-soapy tasters, NSTs) were 75 (34.2%). Overall, 25.1% perceived soapy in only one cheese, 21.9% perceived it in two cheese samples, 8.2% in three, 3.2% in four, 2.7% in five and 4.6% in all six cheese samples (Fig. 2). For each of the six Gorgonzola cheese samples, Table 1 summarizes the characteristics of participants as STs and NSTs.

P95 was the cheese for which the greatest number of individuals perceived the soapy flavor (74 out of 219), while S80 and P85 were those for which fewer individuals perceived the soapy flavor (43 and 44, respectively). No statistically significant differences were found in the distribution of males and females between STs and NSTs. The mean age of STs was lower than the mean age of NSTs for each cheese and was statistically significantly lower for P95, P80 and S75. Considering all

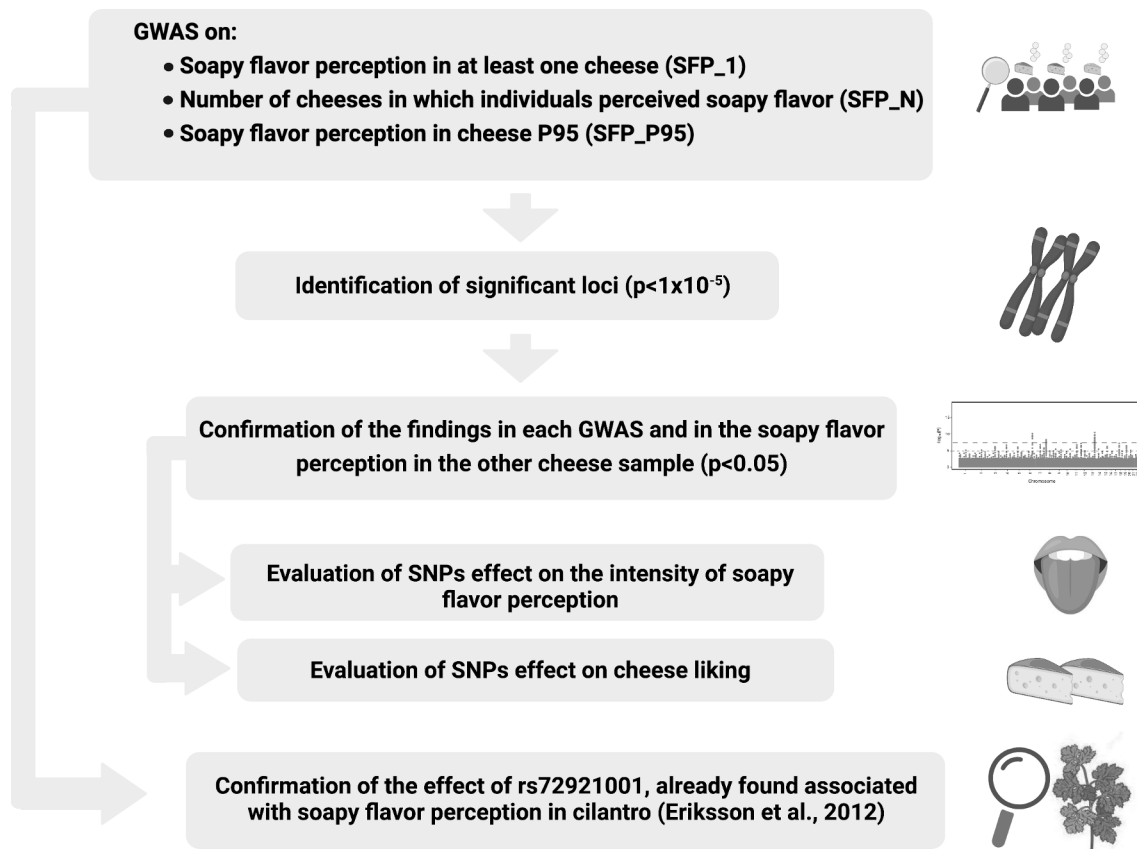
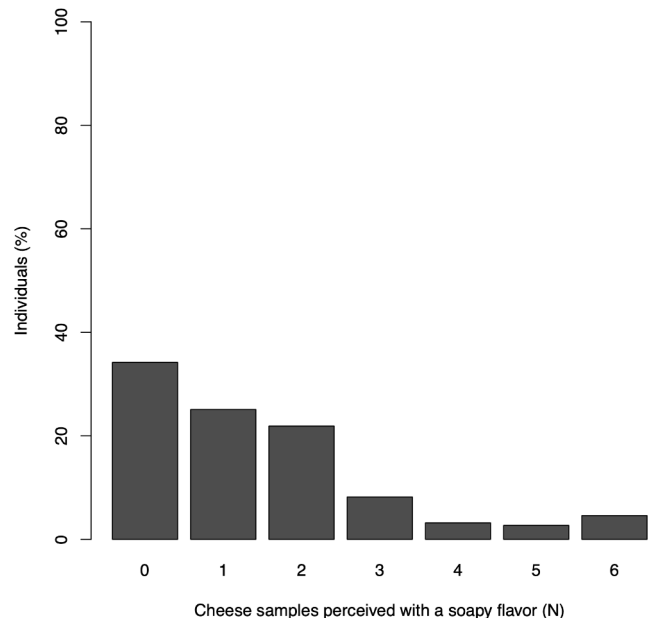


Fig. 1. Workflow applied to the present study.



**Fig. 2.** Distribution of the individuals (n = 219) based on the number of cheese samples in which they perceived the soapy flavor.

cheese samples, the mean age was 40.6 (standard deviation 14.5) for STs and 48.8 (standard deviation 14.9) for NSTs. This difference was significant (T-test p-value < 0.05). The mean intensity of soapy flavour in STs ranged from 20.1 for cheese P85 to 28.3 for cheese P95. The mean likings were significantly higher (p-value < 0.05) for NSTs compared to STs for all cheese samples except for P85.

### 3.2. Loci associated with soapy flavor perception

Figures in Online Resource 1 show the Manhattan and QQ plots of the GWAS conducted on the three considered phenotype traits related to the soapy flavor perception (SFP\_1, SFP\_N, and SFP\_P95), while Table S1 displays the SNPs with p-value <  $1 \times 10^{-5}$ . VEP annotation is available in Table S2.

Table 2 summarizes the best results obtained for each of the three applied GWAS.

The GWAS identified nine loci located in chromosomes 5, 8 (two different loci), 11 and 21 for SFP\_1, in chromosomes 1 and 7 for SFP\_N,

**Table 1**

Characteristics of the participants (n = 219) based on their soapy flavor perception in each Gorgonzola Protected Designation of Origin (PDO) cheese. For each cheese (indicated in the first column), the table shows: the number (and percentage) of soapy-tasters (STs), the number of males/females STs, and the p-value of the Chi-square test comparing the distribution of sex in STs and non-soapy tasters (NSTs), the mean age (and standard deviation) of STs, NSTs, and the p-value of T-test comparing the distribution of age in STs and NSTs, the mean intensity (and standard deviation) of soapy perception in STs (in NSTs the intensity was 0) the mean liking (and standard deviation) expressed by STs and NSTs and the p-value obtained by T-test comparing their liking. In bold are indicated the significant p-value (<0.05).

Cheese	Soapy tasters (STs)		Mean age (standard deviation)			Mean intensity (standard deviation)		Mean Liking (standard deviation)		
	n (%)	males/females (p-value)	Soapy Tasters (STs)	Non-Soapy Tasters (NSTs)	p-value	Soapy Tasters (STs)	Soapy Tasters (STs)	Non-Soapy Tasters (NSTs)	p-value	
P95	74 (33.8)	26/48 (0.1064)	37.8 (13.4)	46.3 (15.1)	<0.001	28.3 (22.6)	57.8 (20.4)	67.1 (17.8)	0.0012	
P85	44 (20.1)	20/24 (0.8882)	40.64 (15.7)	44.1 (14.9)	0.1885	20.1 (18.5)	68.1 (17.8)	66.0 (16.9)	0.4777	
P80	50 (22.8)	24/26 (0.5565)	38.7 (13.4)	44.8 (15.3)	0.0072	21.5 (17.9)	58.1 (21.7)	68.1 (17.2)	0.0038	
S80	43 (19.6)	22/21 (0.3285)	41.4 (13.6)	43.9 (15.4)	0.2910	20.6 (18.2)	61.1 (17.5)	71.3 (16.9)	<0.001	
S75	63 (28.8)	33/30 (0.1193)	39.4 (14.8)	45.0 (15.0)	0.0129	21.0 (16.5)	59.4 (15.9)	65.7 (14.5)	0.0078	
S70	49 (22.4)	23/26 (0.6839)	42.6 (13.6)	43.7 (15.5)	0.6304	20.2 (16.4)	62.0 (17.4)	69.5 (16.1)	0.0087	

and chromosomes 3 and 6 for SFP\_P95.

Table S3 displays the results of the association of the detected SNPs in the three previous GWAS (SFP\_1, SFP\_N and SFP\_P95) and in the analysis regarding the soapy flavor perception in the other five cheese samples (SFP\_P85, SFP\_P80, SFP\_S80, SFP\_S75, SFP\_S70). Fig. 3 summarizes these results.

Since we considered “confirmed” the SNPs that showed association with all the SFP\_1, SFP\_N, SFP\_P95 traits and with the SFP for two additional cheese samples, out of the nine loci identified in the three GWAS, we excluded five loci from further analysis. Indeed, *TRIM36* showed association in only one cheese (SFP\_P95), *KCNU1* did not present association for SFP\_N and any cheese, *ANXA13*, *BRWD1* and *ZCWPW2* showed association for the analysis in only one other cheese (P85, P80 and P85 respectively).

Among the four remaining loci, the first is detected in SFP\_1 analysis by three genome-wide significant SNPs (i.e., p-value <  $5 \times 10^{-8}$ ; top SNP rs11041224). These SNPs are located in chromosome 11, in intergenic region. The nearest coding gene is *SYT9* (closed ~ 70 kb) and the SNPs are located about 300 kb from rs72921001, the SNP already found in association with soapy perception in cilantro (Eriksson et al., 2012). As shown in Fig. 4A and in Table S2, the top SNP is 243 kb from a cluster of olfactory receptor genes and in particular *OR2D3* gene. Significant associations (p-value < 0.05) with these SNPs were found for SFP\_N and soapy flavor perception in cheese samples P95, P85 and S75 (Fig. 3).

Six SNPs identified a locus in *PDE4B* gene (Fig. 4B). This locus was highlighted in SFP\_N and confirmed in SFP\_1 and in SFP analysis for all the six cheese samples.

The GWAS on SFP\_N highlighted another region in chromosome 7 (Fig. 4C) spanning about 93 kb and identifying four protein coding genes: *FKBP9*, *AVL9*, *NT5C3A* and *RP9*. The association were confirmed by the analysis SFP\_1 and SFP analysis for five cheese samples (Fig. 3).

The GWAS on cheese SFP\_P95 identified one locus in chromosome 6 closest 246 kb of *HTR1B* gene (Fig. 4D). This signal was confirmed by SFP\_1, SFP\_N and SFP for cheese samples P85 and P80 (Fig. 3).

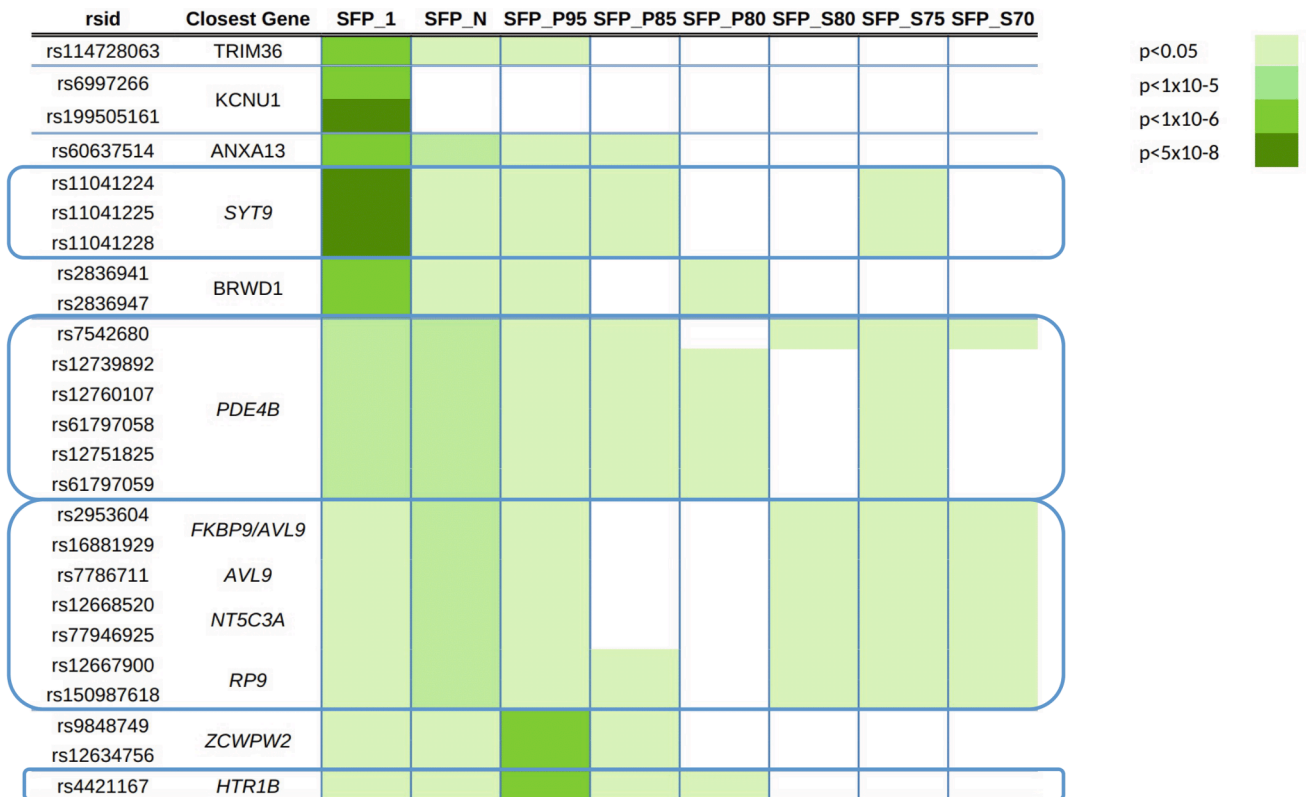
### 3.3. Effect of the SNPs on soapy flavor intensity

For each SNP in the four identified loci, we verified the association with the perceived intensity of soapy flavor in each cheese sample. The results are displayed in Table S4. Although not always with significant p-values, the allele more frequent in STs resulted associated with increased intensity for each SNP and each cheese sample, except for rs4421167 (*HTR1B*) and intensity of soapy perception in S70 cheese. In detail, we found that the perceived intensity of soapy flavor in P95 cheese was

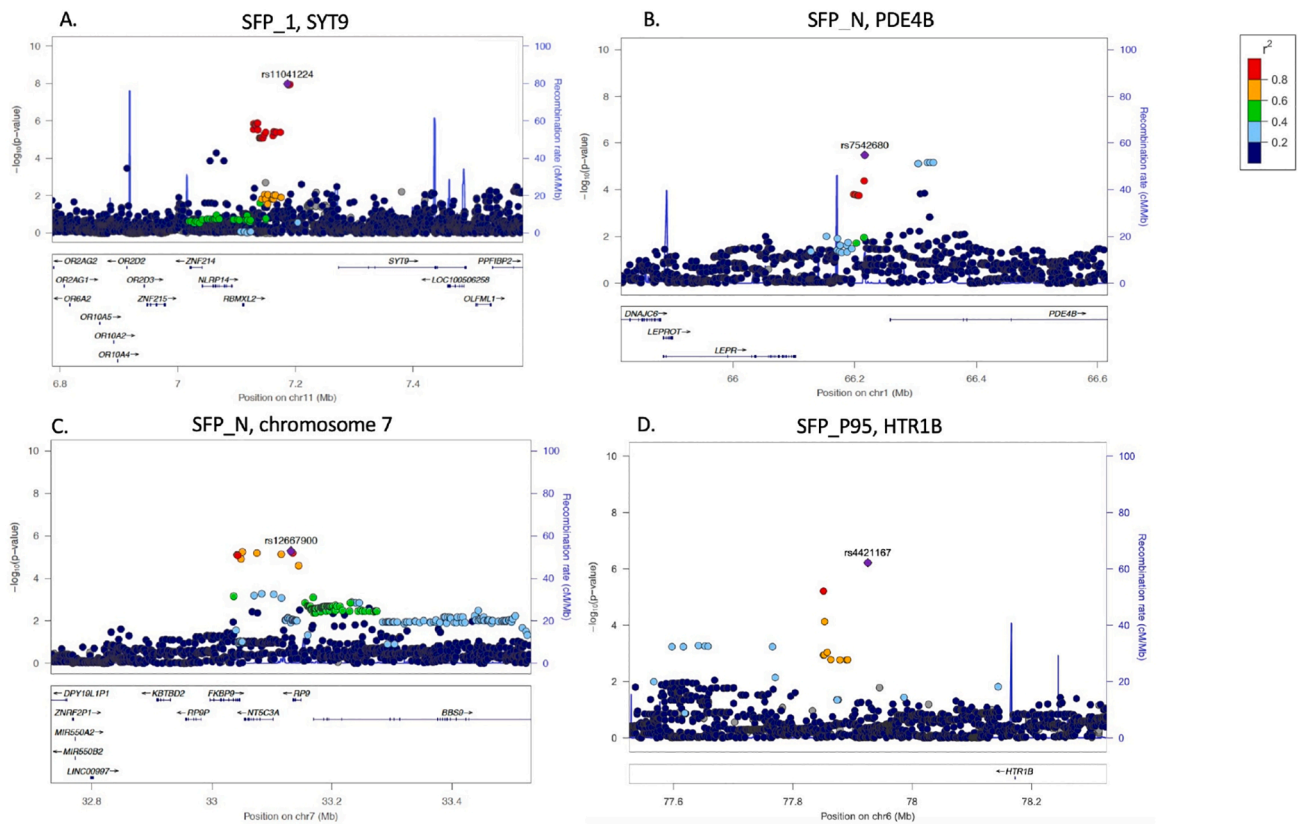
**Table 2**

Best results of the GWAS on soapy flavor perception in at least one cheese (SFP\_1), number of cheese samples in which the individuals perceived the soapy flavor (SFP\_N) and soapy flavor perception in cheese P95 (SFP\_P95). Rsid = SNP name; Chr = chromosome; position = position in base pair (bp); Alleles = effect allele/other allele; N = number of individuals involved in the analysis; MAF = minor allele frequency; Effect referred to Odds Ratio (OR) for binary variables (SFP\_1 and SFP\_P95) and beta for quantitative trait SFP\_N; Consequence = role of the SNP on the gene; Closest gene = the closest coding protein gene in an around of 250 kb; Distance (bp) = the distance of the SNP from the gene in bp. Data refer to 219 subjects.

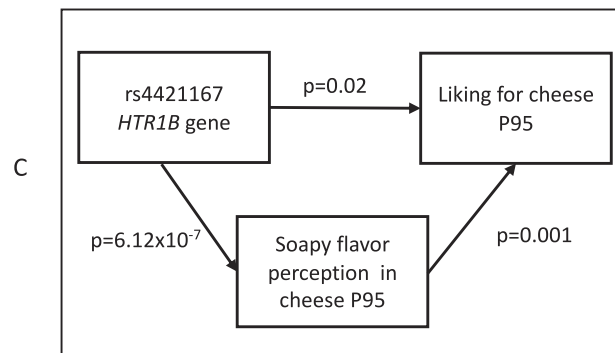
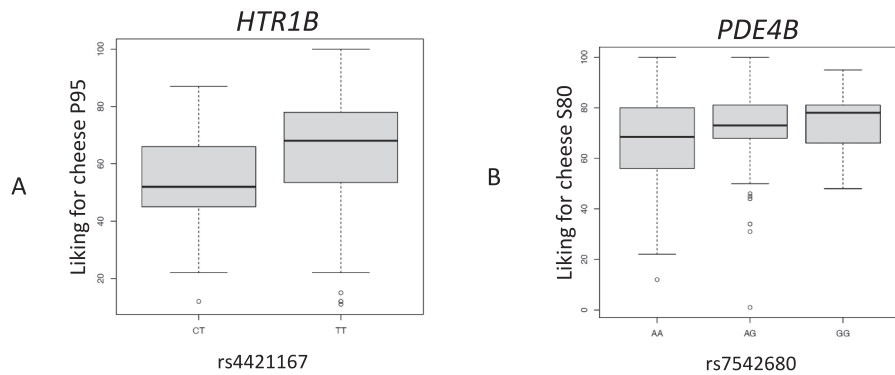
Phenotype	Rsid	Chr	Position	Alleles	MAF	Effect	p-value	Consequence	Closest Gene	Distance (bp)	
SFP_1	rs114728063	5	114404447	A/G	0.030	0.143	$2.87 \times 10^{-7}$	downstream_gene	TRIM36	56012	
	rs6997266	8	36635215	T/C	0.033	0.334	$3.90 \times 10^{-7}$	upstream_gene	KCNU1	6627	
	rs199505161	8	36639731	T/C	0.035	0.275	$1.34 \times 10^{-10}$	upstream_gene	KCNU1	2111	
	rs60637514	8	124749145	A/G	0.225	0.344	$7.65 \times 10^{-7}$	intron	ANXA13	-	
	rs11041224	11	7186458	A/T	0.084	0.296	$1.06 \times 10^{-8}$	upstream_gene	SYT9	73641	
	rs11041225	11	7188457	C/T	0.085	0.301	$1.17 \times 10^{-8}$	upstream_gene	SYT9	71642	
	rs11041228	11	7190680	A/G	0.084	0.298	$1.09 \times 10^{-8}$	upstream_gene	SYT9	69419	
	rs2836941	21	40590899	T/C	0.094	0.272	$5.84 \times 10^{-7}$	intron	BRWD1	-	
	rs2836947	21	40598376	T/G	0.092	0.273	$5.80 \times 10^{-7}$	intron	BRWD1	-	
	SFP_N	rs7542680	1	66216575	A/G	0.263	0.445	$3.37 \times 10^{-6}$	upstream_gene	PDE4B	41622
	rs12739892	1	66304567	T/G	0.219	-0.455	$7.70 \times 10^{-6}$	intron	PDE4B	-	
	rs12760107	1	66304644	A/T	0.219	-0.454	$7.67 \times 10^{-6}$	intron	PDE4B	-	
	rs61797058	1	66319768	A/G	0.218	-0.461	$7.03 \times 10^{-6}$	intron	PDE4B	-	
rs12751825	1	66324394	G/A	0.219	-0.461	$7.08 \times 10^{-6}$	intron	PDE4B	-		
rs61797059	1	66329133	T/C	0.219	-0.461	$7.13 \times 10^{-6}$	intron	PDE4B	-		
rs2953604	7	33042190	C/T	0.162	-0.503	$7.78 \times 10^{-6}$	intron	FKBP9/AVL9	-		
rs16881929	7	33042945	C/T	0.162	-0.500	$8.13 \times 10^{-6}$	intron	FKBP9/AVL9	-		
rs7786711	7	33050940	A/G	0.149	-0.510	$5.40 \times 10^{-6}$	intron	AVL9	-		
rs12668520	7	33075248	G/A	0.150	-0.506	$6.12 \times 10^{-6}$	intron	NT5C3A	-		
rs77946925	7	33115644	C/T	0.155	-0.498	$7.39 \times 10^{-6}$	upstream_gene	NT5C3A	13235		
rs12667900	7	33131729	A/G	0.189	-0.464	$5.03 \times 10^{-6}$	downstream_gene	RP9	2680		
rs150987618	7	33134883	C/T	0.185	-0.462	$6.37 \times 10^{-6}$	missense	RP9	-		
SFP_P95	rs9848749	3	28808234	A/T	0.435	2.497	$3.20 \times 10^{-7}$	downstream_gene	ZCWPW2	241598	
rs12634756	3	28808844	G/T	0.422	2.475	$3.54 \times 10^{-7}$	downstream_gene	ZCWPW2	242208		
rs4421167	6	77925696	C/T	0.040	5.901	$6.12 \times 10^{-7}$	downstream_gene	HTR1B	246252		



**Fig. 3.** Summary of the results of all the analysis on soapy flavor perception (SFP) for the SNPs obtained by the three GWAS (see Table S3). The white cells referred to not significant p-value (>0.05). Inside the rectangles are indicated the four loci shared by all three main analyses (SFP\_1, SFP\_N and SFP\_95) and confirmed in the analysis for at least two other cheese samples: SYT9, PDE4B, FKBP9/AVL9/NT5C3A/AVL9 and HTR1B.



**Fig. 4.** Regional association plots of the loci identified in the three GWAS and confirmed in the other analysis (A: *SYT9*; B: *PDE4B*; C: chromosome 7; D: *HTR1B*). Plots are produced in LocusZoom (2021) (Pruim et al., 2010) and show as purple diamond the most strongly associated SNP.



**Fig. 5.** Boxplot of liking for cheese samples P95 and S80 by the SNP rs4421167 (*HTR1B* gene) (A) and rs7542680 (*PDE4B* gene) (B), respectively. In (C), the effect of the SNP rs4421167 (*HTR1B* gene) on soapy flavor perception and liking for cheese P95 is shown.  $p = p$ -value.

significantly associated with rs11041225 (*SYT9*), with all the SNPs in chromosome 7 and with rs4421167 (*HTR1B*). Moreover, the intensity in P80 was associated with five SNPs in *PDE4B*, while intensity in S80 was associated with one SNP in *PDE4B* and intensity in S75 with all the SNPs in *PDE4B*.

### 3.4. Effect of the SNPs on liking for Gorgonzola cheese

For each SNP in the four identified loci, the association with the liking for cheese samples was verified and the results are displayed in Table S5. We found a significant association of *HTR1B* SNP with liking for P95 cheese and an association of rs7542680 (*PDE4B*) with liking for cheese S80 (Fig. 5A and 5B). As regards *HTR1B* gene, the C allele of rs4421167 was more frequent in STs for cheese P95 (Table 2) and the individuals carriers of the same allele showed lower liking for the same cheese ( $\beta = -10.7$ ,  $p$ -value = 0.02; Fig. 5A, Table S5). Concerning *PDE4B* gene, the A allele of rs7542680 SNP was more frequent in ST for cheese S80 (Table S3) and the same allele was associated with a lower liking for the same cheese ( $\beta = -4.1$ ,  $p$ -value = 0.03; Fig. 5B, Table S5).

Considering that soapy flavor perception affected liking (Table 1) and that the SNP affected, both soapy flavor perception and liking, Sobel test was carried out to understand the possible mediated effect of soapy flavor perception. The result of this test showed that the effect of the SNP rs4421167 (*HTR1B* gene) on liking for cheese P95 was mediated by the effect of the SNP on soapy flavor perception ( $z$ -value = 2.38,  $p$ -value = 0.017, Fig. 5C), while the effect of the SNP rs7542680 (*PDE4B* gene) on liking for cheese S80 was not mediated by the soapy flavor perception in the same cheese ( $z$ -value = 1.77,  $p$ -value = 0.076).

### 3.5. Effect of the SNP rs72921001 (cilantro) on soapy perception

Table S6 summarizes the results of the analysis for the SNP rs72921001, already found associated with soapy flavor perception in cilantro (Eriksson et al., 2012). We found significant association only for soapy flavor perception in cheese P95 (OR 0.64 per A allele,  $p$ -value 0.003), but the liking for this cheese was not affected by the SNP ( $\beta = 2.48$  per A allele,  $p$ -value = 0.17). The effect was the same observed in Eriksson et al. (2012): the A allele is associated with a lower probability to be soapy flavor taster and a greater liking for the cheese (although in our sample not significant). The effect of A allele was confirmed also for the intensity of soapy perception ( $\beta = -0.15$ , standard deviation 0.09) although not significant ( $p$ -value 0.1218). As regards the remaining analysis, the A allele was less frequent in STs compared to NSTs (OR < 1) and with a minor number of cheese in which the individuals perceived soapy (SFP\_N,  $\beta < 0$ ). All these associations are not significant ( $p$ -value > 0.05) (Table S6).

## 4. Discussion

### 4.1. Individual variability in soapy flavor perception

In a review focused on polymorphisms in genes and their relationship with human ingestive behavior (Hayes et al., 2013), the need to increase the research on individual differences in perception ability because they may influence food preference was highlighted. In this study, the soapy flavor of Gorgonzola cheese, observed in a previous research as main driver of disliking (Torri et al., 2021), was further investigated. Collected data allowed to reveal several individual differences in soapy flavor perception among subjects.

Firstly, an individual difference among subjects in the ability to detect or not to detect the soapy flavor in at least one cheese sample was identified, thus it was possible to classify the participants in soapy tasters and non-soapy tasters. The group of the soapy tasters resulted approximately two thirds (65.8%) of the whole tested population. This proportion of soapy-tasters is quite high and in somewhat surprising.

The only information available in literature regarding a similar classification of individuals based on soapy-taste detection concerns cilantro. In particular, a study conducted on 14,604 participants of primarily European ancestry reported that 13.7 % of the population declared to think that cilantro tastes like soap (Eriksson et al., 2012). In comparison, in the present study, the proportion of soapy tasters was much higher. It is possible to assume that this large difference could be due to several reasons. For instance, it is plausible that even if the word used to describe the perception was the same (soapy) for the participants to the cilantro study and those involved in the present work, the volatile organic compounds responsible for the soapy perception are different in cilantro and Gorgonzola cheese. Indeed, it was reported that soapy perception in cilantro was due to the presence of aldehydes, such as decanal and dodecanal (Cadwallader, Benitez, Pojjanapimol, Suriyaphan, & Singh, 2005; Eyres, Dufour, Hallifax, Sotheeswaran, & Marriott, 2005), while the soapy flavor in Gorgonzola cheese was mainly positively correlated to the content of a few alcohols (4-methyl-2-pentanol, 1-pentanol, 2-heptanol) and methyl hexanoate (Torri et al., 2021). Hence, the various volatile molecules associated with the soapy flavor in the two food items could stimulate distinct odor receptors and be interpreted in a different way. Besides, it could be hypothesized that different volatile compounds could be responsible for the same perception named “soapy flavor” because of potential interactions occurring among several compounds present in a very complex food matrix, such as Gorgonzola cheese. In addition, it is relevant to consider that the description of “soapy flavor” could be the results of different interpretations of various olfactory stimuli due to a potential cultural effect. In fact, it was observed that consumers described the same stimuli using very different sensory terms depending on their gastronomic culture (Torri et al., 2017).

Moreover, in the cilantro study (Eriksson et al., 2012) the participants were asked the question “Does fresh cilantro taste like soap to you?” via an online questionnaire without tasting any cilantro sample. That means that participants chose the answer option (Yes/No/I'm not sure) based on their previous consumption experience and recalled perception. It can be assumed that probably some subjects would not associate the soapy flavor to cilantro only because they never specifically focused on it during a real consumption before answering the question. Thus, the percentage of soapy-tasters for cilantro could have been higher if the same question had been asked during a test including the sensory evaluation of a cilantro sample, in which participants could have focused specifically on the presence/absence of the soapy note. On the contrary, in the present work, participants had the opportunity to taste several Gorgonzola cheese samples and to evaluate if they actually perceived or not a soapy flavor. Moreover, the use of the rate-all-that-apply test allowed the participants to choose the term ‘soapy flavor’ among other attributes. This approach reduced the risk of any psychological bias and potential false positive responses that could occur if they had been required to focus only on the soapy flavor perception. Indeed, a comparison of forced yes/no questions with RATA questions revealed an increase in frequency of selection of the emoji for yes/no questions, without a corresponding improvement in sample discrimination (Ares & Jaeger, 2017).

Secondly, a variability was noticed also in terms of number of cheese samples in which each individual perceived the soapy flavor. Non-soapy tasters apart, most of the soapy-tasters (71.5%) perceived the soapy flavor in only one or two cheese samples while the rest of STs perceived the soapy flavor in three or more samples. Thirdly, the individuals perceiving the soapy flavor in each cheese sample varied between 19.6% and 33.8 % (with an average value of 24.6%), indicating that subjects differently identified the soapy flavor in the six tested Gorgonzola cheese. Both last two types of observed individual variability could be partially explained taking into account that the intensity of the soapy flavor was different in the cheese samples and that subjects could have a different perception thresholds for the volatile compounds responsible for the soapy perception. Indeed, responsiveness to retronasal odors



varied greatly across individuals (Flaherty & Lim, 2017) and both odorant-specific and general sensitivity variations are highly prevalent (Hummel & Nordin, 2005; Piochi, Dinnella, Spinelli, Monteleone, & Torri, 2021).

Demographic characteristics like age and gender (Wang, Liang, Lin, Chen, & Jiang, 2020) may influence sensory responsiveness. In this study, no individual differences in soapy flavor perception were found between males and females. On the contrary, gender has a significant effect on cilantro perception, as observed by Eriksson and colleagues; their study showed that women were more likely to detect the soapy taste compared to men (Eriksson et al., 2012). Regarding age, a significant effect was observed on Gorgonzola cheese, with soapy tasters having an average age ( $40.6 \pm 14.5$ ) significantly lower than non-soapy tasters ( $48.8 \pm 14.9$ ). This result is in line with literature reporting that aging is an important contributor to olfactory system deterioration in humans and that olfactory function may begin to decline in the fifth decade of life (Zhang & Wang, 2017).

#### 4.2. Role of the loci significantly associated with the soapy flavor perception

In this work we investigated the genetic bases of the perception of soapy flavor in Gorgonzola PDO cheese. The proposed approach based on the application of GWAS on three specifically defined phenotypic traits (SFP\_1, SFP\_N and SFP\_95) allowed us to identify four significant loci. Our results appeared particularly interesting considering that the four identified regions contain genes involved in pathways related to the perception of taste and smell, and genes expressed in the olfactory bulb of humans or mice.

The first locus was found investigating the perception of soapy flavor in at least one cheese (SFP\_1); this was confirmed in the other two GWAS and in the analysis of soapy perception in two specific cheese samples. The closest gene is *SYT9* (synaptotagmin 9), a neuronal protein belonging to synaptogamines, a family of Ca<sup>2+</sup> + binding proteins involved in the presynaptic transmission. Synaptogamines act mainly as Ca<sup>2+</sup> + sensors mediating the fast release of synaptic potential. This gene is reported to be expressed in mice's olfactory bulb and to assist potential transmission in immature calyx synapses (Kochubey, Babai, & Schneggenburger, 2016). In addition, it deserves to be mentioned that this locus is located on chromosome 11, near a cluster of olfactory receptor genes and near rs72921001, the SNP already associated with cilantro soapy perception (Eriksson et al., 2012). These data and our findings support the involvement of this region in determining the individual differences in the soapy flavor perception.

*PDE4B* (phosphodiesterase 4B) gene was found associated with the number of cheese samples in which the individuals perceived soapy flavor (SFP\_N) and was confirmed in SFP\_1 and SFP for each cheese. This gene is a phosphodiesterase (PDE) responsible for the degradation of the cAMP, a crucial molecule in the olfactory perception. Increased levels of cAMP, created by the activation of olfactory receptors, lead to a Ca<sup>2+</sup> + intake resulting in the depolarization of the olfactory neuron. PDEs degradate cAMP restoring the initial conditions. Regarding animal models, a low expression in the accessory olfactory bulb is reported in mice (Cherry, 2002), but specific *PDE4* inhibition through Rolipram has been proven to impair the perception of decreasing concentrations of odorant and odorant mixtures (Pho, Butman, & Cherry, 2005). Indeed, Pho and colleagues showed that odor perception of increasing dilutions of amyl acetate, citronellal, and 1-propanol was significantly affected by Rolipram treatment thus confirming the involvement of *PDE4* in odor perception and suggesting a role in odor discrimination at low levels of odorant. These findings confirm that this gene is a good candidate to have a role in odor perception and represent a starting point for investigating its involvement in soapy flavor perception.

For the SFP\_N and confirmed by SFP\_1 and SFP in five cheese samples, we detected a region on chromosome 7, that contains four coding protein genes: *FKBP9* (FKBP prolyl isomerase 9), *NT5C3A* (5'-

nucleotidase, cytosolic IIIA), *RP9* (RP9 pre-mRNA splicing factor) and *AVL9* (AVL9 cell migration associate). The first three genes do not seem related to taste or olfactory function. Indeed, *FKBP9* encodes for a peptidyl-prolyl cis-trans isomerase located on the endoplasmic reticulum and it is reported to be involved in the arising of diverse types of cancers, in particular in high-grade gliomas (Xu et al., 2020). *NT5C3A* belongs to the family of the 5'-nucleotidase, a family of enzymes responsible for the dephosphorylation of nucleoside monophosphates to nucleosides and orthophosphate maintaining nucleotide homeostasis. It is described to regulate interferon response in various types of cells (Al-Haj & Khabar, 2018). *RP9* encodes for a pre-mRNA splicing factor and it is widely known as one of many genes which mutation is associated with the arising of Retinitis Pigmentosa, a group of retinal degenerative disorders with high heritability and heterogeneity. As regards the fourth gene, *AVL9*, it encodes for a protein involved in cell migration and cell polarity. Its upregulation is often associated with the arising of various types of cancers. Interestingly, *AVL9* mRNA is detected in the olfactory bulb as reported in Human Protein Atlas (www.proteinatlas.org) although the functions of the gene in the olfactory perception are yet to be studied. Overall, this locus seems particularly interesting since the *AVL9* gene is expressed in the human olfactory bulb and this supports the possible link between this gene and the soapy flavor perception.

Finally, in the GWAS of soapy perception in cheese P95, we found *HTR1B* (5-hydroxytryptamine receptor 1B) gene that encodes for a G-protein that coupled with the serotonin receptor HTR. It can inhibit the activity adenylate cyclase mediating the release of several neurotransmitters, including serotonin, dopamine and acetylcholine. This gene is also involved in taste signal transduction, inhibiting ATP secretion in taste bud cells. In addition, it is reported to be involved in the olfactory perception of lactating rats. Indeed, its expression in the olfactory bulb can influence maternal care (de Moura et al., 2016). Interestingly, for the SNP detected in this gene (rs4421167) we found an association also for the liking for cheese P95. The implication of this gene in taste signal transduction and olfactory perception strongly supports its involvement in the perception of soapy flavor.

To summarize, four genes here identified (*SYT9*, *PDE4B*, *AVL9*, and *HTR1B*) are involved in olfactory or taste processes, suggesting that they could play a relevant role in determining the individual differences in the soapy flavor perception.

#### 4.3. Common genetic results of soapy flavor perception in cheese and cilantro

As regards the SNP rs72921001, already published as associated with soapy perception in cilantro leaves (Eriksson et al., 2012), we confirmed the result for soapy perception in cheese P95. In particular, for this cheese, we found that the A allele for the SNP rs72921001 is significantly less frequent in STs compared to NSTs. The same trend was observed for SFP in other cheese samples and for SFP\_1 and SFP\_N, although the results are not significant. Presumably, the significant association observed for cheese P95 was detected because a higher number of individuals recognized the soapy flavor in that sample. Probably, the higher proportion of STs for cheese P95 was because the soapy flavor in that cheese sample was particularly evident, as shown by the much higher intensity of this attribute in that sample compared to the other tested Gorgonzola cheese samples (Torri et al., 2021), thus the soapy flavor could be more easily detected and recognized by subjects.

#### 4.4. Relationship between genetic variants and liking

Despite various researches found associations between variants in odor/taste receptors genes with differences in taste perception and multiple odor phenotypes, including sensitivity and identification. Limited knowledge is still available regarding the associations of genetic variants with consumers hedonic response (for a review see (Feeney et al., 2021)). Thus, in this study, we investigated the relationship

between the liking for Gorgonzola cheese and the SNPs that we found associated with the soapy flavor perception. The used data analysis approach allowed to find two significant associations: one between the *HTR1B* SNP and liking for cheese P95 and another between one SNP on the *PDE4B* gene and the liking for cheese S80. Interestingly, the association of *HTR1B* SNP with liking for cheese P95 resulted significantly mediated by the soapy flavor perception in the same cheese. This result highlights the complex interplay between genetics, flavor perception, and liking/disliking. Other studies have already suggested that the same genetic variant could affect both perception and liking. For example, Keller and colleagues (Keller et al., 2012) found that variants in the *CD36* gene are associated with oral fat perception and fat preferences. Recently, Pilic and colleagues (Pilic et al., 2020), found that individuals homozygous for the minor allele of the rs8065080 SNP of the *TRPV1* gene had lower ratings of saltiness ( $p = 0.008$ ) and higher ratings of pleasantness of soup ( $p = 0.027$ ) when compared to major allele carriers.

Concerning the SNP rs72921001 on chromosome 11, we found that the A allele tends to be associated with a greater liking for cheese P95 (the most intense sample for soapy flavor), even if not in a significant way. This tendency is in agreement with Eriksson et al. (Eriksson et al., 2012) who reported that the C allele of the same SNP was associated with both detecting the soapy smell and disliking cilantro. The fact that we observed only a trend but not a significant association could be partially explained considering that we tested the individual perception in a real food product. It was argued that, while most of the studies investigated the phenotypic differences in terms of olfactory response to isolated compounds (e.g., androstenone,  $\beta$ -ionone, isovaleric acid, guaiacol, etc.) or watery solutions, using a food that has a very complex matrix (like Gorgonzola cheese) with different physiological characteristics may affect the flavor release and, thus, inhibit or decrease ligand availability in interaction with a target receptor (Feeney et al., 2021). Consequently, the perception of odor and flavor in complex food matrices could provide different and less neat results than when pure compounds are tested.

#### 4.5. Limitations and outlook

The fact that this study was conducted with a sample of subjects recruited without any particular criteria turned out a relevant limitation. Due to the actual composition of the participant group, the results can be referred only to a population of Caucasian subjects or individuals with Caucasian ancestries. Therefore, the results cannot be extended to other populations. It is possible to assume that different proportions of soapy-tasters and non-soapy tasters could be found in groups of subjects with different ancestry, as observed for soapy perception in cilantro leaves (Eriksson et al., 2012). Thus, in future studies, it may be of interest to investigate the proportion of soapy-tasters and non-soapy tasters in populations of different origins. A further avenue for future research would be to focus the investigation on a group of subjects including a high number of relatives, in order to estimate the heritability of soapy flavor detection ability in Gorgonzola cheese. Furthermore, research could be extended to other blue-veined cheeses (e.g. Roquefort and Stilton cheeses) and types of cheese previously described with a soapy flavor (e.g. Cheddar cheese) (Murray & Delahunty, 2000; Kheadr et al., 2002; Kilcawley et al., 2007; Murtaza et al., 2013).

## 5. Conclusions

Investigating the genetic bases of phenotypic traits of soapy flavor perception in Gorgonzola PDO cheese samples, this study contributed to increase the scientific knowledge in the emerging research area linking genetic individual differences to food perception and preferences. Classifying subjects in soapy flavor tasters and non-tasters revealed large variability in this attribute evaluation and allowed to confirm our two initially hypothesis. Firstly, it was found that the perception of 'soapy'

flavor in Gorgonzola cheese was associated to some genetic variations (as previously observed in other foods, like cilantro). Indeed, our work suggested four possible candidate genes (*SYT9*, *PDE4B*, *AVL9* and *HTR1B*), involved in olfactory or taste processes, associated with the perception of soapy flavor. It also partially confirmed the already known locus on chromosome 11 for the soapy perception in cilantro. Secondly, we observed that an existing genetic variant partially explained the variability in liking for the Gorgonzola cheese sample with the strongest soapy flavor intensity. Thus, the soapy flavor perception could contribute to justify that Gorgonzola cheese tend to polarize the consumers' affective responses. In a broader sense, our work provided a starting point to better understand the individual differences in blue-veined cheese perception and its relationship with consumers' acceptability and choice for this cheese category.

Overall, this work contributed to elucidate the genetic bases of different food perceptions influencing food preferences by testing a real food product instead of watery solutions or pure compounds. Thus, the used approach could allow a more reliable understanding of the link between genetic variants, food dietary behavior and, potentially, the health status. In the future, the knowledge of the genetic variants associated with food preferences could help to develop new personalized strategies for the promotion of consumers' health and the prevention of diet-related diseases.

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## CRediT authorship contribution statement

**Maria Pina Concas:** Conceptualization, Methodology, Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Maria Piochi:** Investigation, Writing – original draft, Writing – review & editing. **Giorgia Cabrino:** Investigation, Writing – review & editing. **Alessia Colaianni:** Investigation, Writing – review & editing. **Giuseppe Giovanni Nardone:** Visualization, Writing – review & editing. **Paolo Gasparini:** Resources, Writing – review & editing. **Luisa Torri:** Conceptualization, Methodology, Investigation, Resources, Data curation, Writing – original draft, Writing – review & editing, Supervision, Project administration, Funding acquisition.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.foodqual.2022.104569>.



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