Genetic Polymorphism of Bitter Taste Perception in Tempe, Arizona and its Association with Nutritional Status

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Introduction

Food preferences, nutritional status, and predisposition to obesity have the ability to play a factor in an individual's taste sensitivity as well as be directly linked to specific phenotypes such as cancer and BMI. A preference for sweet food and food rich in fat was observed to decline with increasing perception of bitter taste and subsequent research highlighted the relationship between the ability to taste bitter compounds, BMI, adiposity levels, and risk factors for cardiovascular disease[3]. Phenylthiocarbamide (PTC) taste has been discovered to be a dominant trait within humans, defined by three single nucleotide polymorphisms (SNPs) influencing receptor polymorphism, and the related haplotypes have been proven to correlate with the intensity of the response to PTC bitter taste[5]. In the United States of America, about 70-75% of people are tasters for PTC at five different magnitudes. Thirty percent of the world population are PTC non-tasters. The ability to taste PTC could have a protective advantage by allowing identification of bitter tasting toxic compounds that are present in plants. PTC results for supertasters, non-tasters, and tasters in this research can provide insight on the percentage of the population possessing the dominant trait and how it affects an individual's health status.

Methods

Isolation of genomic DNA. DNA extraction from saliva was optimized in our lab using a commercial DNA purification kit (QIAamp Blood kit, QIAGEN) following a protocol adapted from Rob van Schie et al[4]. DNA was eluted in Tris buffer and DNA yield was determined using a NanoDrop microvolume spectrophotometer. We are currently standardizing a protocol to extract DNA from hair as well.

PTC receptor (TAS2R38) genotyping. PCR was optimized for each of the specific SNPs using 25 µl reactions containing 300 ng of DNA extract, 2.5 µl of 10X PCR Buffer, 200 µM of each dNTP and 0.5 µl of Taq polymerase. PCR were performed with initial denaturation (5 min), then denaturation at 94°C for 40 seconds followed by annealing temperatures corresponding to the SNP under study[2,3] for 40 seconds and extension temperature at 72°C for 40 seconds, before finishing with an extension step of 72°C for 5 min. PCR products were digested with 0.5 units of respective restriction enzyme (HaeIII, Fnu4HI and BamHI for SNPs C/G 145, C/T 785, G/A 886 respectively) at 37 °C for 1 hour. PCR amplified and restriction digested products were separated on 3% agarose and visualized by using SYBR green.

Epidemiological model. We used a compartmental model to produce a system of differential equations and used ODE45, a numerical differential equation solver to solve differential equations. We adapted the SIR compartmental model for our project by grouping the susceptible populations into their phenotypes and determining their proportions. The model incorporated social and genetic parameters associated with obesity, along with their respective death rates. Afterwards, we measured the change in the proportion of the unhealthy population over a time span of 500 years. The proportion of the three phenotypic populations' unhealthy compared to healthy individuals was also analyzed.

Discussion

Based on our results, the population of Tempe, Arizona is at a higher risk of obesity than the United States due to a higher proportion of bitterness tasters and a lower proportion of non-tasters than the US. Differential equations produced from our model show that a higher proportion of non-tasters contributes to a lower rate of obesity, where tasters and supertasters contribute very similarly to an increased rate of obesity. They also show that by year 500, the population will reach an endemic equilibrium.

Acknowledgements

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Feeling unthankful for Brussel sprouts this season? Blame DNA for your health and diet.

Results

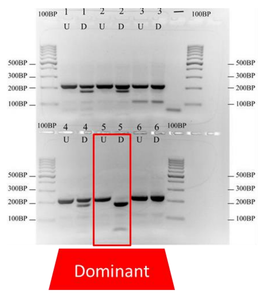

Fig. 1: Gel electrophoresis comparing samples of undigested PTC PA PCR product with the same products digested with HaeIII.

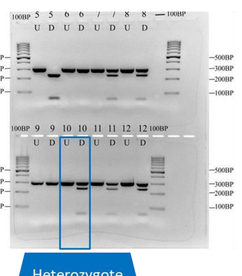

Fig. 2: Gel electrophoresis comparing samples of undigested PTC AV PCR product with the same products digested with Fnu4HI.

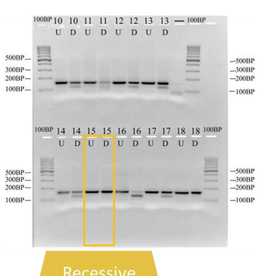

Fig. 3: Gel Electrophoresis comparing samples of undigested PTC VI PCR product with the same products digested with BamHI.

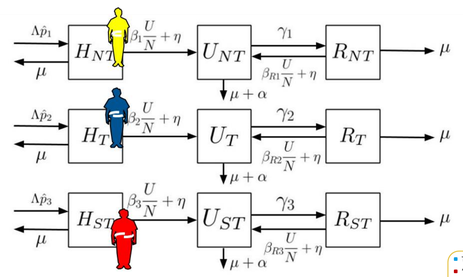

Fig. 4: Compartmental model.

$$\frac{H_{NT}}{dt} = \Lambda p_1 - \beta_1 H_{NT}\frac{U}{N} - (\eta+\mu)H_{NT}$$
$$\frac{H_T}{dt} = \Lambda p_2 - \beta_2 H_T\frac{U}{N} - (\eta+\mu)H_T$$
$$\frac{H_{ST}}{dt} = \Lambda p_3 - \beta_3 H_{ST}\frac{U}{N} - (\eta+\mu)H_{ST}$$
$$\frac{U_{NT}}{dt} = \beta_1 H_{NT}\frac{U}{N} + \eta H_{NT} + \beta_{R1}R_{NT}\frac{U}{N} + \eta R_{NT} - (\gamma_1+\mu+\alpha)U_{NT}$$
$$\frac{U_T}{dt} = \beta_2 H_T\frac{U}{N} + \eta H_T + \beta_{R2}R_T\frac{U}{N} + \eta R_{NT} - (\gamma_2+\mu+\alpha)U_T$$
$$\frac{U_{ST}}{dt} = \beta_3 H_{ST}\frac{U}{N} + \eta H_{ST} + \beta_{R3}R_{ST}\frac{U}{N} + \eta R_{ST} - (\gamma_3+\mu+\alpha)U_{ST}$$
$$\frac{R_{NT}}{dt} = \gamma_1 U_{NT} - \beta_{R1}R_{NT}\frac{U}{N} - (\eta+\mu)R_{NT}$$
$$\frac{R_T}{dt} = \gamma_2 U_T - \beta_{R2}R_T\frac{U}{N} - (\eta+\mu)R_T$$
$$\frac{R_{ST}}{dt} = \gamma_3 U_{ST} - \beta_{R3}R_{ST}\frac{U}{N} - (\eta+\mu)R_{ST}$$

Fig. 5: Differential equations corresponding with compartmental model.

Table 1: Parameter values used for numerical simulations.

Notation	Meaning	Value	Unit
Λ	population birth rate	2150	people/yr
β_1	Infection rate NT	0.0072	1/yr
β_2	Infection rate T	0.04	1/yr
β_3	Infection rate ST	0.045	1/yr
β_{R1}	Relapse rate NT	0.0072	1/yr
β_{R2}	Relapse rate T	0.04	1/yr
β_{R3}	Relapse rate ST	0.045	1/yr
η	Social influence toward obesity	0.005	1/yr
pNT	Proportion of population NT	0	
pT	Proportion of population T	0.521739	
pST	Proportion of population ST	0.478261	
μ	Natural death rate	0.0077	1/yr
α	Obesity induced death rate	0.0086	1/yr
Γ_1	Recovery rate NT	0.0031	1/yr
Γ_2	Recovery rate T	0.0031	1/yr
Γ_3	Recovery rate ST	0.0031	1/yr

Table 2: Model state variables, initial values and their biological meanings.

Variable	Biological Meaning	Initial Value
H_{NT}	Non-taster population	0
H_T	Taster population	37748
H_{ST}	Supertaster population	47026
U	Unhealthy population	97224
R	Recovered population	0

Table 3: Detailed distributions of TAS2R38 haplotypes in the studied populations[5]. The supertaster column is highlighted red, taster blue, and non-taster yellow.

Population	PAV	AVI	AAV	AVV	PAI	PVI	AAI	PVV
All	50.76%	42.70%	2.48%	0.32%	0.18%	0.07%	3.39%	0.10%
Africans	50.76%	35.18%	0.61%	0.08%	0.00%	0.15%	13.22%	0.00%
Asians	64.51%	35.31%	0.00%	0.17%	0.00%	0.00%	0.00%	0.00%
Europeans	45.66%	49.22%	3.56%	0.49%	0.32%	0.03%	0.55%	0.17%
Americans	68.61%	26.69%	2.26%	0.00%	0.00%	0.19%	2.26%	0.00%

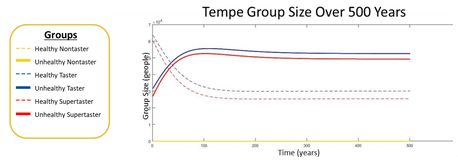

Fig. 6: Proportions of taster groups in Tempe over 500 years.

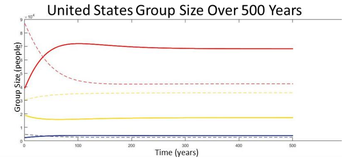

Fig. 7: Proportions of taster groups in the United States over 500 years.

References

1. Deshaware, S., Singhal, R. (2017). Genetic variation in bitter taste receptor gene TAS2R38, PROP taster status and their association with body mass index and food preferences in Indian population. Gene, 627, 363-368.
2. Merritt, R. B., Bierwert, L. A., Slatko, B., Weiner, M. P., Ingram, J., Sciarra, K., Weiner, E. (2008). Tasting phenylthiocarbamide (PTC): a new integrative genetics lab with an old flavor. The American Biology Teacher, 70(5).
3. Ooi, S. X., Lee, P. L., Law, H. Y., Say, Y. H. (2010). Bitter receptor gene (TAS2R38) P49A genotypes and their associations with aversion to vegetables and sweet/fat foods in Malaysian subjects. Asia Pacific journal of clinical nutrition, 19(4), 491-498.
4. R. V. Schie and M. Wilson. (1997). Saliva: a convenient source of DNA for analysis of bi-allelic polymorphism of Fc gamma receptor (CD32) and Fc gamma receptor IIIB (CD16). Pages 91–101.
5. Risso, D. S. et al. (2016). Global diversity in the TAS2R38 bitter taste receptor: revisiting a classic evolutionary PROPosal. Sci. Rep. 6, 25506.