Bitter Taste Receptor Polymorphisms and Colorectal Cancer Risk

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INTRODUCTION

Epidemiology

**Estimated New Cases Worldwide**

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>Breast</td>
</tr>
<tr>
<td>1,095,200</td>
<td>1,383,500</td>
</tr>
<tr>
<td>Prostate</td>
<td>Colon &amp; rectum</td>
</tr>
<tr>
<td>903,500</td>
<td>570,100</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>Cervix uteri</td>
</tr>
<tr>
<td>563,600</td>
<td>529,860</td>
</tr>
<tr>
<td>Stomach</td>
<td>Lung &amp; bronchus</td>
</tr>
<tr>
<td>640,600</td>
<td>513,600</td>
</tr>
<tr>
<td>Liver</td>
<td>Stomach</td>
</tr>
<tr>
<td>522,400</td>
<td>349,000</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Corpus uteri</td>
</tr>
<tr>
<td>326,600</td>
<td>287,100</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>Liver</td>
</tr>
<tr>
<td>297,300</td>
<td>225,960</td>
</tr>
<tr>
<td></td>
<td>Ovary</td>
</tr>
<tr>
<td></td>
<td>225,560</td>
</tr>
<tr>
<td></td>
<td>Thyroid</td>
</tr>
<tr>
<td></td>
<td>163,000</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>All sites but skin</td>
</tr>
<tr>
<td>195,600</td>
<td>6,625,100</td>
</tr>
<tr>
<td>Leukemia</td>
<td>Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>195,900</td>
<td>156,360</td>
</tr>
<tr>
<td>Oral Cavity</td>
<td>All sites but skin</td>
</tr>
<tr>
<td>170,300</td>
<td>6,625,100</td>
</tr>
</tbody>
</table>

Jemal et al. CA CANCER J CLIN (2011)

SNPs in Bitter Taste Receptor Genes (TAS2Rs)

<table>
<thead>
<tr>
<th>Vegetables</th>
<th>Alcohol</th>
<th>Grapefruit Juice</th>
<th>Coffee</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs713598, rs1726866, rs10246939 (TAS2R38)</td>
<td>rs1015443 (TAS2R13)</td>
<td>rs10772420 (TAS2R19)</td>
<td>rs765007, rs2234001, rs2227264, rs2234012 (across TAS2R3, -4 and -5)</td>
</tr>
<tr>
<td>rs846672, rs846664 (TAS2R16)</td>
<td>rs1726866, rs10246939 (TAS2R38)</td>
<td>rs4595035 (TAS2R60)</td>
<td></td>
</tr>
</tbody>
</table>

Hill et al. AJHG

Etiology

- 50% attributed to diet and lifestyle (Anderson et al., 2013)

Vegetables Alcohol

25 TAS2Rs

CRC risk

Bitter taste perception

Consumption of a Less nutritive diet

Hayes et al. FOOD QUAL PREFER (2013)
AIMS

Selection of a set of highly informative SNPs

Determination of the genotype frequencies

Investigation of potential trends in dietary intake across the TAS2R genotypes/haplotypes and their associations with CRC risk.
Extraction of SNP data

Pairwise Tagging

SNP Selection

Showing 93.38 kbp from chr5, positions 9,677,109 to 9,770,490

Instructions:

Searching: Search using a sequence name, gene name, locus, or other landmark. The wildcard character “*” is allowed.

Navigating: Click one of the rulers to center on a location, or click and drag to select a region. Use the Zoom/Zoom buttons to change magnification and position.

Examples: Chr20, Chr5:000,000-500,000, SNP:rs8479050, MMU_153514, D Allen 1, Sp3, Enm010, gpa2, PARK5.

[Back/Forward (Upload your own data) (Hide banner) (Share these tools) (Link to image) (SNP genotype data) (High-res image) (Help) (Reset)

Population descriptors: ASW: African ancestry in Southwest USA, CEU: Utah residents with Northern and Western European ancestry from the CEPH collection, CHB: Han Chinese in Beijing, China.

Haploview 4.2 -- dumped_region_test2/1 transcript 1 --> 5000

Tests

Alleles captured by Current Selection

rs41467
rs1513027
rs2234231
rs9881081
| Chr. 5 | TAS2R1 | 4 SNPs in 4 tests captured 5 of 5 (100%) alleles at \( r^2 \geq 0.8 \)  
Mean max \( r^2 \) is 1.0 |
|---|---|---|
| TAS2R16 | 5 SNPs in 5 tests captured 12 of 12 (100%) alleles at \( r^2 \geq 0.8 \)  
Mean max \( r^2 \) is 0.974 |
| TAS2R3 \( \rightarrow \) 5 | 3 SNPs in 3 tests captured 36 of 36 (100%) alleles at \( r^2 \geq 0.8 \)  
Mean max \( r^2 \) is 0.997 |
| TAS2R38 | 3 SNPs in 3 tests captured 5 of 5 (100%) alleles at \( r^2 \geq 0.8 \)  
Mean max \( r^2 \) is 0.992 |
| TAS2R39 \( \rightarrow \) 40 | 5 SNPs in 5 tests captured 13 of 13 (100%) alleles at \( r^2 \geq 0.8 \)  
Mean max \( r^2 \) is 1.0 |
| TAS2R60 \( \rightarrow \) 41 | 10 SNPs in 10 tests captured 35 of 35 (100%) alleles at \( r^2 \geq 0.8 \)  
Mean max \( r^2 \) is 0.955 |
| TAS2R7 \( \rightarrow \) 42 | 15 SNPs in 15 tests captured 276 of 276 (100%) alleles at \( r^2 \geq 0.8 \)  
Mean max \( r^2 \) is 0.975 |

**45 tagSNPs**

**Representations of Variability**

**Significance in the Literature**

**14 tagSNPs**
1- TAS2R31: rs10845293
Genotype Frequencies

2- TAS2R16: rs12706460
Genotype Frequencies

3- TAS2R9: rs3741845
Genotype Frequencies

4- TAS2R38: rs1726866
Genotype Frequencies

5- TAS2R38: rs713598
Genotype Frequencies

All 5 SNPs are in Hardy Weinberg Equilibrium (HWE)
Finding Associations

Clinical Data:

- Sample
  - Normal (clean colon)
  - Polyps (Number / Size / Location)
  - General Health Status
    - Adenoma
    - Adenocarcinoma
    - BMI
    - Smoker / Nonsmoker
    - Alcohol drinker / no
  - Hyperplastic
  - Low grade
  - High grade

Food Questionnaires:
- 6 bitter Beverages
- 6 Bitter Vegetables
- Other bitter foods

Qual è il suo gradimento per i ...? (Assolutamente graditi / Sgraditi)

□ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9

Con quale frequenza lei consuma ...?

□ Raramente o Mai

$N^0$ di volte al giorno ____
$N^0$ di volte alla settimana ____
$N^0$ di volte al mese ______

Qual è l’intensità di amaro che, mediamente, assocerebbe ai ...?

□ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9

Bassissima intensità □ □ □ □ □ □ □ □
Media intensità □ □ □ □ □ □ □ □
Altissima intensità □ □ □ □ □ □ □ □
GRAZIE PER L’ATTENZIONE