Alcohol Flush Reaction

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Gene 210
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Alcohol flush reaction (Asian flush)
Symptoms: dizzy, nauseous, headaches, face and neck turning bright red
Introduction

NAD$^+$  NADH  NAD$^+$

ADH

CH$_3$CH$_2$OH $\rightarrow$ CH$_3$CHO $\rightarrow$ CH$_3$COOH

Ethanol  Acetaldehyde  Acetic acid
Introduction

Metabolism of Ethanol and Acetaldehyde in Hepatocyte

\[
\begin{align*}
\text{CH}_2\text{CH}_2\text{OH} \quad (\text{mM}) & \quad \text{CH}_2\text{CHO} \quad (\mu\text{M}) \\
\text{ADH} & \quad \text{ALDH}1 \\
\text{NAD}^+ & \quad \text{NADH} \\
\text{NADH} & \quad \text{NADH} \\
\text{NADH Shuttle} & \quad \text{CIRCULATION} \\
\text{CH}_3\text{CHO} & \quad \text{CH}_2\text{COOH} \quad (\text{mM}) \\
\text{ALDH}2 & \quad \text{TCA} \\
\text{CH}_3\text{COOH} & \quad \text{CO}_2 \\
\text{electron transport} & \quad \text{H}_2\text{O} \\
\text{MITOCHONDRION} & \quad \text{ATP} \\
\text{Energy Yield: } 7 \text{ Kcal/s/g}
\end{align*}
\]
Two genes responsible for flush reactions

- ALDH2
- ADH1B
ALDH2: rs671

- A allele causes glutamine to lysine substitution
- Inactive ALDH2 enzyme, building up acetaldehyde

<table>
<thead>
<tr>
<th>SNP</th>
<th>Chrom.</th>
<th>Ref</th>
<th>Alternative</th>
<th>Trait</th>
<th>OR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs671</td>
<td>12</td>
<td>G</td>
<td>A</td>
<td>Flush</td>
<td>33.0</td>
<td>N.A.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Alcoholism</td>
<td>0.2</td>
<td>&lt;0.0001</td>
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</tbody>
</table>
ALDH2-deficiency (AA & AG) is more common in East Asians

- At least 540 million ALDH2-deficient individuals
- 8% of the global population
- 40% of the East Asian population
Treating alcoholics

- Commercial drug: disulfiram (trade name Antabuse)
- Chinese herbal medicine: daidzin (extracted from Kudzu root)
Diseases associated with rs671 (A allele) in frequent drinkers

- Esophageal cancer
- Colorectal cancer
- Lung cancer
- Liver cancer
- Coronary artery disease
- Hypertension
- ...
ADH1B: rs1229984

- A allele causes arginine to histidine substitution
- Fast metabolizing ADH1B, also accumulating acetaldehyde

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<tbody>
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<td>rs1229984</td>
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<td>Alcoholism</td>
<td>7.8</td>
<td>8.2E-23</td>
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</table>
ADH1B: rs1229984

rs1229984 A allele is found in:

- Less than 10% of the white population
- More than 80% of the East Asian population

rs1229984 A allele protects from:

- Alcoholism
- Esophageal cancer
Thank You!

Questions?