Explore a Trait Assignment - Alcoholism Scenario

Victor Morales has joined one of the largest fraternities on campus. He is turning 21 next week, and his brothers are hosting a big bash to celebrate. Victor knows that alcoholism runs in his family. His uncle is a serious alcoholic, but his uncle didn’t drink much until he was in his 40s. Until now, Victor has been able to say no to his friends because he wasn’t legal. Now that he can’t use the excuse of being underage, he wants to figure out if he is prone to alcoholism. If he is, he plans to limit his drinking to just a few on the weekends and he’ll only drink beer and wine. If he is not likely to be an alcoholic, then he knows he doesn’t have to worry. He learned that direct-to-consumer genetic tests include testing for genes associated with alcoholism. He wants your advice – should he get tested?

1. After reading the “23AndMe Facts on Alcoholism” provided below, write a one-paragraph summary in your own words of the information provided. Include answers to the following questions:
   - What percentage of alcoholism has a genetic cause? Environmental?
   - What are the mutations that are currently tested for by 23AndMe for alcoholism and alcohol dependence?
   - If Victor tested positive for one of these mutations, describe his increased risk for developing alcoholism?
   - What is the likelihood of developing alcoholism if you test positive for these mutations?

2. Several research studies are referenced after the “23AndMe Facts on Alcoholism” please summarize what is found in one of these research studies including a decision about how it would influence Victor’s decision to be tested.

3. Considering Victor’s likely Hispanic ethnic background, find a source that provides information tested in his ethnicity.

23AndMe Facts on Alcoholism:
Alcohol dependence is a complex disorder that combines alcohol abuse – continued drinking despite negative consequences – with physical symptoms of tolerance, withdrawal and uncontrollable craving for alcohol. The heritability of alcohol dependence is estimated to be between 38% and 64%. This means genetic and environmental factors contribute varying amounts to risk for this condition, probably depending on the population in question. Environmental factors that may increase risk include a family history of alcohol or drug abuse, having peers who exhibit common alcohol abuse, being male, cultural background, psychiatric disorders such as anxiety or depression and drinking at an early age. Genes that may play a role in alcohol dependence include those that affect brain chemistry and the liver’s ability to process alcohol.

4 Markers Examined by 23AndMe:
I. Alcohol dependence in Asians:
   - Journal: Hum Genet
   - Study Size
   - Replications: None
   - Contrary Studies: None
   - Applicable Ethnicities: Asian
   - Marker: rs671

   In this study, researchers compared 9,478 individuals with clinically-diagnosed alcohol dependence to 7,080 individuals without alcohol dependence, all of Asian descent. They found that each copy of an A at rs671 in the ALDH2 gene was associated with about 0.23 times the odds of alcohol dependence. Individuals with an A at rs671 are also known to flush in response to alcohol and are at increased risk for esophageal cancer.

   - SNP Phenotype
   - GG: Typical odds of alcohol dependence.
   - AG: Substantially decreased odds of alcohol dependence.
   - AA: Greatly decreased odds of alcohol dependence.

   Citation

II. Alcohol dependence in men
   - Journal: Arch Gen Psychiatry
   - Study Size

Citation

In this study, researchers compared 1,460 men with clinically-diagnosed alcohol dependence to 2,332 men without alcohol dependence, all of European ancestry. They found that each copy of a G at rs7590720 was associated with about 1.35 times higher odds of alcohol dependence.

### Genotype What It Means
- **GG**: Moderately higher odds of alcohol dependence in men.
- **AG**: Slightly higher odds of alcohol dependence in men.
- **AA**: Typical odds of alcohol dependence in men.

Citation:

### III. Alcoholism

This analysis combined data from a number of previous studies that looked at the correlation between rs1800497 and alcoholism in a total of more than 10,000 people. The results of those studies may have varied in part because alcoholism has multiple definitions that are similar to, but not identical to, alcohol dependence. But taken together, the combined studies indicated that each copy of A at rs1800497 increased a subject's odds of alcoholism by about 1.2 times. (Note: this SNP is commonly referred to in the literature as the DRD2 TaqIA polymorphism. Having a copy of the DRD2 TaqIA A1 allele is equivalent to having an A at rs1800497, while having the A2 allele is equivalent to having a G.)

### Genotype What It Means
- **AA**: Slightly increased odds of alcoholism.
- **AG**: Slightly increased odds of alcoholism.
- **GG**: Typical odds of alcoholism.

Citation:

### IV. Alcohol withdrawal seizures

Withdrawal seizures are one indication of alcohol dependence, though their absence does not necessarily rule out that diagnosis. This study compared 60 alcohol-dependent subjects who had withdrawal seizures to 190 alcohol-dependent subjects who did not. The authors found that alcohol-dependent people with at least one T at rs27072 had about half the odds of experiencing withdrawal seizures compared to those with none.

### Genotype What It Means
- **CC**: Typical odds of alcohol withdrawal seizures (if alcohol-dependent).
- **CT**: Moderately lower odds of alcohol withdrawal seizures (if alcohol-dependent).
- **TT**: Moderately lower odds of alcohol withdrawal seizures (if alcohol-dependent).

Citation:

**Alcohol Flush Reaction:**
Alcohol is a social lubricant for some and an addictive substance for others. But for people with the alcohol flush reaction, alcohol has such an unpleasant, noxious effect that they tend to avoid it altogether. Even a single drink may cause people sensitive to alcohol to become dizzy or nauseous, have headaches, and turn bright red. The alcohol flush reaction is primarily due to variations in two genes that encode proteins responsible for breaking down alcohol in the bloodstream.

**Genes vs. Environment:**
Sensitivity to alcohol—the alcohol flush reaction—depends almost entirely on a person's genotype at two genes, ALDH2 and ADH1B. 23andMe currently reports your genotype at a SNP in ALDH2. It is possible that those with the AG or GG genotypes at the SNP are more sensitive to alcohol due to their genotype at ADH1B (which 23andMe does not report).

**Your Genetic Data**

<table>
<thead>
<tr>
<th>Genotype</th>
<th>What It Means</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>No working copies of ALDH2. <strong>Extreme</strong> flushing reaction to alcohol. Highly unlikely to become dependent on alcohol.</td>
</tr>
<tr>
<td>AG</td>
<td>One working copy of ALDH2. <strong>Moderate</strong> flushing reaction to alcohol. Somewhat less likely than average to become dependent on alcohol.</td>
</tr>
<tr>
<td>GG</td>
<td>Two working copies of ALDH2. <strong>Little or no</strong> flushing reaction to alcohol.</td>
</tr>
</tbody>
</table>

**References:**
- *Peng et al. (1999)* "Involvement of acetaldehyde for full protection against alcoholism by homozygosity of the variant allele of mitochondrial aldehyde dehydrogenase gene in Asians." *Pharmacogenetics* 9(4):463-76.