



# **ALDH2, Alcohol Sensitivity, Ethnicity and Acculturation: A Pilot Study of the Japanese and Vietnamese in St. Louis**

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## Abstract

**Background:** The protective effect of ALDH2 among subgroups of Asians is well known. However, recent general-population epidemiologic surveys results are inconsistent with the genetic protection hypothesis; they show wide differences between the Japanese and the Vietnamese. **Objective:** To examine relative strengths of association of ALDH2, alcohol sensitivity, ethnicity, and indices of acculturation and socio-economic status. **Methods:** A total of 123 Japanese or Vietnamese residents in St. Louis, ages 15 to 54, were interviewed in person. Genotypes were obtained from buccal brush DNA by fluorescent sequencing of a PCR-amplified fragment including exon 12. **Results:** ALDH2 genotype distributions were similar for the Japanese and Vietnamese and clearly differentiated alcohol reaction patterns. Several acculturation/SES measures were associated with a variety of alcohol and other substance use/abuse phenotypes. Beyond the powerful effect of \*2/\*2, interactions were found between being heterozygous (\*2/\*1) and ethnicity and gender for alcohol dependence syndrome but not other phenotypes. **Summary:** Though a small sample, the importance of interactions of genotypes with gender, ethnicity and potentially acculturation was shown for the two ethnic subgroups of Asians in the St. Louis.

# Introduction (1)

Understanding the role of gene\*environment (G\*E) interactions underlying susceptibility (or immunity) for complex diseases is advocated in the roadmap for future NIH research. With rapidly advancing technology and reduced costs for genotyping, it is now very feasible to conduct a genetic association study within the standard epidemiologic design framework.

ALDH2 as a major drug metabolizing enzyme (DME) candidate gene: Ethanol is converted by the enzyme alcohol dehydrogenase to the toxic metabolite acetaldehyde, which is in turn converted by the enzyme acetaldehyde dehydrogenase to acetic acid. A single point mutation in the mitochondrial ALDH2 gene, on chromosome 12, leads to an inactive enzyme causing side effects of alcohol consumption that include a dozen reaction symptoms. In the Japanese population, 47.6% are normal homozygotes (\*1/\*1), 46% are heterozygotes (\*2/\*1) and 6.4% are mutant homozygotes (\*2/\*2). One study reported ALDH2 deficiency of 57% (\*2/\*2 and\*2/\*1) among a Vietnamese sample. To date, single candidate gene effects on substance abuse as large as the effects of ALDH2 on alcoholism have not been observed among other racial/ethnic groups in the U.S. Evidence for G\*E interactions of ALDH2 is shown by increases in the proportion of alcoholics with 2\*/\*1 or\*2 in a Japanese hospital from 2.5% in 1979 to 13% in 1992, and large differences of alcohol consumption reported between Japanese men and women, irrespective of genotypes (Table 1). Evidence is inconclusive regarding protective effects of ALDH2 extending to other substance use/abuse.

## Introduction (2)

Contrary epidemiologic data: The population epidemiologic data in the U.S. show wide differences in the prevalence of both licit and illicit substance use/abuse across major subgroups of Asians in the U.S. (Table 2 & 3). These data contradict the expectations based on the genotype distributions among specific Asian subgroups reported in the genetic literature. Among the five most representative Asian subgroups, the Japanese and Vietnamese have the most contrasting patterns of substance use and abuse across all major types of psychoactive substances, even though ALDH2 genotype frequencies were presumably similar between the two subgroups. In the U.S., the two subgroups also have the most contrasting backgrounds with respect to immigration history, acculturation and socio-economic achievement. Sufficient evidence also exists for increased risk for licit as well as illicit substance use and abuse among mixed-race. Up to a four-fold increase in problem alcohol use and regular cigarette smoking is observed among Vietnamese mixed-race adolescents.

Need to integrate genetic and epidemiologic perspectives: incorporating information on population dynamics, contextual measures, individual risk and protective factors into measures of genetic (in)vulnerability, is necessary to fully address the relative importance of the effects of the candidate genes on the development of alcoholism. Incorporating this information also informs pathways to other substance use/abuse and provides a better understanding of the gene\*environment interaction that affects those pathways.

# Methods (1)

**Sample:** A total of 142 self-identified Japanese and Vietnamese aged 15 to 54 were recruited from St. Louis City and St. Louis County by using major ethnic specific community-based organizations (CBO)'s (including retail stores) as entry points.

**In-Person Interviews:** Eligible respondents were interviewed by bi-lingual interviewers (English and Japanese or English and Vietnamese). Two versions (English or mother tongue) were tailored specifically to some of the Japanese and Vietnamese customs from an English version using standard translation and back-translation procedures. The measures include demographics, detailed assessment of ethnicity of the probands and relatives, ethnic identification, socio-economic status (SES), acculturation, citizenship, prosocial and antisocial activities, trauma and post-traumatic stress symptoms, depression, drinking patterns, reaction to alcohol use and alcohol dependence symptoms, tobacco use, reaction to tobacco, symptoms of dependence, and illicit drug use. DNA was obtained by collecting cheek cells using 4-6 buccal brushes per proband.

**DNA Processing:** The basic protocol described by Richards et al (1993) was: **a)** immerse the brush in 50 mM NaOH in a tube; **b)** vortex moderately for 10 seconds; **c)** heat the tube at 95°C for 5 minutes; **d)** remove the brush and neutralize the NaOH with 0.1X volume of 1M Tris, pH 8, vortexing to mix. Store at 4°C.

Modifications included: **a)** two brushes were processed with the same aliquot of 50 mM NaOH to increase the concentration of DNA in the resultant solution; **b)** aliquots of the DNA solution were concentrated by adding 0.1X volume of 3M sodium acetate and 2.5X volumes of ethanol to precipitate the DNA and resuspend it in a smaller volume; **c)** aliquots of the DNA solution were cleaned by adding Proteinase K (final concentration of 0.2 mg/ml) and placing at 55°C for one hour, followed by 50:50 phenol:chloroform extraction of the solution, ethanol precipitation, and resuspension in a smaller volume, or **d)** the Proteinase K treatment was followed by a protein precipitation step (not phenol-chloroform extraction) and a subsequent isopropanol precipitation and resuspension in a smaller volume.

## Methods (2)

**Determination of ALDH2 Genotypes:** The study sample DNA was genotyped for a point mutation (g→a) in exon 12 of the DNA, which codes for amino acid position 487 of the ALDH2 protein, by amplifying a 322 bp fragment of the DNA sequence containing exon 12, then sequencing from an internal priming site. In the sequence illustrated below, the exon is represented by capital letters, the point mutation is indicated as **G/A**, and the primers used for amplification and sequencing are indicated as follows:

PCR amplification forward primer (F2): **tgggcaacagagaaagattctatc**

PCR amplification reverse primer (R2): **ccaccagcagaccctcaag**

Sequencing primer (F1): **taaccataacccccaaga**

**tgggcaacagagaaagattctatc**tcaaaaaaaaaaatttttttttaagttaaaaataaaataaagactttg  
gggcaatacagggggtcctgggagtg**taaccataacccccaaga**gtgatttctgcaatctcgtttcaaatt  
ac**ag**GGTCAACTGCTATGATGTGTTTGGAGCCCAGTCACCTTTGGTGGCTACAAGATGTCGGGGAGTGGCC  
GGGAGTTGGGCGAGTACGGGCTGCAGGCATACT**G/A**AAGTGAAAAGT**gt**gagtgtgggacctgctggggg  
ctcagggcctggtgggg**cttgagggtctgctggtgg**

The ALDH2 exon 12 PCR products were sequenced with a BigDye terminator sequencing kit (PE Applied Biosystems, Foster City, CA). After ethanol precipitation and resuspension in TE (10 mM Tris (pH 8), 1 mM EDTA) 15-150 nanograms of PCR product were combined with 2-4 µl of BigDye terminator mix and 5-10 picomoles of primer in a total reaction volume of 5-10 µl. A Perkin Elmer 9600 thermal cycler was used for the cycle sequencing according to the following protocol for 25 cycles: rapid thermal ramp to 96°C to hold for 10 seconds, rapid thermal ramp to 50°C to hold for 5 seconds, and rapid thermal ramp to 60°C to hold for 4 minutes. The reaction was then held at 4°C until further processing. Extension products were precipitated by the addition of EDTA (to 25 mM final concentration) and 100% ethanol (to 66% final concentration) and were left at room temperature for 15 minutes. The precipitate was pelleted; the pellet was washed with 70% ethanol and resuspended in 25 µl of Template Suppression Reagent (PE Applied Biosystems). The DNA was then denatured at 95°C for 3 minutes and rapidly cooled on ice before analysis on an ABI Prism 310 Genetic Analyzer.

# Measures and Analyses

## Measures:

- Phenotypes: Based on self-report several use and clinical measures were developed including: alcohol use ever, 3+ DSM-IV alcohol dependence symptoms, ever gotten drunk, ever smoked cigarettes, 2+ tobacco dependence symptoms, marijuana use ever, and any illicit use ever.
  - Genotypes: three genotypes were used in bivariate analyses; single allele mutation (\*2/\*1 or 2\*2) and double allele mutation (2\*2) were entered in multivariate analyses.
  - Alcohol reaction: 13 items reaction items included become anxious, pounding in head, perspire, nauseated, felt weak, chills, itchy, dizzy, shortness of breath, headache, fast heartbeat, non facial flush, and facial flush. The items were assessed for one sip, one drink and 1+ drink.
  - Demographics and SES: gender, ethnicity, mixed heritage (any of multiple ethnicities or races), education, income were included in bivariate and multivariate analyses.
  - Acculturation measures included mixed heritage, country of birth, language of interview, scores of modified Suinn-Lew acculturation items (based on factor analyses, a simplified trichomous measure was used).
- Analyses: Simple bivariate analyses and multivariate logistic regression were used. To assess interaction patterns, classification tree analysis was used for selected measures.

# Results (1)

**Demographics:** Of 123 interviewed, 62 were Japanese and 61 were Vietnamese (Tab. 4). The mean age was 32.8, 41.4% were male and 7.3% were of mixed heritage, indicating some ascertaining bias. More women, more unmixed heritage respondents were interviewed than expected from the 2000 Census).

**Association of demographics, SES, acculturation with phenotypes:** In general, Japanese, those of mixed heritage, males, those with higher income, those with higher education, those who were interviewed in English, and those with higher Westernness scores had higher rates of substance use or problem use. Tobacco use and dependence syndrome did not always follow this general pattern (Tab. 5).

**Ethnic heritage, gender and ALDH genotypes:** Probably this study provides the first report of ALDH2 genotypic distribution among Vietnamese in U.S. We found that the genotype distributions were very similar between the Japanese and Vietnamese. While the \*2/\*2 was absent among mixed heritage individuals, overall differences were not significantly different (Tab. 6). Small insignificant gender differences are found, which probably reflect a degree of ascertainment bias.

## Results (2)

**Alcohol reactions and ALDH2:** Differences in alcohol reactions are clearly seen with one sip of alcohol. Facial flush, non-facial flush, fast heartbeat, headache were more common among \*2/\*2 than other types. Except facial and non-facial flushing, the differences between \*2/\*1 and \*1/\*1 are not pronounced (Fig. 1). However, with one drink, wider differences appear between \*2/\*1 and \*1/\*1.

**Association of ALDH2, ethnicity and gender with alcohol and tobacco dependence syndrome:** So powerful is the protective effect of having two mutant alleles (\*2/\*2) on alcohol dependence syndrome, this variable resulted in quasi-separation (i.e., \*2/\*2 had no positive) (Tab.7). Although ethnicity was shown to have associated with the variety of phenotypes, it appears that the association is primarily due to the interaction of ethnicity and having one mutant allele (1MA) (OR=10.1). Gender, on the other hand, showed both a large main effect (OR=25.0) and interactive effect with 1MA (OR=14.3). Results essentially held when abstainers were removed from the sample. The interactive effect of 1MA and ethnicity or gender was not observed for tobacco dependence syndrome, although a main effect of gender is still shown. It appears the protective effect of \*2/\*2 extends to tobacco dependence syndrome. The interactive model (Fig. 2) picked the acculturation measure to be the second important measure in predicting alcohol dependence syndrome, even though it was not a significant predictor in the logistic regression models. Ethnicity was not a prominent predictor once acculturation was taken into account.

**Role of alcohol reaction symptoms:** Although the patterns of alcohol reactions were different between the three genotypes, the alcohol reaction measure was not an important predictor of alcohol dependence syndrome.

# Discussion

Although sample size was small, with use of ALDH2, role of this major candidate gene, gender, ethnicity and acculturation on a variety of substance use/abuse behaviors were delineated.

**Role of ALDH2 on alcohol dependence syndrome:** As repeatedly shown, having two mutant alleles were so protective that socio-cultural influences are not inferred. The interaction effects of having one allele (\*2/\*1) with environmental factors were captured for ethnicity and gender. Despite the fact that the Japanese and Vietnamese have similar genotype frequencies, the phenotypic expression was different for the heterozygotes. The association of ethnicity with the genotype appears attributable to the elasticity of \*2/\*1 according to environments, rather than a direct association of ALDH2 genotypes with drinking patterns. It is still possible that interactions of ALDH2 with other genes play a role, if their polymorphisms are also differentiated along the ethnicity or gender line.

**Role of acculturation on alcohol dependence syndrome:** The association of acculturation with the phenotype may not be linear; thus its association was insignificant in a linear logistic model, while it was an important predictor in the interactive classification tree.

**Role of alcohol reactions on phenotypic expression:** Although ALDH2 genotypes differentiated alcohol reaction patterns, reactions do not seem to predict a clinical syndrome of alcoholism when the population is limited to Asians.

**Role of ALDH2 on other substance use/abuse:** The powerful protective effect of \*2/\*2 appears to extend to tobacco dependence. The same protection does not appear to hold for ever tobacco use. A lack of cross-tolerance development may reduce tobacco dependence syndrome.

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## Properties of Human Aldehyde Dehydrogenases

Gene Locus	Structure	$K_m$ (Acetaldehyde)	Tissue Distribution
<i>Class I</i> (cytosolic)			
ALDH1	$\alpha 4$	$30 \mu\text{M}$	Most tissues
<i>Class II</i> (mitochondrial)			
ALDH2	$\alpha 4$	$< 1 \mu\text{M}$	Liver > kidney > lung
<i>Class III</i>			
ALDH3	$\alpha 2$	11 mM	Stomach, liver

Source: Crabb, et al., 1995.

## Table 1. Evidence of interaction of ALDH2 with Environmental Factors

A) Over time changes in heterozygous ALDH2 among alcoholics.<sup>1</sup>

Genotypes	1979	1986	1992
<b>*2/*2</b>	0.0	0.0	0.0
<b>*2/*1</b>	2.5	8.0***	13.0**
<b>*1/*1</b>	97.5	92.0	87.0

B) Gender differences in average monthly alcohol consumption (ml pure alcohol) by ALDH2 genotypes<sup>2</sup>

Genotypes	Men	Women
<b>*2/*2</b>	1054.7	104.9
<b>*2/*1</b>	390.9	46.6
<b>*1/*1</b>	94.1	3.3

Source: 1. Higuchi et al., 1994. 2. Higuchi et al., 1996.

## Genotype Distributions of ALDH2 and CYP2A6

	ALDH2 Genotypes (%)			CYP2A6 Allelic (%) Frequency		
	*1/*1	*2/*1	*2/*2	6*1 <sup>1</sup>	6*2(v1) <sup>2</sup>	6*3(v3)
Caucasian	100 <sup>3</sup>	0	0	85 <sup>4</sup>	15 <sup>4</sup>	0 <sup>4</sup>
Japanese	56.4	39.4	4.2	98.6 <sup>5</sup>	1.4 <sup>5</sup>	?
Filipino	87.3	12.7	0	Not Available		
Korean	71.6	26.6	1.8	Not Available		
Chinese	59.0	35.9	5.1	83 <sup>6</sup>	11 <sup>6</sup>	6 <sup>6</sup>
Vietnamese	43.0	57.0		Not Available		

Source Harada, 1991; Goedde et al., 1985. 1.Wildtype. 2.Inactive. 3.European. 4.Finnish; based on the PCR amplifiers confined with diagnostic restriction digestion. 5.Finnish; based on a two-step PCR method 6.Taiwanese

## Table 2. Alcohol Use Patterns among the Five Largest AAPI Subgroups

<b>ADULTS (NLEAS)</b>	<b>Caucasian</b> (n=34,489)	<b>Japanese</b> (n=314)	<b>Filipino</b> (n=185)	<b>Chinese</b> (n=230)	<b>Korean</b> (n=123)	<b>Vietnamese</b> (n=89)
% Drinking past year	46.9	37.5	31.5	19.5*	28.9	18.1*
% Alcohol Dep. (DSM-IV)	14.2	12.8	10.1	4.5	9.7	3.4*
<b>ADOLESCENTS (ADD HEALTH)</b>	<b>Caucasian</b> (n=50,397)	<b>Japanese</b> (n=512)	<b>Filipino</b> (n=1,579)	<b>Chinese</b> (n=749)	<b>Korean</b> (n=664)	<b>Vietnamese</b> (n=499)
% Drank 2-3 times, ever	58.1	56.4	52.7	41.1*	48.0	35.8*
% Drank beer, wine, liquor, past year	55.5	51.5	50.6	38.9*	44.4	36.5*
% Got drunk, past year	33.2	31.7	28.7	16.4*	21.0	20.5

Source: National Longitudinal Alcohol Epidemiology Survey (NLAES, 1992), National Longitudinal Study of Adolescent Health (Add Health, 1994-5), Price et al., 2002. The NLAES data were weighted to be generalizable to the U.S. population according to the 1990 Census; The Add Health data were weighted to be generalizable to the U.S. population of adolescents in grade 7 through 12 in 1994-6. Standard errors adjusted using SUDAAN for both datasets: \*, significantly lower than the Japanese.

## Table 3. Cigarette and Illicit Drug Use Patterns among the Five Largest AAPI Subgroups

<b>ADULTS (NLAES)</b>	<b>Caucasian</b> (n=34,489)	<b>Japanese</b> (n=314)	<b>Filipino</b> (n=185)	<b>Chinese</b> (n=230)	<b>Korean</b> (n=123)	<b>Vietnamese</b> (n=89)
% Smoking, past year	30.0	26.4	15.8*	8.8*	33.5	11.5*
% Illicit drug use, past year	5.3	4.2	2.5	2.3	2.3	0.0
% Sedative use, 12+ times	2.4	3.0	1.5	0.6*	0.0	0.8
% Stimulant use, 12+ times	4.5	5.1	2.5	3.0	0.0	0.0
% Marijuana use, 12+ times	14.6	12.8	8.5	2.3*	3.1*	0.0
% Cocaine use, 12+ times	3.9	4.0	1.7	0.0	0.0	0.0
<b>ADOLESCENTS (ADD HEALTH TOTAL SAMPLE)</b>	<b>Caucasian</b> (n=50,397)	<b>Japanese</b> (n=512)	<b>Filipino</b> (n=1,579)	<b>Chinese</b> (n=749)	<b>Korean</b> (n=664)	<b>Vietnamese</b> (n=499)
% Smoked cigarettes, past year	39.7	36.0	36.0	21.7*	31.6	24.4*
<b>ADOLESCENTS (ADD HEALTH SUBSAMPLE)</b>	(n=11,621)	(n=103)	(n=662)	(n=389)	(n=113)	(n=75)
% Marijuana use, ever	25.9	31.6	28.6	19.3	11.1*	4.7*
% Cocaine use, ever	3.6	3.7	4.7	3.3	0.0	0.0
% Inhalant use, ever	6.8	6.4	3.6	6.1	5.5	2.1
% other illicit drug use, ever	9.4	12.0	6.4	7.6	2.6	2.2*

Source: National Longitudinal Alcohol Epidemiology Survey (NLAES, 1992), National Longitudinal Study of Adolescent Health (Add Health, 1994-5), Price et al., 2002. The NLAES data were weighted to be generalizable to the U.S. population according to the 1990 Census; The Add Health data were weighted to be generalizable to the U.S. population of adolescents in grade 7 through 12 in 1994-6. Standard errors adjusted using SUDAAN for both datasets: \*, significantly lower than the Japanese.

# Acculturation Indicators Among the Five Largest AAPI Subgroups in the U.S.

	Japanese	Filipino	Chinese	Korean	Vietnamese
<b>% Foreign born*</b>	<b>31.2</b>	<b>66.3</b>	<b>70.6</b>	<b>73.2</b>	<b>80.1</b>
<b>% Foreign born migrated 1975 or later</b>	<b>20.0</b>	<b>42.7</b>	<b>50.8</b>	<b>56.3</b>	<b>76.9</b>
<b>Median age</b>	<b>36.3</b>	<b>31.1</b>	<b>32.1</b>	<b>29.1</b>	<b>25.2</b>
<b>Number in household</b>	<b>3.1</b>	<b>4.0</b>	<b>3.6</b>	<b>3.6</b>	<b>4.4</b>
<b>% High school graduate*</b>	<b>90.1</b>	<b>85.0</b>	<b>78.3</b>	<b>90.2</b>	<b>69.8</b>
<b>% Speak native tongue at home</b>	<b>42.8</b>	<b>66.0</b>	<b>82.9</b>	<b>80.8</b>	<b>92.5</b>
<b>Per capita income*</b>	<b>\$21,271</b>	<b>\$15,985</b>	<b>\$16,477</b>	<b>\$19,134</b>	<b>\$12,543</b>

Source: We the Americans: Asians, 1993; Bureau of the Census. \*, figures were updated from the 2000 Census.

## St. Louis County Asian Subgroup Populations

	Unmixed N	Mixed N	Mixed %	Total N
<b>Japanese</b>	1,354	625	31.6	1,979
<b>Korean</b>	2,637	451	19.6	3,088
<b>Chinese</b>	7,913	263	3.2	8,176
<b>Vietnamese</b>	4,876	369	7.0	5,245
<b>Total</b>	16,780	1,708	9.2	18,488

Source: Census 2000. A few individuals may be counted in Mixed Heritage groups of two or more ethnic groups.

## Table 4. Demographic Characteristics among the Japanese and Vietnamese

	Japanese	Vietnamese	Total
<b>Ascertained</b>	<b>67</b>	<b>75</b>	<b>142</b>
<b>Interviewed</b>	<b>62</b>	<b>61</b>	<b>123</b>
<b>Genotype data available</b>	<b>61</b>	<b>60</b>	<b>121</b>
<b>Analysis sample size</b>	<b>n=62</b>	<b>n=61</b>	<b>n=123</b>
<b>Demographics</b>			
<b>Age (years)</b>	<b>32.2</b>	<b>33.5</b>	<b>32.8</b>
<b>Male (%)</b>	<b>40.3</b>	<b>42.6</b>	<b>41.4</b>
<b>Mixed heritage</b>	<b>12.9</b>	<b>1.6</b>	<b>7.3</b>
<b>Education (%)</b>			
<b>No H.S. diploma</b>	<b>1.6</b>	<b>54.1</b>	<b>27.6</b>
<b>H.S. diploma</b>	<b>21.0</b>	<b>36.1</b>	<b>28.5</b>
<b>College degree</b>	<b>77.4</b>	<b>9.8</b>	<b>43.9</b>
<b>Language of interview (%)</b>			
<b>English</b>	<b>67.7</b>	<b>21.3</b>	<b>44.7</b>
<b>Mother tongue</b>	<b>32.3</b>	<b>78.7</b>	<b>55.3</b>

1. All participants consented to buccal brush DNA collection, however, two samples failed to produce viable DNA.

2. Boxed pairs indicate significant differences between the Japanese and Vietnamese by Pearson  $\chi^2$ ,  $p \leq .05$ .

## Table 5. Acculturation and Substance Use Phenotypes (n=123)

		N	Alcohol use ever	3+ alcohol dependence sxs <sup>1</sup>	Ever gotten drunk	Ever smoke	2+ tobacco sxs <sup>1</sup>	Marijuana use ever	Any illicit drug use ever
Ethnicity	Japanese	62	95.2	20.3	85.3	76.2	31.1	30.7	11.3
	Vietnamese	61	73.8	17.8	32.8	29.5	66.7	9.8	3.3
Mixed heritage	Mixed	9	100	22.2	88.9	66.7	0	55.6	22.2
	Unmixed	114	83.3	19.0	56.6	50.0	45.6	17.5	6.1
Country of birth	U.S.	16	93.8	20.0	66.7	50.0	25.0	56.3	31.3
	Other	107	83.2	19.1	57.9	51.1	43.6	15.0	3.7
Gender	Male	51	94.1	31.3	80.0	72.6	54.1	29.4	11.8
	Female	72	77.8	8.9	44.4	36.1	23.1	13.9	4.2
Education	No H. S.	34	61.8	28.6	32.4	26.5	88.9	11.8	2.9
	H. S.	35	94.3	18.2	45.7	54.3	31.6	28.6	14.3
	B. A.	54	92.6	16.0	84.9	64.8	34.3	20.4	5.6
Income	\$30K or less	52	80.8	14.3	51.9	46.2	41.7	11.5	1.9
	More than \$30K	63	92.1	22.4	69.4	55.6	37.2	30.2	12.7
Language of interview	English	55	96.4	20.8	72.2	61.8	48.3	34.6	12.7
	Mother tongue	68	75.0	17.7	48.5	42.7	35.3	8.8	2.9
Suinn-Lew acculturation indices	Asian	40	82.5	12.2	60.0	52.5	42.9	7.5	2.5
	Asian/Western	41	87.8	16.7	61.0	61.0	36.0	22.0	2.4
	Western	42	83.3	28.6	56.1	40.5	47.1	31.0	16.7

1. Conditioned on use (ever use alcohol (n=104) or ever use tobacco (n=59)).  
 2. Boxes indicates statistically significant differences by the Pearson X<sup>2</sup>, p<.05.

## Table 6. Ethnic Heritage and Gender by ALDH2 Genotypes<sup>1</sup>

Ethnic Heritage and Gender		N	Genotypes %		
			*2/*2	*2/*1	*1/*1
Heritage	Japanese	(n=61)	6.6	36.1	57.4
	Vietnamese	(n=60)	6.7	31.7	61.7
Mixed Heritage	Mixed	(n=9)	0	22.2	77.8
	Unmixed	(n=112)	7.1	34.8	58.0
Gender	Male	(n=50)	4.0	34.0	62.0
	Female	(n=71)	8.4	33.8	57.8

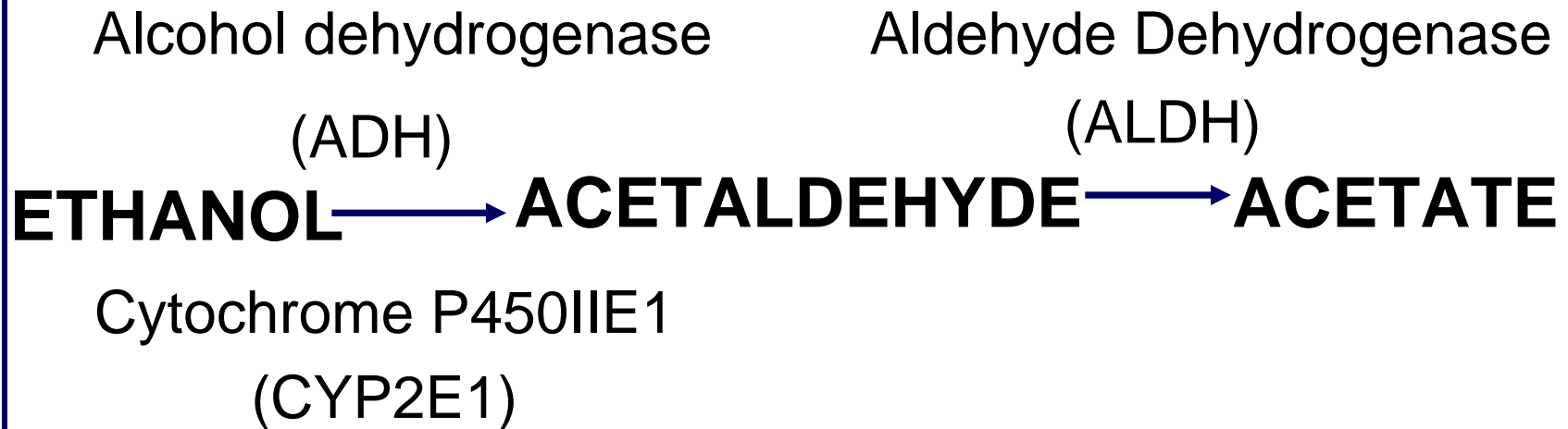
1. None of the differences were statistically significant at p=.05.

## Table 7. ALDH2, Ethnicity and Gender on Alcohol and Tobacco Dependence Syndrome

Covariates	Phenotypes					
	3+ alcohol dependence symptoms			2+ tobacco dependence symptoms		
	All (n=121)		Drinkers only (n=103) <sup>1</sup>		All (n=121) <sup>2</sup>	
	O.R.	p	O.R.	p	O.R.	p
One mutant allele (1MA) <sup>3</sup>	NS	-	NS	-	NS	-
Two mutant alleles (2MA) <sup>4</sup>	<b>QS</b>	≈.00	<b>QS</b>	≈.00	<b>QS</b>	≈.00
Ethnicity (Japanese = 1)	NS	-	NS	-	NS	-
Ethnicity*1MA	9.6	.09	7.8	.13	NS	-
Gender (male = 1)	25.6	.003	17.5	.008	5.8	.006
Gender* 1MA	19.6	.03	13.3	.06	NS	-
C index	0.81		0.78		0.73	

NS: Non-significant; QS: quasi-separation. 1. One respondent was deleted from the analysis due to inconclusive genotype result. 2. Logistic regression for smokers only had no significant predictors included here, except 2MA, which was QS. 3. (\*1/\*2 or \*2/\*2) = 1. 4. 2\*/2 = 1.

# Genes Associated with Alcohol Metabolization

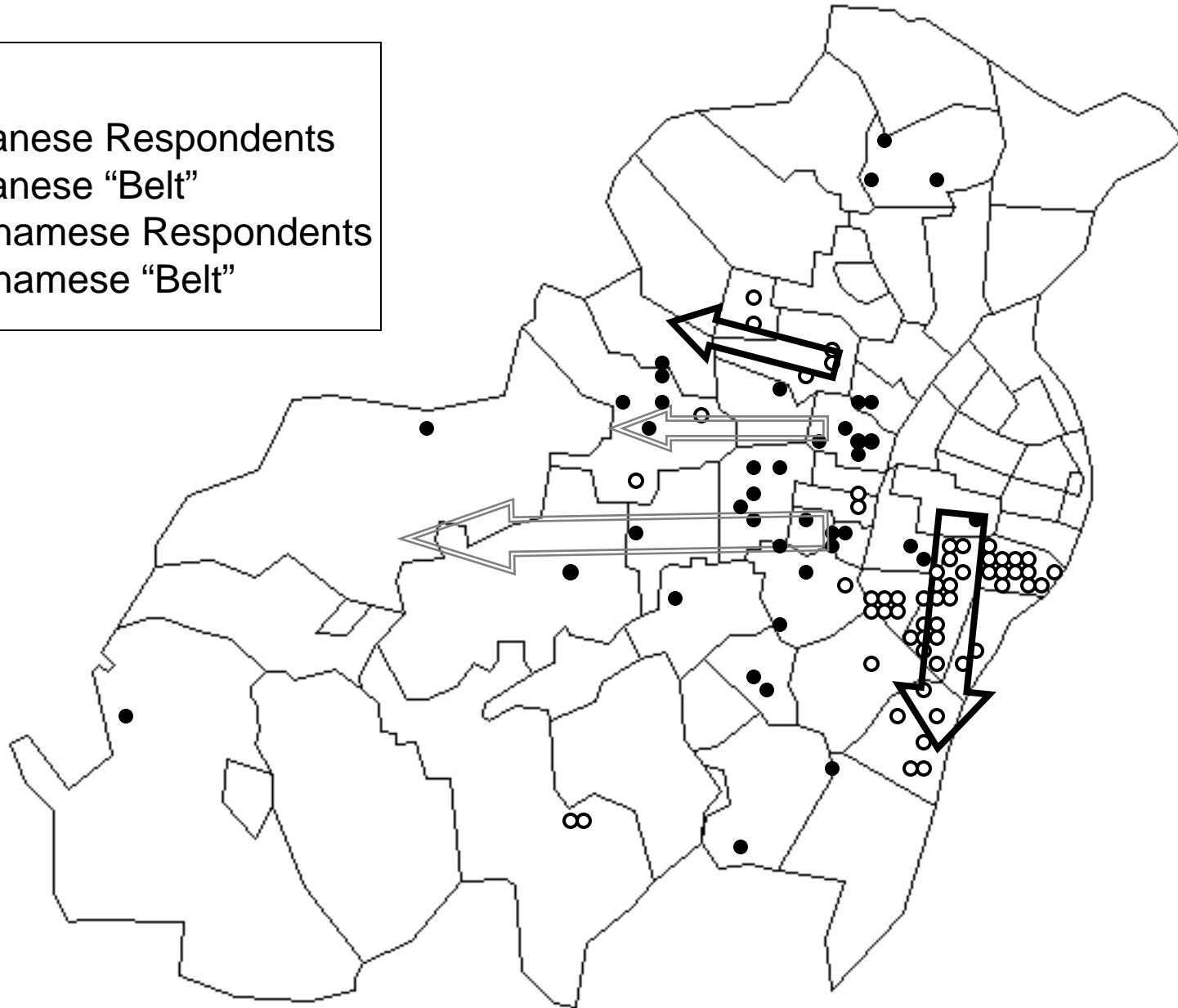


Source: Crabb et al., 1995

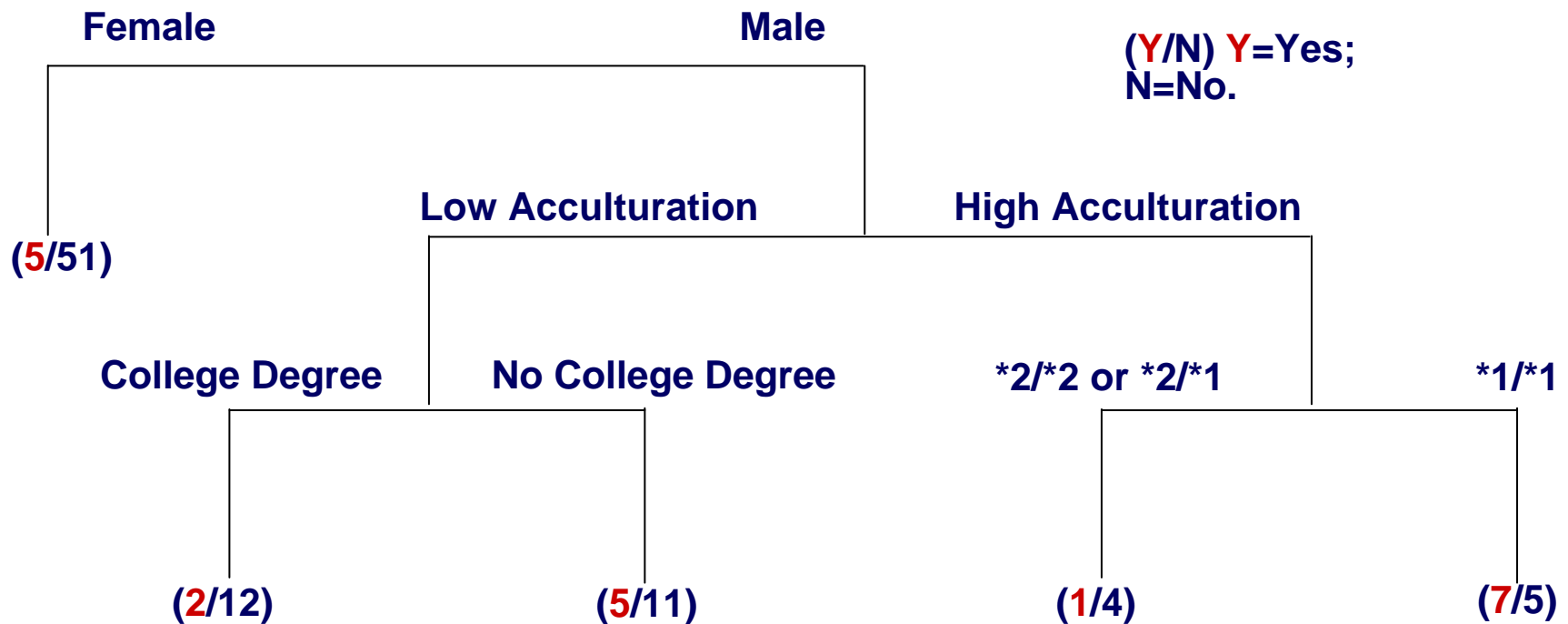
# St. Louis Asian Health Pilot Study Sample Ascertainment

**Legend:**

- Japanese Respondents
- ← Japanese "Belt"
- Vietnamese Respondents
- ← Vietnamese "Belt"



# Figure 2. Predictors of Alcohol Dependence Syndrome: Interactions of ALDH2 Genotypes, Gender and Acculturation<sup>1</sup>



1. Cross-validated tree to minimize a deviance score and then manually pruned to maintain the minimum node size of five. Life time abstainers and one respondent with inconclusive genotype result are excluded from the classification tree analyses (n=103).