Genetics of alcohol metabolism in the Ugandan Population

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Alcohol burden

❖ **Consumption (Age,15+): 43% (world population) 32.3% (African population) are current alcohol consumers (WHO, 2018)**

✓ In Uganda: 36.3% (7.61 million) (WHO,2018), 30.5% (Swahn *et al.,* 2018) and 26.8% (Kabwama *et al.,* 2016)

❖ **Effects: 3M deaths per year, 5.1% of the disease burden (WHO, 2018)**

✓ In Uganda: 7.1% Alcohol Use Disorders, 2.5% Alcohol Dependence, Alcohol Attributable Fractions: 58.8% liver cirrhosis, 30.7% road traffic injuries, 5.8% cancer (WHO, 2018)

Alcohol metabolism

❖ **In the liver: >90%, breath: ≈0.7%, urine: ≈ 0.3%, sweat: ≈ 0.1%**
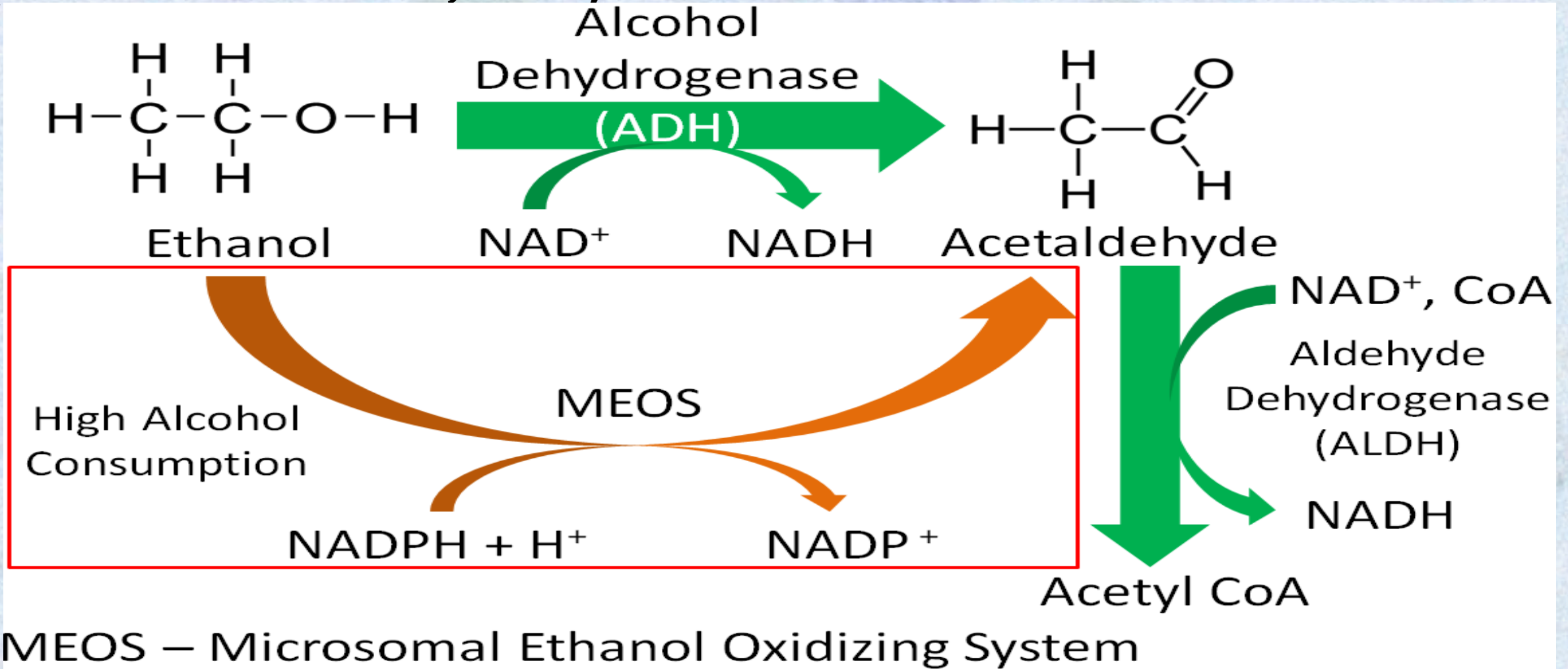**(Ramchandani *et al.,* 2001)**

Fig.1: Enzymatic alcohol breakdown

Alcohol & Aldehyde dehydrogenases

❖ **Class I ADH enzymes encoded by *ADH1B* & *ADH1C* genes account for most alcohol oxidizing activity**

❖ **ALDH2 enzyme encoded by *ALDH2 gene* is the major aldehyde dehydrogenase**

Table 1: Functional SNPs in ADH1B & ADH1C

Gene	SNP	Allele	Effect
ADH1B	rs1229984 – G (Arg) 47 A (His)	ADH1B*1 (Arg47Arg370)	70 to 80 times higher turn over rate than the wild type
	rs2066702 – C (Arg) 370 T (Cys)	ADH1B*2 (His47Arg370)	
		ADH1B*3 (Arg47Cys370)	
ADH1C	rs1693482 – G (Arg) 272 A (Gln)	ADH1C*1 (Arg272Ile350)	70% higher turn over rate than mutant
	rs698 - A (Ile) 350 G (Val)	ADH1C*2 (Gln272Val350)	
ALDH2	rs671 - G (Glu) 487 A (Lys)	Loss of enzyme activity in the mutant	

The alcohol genetics study in Uganda

❖ **250 Blood donors aged 16 – 56 yrs.**

❖ **Extracted DNA**

❖ **Genotyping by PCR-RFLP & Tetra ARMS PCR**

❖ **5 polymorphisms genotyped**
  - ❖**ADH1B rs1229984**
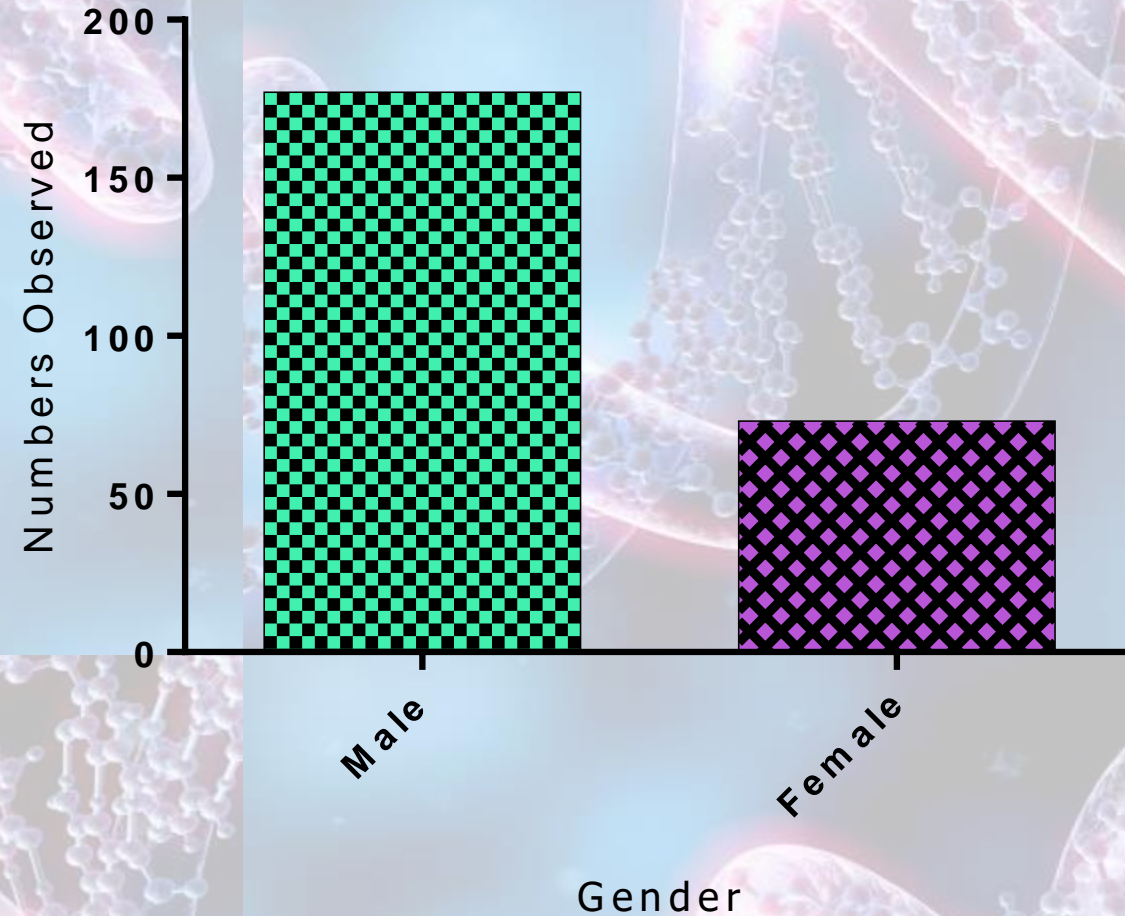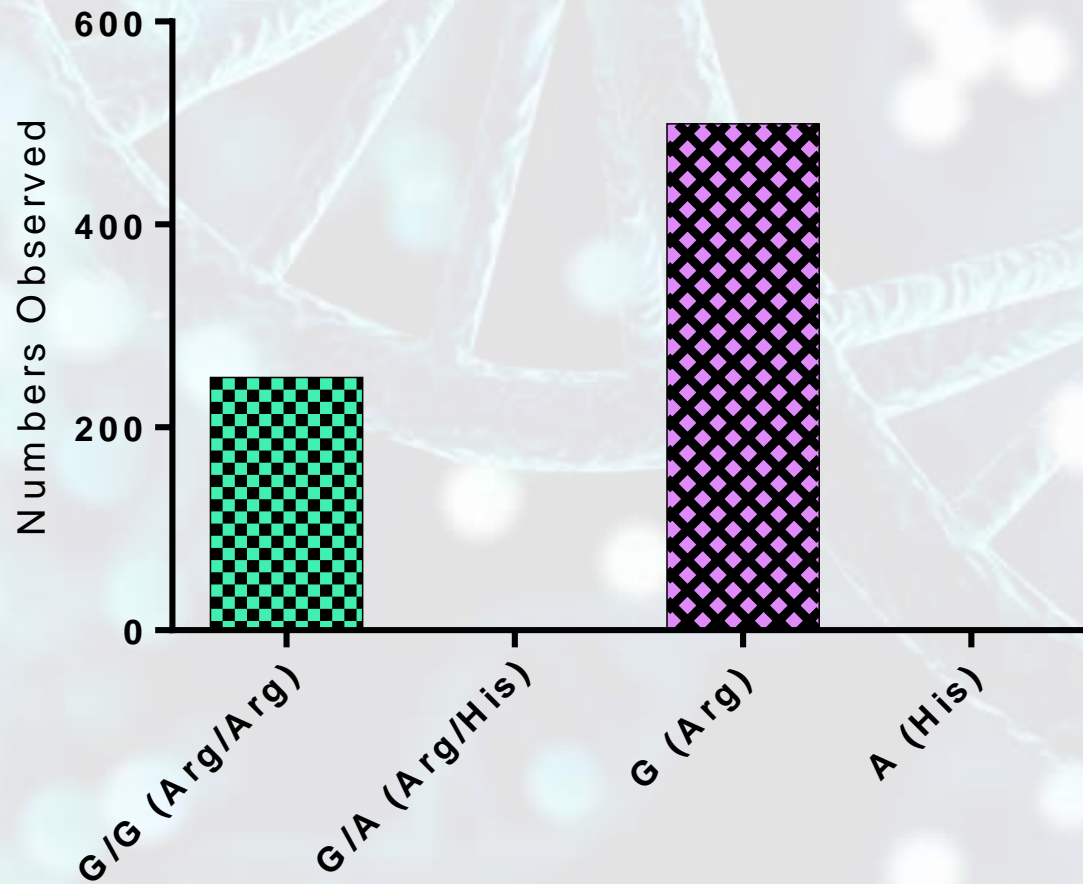 - ❖**ADH1B rs2066702**
  - ❖**ADH1C rs1693482**
  - ❖**ADH1C rs698**
  - ❖**ALDH2 rs671**

Fig.2: Study participants
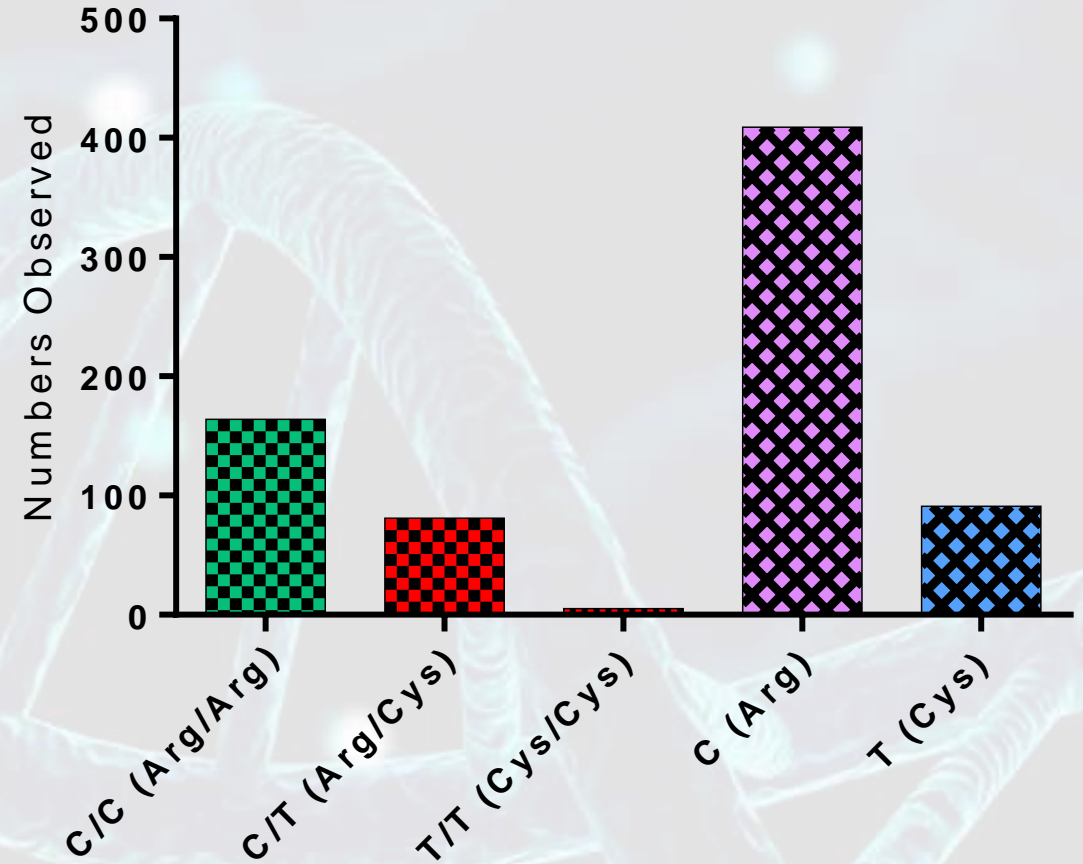
Genotyping Results

Fig. 3 & 4: ADH1B Genotype frequencies

Genotyping Results
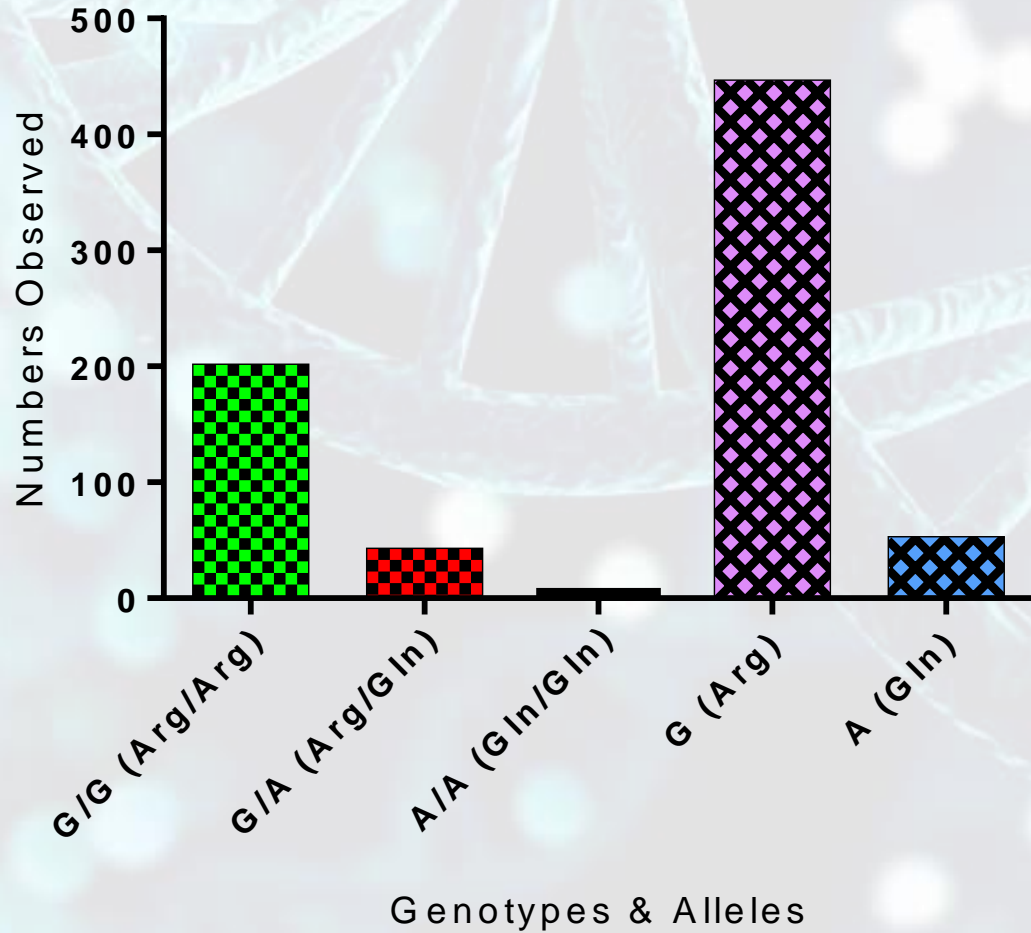
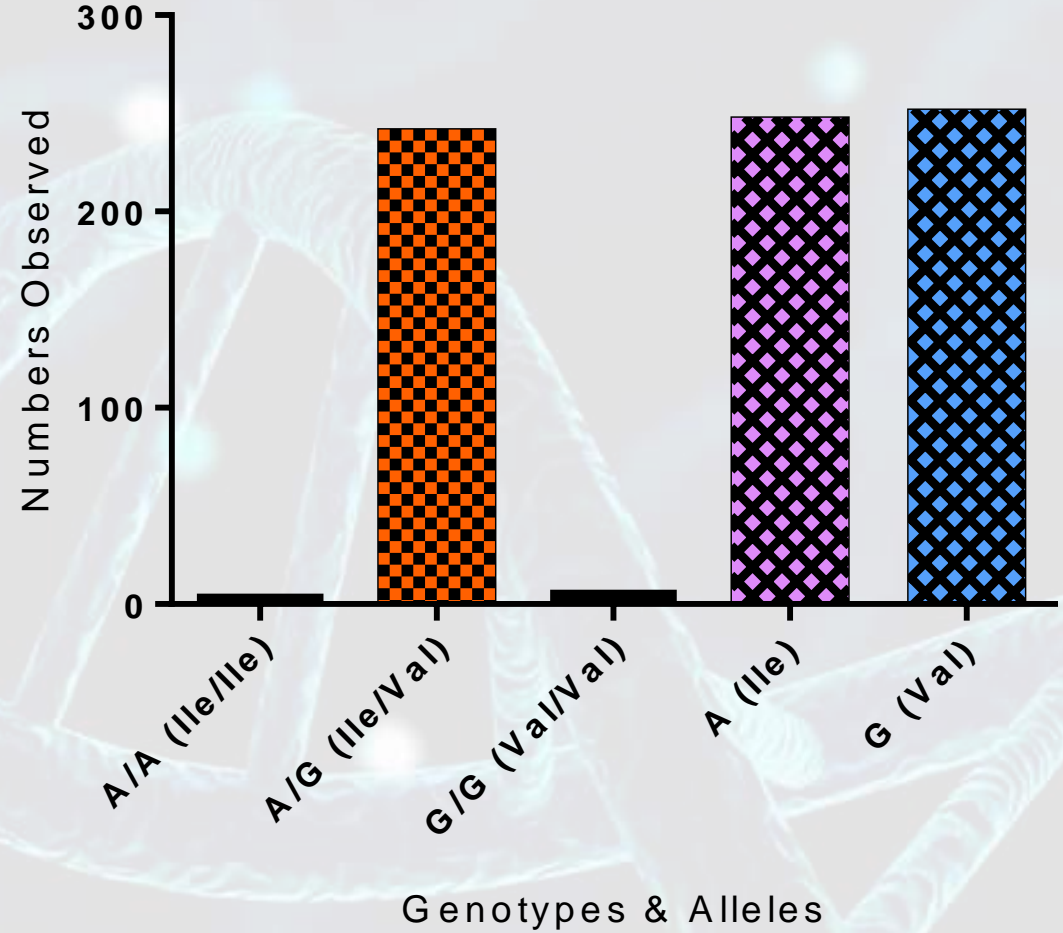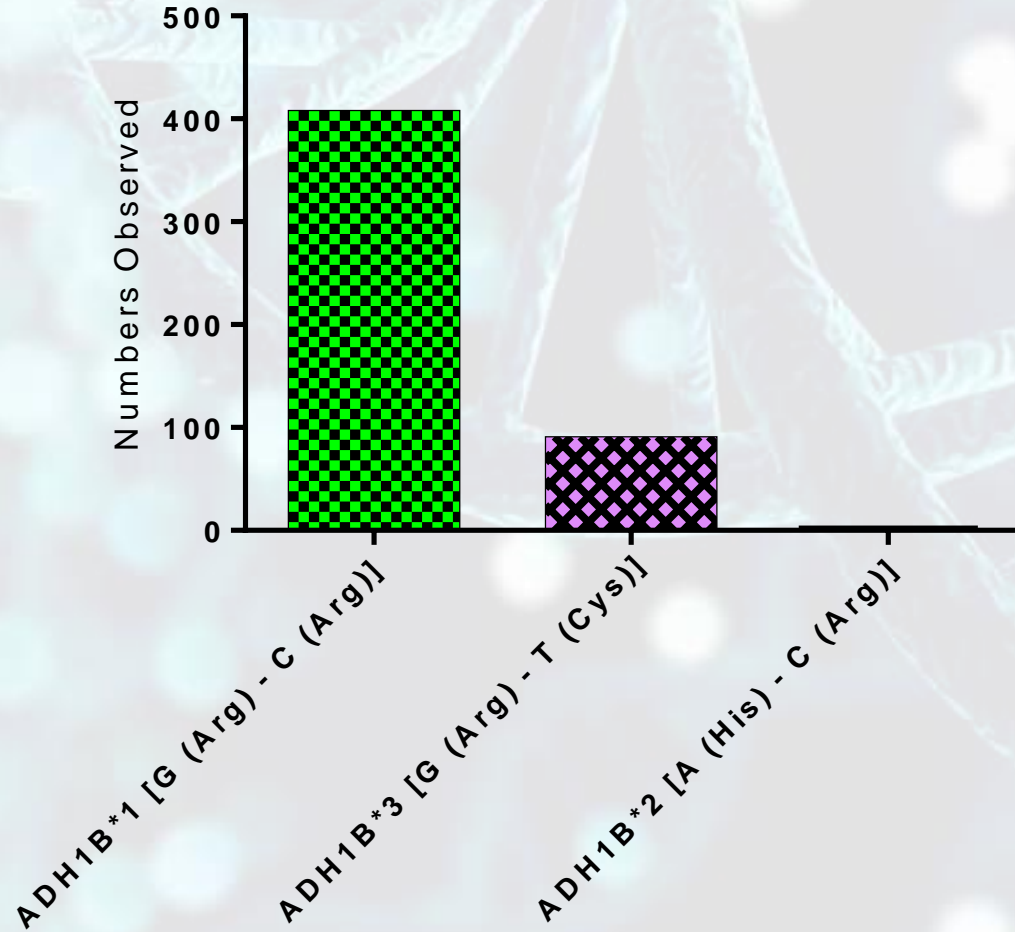*Fig. 5 & 6: ADH1C Genotype frequencies*

Allele frequencies
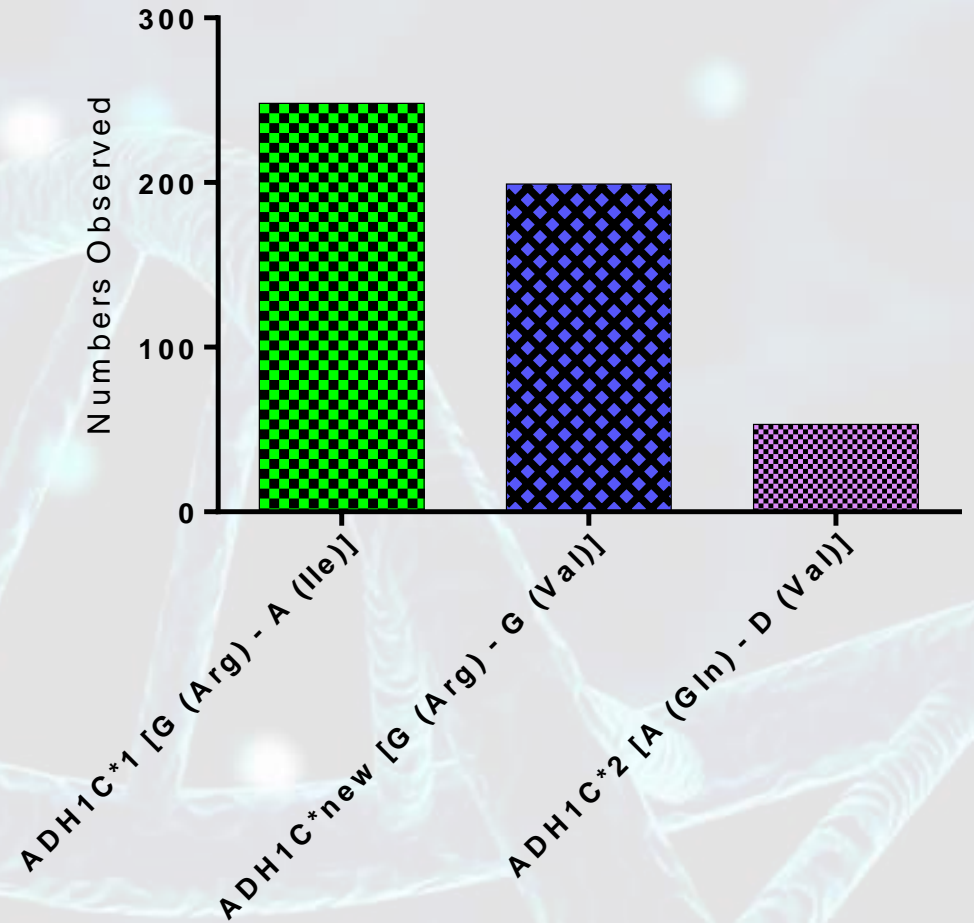
Fig. 7 & 8: ADH1B & ADH1C Allele/Haplotype frequencies

Haplotype frequencies

A D H 1 B - A D H 1 C   H A P L O T Y P E S

Fig. 9: ADH1B & ADH1C Haplotype frequencies
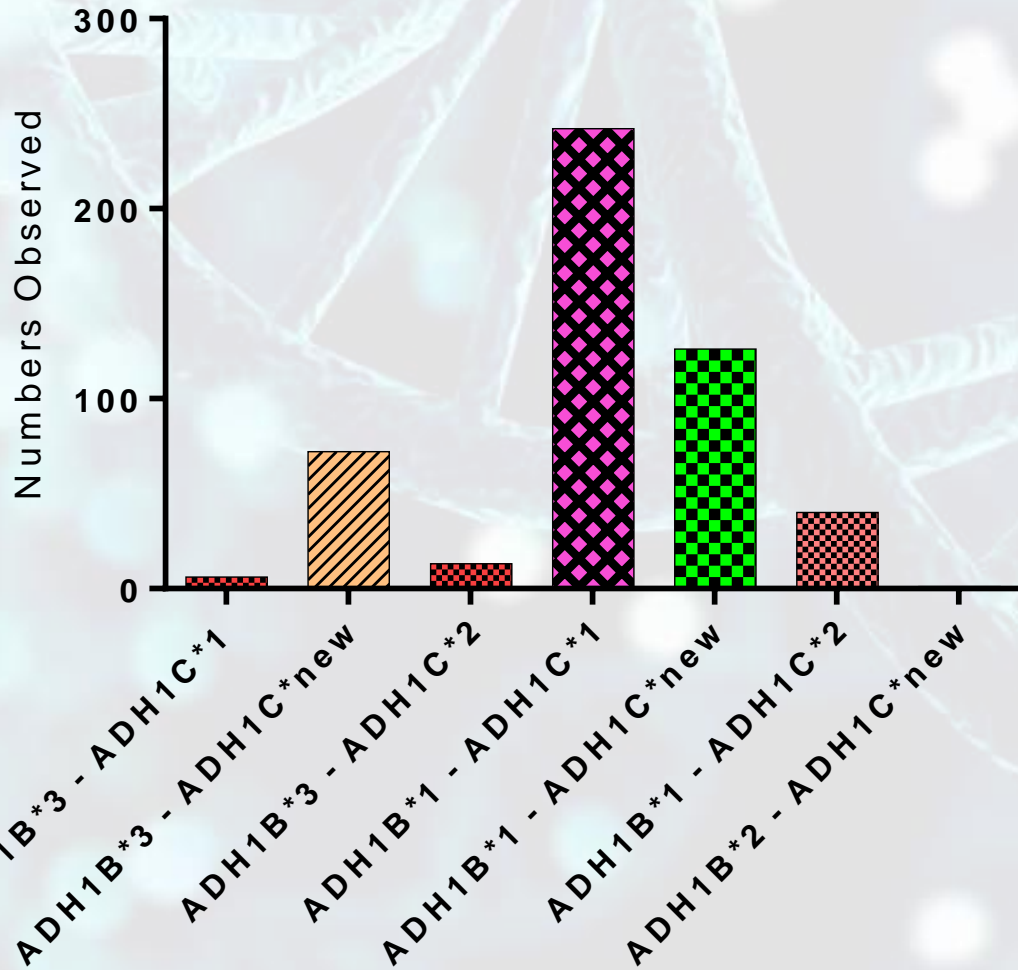
Table 2: Effects of ADH1B & ADH1C Alleles

Allele	Effect
ADH1B*1	Wild type
ADH1B*2	40-fold higher Vmax than wild type
ADH1B*3	30-fold higher Vmax than wild type
ADH1C*1	Wild type
ADH1C*2	Half Vmax of the wild type
ADH1C*new	Unknown

Agarwal, 2001; Edenberg, 2007; Edenberg et al., 2006; Zhakari, 2006

Discussion

❖ **ADH1B*1 - ADH1C*1 (48.4%) & ADH1B*3 - ADH1C*1 (1.2%) imply less acetaldehyde generation following alcohol intake**

❖ **100% G/G genotype means no loss of enzyme activity**
- ✓ **No protection against alcohol dependence & alcoholism**
- ✓ **Protection against alcohol induced tissue damage, esophageal, head, neck & colon cancers**

Outcome

❖ **Per capita alcohol consumption: Uganda 9.5, is higher than African (6.3) & the Global (6.4) (WHO, 2018)**

Way forward/recommendations

❖ **Large scale studies with field samples for SNP distribution**
- ✓ **Alcoholics**
- ✓ **Regional/ethnic samples**
- ✓ **Sequencing**

❖ **Diagnostic/preventive markers**

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