

# Genetic Risks for Alcohol Dependence and Smoking

Laura Jean Bierut, MD  
Washington University

# Alcohol Dependence and Smoking

- Alcohol dependence is a serious public health problem.
- Increasing prevalence of alcohol dependence in younger generations.
- Smoking is the number 1 cause of preventable death in the U.S. Over 400,000 people die every year from a smoking related illness.

# A Part of Medicine

- As with many illnesses in medicine, alcoholism and smoking are complex disorders.
- Clusters in families.
- Genetic contribution.
- Changing environment influences the risk.

# Alcohol Dependence Clusters in Families

- Children of alcoholics are at 2- to 4-fold higher risk for developing alcohol problems.
- About 50% of brothers and 25% sisters of an alcoholic are also alcoholic.
- Yet, most individuals in a family are not affected with alcoholism.

# Understanding Genetic and Environmental Influences Using Twin Studies



MZ Twins

100% genes

100% home environment



DZ Twins

50% genes

100% home environment

If MZs > DZs → Additive Genetic Influence (A)

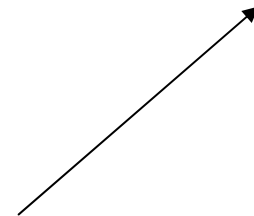
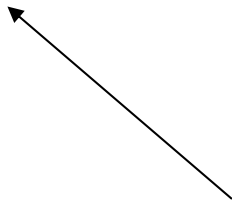
If DZs = MZs → Common Environmental Influence (C)

If MZs < 1 → Unique Environmental Influence (E)

# Adoption Studies

Adoptive Parents

Biologic Parents



# Substance Dependence - A Genetic Disorder

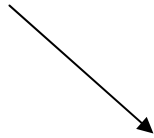
- Several lines of evidence
  - Family studies
  - Adoption studies
  - Twin studies
  - Animal and human genetics

# Substance Dependence - A many step process

Initiation

# Substance Dependence - A many step process

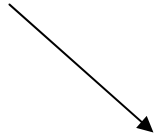
Initiation



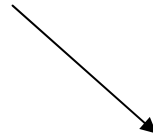
Regular Use

# Substance Dependence - A many step process

Initiation



Regular Use



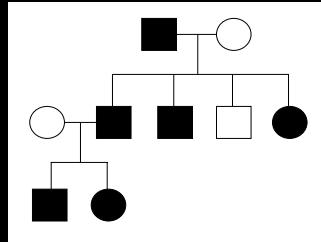
Substance Dependence

# Genetic Studies

- Family based studies – Family studies examine affected individuals and see what regions of their genes are shared among affected individuals.

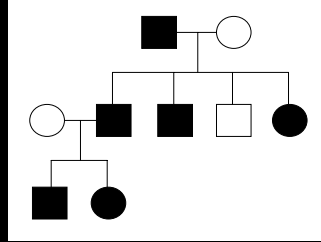
# Genetic Strategy

1. Recruit families affected with alcoholism

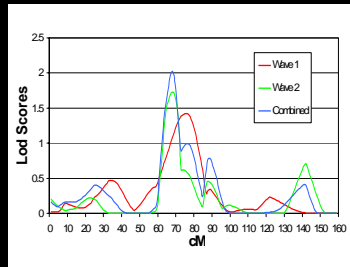


# Genetic Strategy

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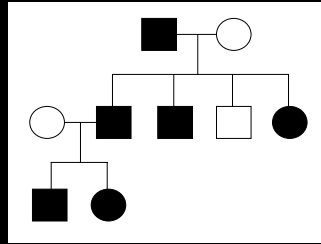
2. Linkage analyses to identify chromosomal regions



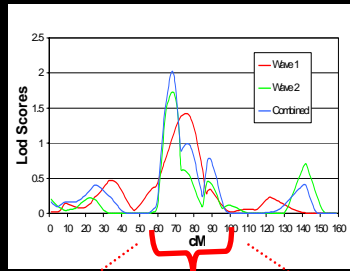
↑ allele-sharing among affecteds within a family

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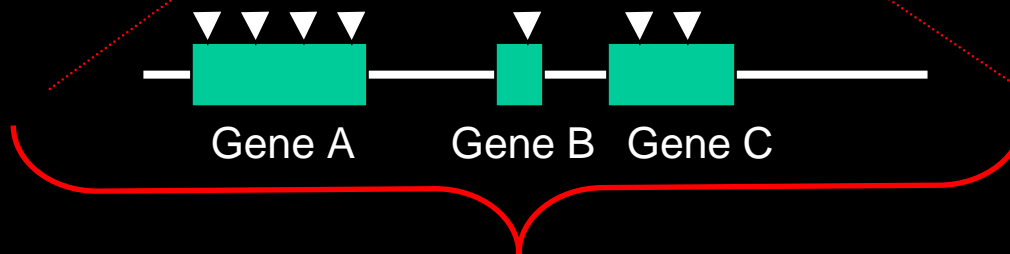


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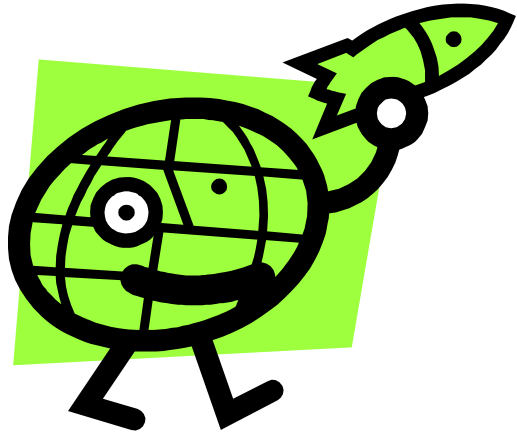


↑ allele-sharing among affecteds within a family

3. Association analyses to identify specific genes



# Case Control Study



A - 38%



A - 64%

Compare the frequency of genetic variants in cases and controls

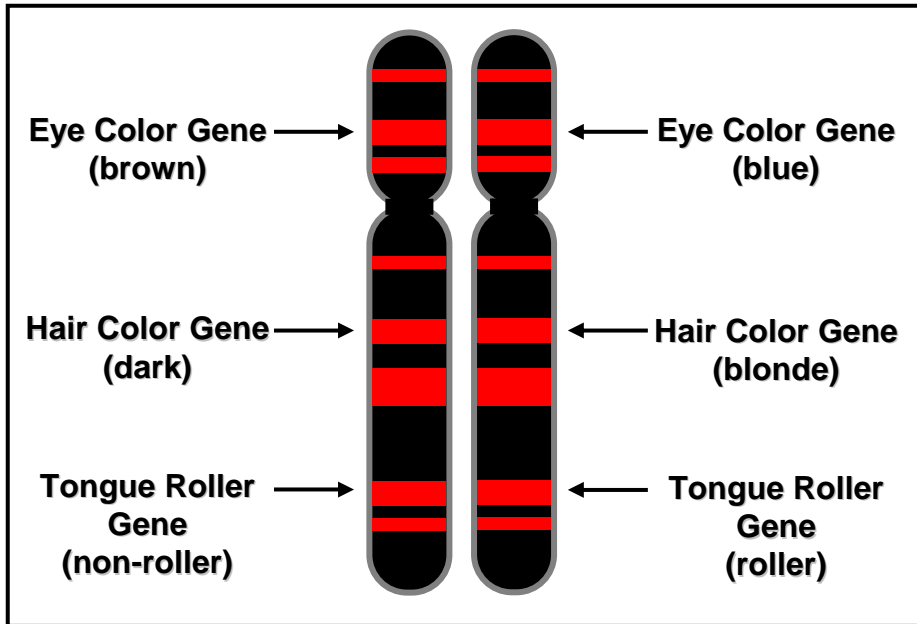
# Genes Associated with Alcoholism

- Multiple genes are associated with alcoholism.
- Several independent studies replicated findings.
- We now have genes that influence the risk for the development of alcoholism.

# Genes Associated with Alcoholism

ALDH	Aldehyde metabolism	Thomasson et al, 1992
GABRA2	Gaba receptor	Edenberg et al, 2004
GABRG3	Gaba receptor	Dick et al, 2004
CHRM2	Muscarinic receptor	Wang et al, 2004
OPRM1	Opioid receptor	Bart et al, 2005
TAS2R16	Taste receptor	Hinrichs et al, 2006
ADH4	Alcohol metabolism	Edenberg et al, 2006

# Genetic Variants



- **There are millions of variants catalogued across our genome.**
- **Many genes have multiple variants.**
- **Another commonly used name for allelic variant is polymorphism.**

What does the future bring?

# Genetics is here to stay

- Genetic findings open valuable possibilities for the future of medicine
  - Greater understanding of biologic pathways is disorders.
  - Understanding of environmental influences
  - New targets for personalized medicine