

# Genetics is largely the study of genetic variation

## Induced variation

- experimental alteration of the genome or its gene products

## Natural variation

- alterations of the genome that exist in natural populations

## Induced variation

Used in *model organisms* to dissect biological phenomena  
- identify genes that function in a biological process,  
understand how they act together to orchestrate  
the process as well as to understand the mechanistic  
basis of human disease.

## Natural variation

The basis of *population and quantitative genetics*.  
The basis of variation in *human genetics* that underlies  
traits (phenotypes) such as height and diseases.

# Model Organism Genetics

One or a few strains are chosen as the wild-type/canonical version (e.g. Bristol N2 for *C. elegans* or S228c for yeast). Also used as the reference genome sequence.

Genetic background homogeneous (inbred, limited variation between strain versions used by the community)

Genetic variation (mutations) experimentally induced

- allows comparison of mutant phenotypes between laboratories without the issue of genetic modifiers.

- obtained variation (mutations) can have strong, deleterious and pleiotropic phenotypes (null alleles, gain-of-function alleles), that are very informative for understanding gene function and can be maintained in the laboratory.

# Population & quantitative genetics

Individuals/ strains obtained from natural (wild) populations.

Genetic background heterogeneous  
(usually not inbred, variation (alleles) usually heterozygous).

Genetic variation found in the population - most is silent while some may be of selective advantage in certain environments. Deleterious pleiotropic alleles are usually rapidly lost from natural populations.

Experimentally, examine the variance in phenotype and identify the genes that contribute to this variance. Natural phenotypic variation is usually not from null alleles, often from missense and non-coding changes.

# Human Genetics

Natural populations, that at most show limited inbreeding; significant number of sequence differences between individuals (no "reference genome sequence").

Observed genetic variation is based on historical breeding patterns, that distributed ancestral variation, and newly arising variation.

Experimentally, traits are considered monogenic (Mendelian) or polygenic (complex); particularly for complex traits it can be difficult to demonstrate a causative association of genotype with phenotype.

The course will use Model Organisms to

- illustrate principles and concepts in genetics and the logic of genetic analysis, much of which is organism independent.
- illustrate how to perform genetic analysis in various model organisms.

{Importance of Model Organism Genetics in driving discovery and knowledge to translate (Alberts' Editorial)}

Natural variation will be discussed primarily in the sections on Quantitative Genetics, Human Genetics and Cancer Genetics.



# Course expectations:

50% of grade is from homework and discussion sections

50% from the research proposal and study section

For Small Group Discussions of papers:

Write 1 to 1.5 page (single spaced) evaluation of the paper that covers:

- Significance of the study
- Take home points
- Approach/ methods
- What is the next set of experiments?

Turn in at the beginning of the Discussion Section

Homework: type out answers and where necessary draw neatly.

Assignments should be turned in on time, except with permission.