The Multiethnic Cohort Study

UNIVERSITY OF HAWAI'I CANCER CENTER

USC University of Southern California

Genetic Variation and Cancer

GENETIC VARIATION

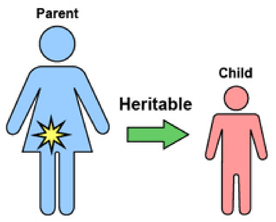
SOMATIC DNA MUTATIONS — **GERMLINE DNA MUTATIONS and VARIANTS (SNPs)**

- Occur in ***nongermline*** tissues
- Cannot be inherited

Nonheritable

Mutation in tumor only (for example, breast)

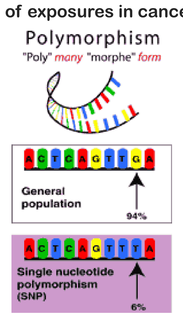
RARE MUTATIONS
- Present in egg or sperm
- Can be inherited
- Cause cancer family syndrome



Mutation in egg or sperm

All cells affected in offspring

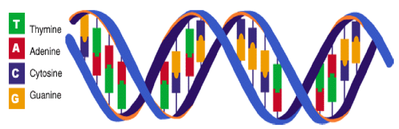
COMMON POLYMORPHISMS -SNPs
- Present in egg or sperm
- Are inherited
- Can lessen or increase the effect of exposures in cancer risk



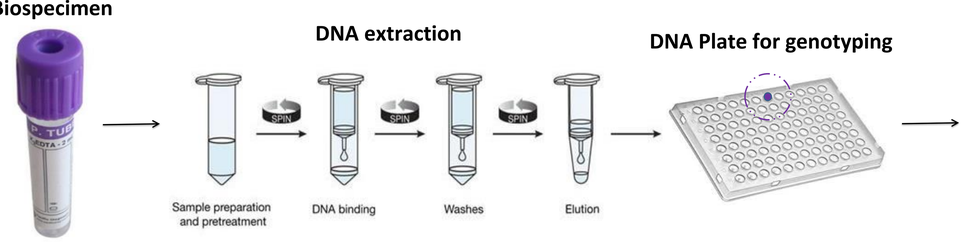
SNPs are studied in GWAS

Adapted from the National Cancer Institute and the American Society of Clinical Oncology

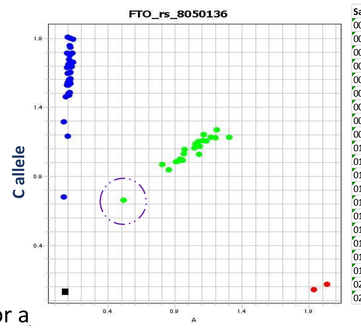
DNA GENOTYPING



De-identified Biospecimen



DNA genotyping results for multiple individuals

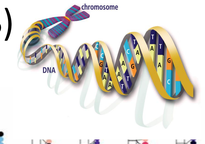


Sample Id	Genotype
001	AA
002	CC
003	AC
004	AC
005	CC
006	AC
007	AA
008	CC
009	CC
010	CC
011	AC
012	AC
013	CC
014	AC
015	AC
016	CC
017	CC
018	CC
019	AC
020	CC
021	AC

A MEC-participant's blood sample was extracted for DNA at the genomics laboratory and genotyped for a SNP in the FTO gene together with other participants' samples. For this particular person, heterozygosity (AC-genotype) for the SNP was observed, meaning that this person has inherited both the more common allele C and the risk-associated variant allele A from his/her parents. This means that this MEC member is at greater risk for Early Onset Obesity and Type-2 Diabetes, as compared to the participants with two common alleles, but is at lower risk than those with two risk-associated variant alleles.

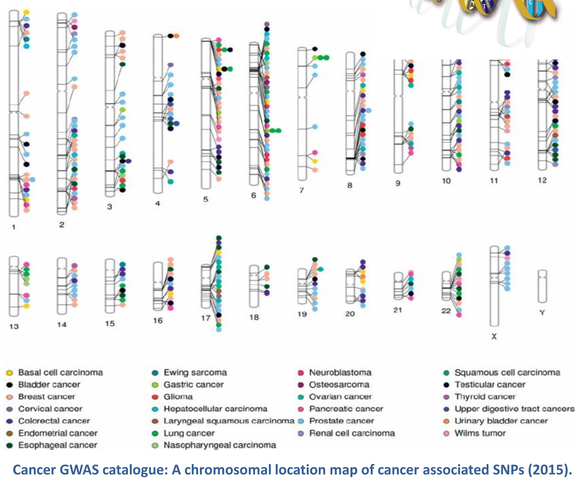
GENOME-WIDE ASSOCIATION STUDIES (GWAS)

HOW DOES DNA VARIATION (SNPs) RELATE TO RISK FOR DISEASE



GWAS studies associations between SNP variants and phenotypes. The goal is to identify **gene variants related to human disease.**

Phenotype is a set of observable characteristics resulting from the interaction between genotype and environment, such as:
- Chronic diseases, such as diabetes and cancer
- Traits, such as body size and shape
- How your body responses to diet, exercise, smoking, etc.



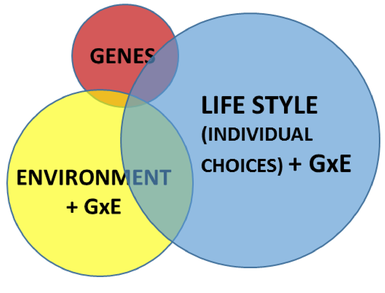
Cancer GWAS catalogue: A chromosomal location map of cancer associated SNPs (2015).

GENES AND ENVIRONMENT + LIFESTYLE

Gene-environment interaction **(GXE)** is when different genotypes respond to an exposure in different ways.

"Genetics loads the gun, lifestyle pulls the trigger"

-Caldwell Esselstyn-

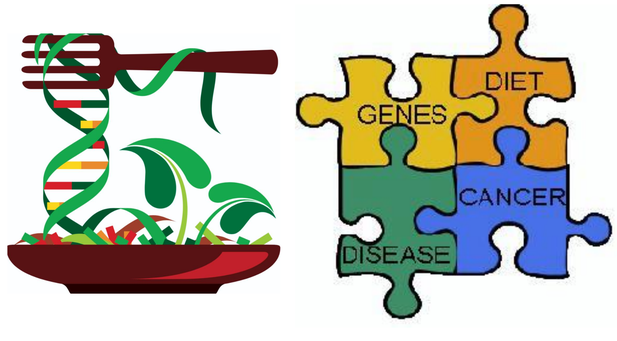


The majority; 90–95% of all cancer cases have their roots in the lifestyle (up to 65%) and environment (up to 30%).

GxE: the effects of the lifestyle and environment can be affected by the individual's genetic background (SNPs etc).

Only 5–10% of cancer cases can be attributed solely to inherited "bad genes" = germline mutations.

NUTRIGENETICS - YOUR GENES AND YOUR DIET



Nutrigenetics is the study of individual differences at the genetic level (SNPs) influencing the body's response to diet.

MEC HI Genomics team: Maarit Tiirikainen, Annette Lum Jones, Ann Seifried and Karolina Peplowska at the University of the Hawaii Cancer Center's Genomics Shared Resource