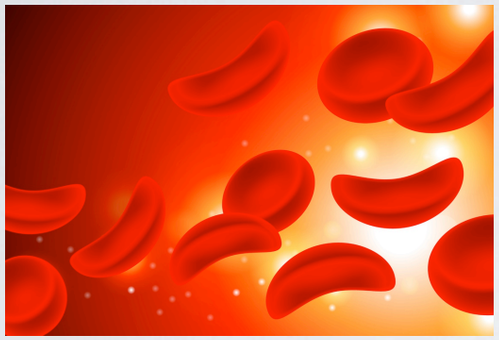
Genetics and Genomics in Clinical Research

An Immersion Course for Clinical Investigators at UAB

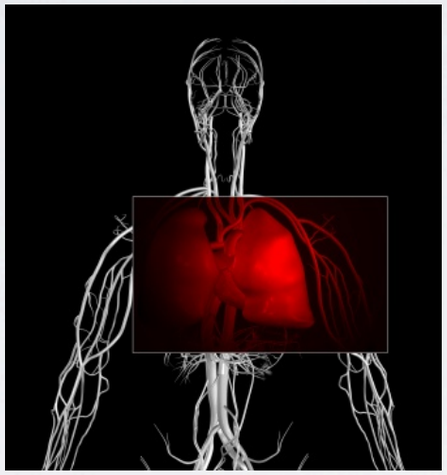
Introduction and Overview

Bruce R. Korf, MD, PhD

Human “Phenome”

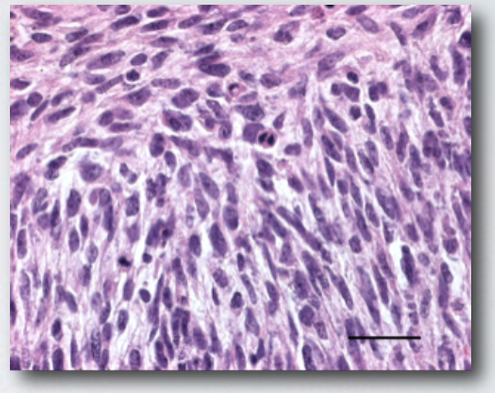


Single Gene



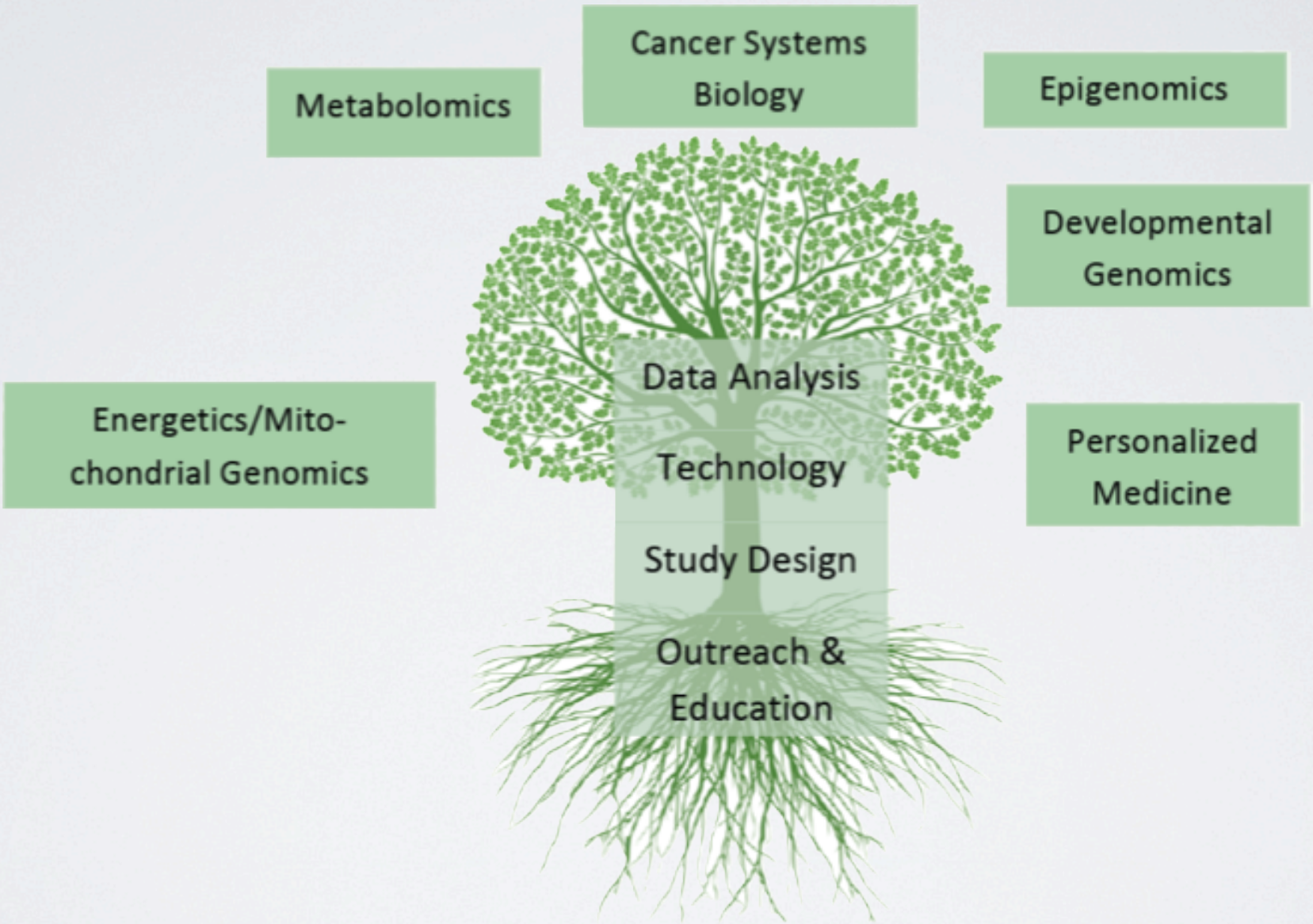
Multifactorial

Pharmacogenetic



Cancer

Genomics at UAB



Goals

This immersion course is intended to provide a review of the principles, major technologies, and experimental approaches in genetics and genomics through both lectures and hands-on activities. Earn up to 20 hours CME credit at no charge.

Register online at The Heflin Center for Genomic Sciences

Learning Objectives:

1. Design an approach to identification of a gene responsible for a phenotype in a family that segregates in a Mendelian manner.
2. Devise an appropriately powered case-control or transmission disequilibrium study to identify single nucleotide polymorphisms in linkage disequilibrium with a multifactorial disorder.
3. Develop a study comparing patterns of gene expression or methylation levels in normal vs. pathological tissue.
4. Formulate a protocol involved human research subjects for a genetic or genomic study to be submitted for IRB review.
5. Choose between alternative genotyping or next generation sequencing platforms appropriate for specific applications.
6. Utilize major bioinformatic databases to analyze genomic data.

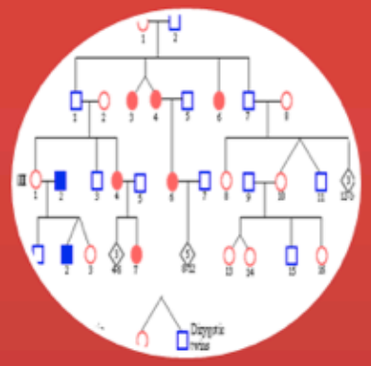
Schedule

September 30 to October 4, 2013

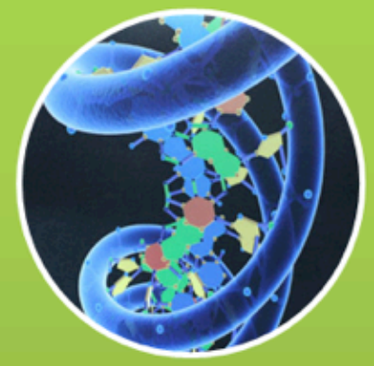
	MON	TUES	WED	THURS	FRI
7:30 – 8:00	Breakfast	Breakfast	Breakfast	Breakfast	Breakfast
8:00 - 9:00	Introduction *Dr. Bruce Korf*	Genotyping Technologies and Copy Number Variation Analysis *Drs. Michelle Amaral & Fady Mikhail*	Next-Generation Sequencing *Dr. Mike Crowley*	Approaches to Bioinformatic Data Analysis *Dr. David Crossman*	Genetic Linkage Analysis *Dr. Hemant Tiwari*
9:15 - 10:15	Approaches to Gene Discovery *Dr. Bruce Korf*	Microarray-Based Approaches for Gene Expression and Methylation Status *Dr. Michelle Amaral*	Whole Genome Functional Assays *Dr. Mike Crowley*	Bioinformtic Pathway and Ontology Analysis *Dr. David Crossman*	Design and Analysis of Genetic Association Studies *Dr. Hemant Tiwari*
10:30 - 11:30	Case Studies/ Translational Genomics *Dr. Bruce Korf*	Analysis of Microarray Data *Dr. David Crossman*	Functional Genomics *Dr. Mike Crowley*	Use of Bioinformatic Databases *Dr. David Crossman*	

Genetics

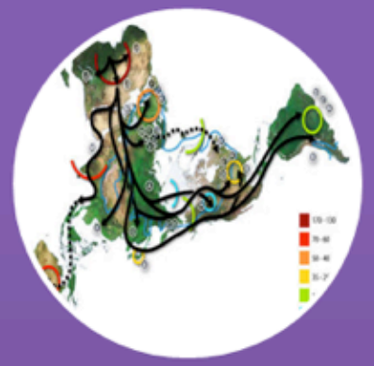
Scientific discipline that deals with the variability and transmission of biological traits.



Transmission through families



Flow of information in cell



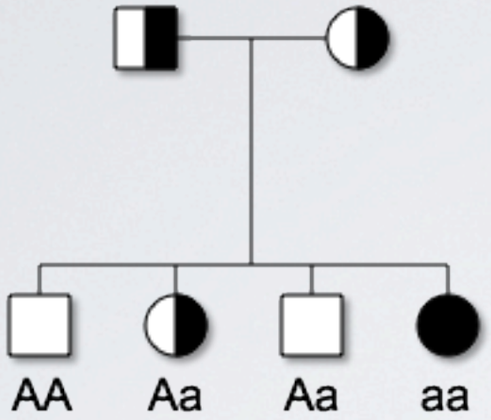
Population forces and evolution

Genomics

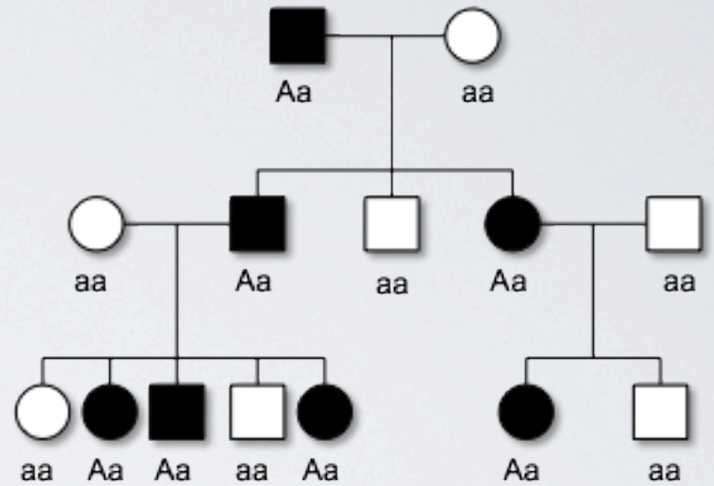
"For the newly developing discipline of mapping/sequencing (including analysis of the information) we have adopted the term GENOMICS. We are indebted to T. H. Roderick of the Jackson Laboratory, Bar Harbor, Maine, for suggesting the term. The new discipline is born from a marriage of molecular and cell biology with classical genetics and is fostered by computational science."

(Victor A. McKusick and Frank H. Ruddle. A new discipline, a new name, a new journal [editorial]. Genomics 1987 Sep; 1:1-2.)

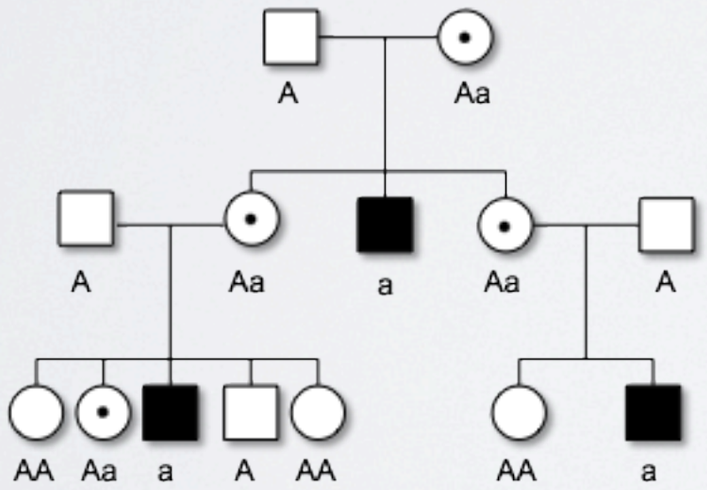
Mendelian Genetics



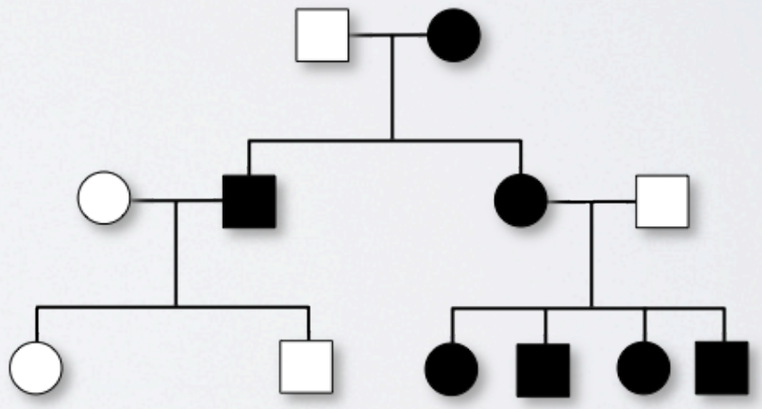
Autosomal Recessive



Autosomal Dominant

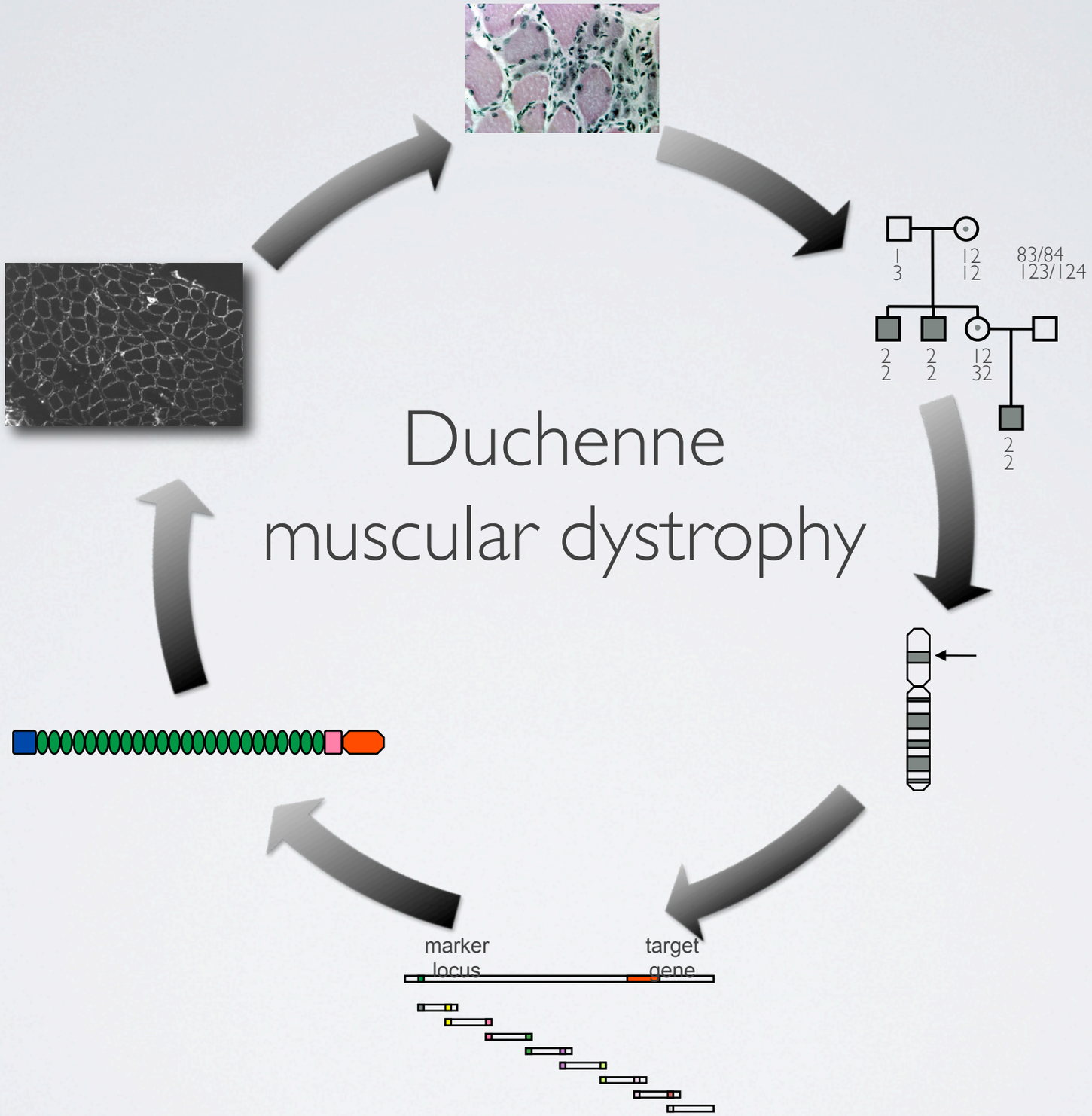


X-linked



Mitochondrial

Positional Cloning



SNP Association Case-control Study

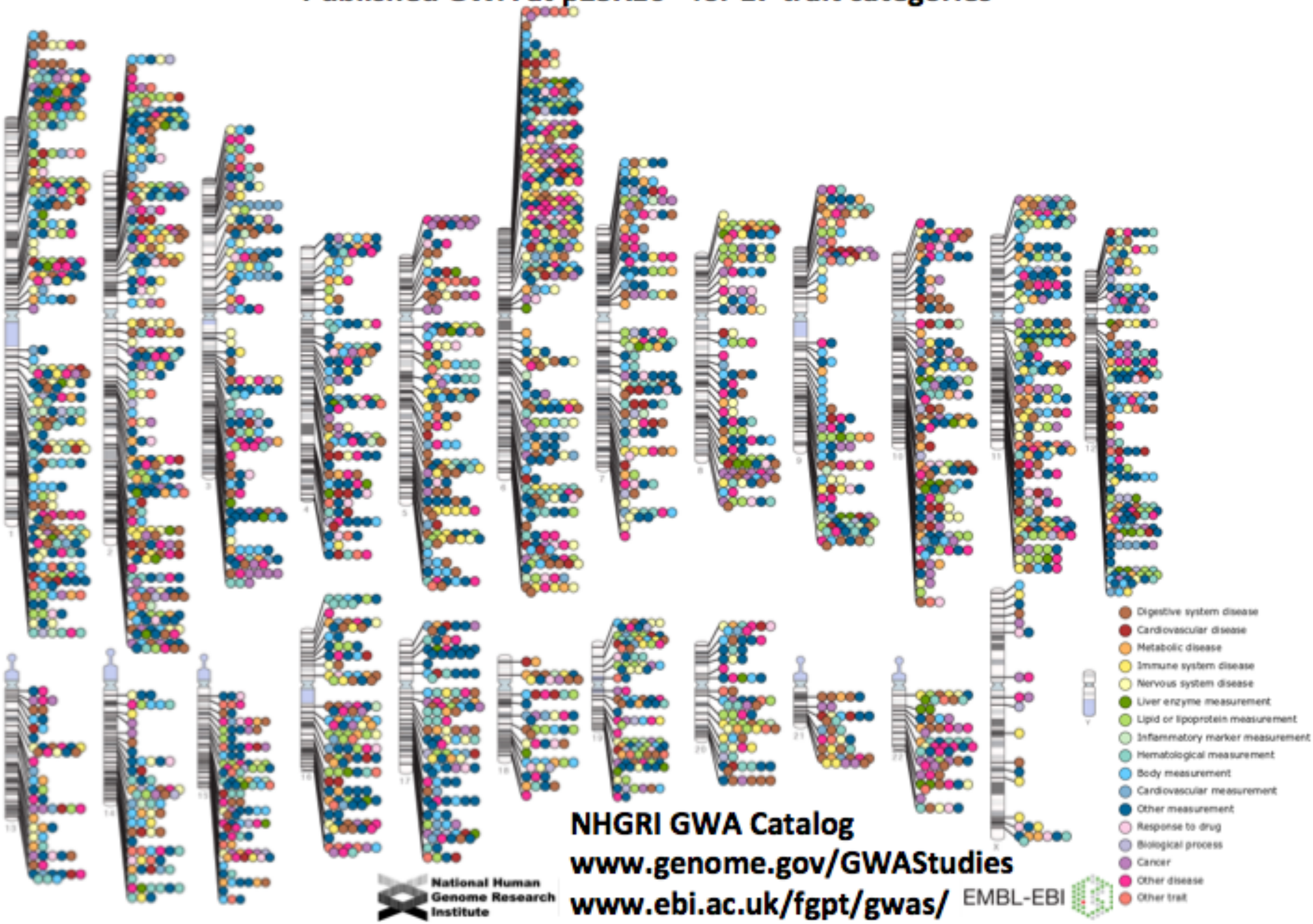
ACTAGGA **Allele 1**

ACTCGGA **Allele 2**

	Asthma	No Asthma
Allele 2 Present	300	100
Allele 2 Not Present	700	900

Hypothesis: Allele 2 is associated with an increased risk of asthma

Published Genome-Wide Associations through 12/2012
Published GWA at p≤5X10^{-8} for 17 trait categories



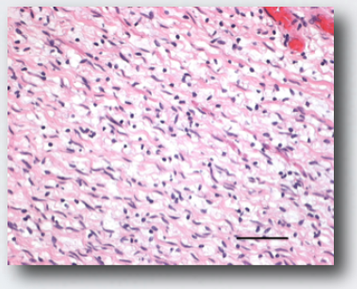
NHGRI GWA Catalog
www.genome.gov/GWAStudies
www.ebi.ac.uk/fgpt/gwas/

National Human Genome Research Institute

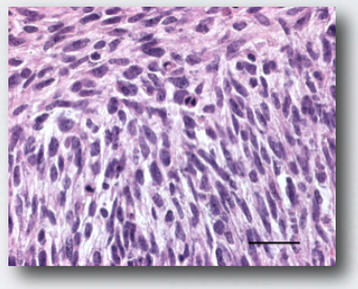
EMBL-EBI

Cancer Genomes

Normal



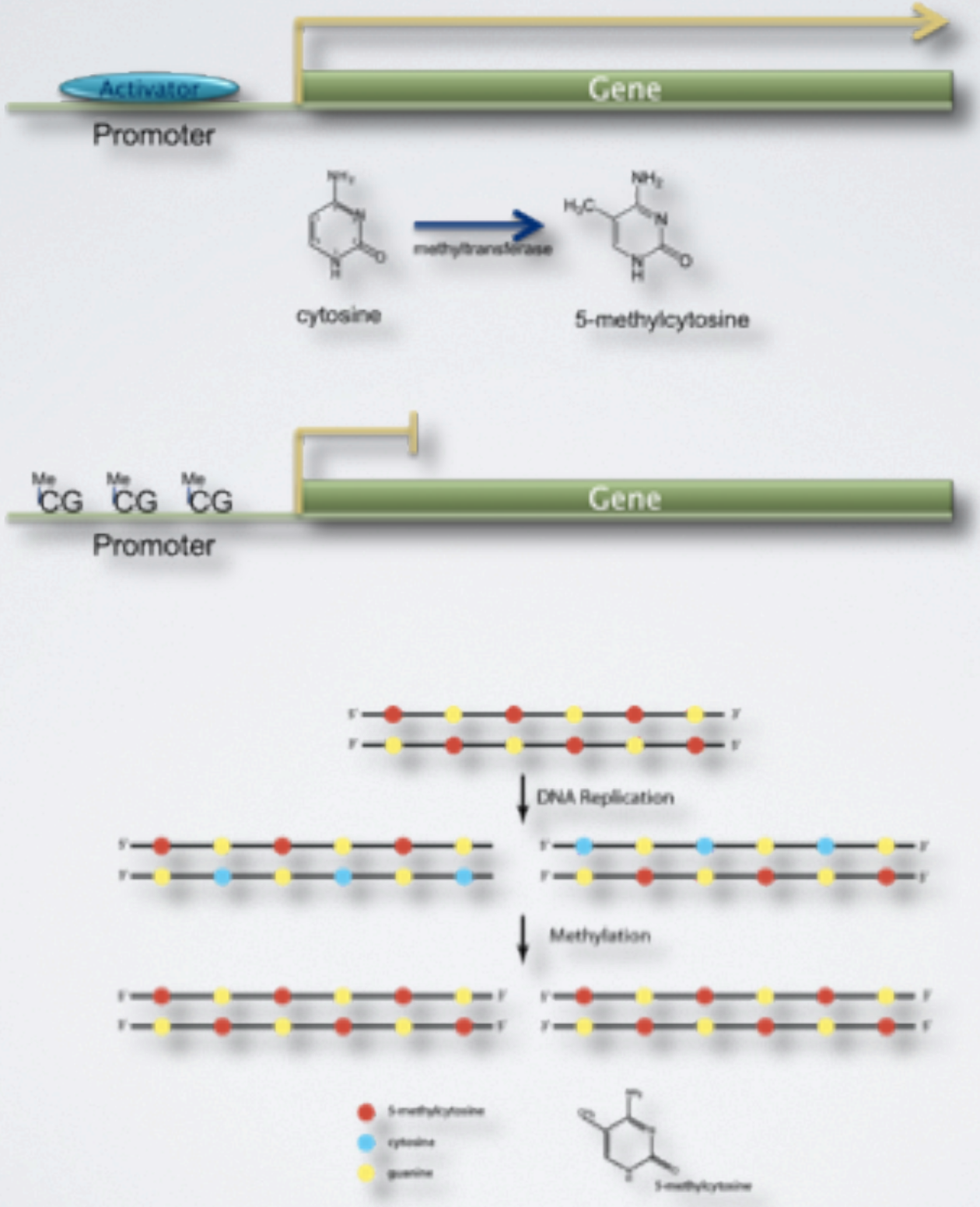
Tumor



Sequence

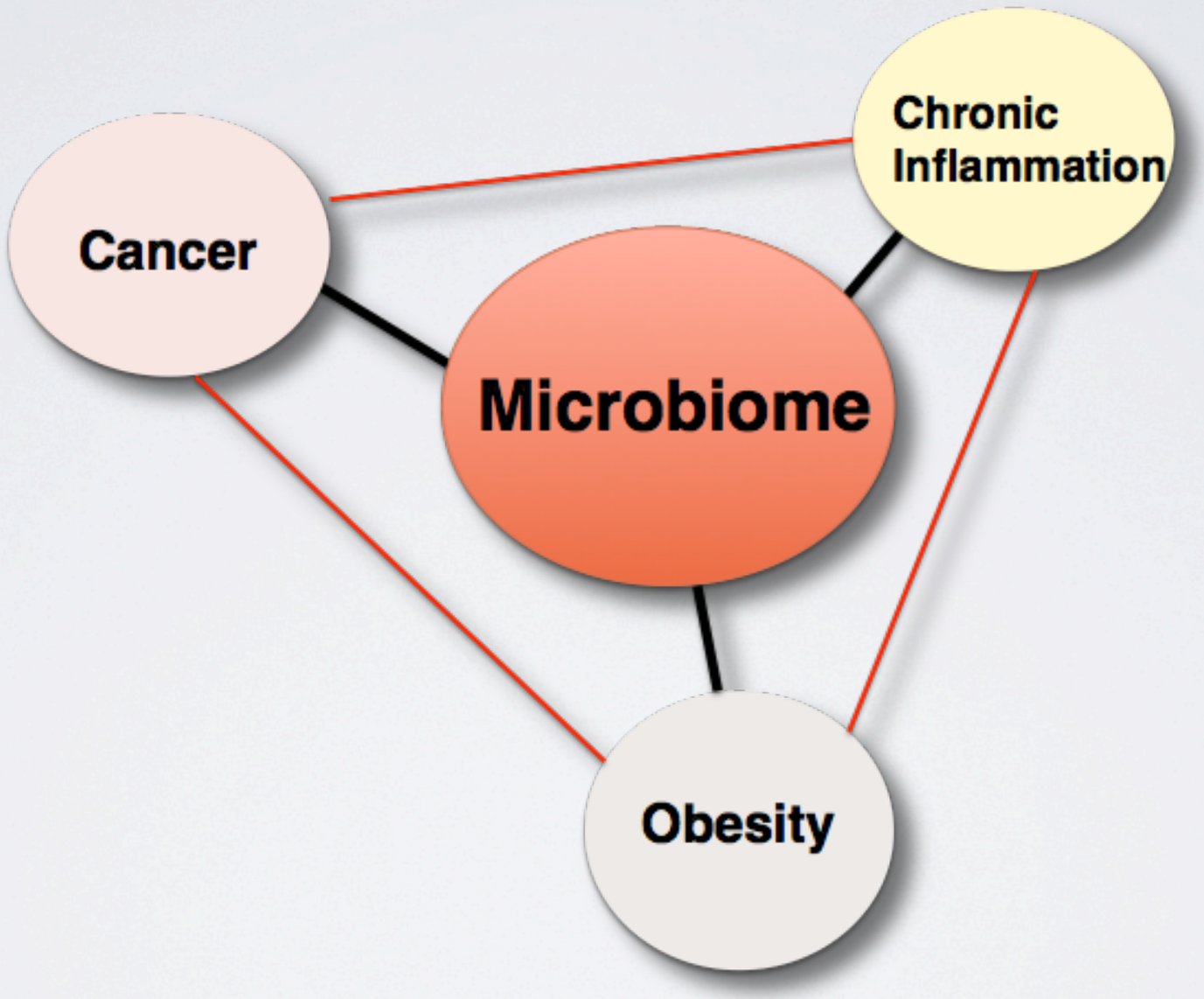
Difference =
cancer-specific genetic changes

Epigenetics



Functional Genomics

Microbiome



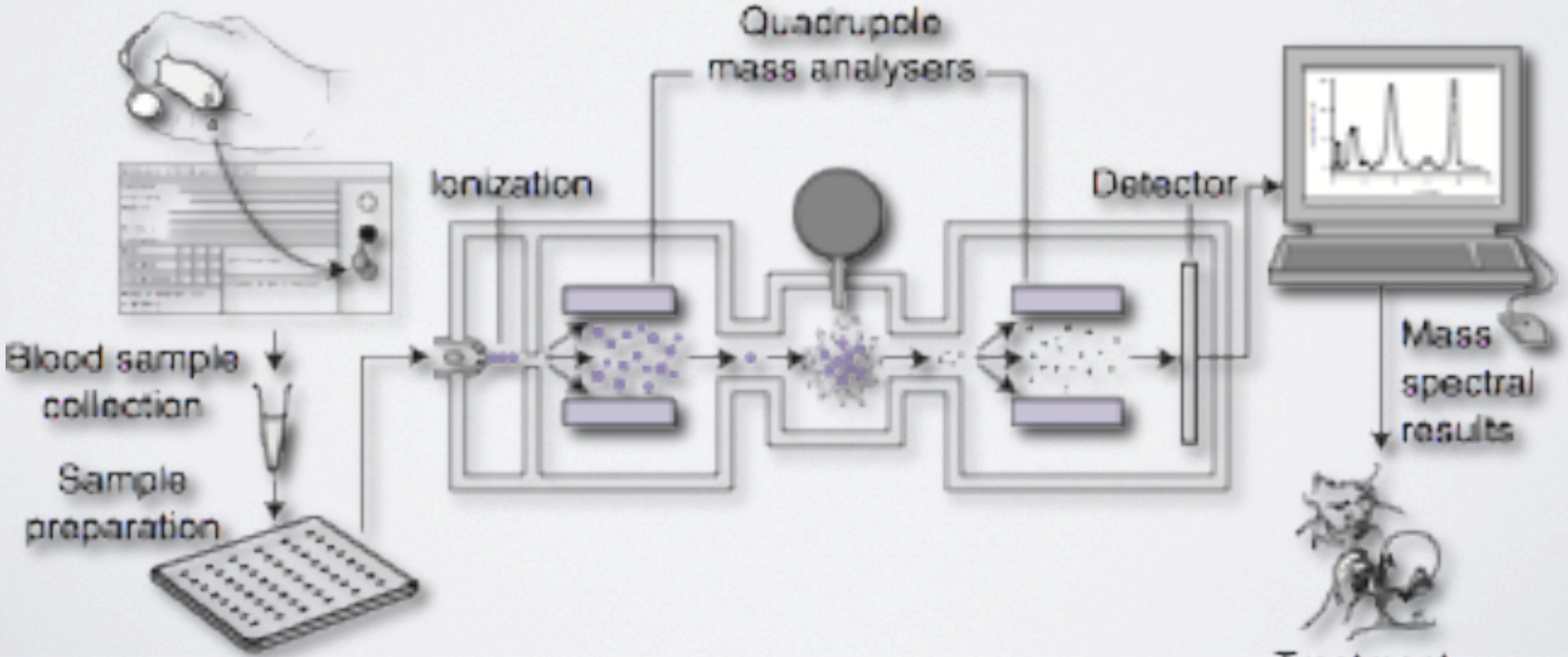
Genetics in Medicine

Prevention

Diagnosis

Treatment

Prevention

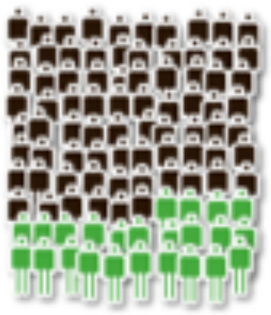

Quadrupole
mass analysers
Ionization
Detector
Blood sample
collection
Sample
preparation
Mass
spectral
results

Direct-to-Consumer Testing

Your Genetic Data

Show information for **Bruce Korf** assuming **European** ethnicity and an age range of **20–79**

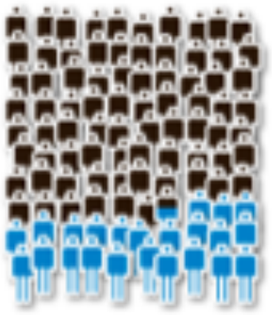
Where's mine?



Bruce Korf

24.3 out of 100

men of European ethnicity who share Bruce Korf's genotype will get Type 2 Diabetes between the ages of 20 and 79.



Average

23.7 out of 100

men of European ethnicity will get Type 2 Diabetes between the ages of 20 and 79.

What does the Odds Calculator show me?

Use the ethnicity and age range selectors above to see the estimated incidence of Type 2 Diabetes due to genetics for men with **Bruce Korf**'s genotype. The 23andMe Odds Calculator assumes that a person is free of the condition at the lower age in the range. You can use the name selector above to see the estimated incidence of Type 2 Diabetes for the genotypes of other people in your account.

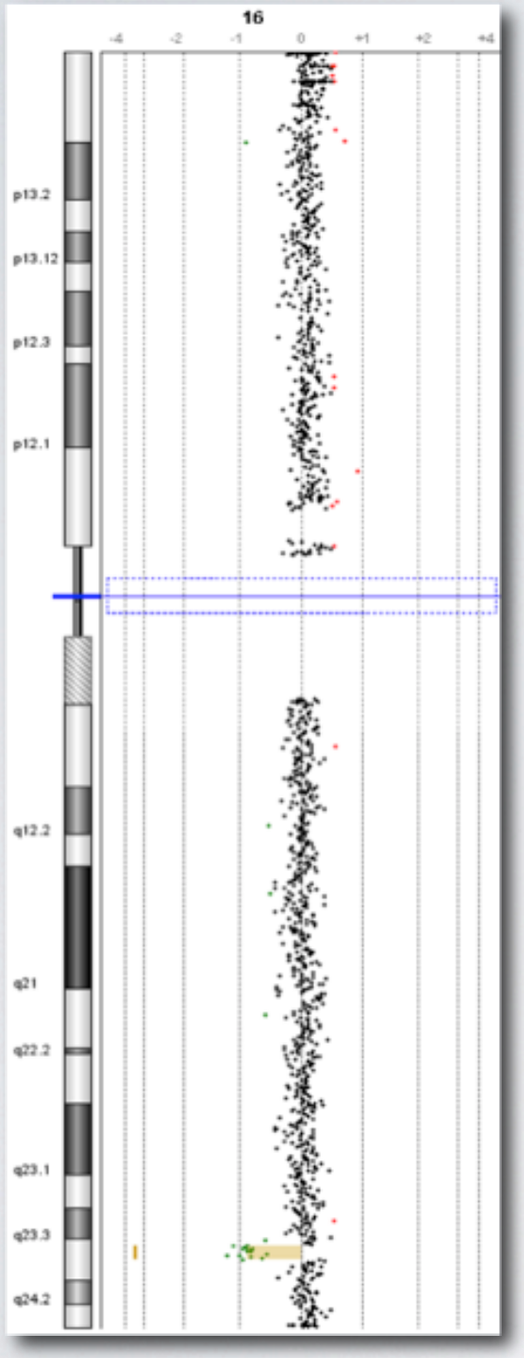
The 23andMe Odds Calculator only takes into account effects of markers with known associations that are also on our genotyping chip. Keep in mind that aside from genetics, environment and lifestyle may also contribute to one's chances of developing type 2 diabetes.

Genes vs. Environment

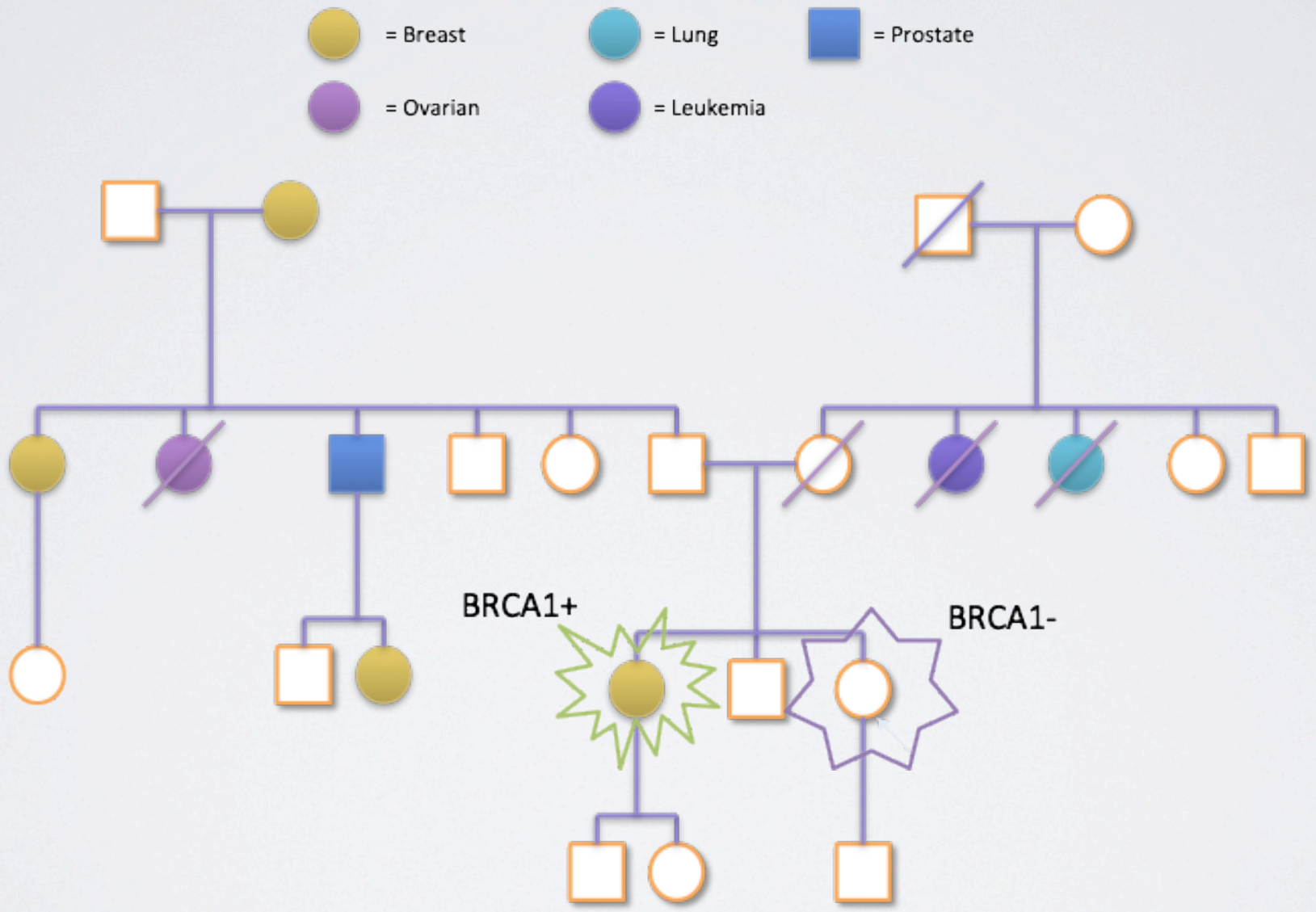
26 %
Attributable to Genetics

The heritability of type 2 diabetes is estimated to be 26%. This means that environmental factors contribute more to differences in risk for this condition than genetic factors. Genetic factors that play a role in type 2 diabetes include both unknown factors and known factors such as the SNPs we describe here. Environmental factors include obesity, gestational diabetes, giving birth to at least one baby weighing nine pounds or more, high blood pressure, abnormal cholesterol levels, physical inactivity, polycystic ovarian syndrome, other clinical conditions associated with insulin resistance, a history of impaired glucose tolerance or impaired fasting glucose, and a history of cardiovascular disease. (sources)

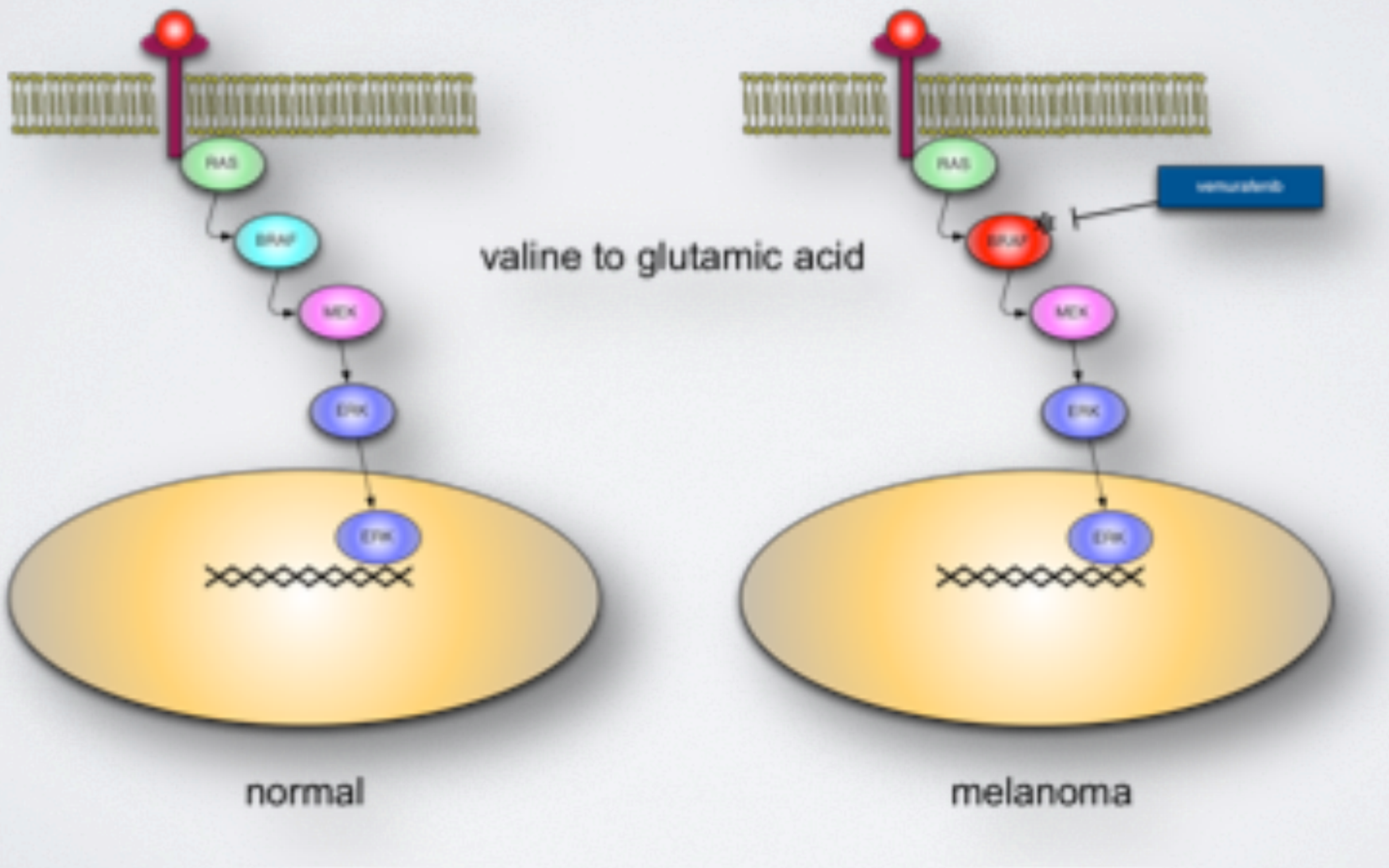
Diagnosis



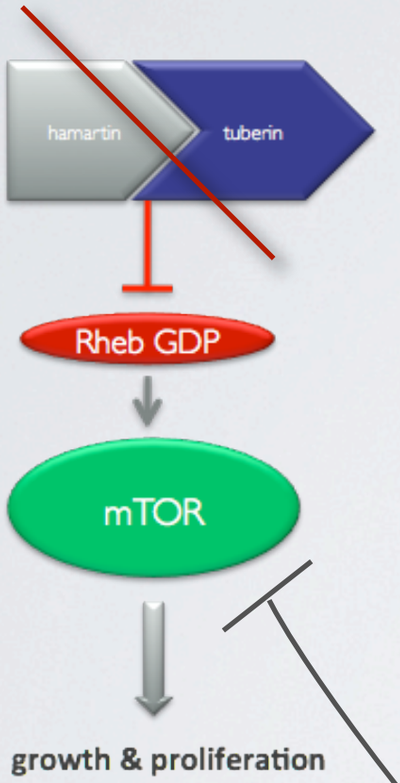
Presymptomatic Diagnosis

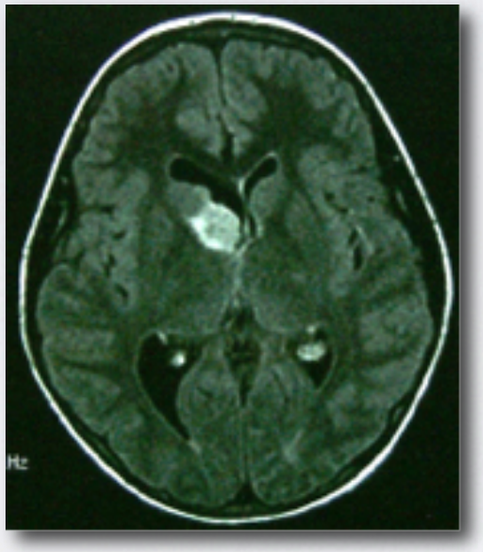


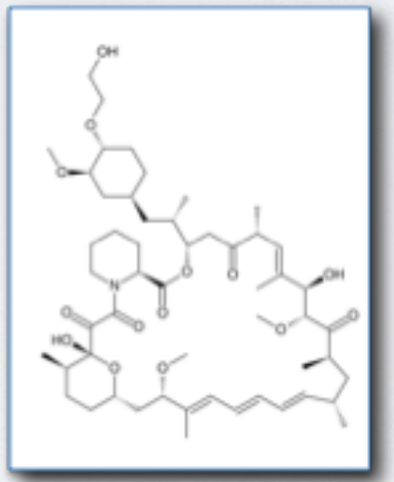
Therapeutics

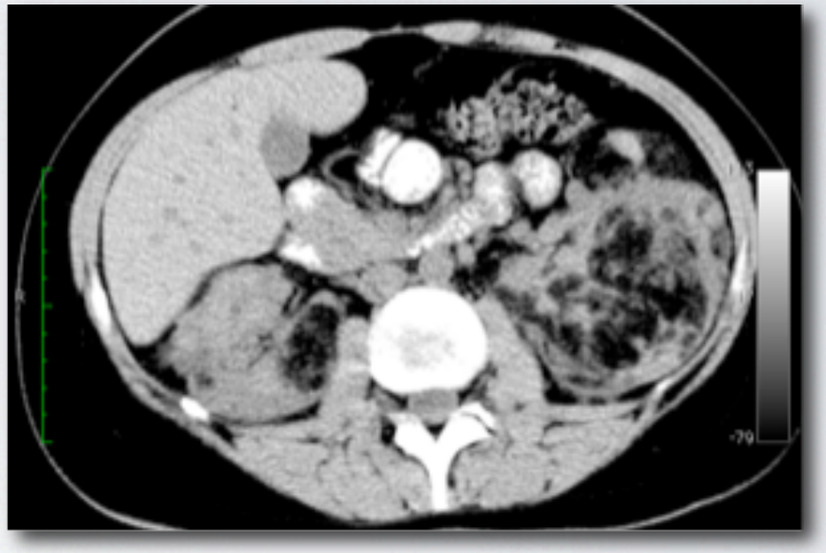


Everolimus and Tuberous Sclerosis









Genomics at UAB

HEFLIN CENTER FOR GENOMIC SCIENCE

Knowledge that will change your world

HUDSONALPHA INSTITUTE FOR BIOTECHNOLOGY

The best way to predict the future is to invent it.

Alan Kay
Computer Scientist