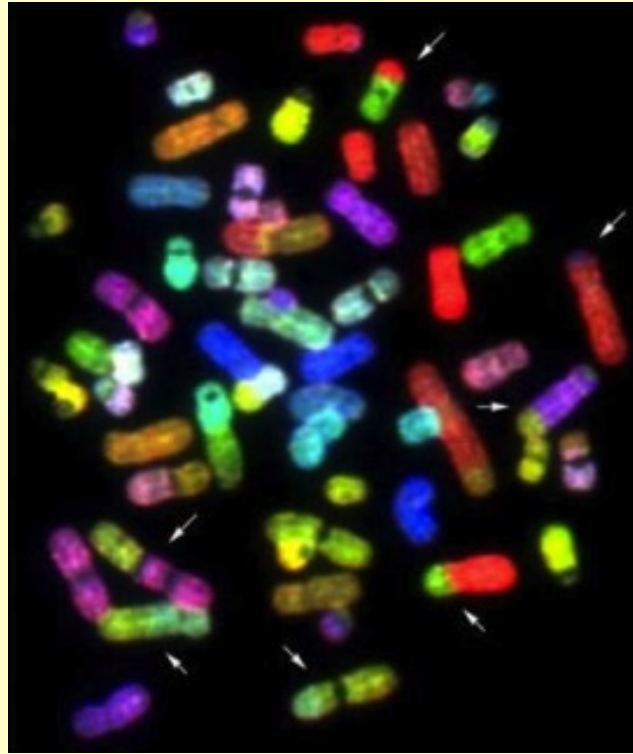


Genomics & Medicine

<http://biochem118.stanford.edu/>

Sophomore Seminar



Doug Brutlag, Professor Emeritus
Biochemistry and Medicine (by courtesy)
brutlag@stanford.edu

Seminar Topics

<http://biochem118.stanford.edu/>

Topics	Slide Links
Introduction to Genomics and Medicine	Slides
Diseases and Disease Databases	Slides
Sequencing the Human Genome	Slides
Finishing the Human Genome Sequence	Slides
Next Generation Sequencing	Slides
Genome Databases	Slides
Bioinformatics and Functional Genomics	Slides
Sequence Variations in the Human Genome	Slides
Structural Variations in the Human Genome	Slides
Discovering Variations Associated with Disease	Slides
Personal Genomics	Slides
Stem Cells	Slides
Stem Cell Therapies	Slides
Gene Expression and Cancer Diagnostics	Slides
MicroRNA Regulatory Networks	Slides
Epigenetics	Slides
Drug Discovery	Slides
Pharmacogenomics	Slides
Bibliographic Search	Slides
Ethical and Societal Issues	

Seminar Topics

<http://biochem118.stanford.edu/>

- Inherited diseases, disorders and traits
 - Disease databases and websites
 - Case presentations
- Genomics and novel diagnostics
 - Sequencing human genome
 - Genomic databases and websites
 - Genome variations leading to diseases and traits
 - Genome wide association studies
- Personal genomics
 - Carrier Status
 - Predisposition to disease
 - Pharmacogenomics
 - Family, genealogies and ancestry
- Gene expression and disease
 - Cell signaling and transcriptional regulation
 - MicroRNAs and translational regulation
 - Protein modification and regulation

Seminar Topics (continued)

- Bioinformatics and drug development
 - Analyzing the function of genes and regulatory regions
 - Drug target identification and validation
 - Identifying new potential drug targets via bioinformatics methods
 - Drug development paradigm and effect of genomics
 - Personalized medicine and medications
- Novel Therapies
 - Gene therapy approaches
 - Stem cell therapies
 - Pluripotent human embryonic stem cells
 - Adult stem cell approaches
 - Induced pluripotent stem cells
- Ethical issues
 - Discrimination for employment and insurability
 - Privacy of genetic information
 - Genetic selection and eugenics
 - Interventions in procreation

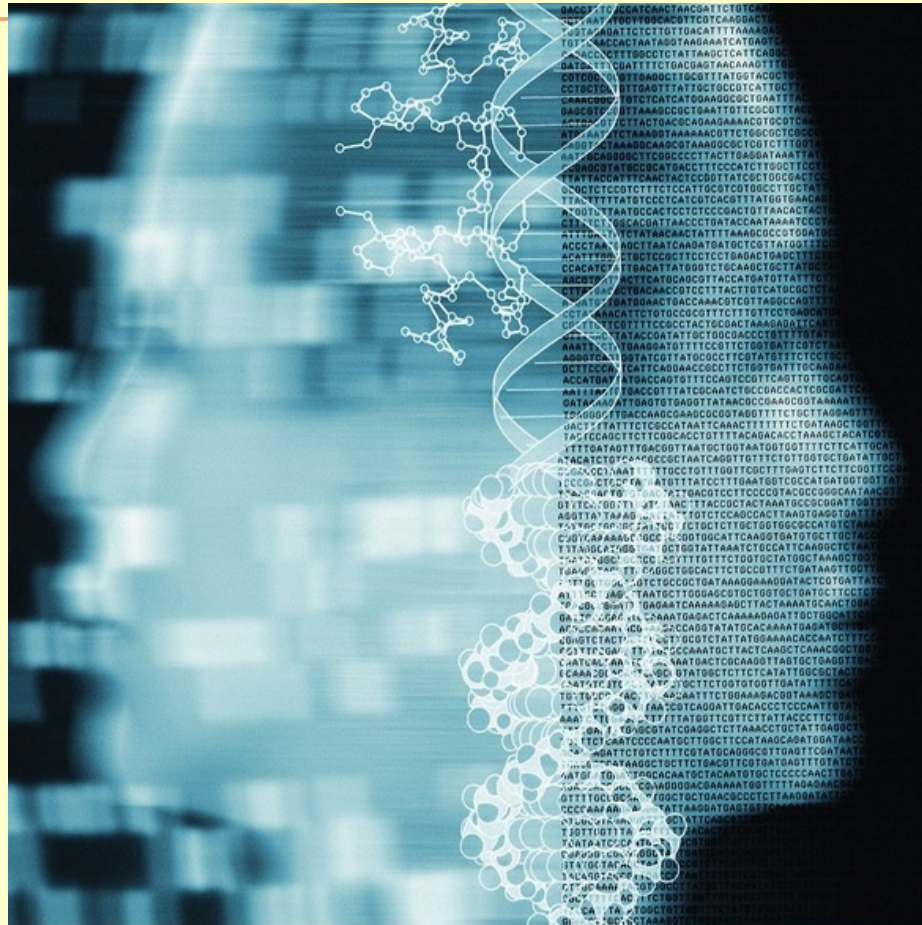
Seminar Requirements

- Five homework assignments
 - Mendelian Disease in class case presentation
 - Bioinformatics analysis of gene function
 - Description of a genome wide association study
 - Describe the kinds of mutation known to cause a Mendelian Disease
 - Description of a stem cell therapeutic approach to a disease
- Final presentation on
 - An ethical, legal or social issue in genomics or medicine
 - The molecular basis of a disease
 - A novel diagnosis or treatment of a disease
 - A technological advance in genomics & disease
- Class participation
 - Asking questions
 - Providing answers, insights or opinions



Gibson: A Primer of Human Genetics

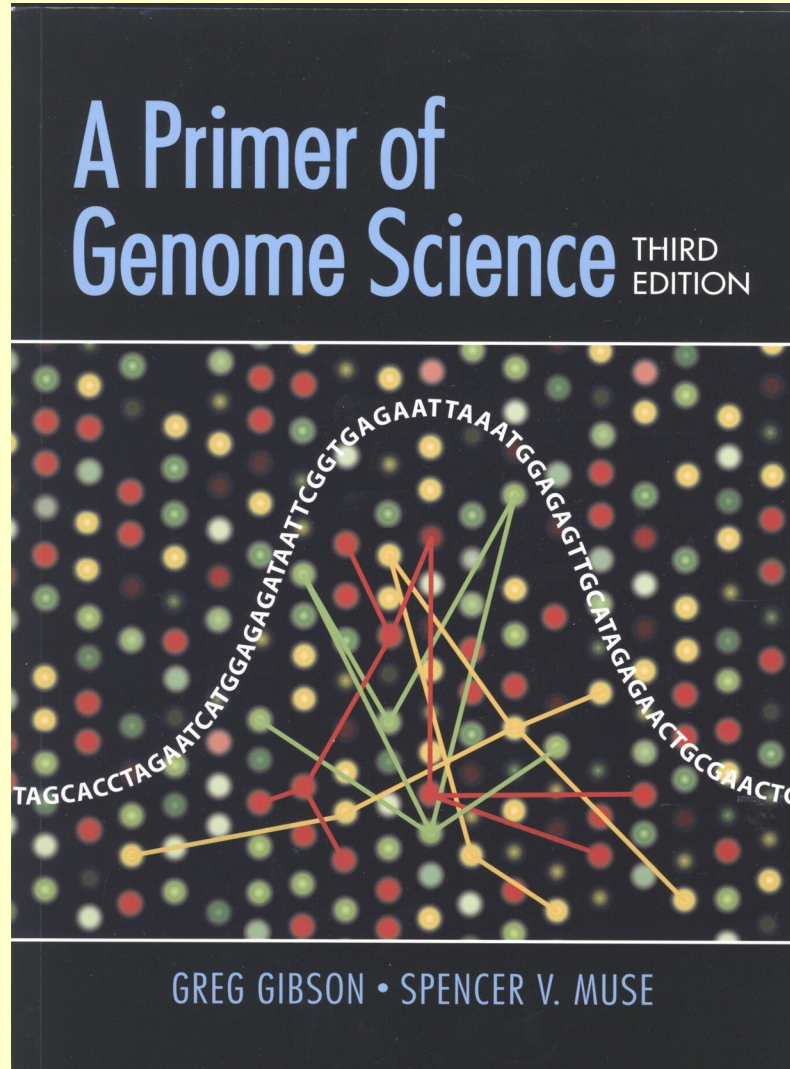
Sinuer Associates



A Primer of Human Genetics

Greg Gibson

Greg Gibson & Spencer V. Muse
A Primer of Genome Science 3rd Ed.



\$73 on
Amazon

Genetics Home Reference Handbook

<http://ghr.nlm.nih.gov/handbook.pdf>



Genetics Home Reference

Your Guide to Understanding Genetic Conditions

Handbook

Help Me Understand Genetics

Reprinted from Genetics Home Reference (<http://ghr.nlm.nih.gov/>)

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services

Published January 1, 2012

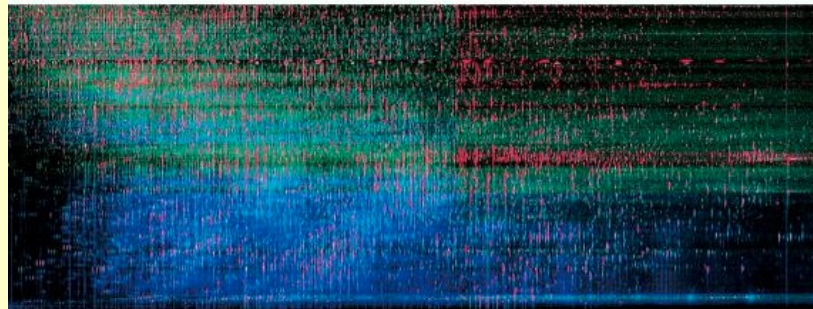
Free to
download

Douglas Brutlag, 2015

The End of Illness David B. Agus

#1 NEW YORK TIMES BESTSELLER

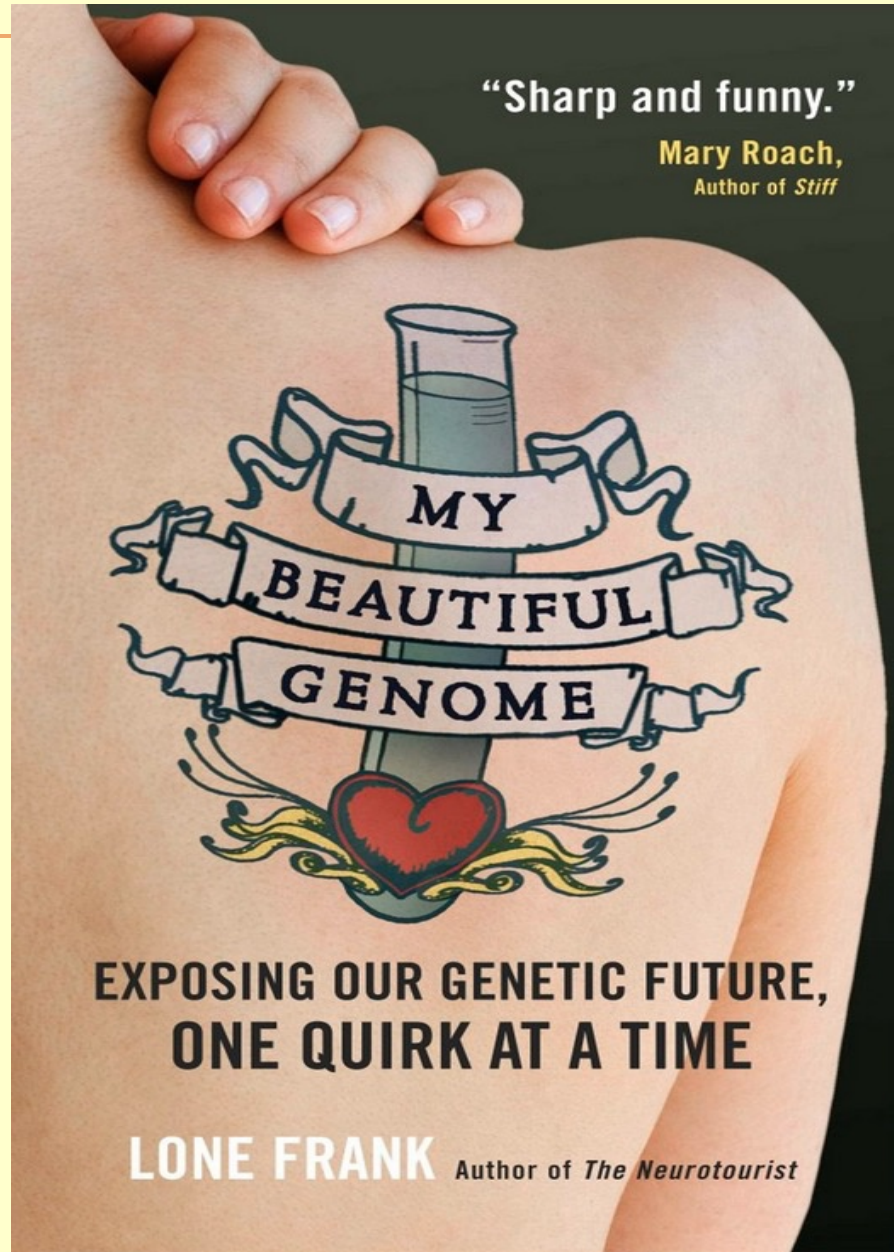
THE END *of* ILLNESS



David B. Agus, MD

\$12 on
Amazon

My Beautiful Genome by Lone Frank



“Sharp and funny.”

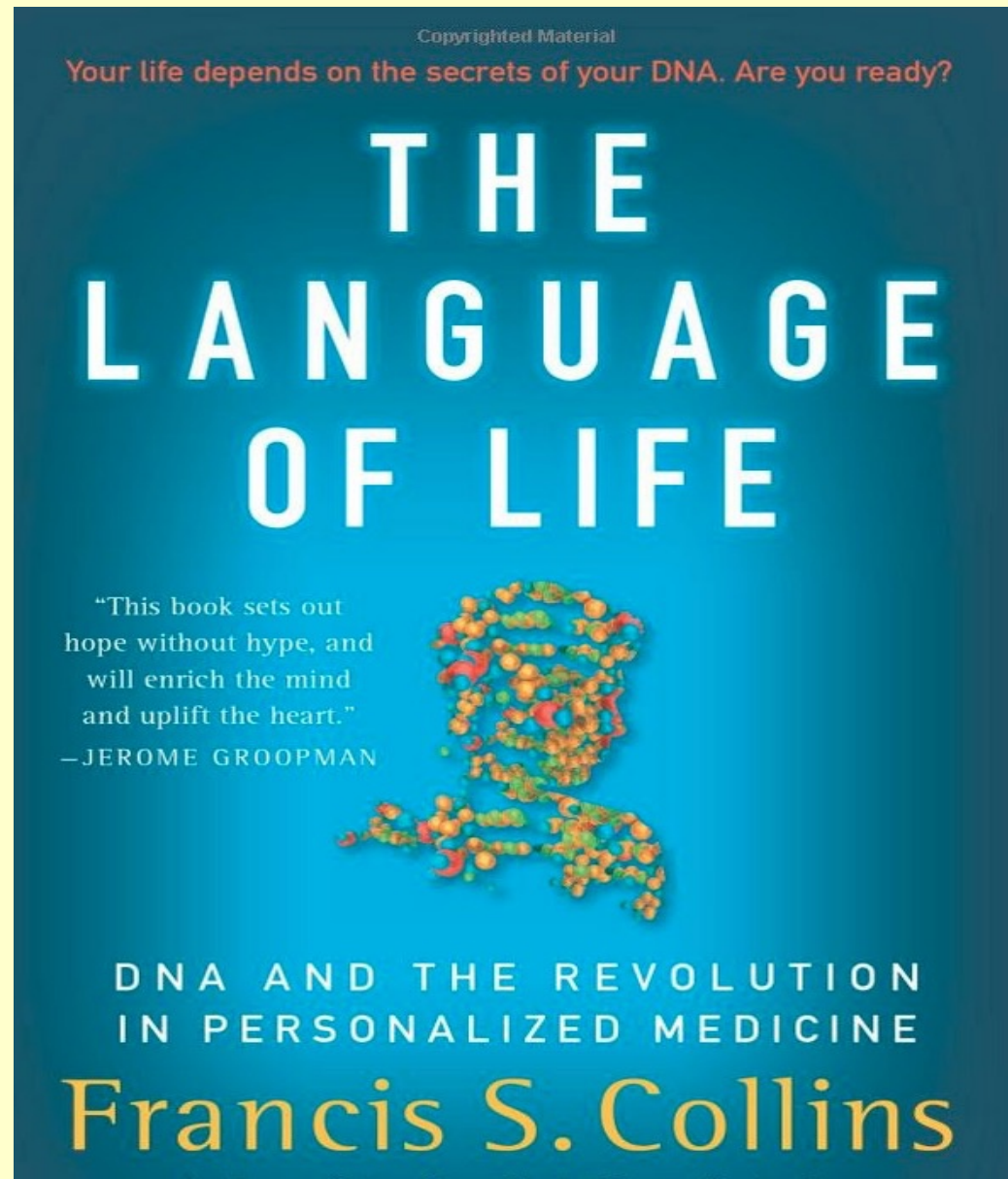
Mary Roach,
Author of *Stiff*



EXPOSING OUR GENETIC FUTURE,
ONE QUIRK AT A TIME

LONE FRANK Author of *The Neurotourist*

The Language of Life: DNA and the Revolution



Cognate Courses

Undergraduate Courses

- Biochem 158 Genomics, Bioinformatics and Medicine
- Bio 109A and 109B (HumBio 158A and B) The Human Genome and
- HumBio 157 The Biology of Stem Cells
- HumBio 159 Genes and Environment in Disease Causation

Graduate Level Courses

- Genetics 210 Genomics and Personalized Medicine
- Genetics 211 Genomics
- CS 262 Computational Genomics
- CS 273A A Computational Tour of the Human Genome
- BMI 214 / CS 274 Representations and Algorithms for Computation
- BMI224 Principles of Pharmacogenomics

BioMedical Seminars

Biomedical Seminars Calendar



Medical Grand Rounds

<http://lane.stanford.edu/biomed-resources/medgrandrounds.html>

- Mike Snyder, Chairman of Genetics
 - Integrating Genomics into Medicine: Where we are and where we should go
- Atul Butte, Stanford Systems Medicine
 - Systems Medicine: Translating 300 billion points of data into Diagnosis
- Muin Khoury, Director Office of Public Health CDC
 - Genomic Medicine in the 21st Century From Science to Action

Henry Stewart Talks

<http://hstalks.com/>

- Biomedical and Life Sciences Collection Topics
 - Cancer: apoptosis, epigenetics, monoclonal antibody therapy, evolution and medicine
 - Diseases, Disorders and Treatments: Alzheimers, autoimmunity, autism and ASD, diabetes, cardiovascular disease, neurodegenerative diseases, obesity, prions, RNA interference, bioinformatics and genome analysis
 - Drug Discovery: antivirals, biomarkers, cancer therapy, monoclonals, small molecules
 - Genetics: Copy number variation, DNA methylation, epigenetics, eukaryotic gene regulation, human genetics, population genetics
- Name and Password

Introductions



Questions?



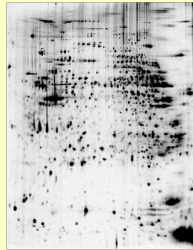
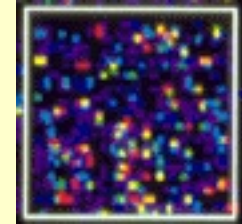
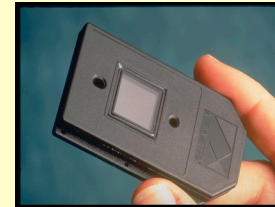
Questions

- Which costs more, treating a disease or preventing a disease
- Why?
- How should patients be motivated to use preventive methods?
- How should doctors be incentivized to use preventive medicine?
- Should preventive care be covered by insurance?
- Should insurance companies cover preventable diseases if the patient did not use preventative methods?
- Should the government (Medicare and Medicaid) cover treatments for preventable diseases?

Leveraging Genomic Information

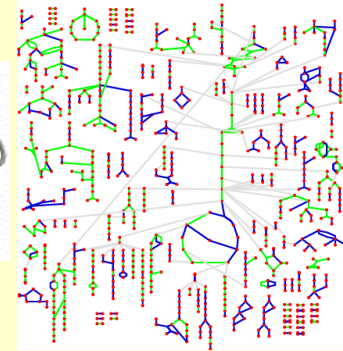
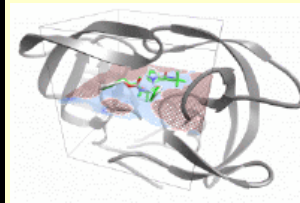
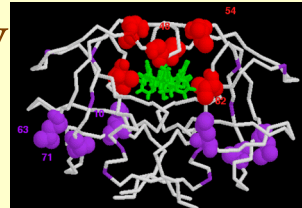
Novel Diagnostics

Microchips & Microarrays - DNA
Gene Expression - RNA
Proteomics - Protein



Novel Therapeutics

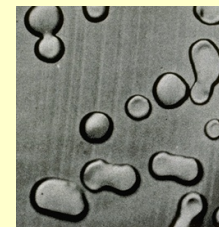
Drug Target Discovery
Rational Drug Design
Molecular Docking
Gene Therapy
Stem Cell Therapy



Understanding Metabolism

Understanding Disease

Inherited Diseases - OMIM
Infectious Diseases
Pathogenic Bacteria
Viruses



Preventive Medicine

上医医未病之病

中医医将病之病

下医医已病之病

~黄帝内经~

“Superior Doctors Prevent the Disease.
Mediocre Doctors Treat the Disease Before Evident.
Inferior Doctors Treat the Full Blown Disease.”

-Huang Dee: Nai - Ching (2600 B.C. 1st Chinese Medical Text

Founder of Preventive Medicine: Louis Pasteur



When thinking about diseases, I never think about how to cure them, but instead I think about how to prevent them.

Immunization: *A Fragile Fortress*





Preventive Medicine

- Prevent disease from occurring
- First one must identify the cause of the disease
- Treat the cause of the disease rather than the symptoms
 - Example 1: Peptic ulcers
 - Example 2: Pyrogens
- Genomics identifies genetic causes of inherited disease
- “All medicine may soon become pediatrics”
 - Paul Wise, Stanford Pediatrician.
- Overlooked acquired disease such as infectious disease, autoimmune disease, aging, accidents and environmental diseases
- Health care costs can be greatly reduced if
 - invests in preventive medicine
 - one targets the cause of disease rather than symptoms
 - controls environmental and behavioral effects

Health Care Policy

- Current health care treats disease rather than maintaining health (illness care?)
- Future health care prevent disease
- Reduce need for expensive interventions
- Need policies that incentivize patients and doctors to prevent disease.
- Need social pressures to control behavior and increase vigilance.

Personalized Medicine



Courtesy of Felix W. Frueh US FDA

Personalized Medicine

- Medicine is personal:
 - We are all different.
 - Some of our genetic differences translate into how we react to drugs as individuals.
 - This is why personalized medicine is important to everyone.
- Why does someone need twice the standard dose to be effective?
- Why does this drug work for you but not me?
- Why do I have side-effects and you don't?
- Why do some people get cancer and others don't?
- Why is anecdotal information irrelevant to your own health and treatment?

Is Medicine a Science or an Art?

If it were not for the great variability among individuals, medicine might well be a science, not an art.

- Sir William Osler, Physician 1892
- Johns Hopkins School of Medicine
- Johns Hopkins Hospital
- Father of modern medicine

Questions

- What are the three macromolecular metabolic levels we need to understand development and disease? Why is each important?
- How can some mutations themselves cause a disease (usually a Mendelian single gene disease) and how can some mutations merely lead to a predisposition to a disease?
- Why can mutations in many different genes cause the same disease?
- Mutations in what kind of genes / pathways can lead to a predisposition to disease?
- Name a few areas of medicine that have been influenced by genomics.
- What is the primary knowledge one must have to prevent a disease?
- Why does treating symptoms often exacerbate a disease?

Huntington Disease

- Autosomal Dominant
 - On the tip of the short arm of chromosome 4
 - One bad gene causes disease (dominant)
 - Brain degeneration over 10-15 years until death
- Neurodegenerative disease
 - Loss of movement control
 - Loss of cognitive skills (dementia) and hallucinations
 - Depression, hostility, aggression and loss of inhibitions
- Dyskinesias
 - Chorea: uncontrollable tics and involuntary movements of extremities, hyperkinesias
 - Dystonia uncontrollable muscle contractions
 - Bradykinesia, slow uncertain movements
 - Dysphagia (difficulty in swallowing) and uncontrollable oral buccal dyskinesia

The Inheritance

- You are 18 years old.
- Your father abandoned you and your mother when you only 2 years old.
- Your father died this year and left you an inheritance.
- He died from an autosomal dominant disease known as Huntington's Disease.
- Since Huntington's disease is autosomal dominant, you have a 50% chance of inheriting this invariably fatal neurodegenerative disease.
- But there is a genetic test for this disease that can tell you if you have the disease, and if you do, when you will experience the symptoms and when you will die from it.
- Would you take the genetic test or not?
- Why?

Impact of Genomics on Medicine

I. Diagnostics

- Genomics: Identifying all known human genes
- Functional Genomics: Functional analysis of genes
 - What tissues are they important
 - When in development are the genes used
 - How are they regulated
- Novel diagnostics
 - Linking genes to diseases and to traits
 - Predisposition to diseases
 - Expression of genes and disease
- Personal Genomics
 - Understanding link between genomics and environment
 - Increased vigilance and taking action to prevent disease
 - Improving health care

Impact of Genomics on Medicine

II. Therapeutics

- Novel Drug Development
 - Identifying novel drug targets
 - Predicting toxicity and adverse reactions
 - Improving clinical trials and testing
- Gene therapy
 - Replacing the gene rather than gene product
- Stem cells therapies
 - Replacing the entire cell type to cure a disease
- Pharmacogenomics
 - Personalized medicine
 - Adjusting drug, amounts and delivery to suit patients
 - Maximize efficacy and minimize side effects
 - Identify genetics of adverse reactions
 - Identify patients who respond optimally

Impact of Genomics on Medicine

III. Ethical, Legal and Social Issues

- Personal Privacy
- Insurability
- Employability
- Discrimination
- Eugenics
- Cosmetic genetics
- Patentability of genes, proteins and other natural products

Impact of Genomics on Medicine

IV. Strategic

- Genomics can discover disease associated genes
- Genomics can discover disease causing genes.
- Genomics provides understanding of disease
- Genomics and bioinformatics provides basis for novel drug development
- Genomics provides basis for novel genetic and stem cell therapies
- Genomics provides the basis for preventive medicine.