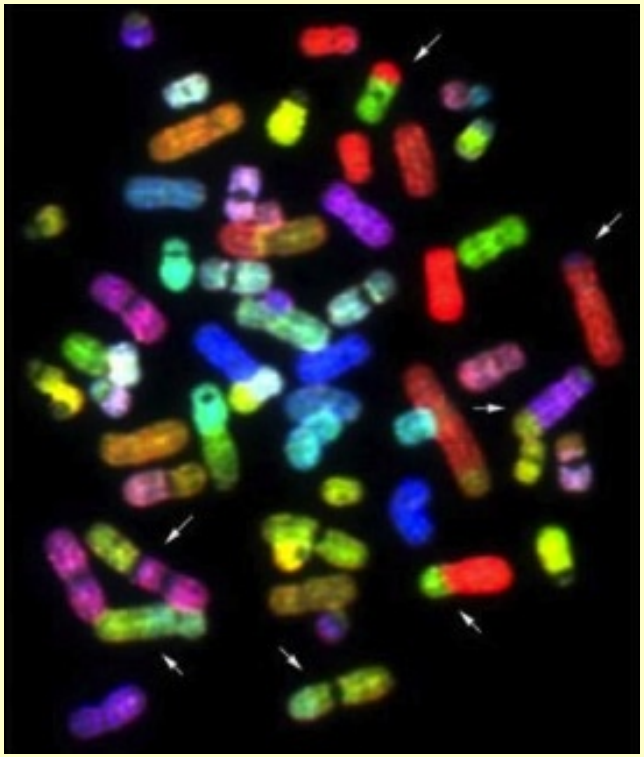
Genomics Bioinformatics & Medicine

http://biochem158.stanford.edu/

Biochem 158/258, BMI 258 and HumBio 158G



Doug Brutlag
Professor Emeritus
Biochemistry and Medicine (by courtesy)
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Course Syllabus

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Date	Topic
Jan 6	Introduction to Genomics and Medicine
Jan 8	Diseases and Disease Databases
Jan 13	Sequencing the Human Genome
Jan 15	Finishing the Human Genome Sequence
Jan 20	Next Generation Sequencing
Jan 22	Genome Databases
Jan 27	Bioinformatics and Functional Genomics I
Jan 29	Bioinformatics and Functional Genomics II
Feb 3	Sequence Variations in the Human Genome
Feb 5	Structural Variations in the Human Genome
Feb 10	Discovering Variations Associated with Disease
Feb 12	Personal Genomics
Feb 17	Clinical Genomics
Feb 19	Stem Cells
Feb 24	Stem Cell Therapies
Feb 26	Gene Expression and Cancer Diagnostics
Mar 3	MicroRNA Regulatory Networks
Mar 5	Epigenetics
Mar 10	Drug Discovery
Mar 12	Pharmacogenomics
Extra	Bibliographic Search

Homework Research Projects

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Topic	Date Due
Letter of introduction (2 page max)	Jan 15
Mendelian disease case presentation (4 page max)	Jan 22
Functional analysis of a human gene (4 page max)	Feb 5
Summary of a genome-wide association study (4 page max)	Feb 19
Describe genomic variations known to cause a specific inherited disease (4 page max)	Feb 26
Describe a disease that could be cured using stem cell therapy (4 page max)	Mar 5
Final project (10 page max)	Mar 15

Short Research Project Format

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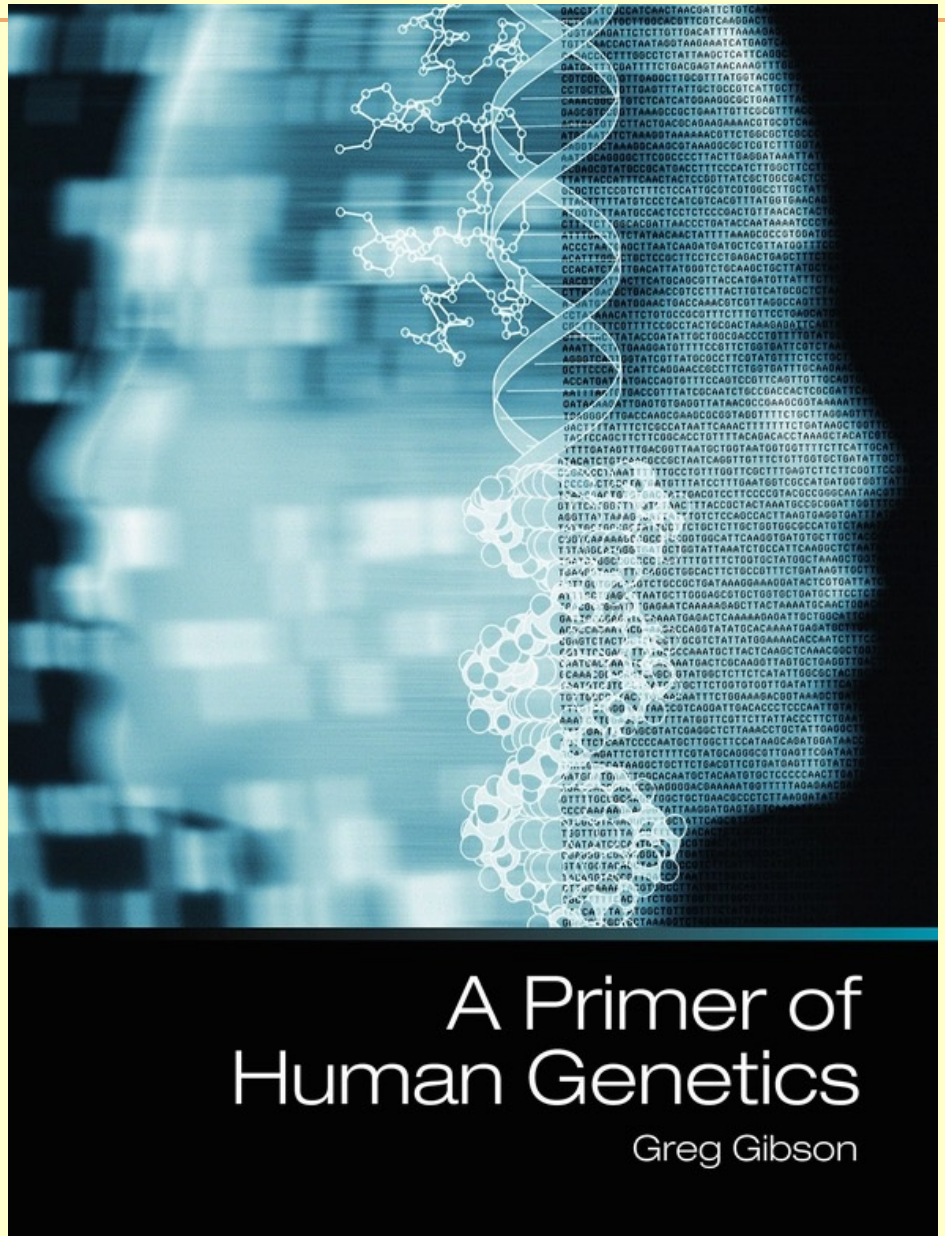
- Title of Project and header (name, course, date)
- Introduction: why you are interested in the topic
- Methods: list of web databases for your topic including actual web pointers (URLs).
- Results as outlined in assignment
- Conclusions
- References including Web pointers (URLs) to Web sites and to literature papers

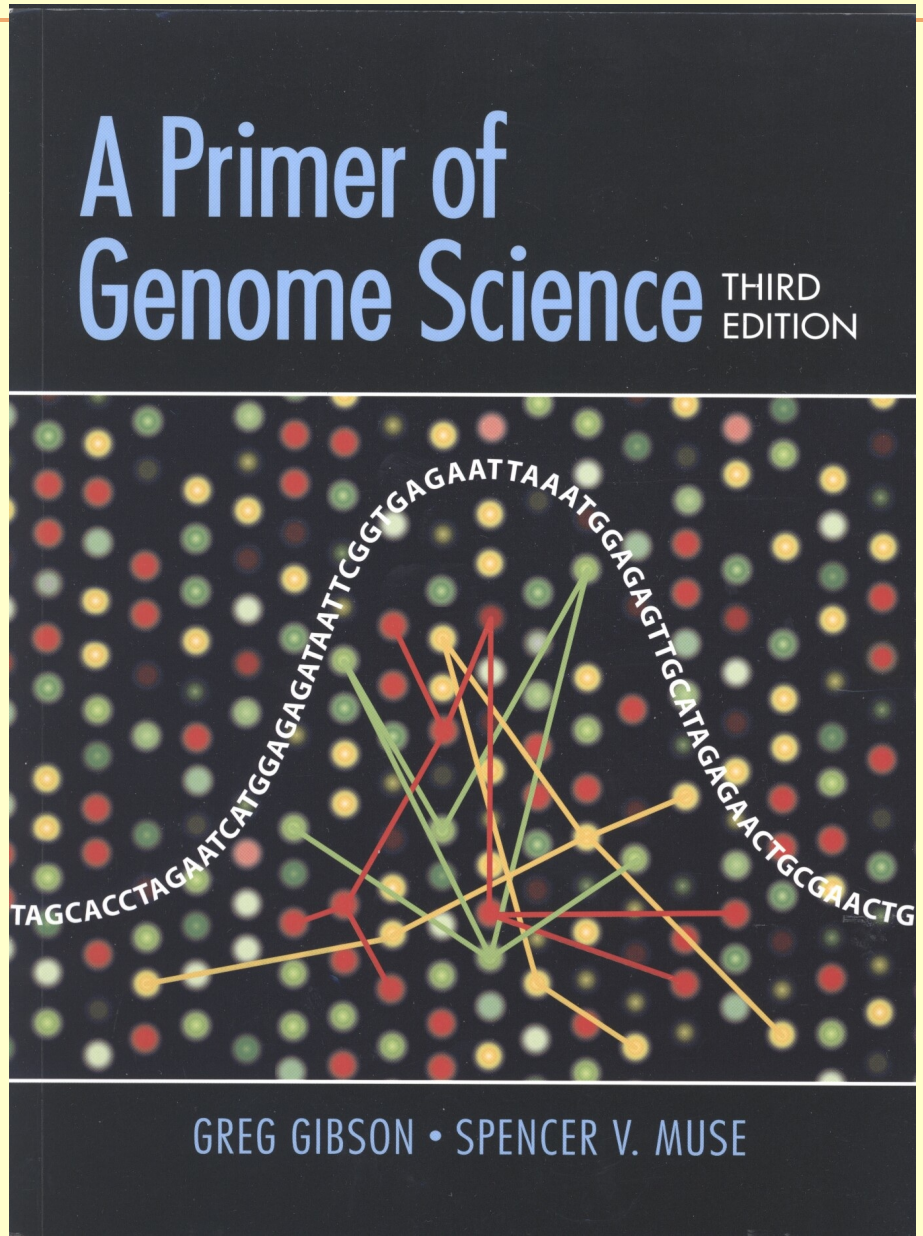
Sinauer Associates

Gibson: A Primer of Human Genetics



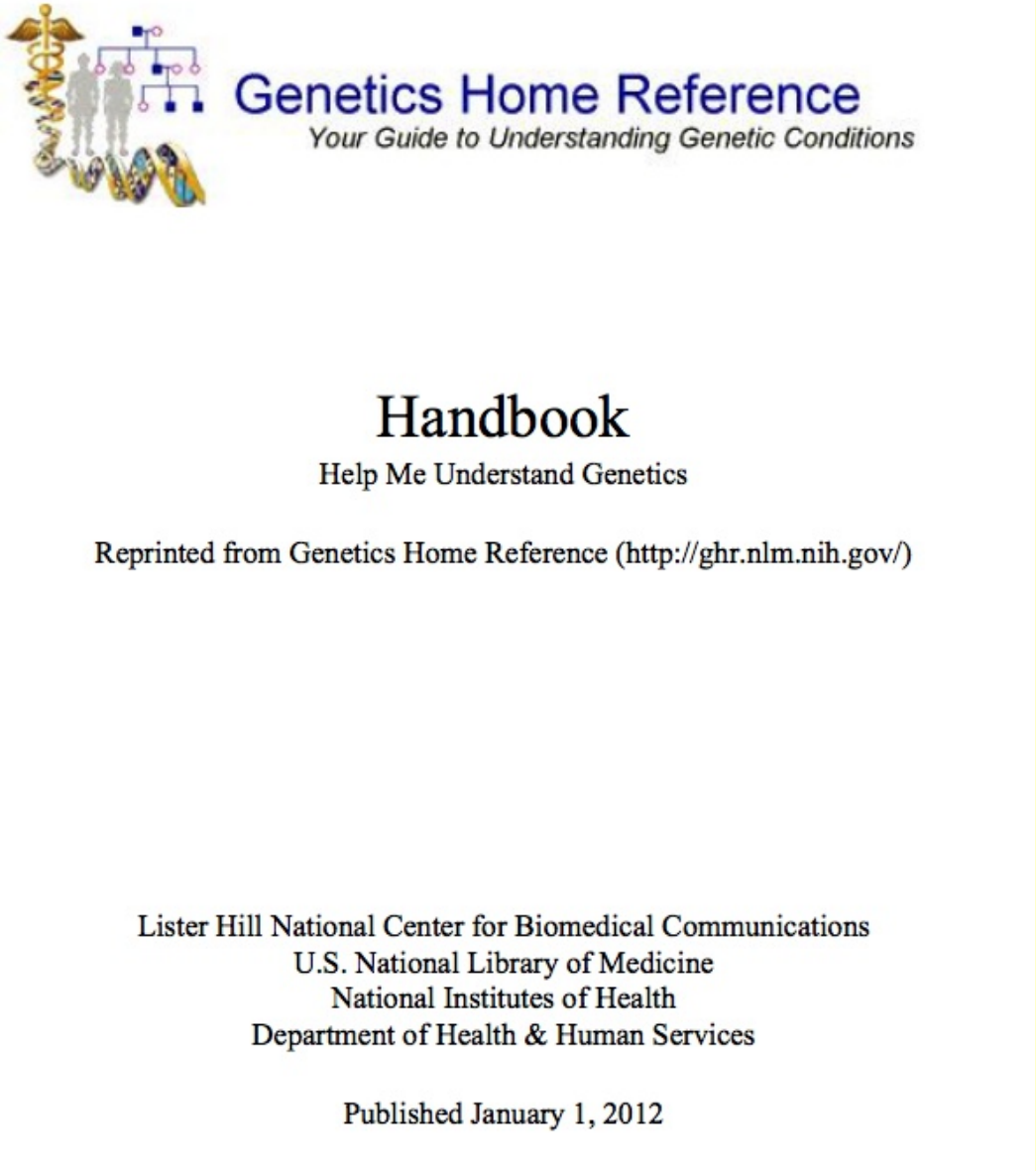
Sinauer Associates

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



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

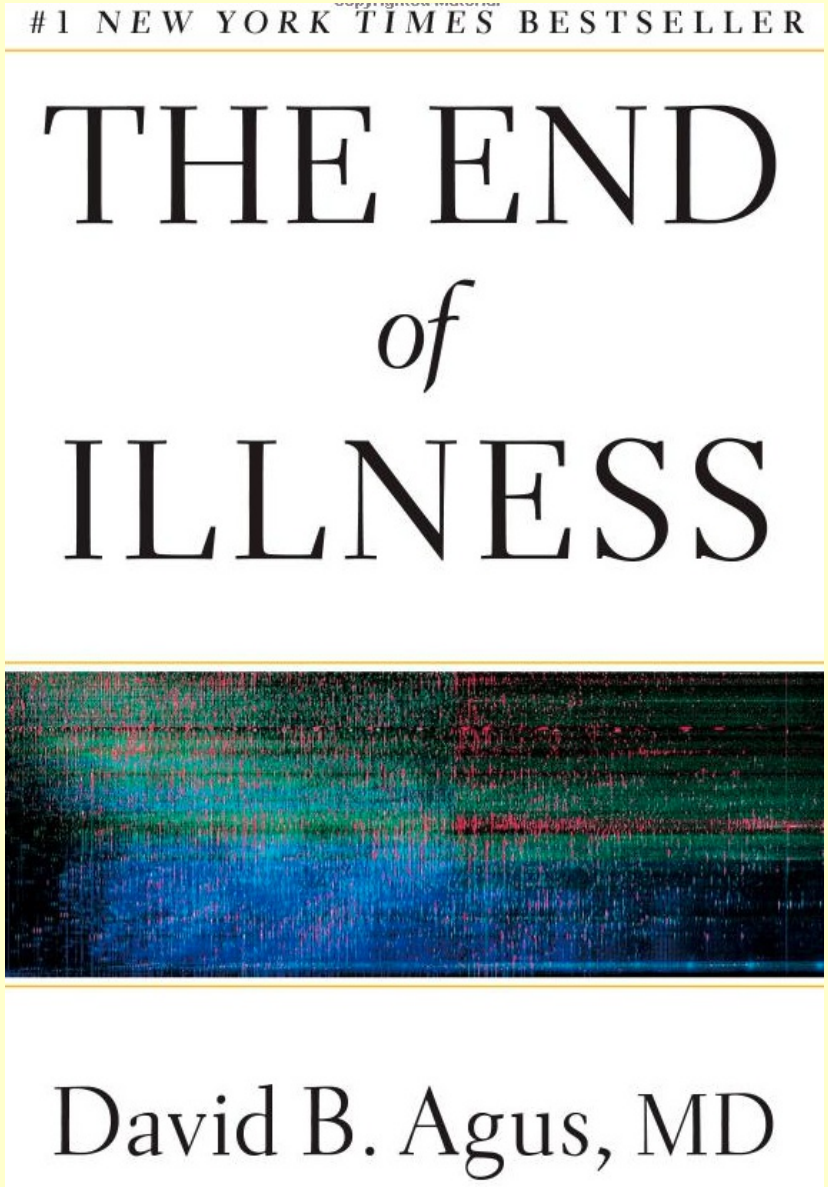
Free download

Genetics Home Reference Handbook

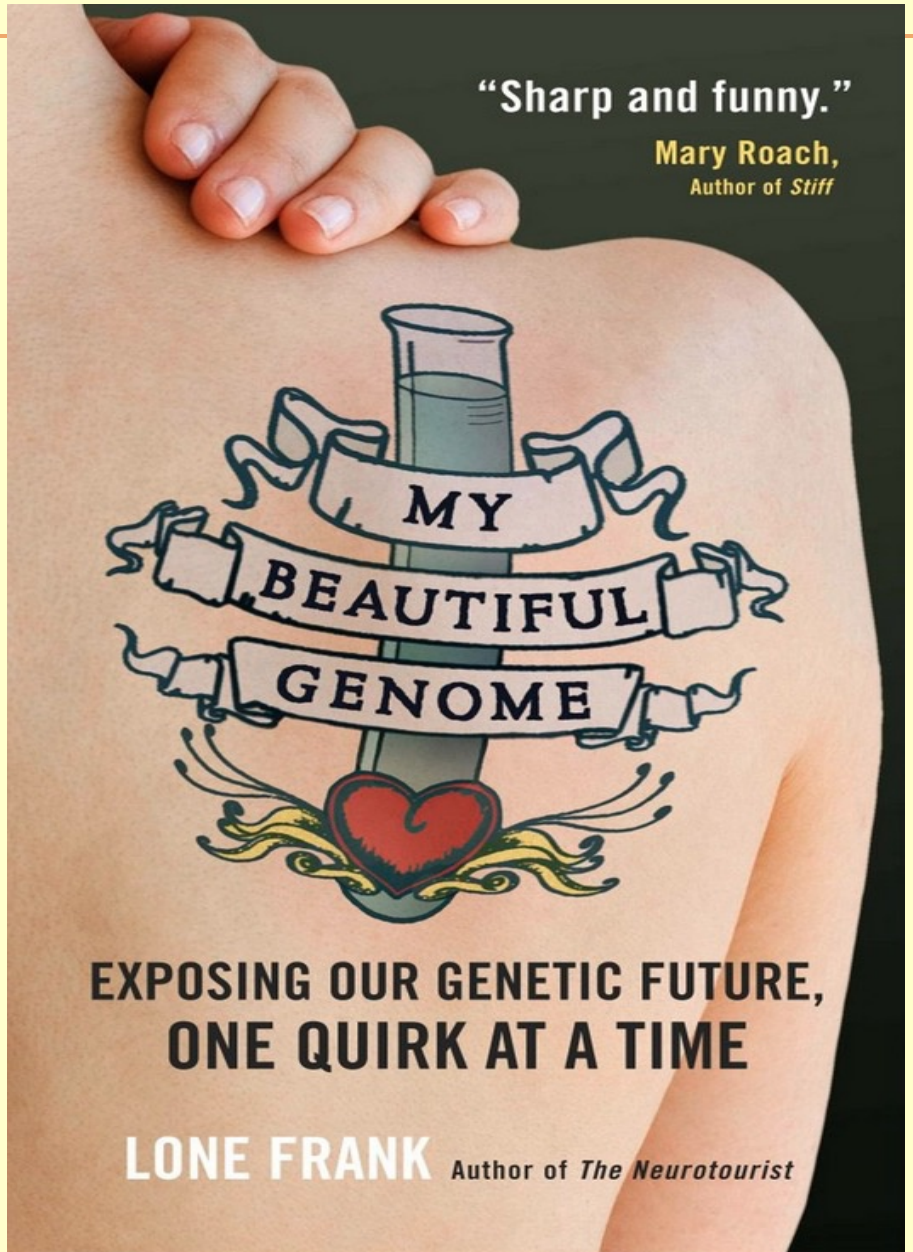
http://ghr.nlm.nih.gov/handbook.pdf

Table of Contents

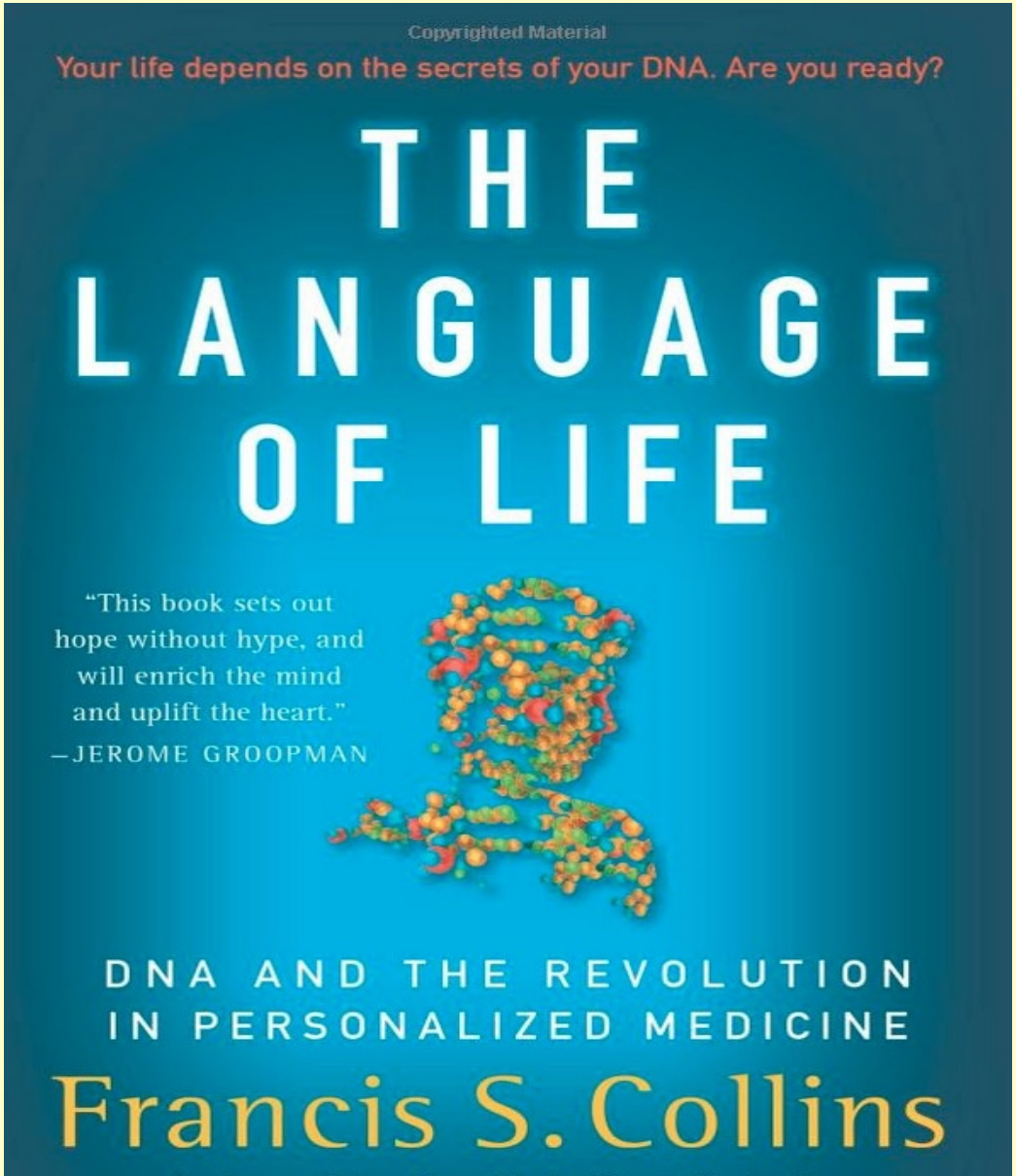
The End of Illness David B. Agus



My Beautiful Genome by Lone Frank



The Language of Life: DNA and the Revol



Cognate Courses

Undergraduate Courses

- Bio 109A and 109B (aka HumBio 158A and B) The Human Genome and Disease
- 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

BioMedical Seminars

Biomedical Seminars Calendar

The Next 3 Weeks

Jan 06, 2015 (Tue) | 7:00 AM - 8:00 AM | Surgery

Surgery Grand Rounds: - Amanda Wheeler, MD - "The Evolution of Breast Surgery"

LKSC - LK130 : Stanford, CA

Details

Jan 06, 2015 (Tue) | 1:30 PM - 3:00 PM | Health Research & Policy - Epidemiology

Epidemiology Research Seminar: Curing the flaw of averages or ending an epidemic of erroneous models

CCSR 4205 : Stanford, CA

Details

Jan 07, 2015 (Wed) | 8:00 AM - 9:00 AM | Medicine

Medicine Grand Rounds - Mentorship in an academic medical enterprise

LKSC, Berg Hall, B&C Conf. Room : Stanford, CA

Details

Jan 07, 2015 (Wed) | 12:00 PM - 1:00 PM | Microbiology & Immunology

Attenuated hyperfusogenic mutants of varicella zoster virus modify the host transcriptional response to infection

Munzer Auditorium : Stanford, CA

Details

Jan 07, 2015 (Wed) | 1:00 PM - 5:30 PM | Institute for Immunity, Transplantation and Infection

Computational Approaches to Problems in Immunology and Infectious Diseases

ALWAY M106 : Stanford, CA

Details

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 sh
- Atul Butte, Stanford Systems Medicine
  - Systems Medicine: Translating 300 billion points of data into Diagnos
- 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

Impact of Genomics on Medicine
I. Diagnostics

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

Impact of Genomics on Medicine
II. Therapeutics

- Gene therapy
  - Replacing the gene rather than the gene product
- Stem cells therapies
  - Replacing the entire cell type or tissue to cure a disease
- Novel Drug Development
  - Identifying novel drug targets
  - Validating drug targets
  - Predicting toxicity and adverse reactions
  - Targeted gene therapies
- 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

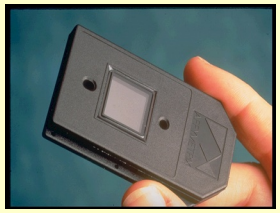
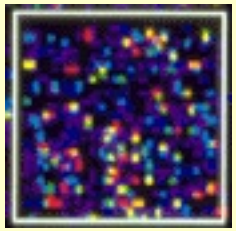
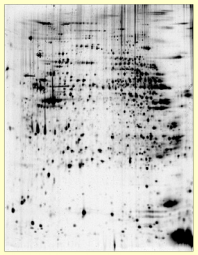
Impact of Genomics on Medicine
III. Strategic

- 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.

Leveraging Genomic Information

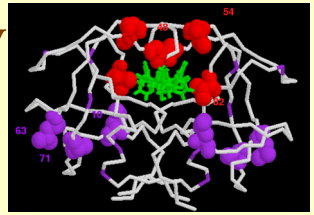
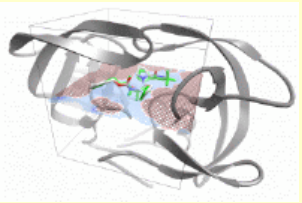
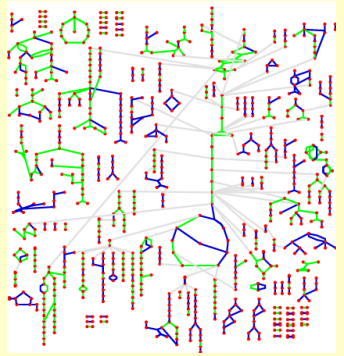
Novel Diagnostics

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

Novel Therapeutics

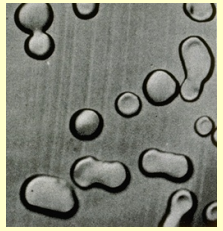
- Drug Target Discovery
- Rational Drug Design
- Molecular Docking
- Gene Therapy
- Stem Cell Therapy

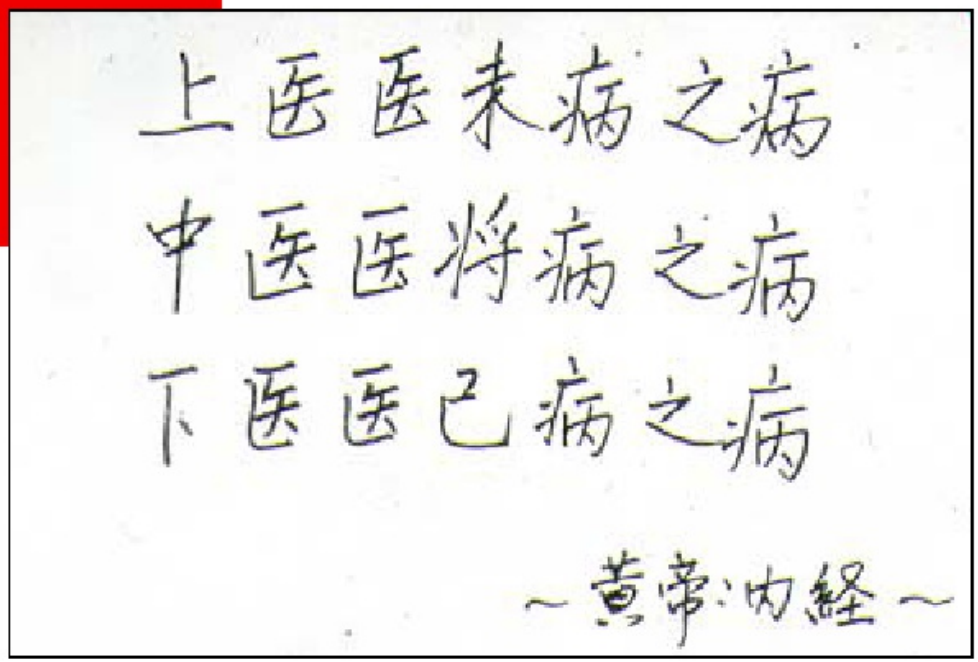
Understanding Metabolism

Understanding Disease

- Inherited Diseases - OMIM
- Infectious Diseases
  - Pathogenic Bacteria
  - Viruses




Preventive Medicine



"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

- The goal is to 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.
- When Paul Wise (a Stanford pediatrician) heard that we may soon sequence every child's genome at birth, he stated:
  - **"… all medicine may soon become pediatrics!"**
- Overlooked accidents, infectious disease or acquired disease such as aging, cancer or auto immune disease
- 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 will 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

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

Personalized Medicine

Courtesy of Felix W. Frueh US FDA

Personalized Medicine

- Medicine is personal:
  - We are all different and respond to disease differently
  - Every cancer is different
  - Some of our genetic differences translate into how we react to drugs as individuals.
  - This is why personalized medicine is important
- Why does someone need twice the "standard" dose to be effective and others need less?
- 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?

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 – Movement disorders
  - 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

Senario 1: The Inheritance

- You are 20 years old.
- Your father abandoned you and your mother when you only 3 years old.
- Your father died this year and left you an inheritance.
- He died from an autosomal dominant disease known as Huntington's Chorea or Huntington's Disease.
- 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 not only if you have the disease, and if you do, when you will die from it.
- Would you take the genetic test or not?
- Why?

Diseases and Disease Databases

http://biochem158.stanford.edu/Diseases.html

- Lecture Materials
  - Diseases and Disease Databases Slide
  - Genomics and Mendelian Diseases
  - Huntington Disease
    - Cassandra's Connundrum
    - Nancy Wexler
    - Francis O. Walker - Review of Huntington Disease
    - Molecular Mechanisms of Huntington Disease
    - Huntington Consortium Publication of Gen
    - Adverse Psychological Events one year after diagnosis
    - Adverse Psychological events five years after diagnosis
    - Facing Life with a Lethal Gene
    - Towards a Cure for Huntington Disease
    - Testing for Huntington Disease: Making An Informed Choice