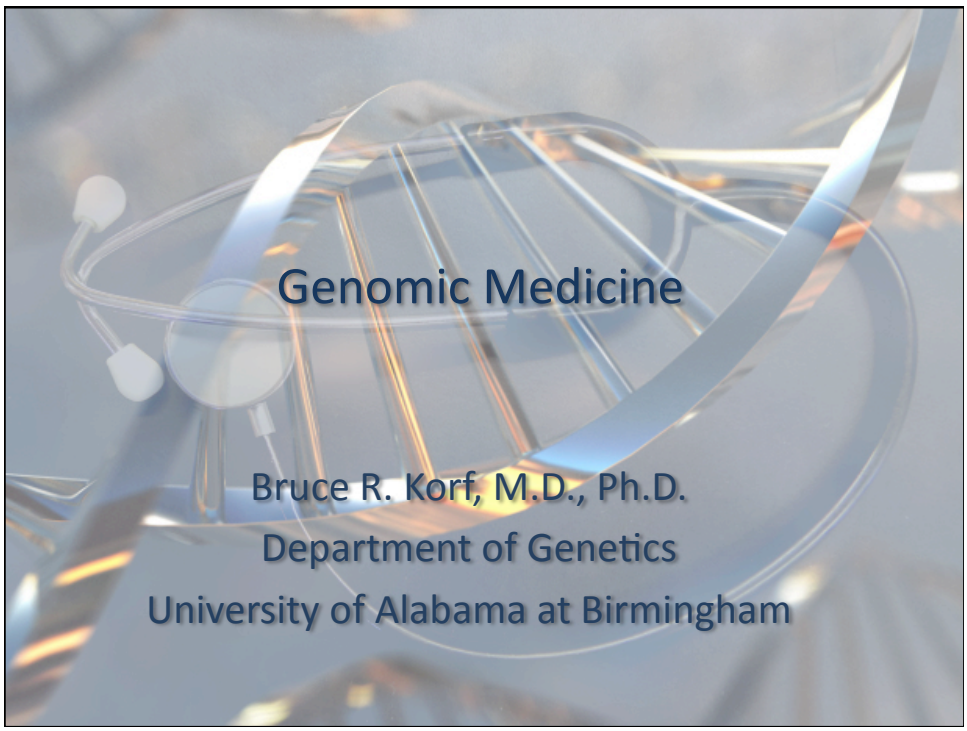
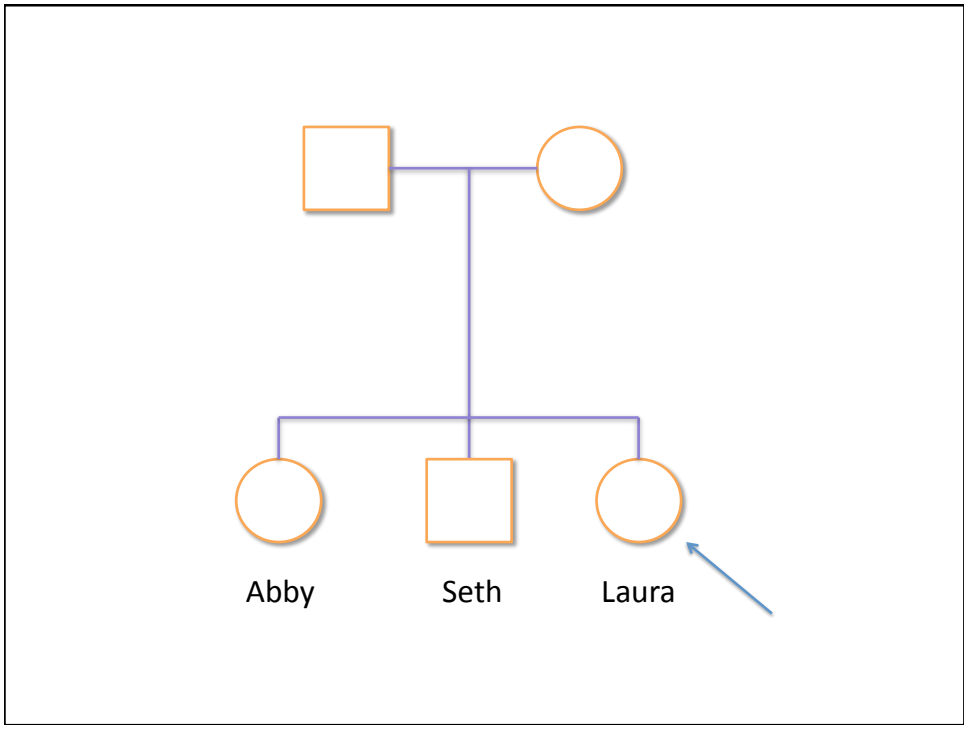
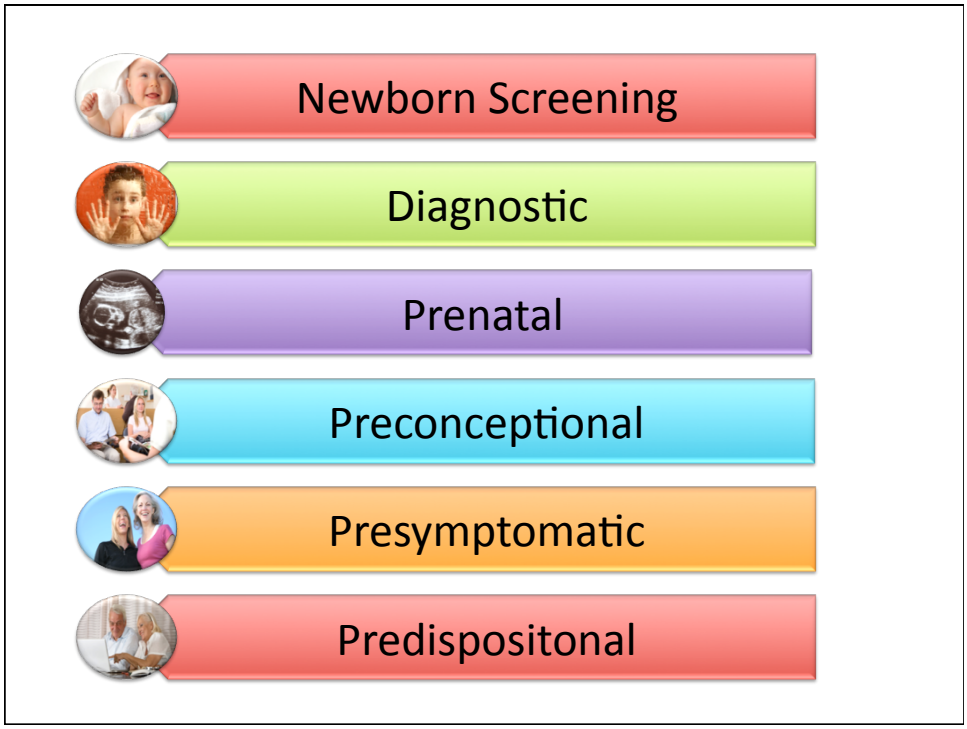


Disclosures

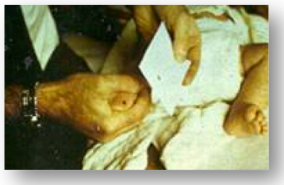
- Medical Director, UAB Medical Genomics Laboratory
- Chair, Medical Affairs Committee, Children's Tumor Foundation
- Grant Funding: NIH, Department of Defense, Novartis
- Advisory Boards: Novartis NF Advisory Board, March of Dimes

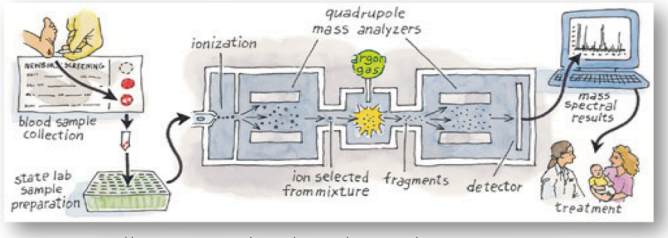

Abby
Seth
Laura


Newborn Screening
Diagnostic
Prenatal
Preconceptional
Presymptomatic
Predispositonal

Newborn Screening

Shortly after birth, blood is taken from Laura's heel and sent to the State Newborn Screening Laboratory. Her parents are told that this is a routine test. No problems are found, and no follow-up is needed.





http://www.sigmaxi.org/amsci/articles/02articles/millingtoncap3.html

Newborn Screening by DNA Sequencing?

RESEARCH ARTICLE

HUMAN GENOMICS www.ScienceTranslationalMedicine.org 12 January 2011 Vol 3 Issue 65 65ra4

Carrier Testing for Severe Childhood Recessive Diseases by Next-Generation Sequencing

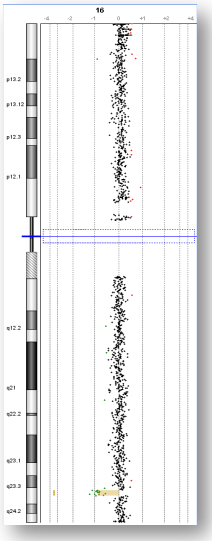
Callum J. Bell,[1]* Darrell L. Dinw
Elena E. Ganusova,[1] Joann Mud
Faye D. Schilkey,[1] Vrunda Shetl
Gary P. Schroth,[3] Ryan W. Kim,[1]

"We found an unexpectedly high proportion of literature-annotated disease mutations that were incorrect, incomplete, or common polymorphisms."

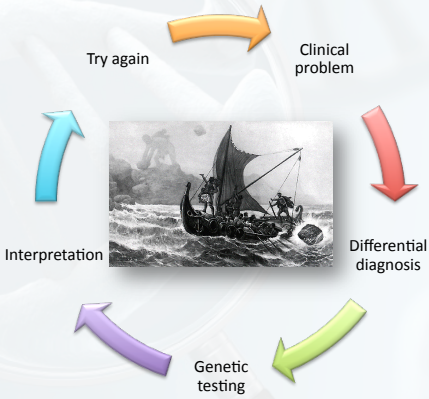
Diagnostic Testing

Laura is now 3 and her brother Seth is 5. Seth has been experiencing developmental problems, and is diagnosed as having autism

Genetic Evaluation in Autism



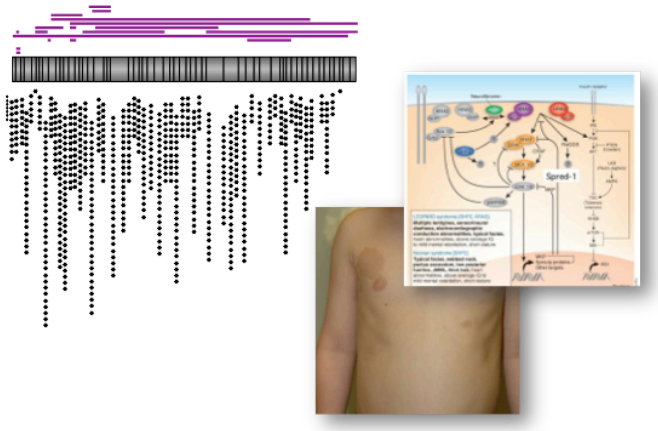
The Diagnostic Odyssey



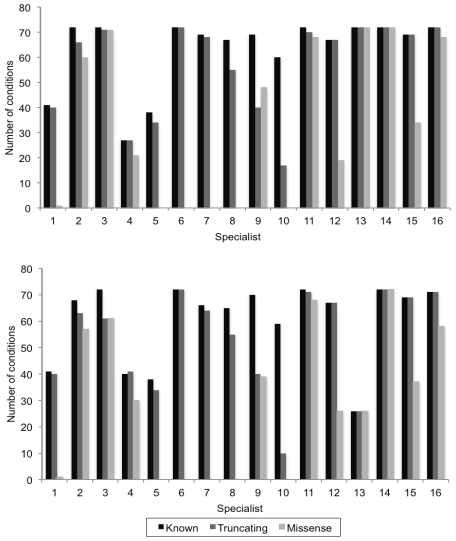
Making a definitive diagnosis: Successful clinical application of whole exome sequencing in a child with intractable inflammatory bowel disease

Elizabeth A. Worthey, PhD[1,2], Alan N. Mayer, MD, PhD[2,3], Grant D. Syverson, MD[2], Daniel Helbling, BSc[2], Benedetta B. Bonacci, MSc[2], Brennan Decker, BSc[2], Jaime M. Serpe, BSc[2], Trivikram Dasu, PhD[2], Michael R. Tschannen, BSc[2], Regan L. Veith, MSc[2], Monica J. Basehore, PhD[4], Ulrich Broeckel, MD, PhD[2,5], Aoy Tomita-Mitchell, PhD[1,2,5], Marjorie J. Arca, MD[2,5], James T. Casper, MD[2,5], David A. Margolis, MD[2,5], David P. Bick, MD[1,2,5], Martin J. Hessner, PhD[1,2], John M. Routes, MD[2,5], James W. Verbsky, MD, PhD[2,5], Howard J. Jacob, PhD[1,2,3,6], and David P. Dimmock, MD[1,2,5]

Genome Annotation



Secondary Findings

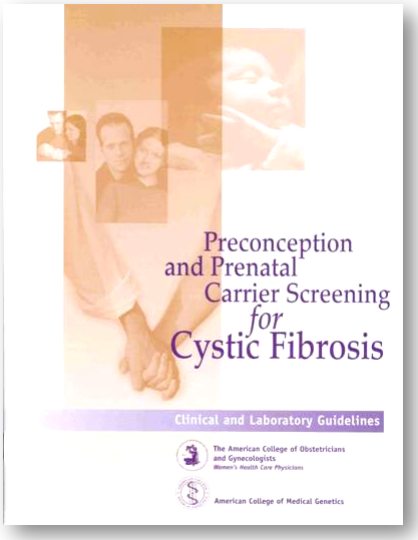


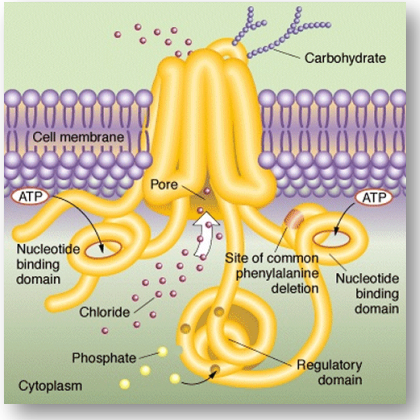
Green R, et al. *Genetics in Medicine* (2012) **14**, 405–410

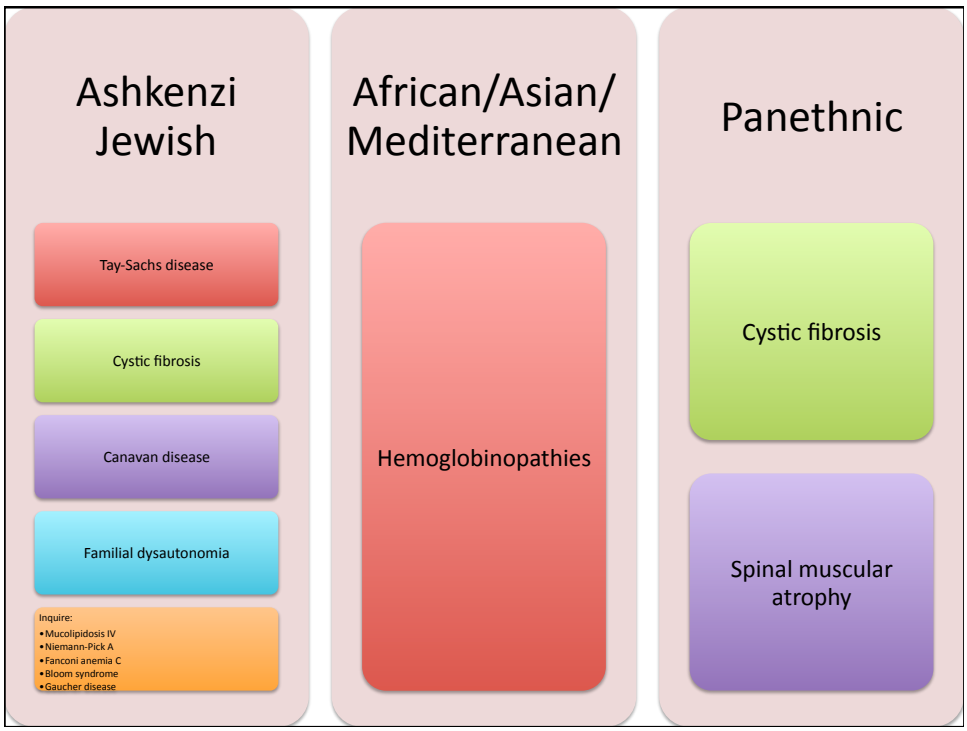
Preconceptional Testing

Laura is now married. She and her husband are considering starting a family and meet with her obstetrician-gynecologist. They are both of Northern European ancestry and are offered carrier testing for cystic fibrosis.

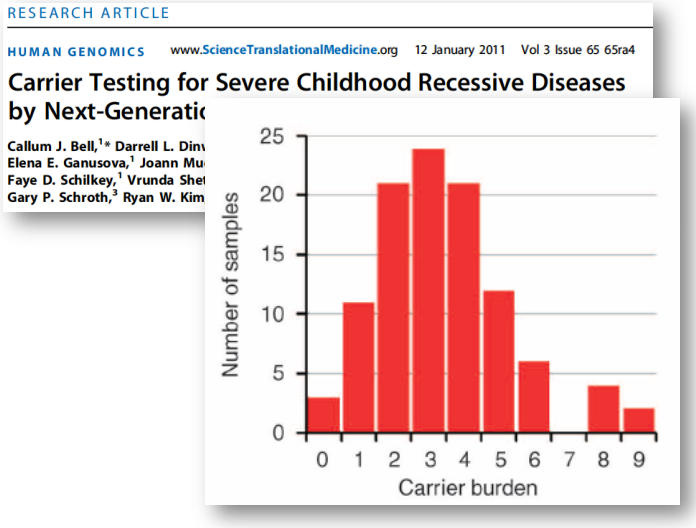
CF Carrier Screening



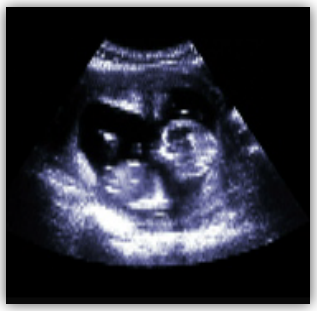




Genomic Carrier Testing

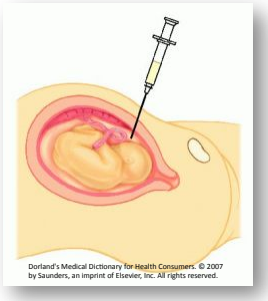


Prenatal Testing

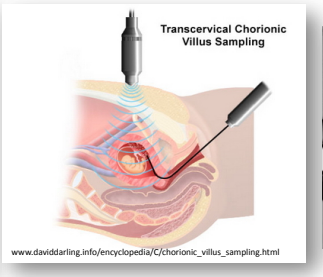


Laura and her Tom are indeed found to both be cystic fibrosis carriers. They elect to have prenatal diagnosis by amniocentesis at 16 weeks of pregnancy. The fetus is found to be a CF carrier.

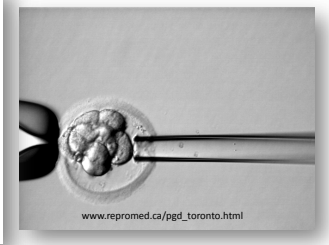
Prenatal Diagnosis



amniocentesis



chorionic villus biopsy



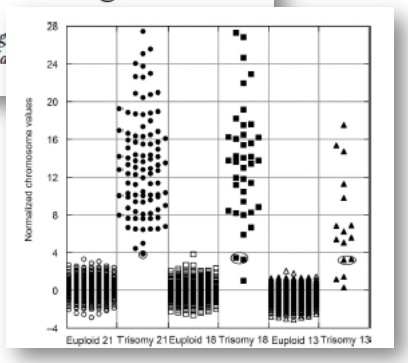
preimplantation diagnosis

Next Generation Prenatal Screening

Genome-Wide Fetal Aneuploidy Detection by Maternal Plasma DNA Sequencing

Diana W. Bianchi, MD, Lawrence D. Platt, MD, James D. Goldberg
Amy J. Sehnert, MD, and Richard P. Rava, PhD, on behalf of the Ma
*Accurately diagnose fetal aneuploidy (MELISSA) Study Group**

(Obstet Gynecol 2012;119:00–00)
DOI: 10.1097/AOG.0b013e31824fb482

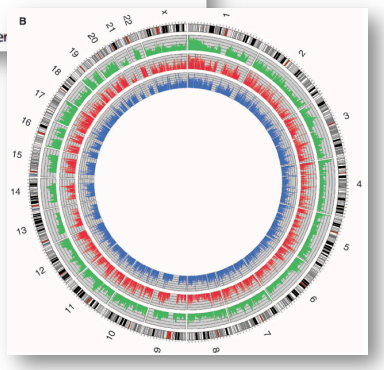


Genomic Prenatal Diagnosis

Maternal Plasma DNA Sequencing Reveals the Genome-Wide Genetic and Mutational Profile of the Fetus

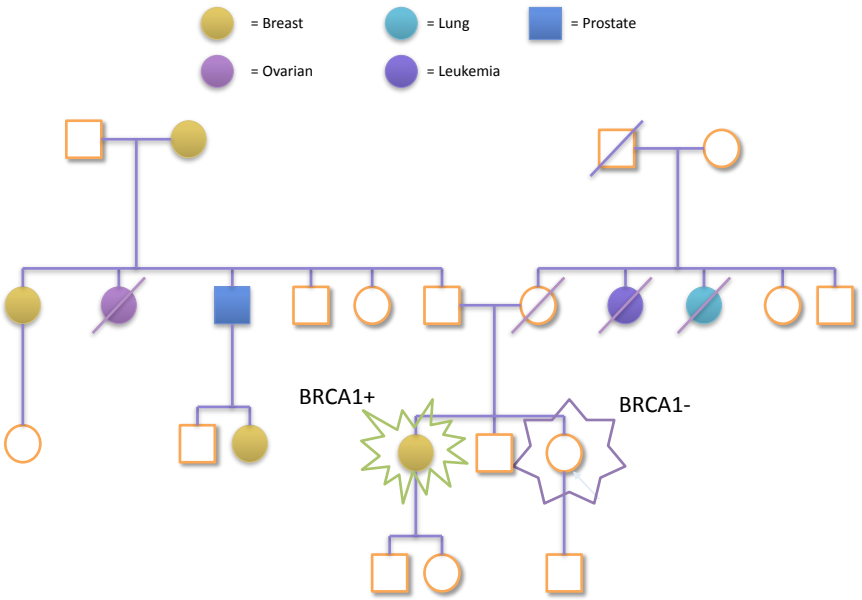
Y. M. Dennis Lo,[1,2]* K. C. Allen Chan,[1,2] Hao Sun,[1,2] Eric Z. Chen,[1,2] Peiyong Jiang,[1,2] Fiona M. F. Lun,[1,2] Yama W. Zheng,[1,2] Tak Y. Leung,[3] Tze K. Lau,[3] Charles R. Cantor,[4] Rossa W. K. Chiu[1,2]

(Published 8 December 2010; Volume 2 Issue 61 61ra91)
www.ScienceTranslationalMedicine.org 8 December

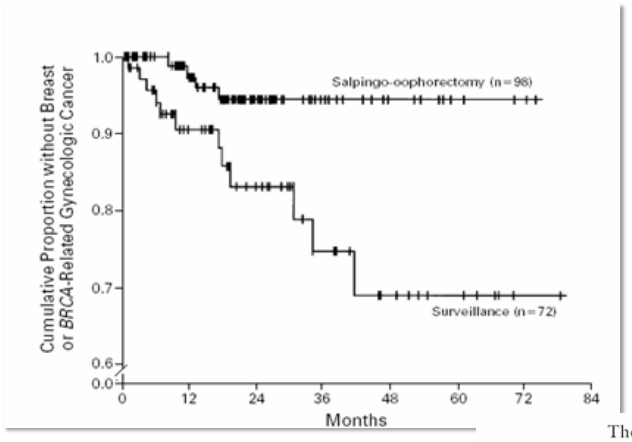


Presymptomatic Testing

Laura is now 45. She has just learned that her older sister Abby, age 49, has been diagnosed as having breast cancer. She is concerned about her own risks, given that there is a family history of others with breast cancer.



Breast Cancer Prevention

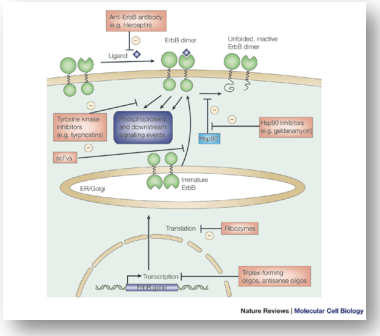



The New England Journal of Medicine

RISK-REDUCING SALPINGO-OOPHORECTOMY IN WOMEN WITH A *BRCA1* OR *BRCA2* MUTATION

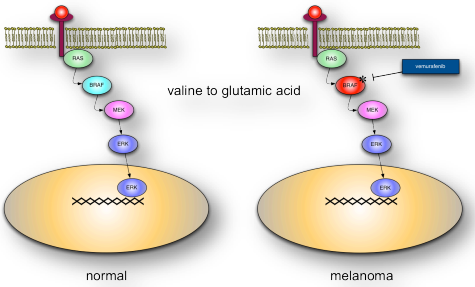
Therapeutics

Herceptin



Nature Reviews Molecular Cell Biology **2**, 127-137 (2001)

BRAF V600E in Melanoma



The Redactome

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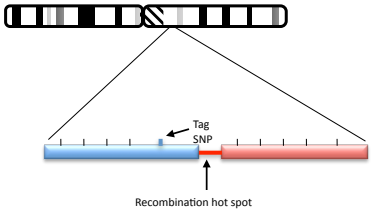
ttaaaaacagtgatgggagtgtagctgggaatggtggggtg

Predispositional Testing

Laura is now 60 years old. She has been in good health. She and her husband have heard about the possibility of having genomic testing, and explore the possibilities on the internet.

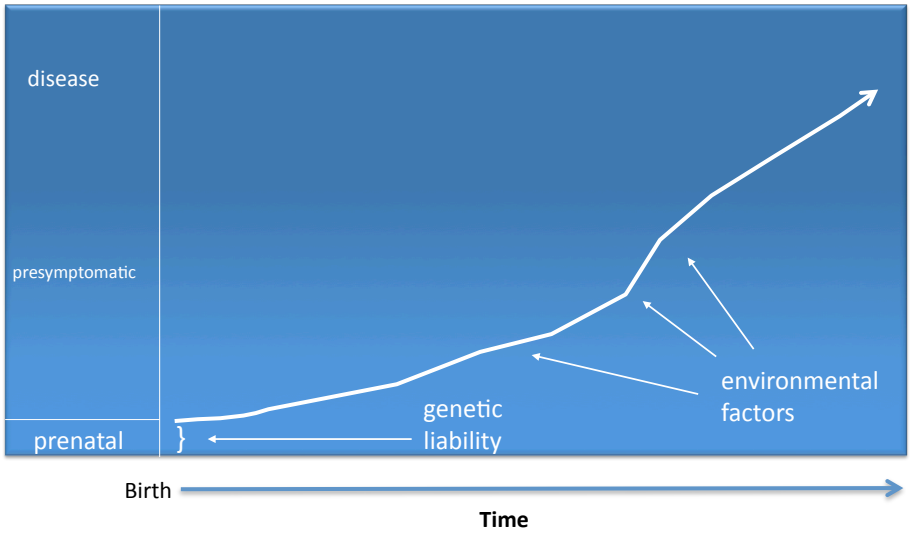
Genome-Wide Association Studies



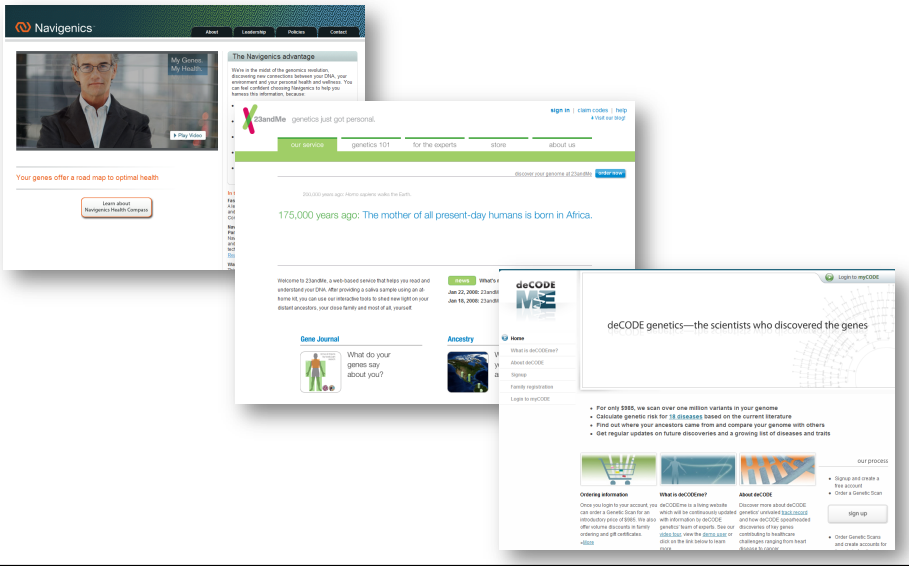
Gene	Symbol
Interleukin	*IL-4, IL-13*
Cluster of differentiation	*CD14*
β_2-Adrenergic receptor	*B2AR*
Human leukocyte antigen DRB1, DQB1	*HLA-DRB1, HLA-DQB1*
Tumor necrosis factor	*TNF*
High-affinity IgE receptor β	*FCER1B*
Interleukin-4 receptor	*IL4RA*
Disintegrin and metalloproteinase domain 33	*ADAM33*

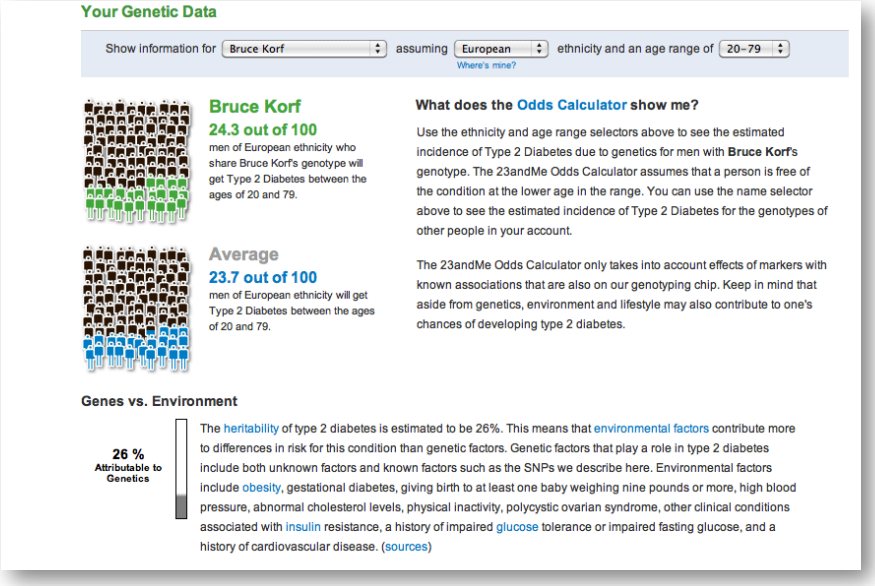
Bierbaum, S., Heinzmann, A. Resp Med
doi:10.1016/j.rmed.2007.01.018

Paradigm of Genetic Prevention



Direct to Consumer Genomic Testing

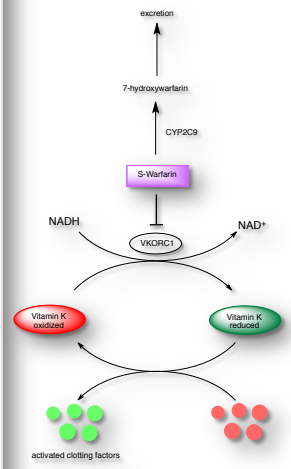




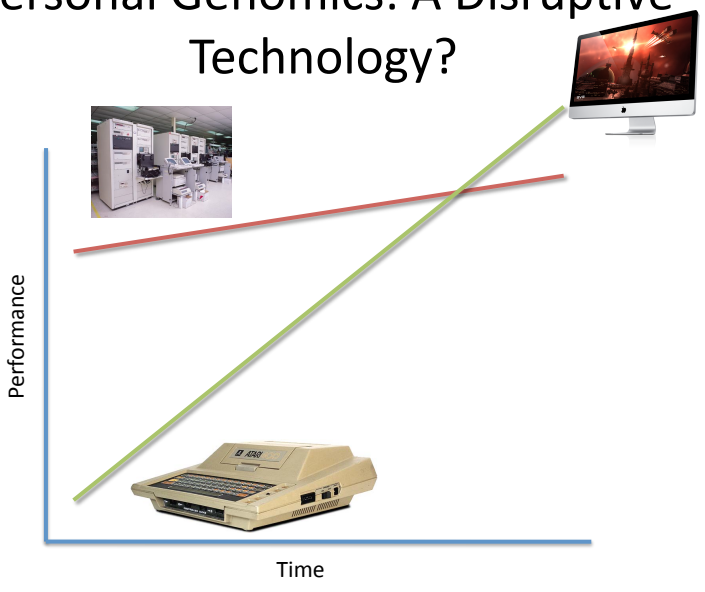
Pharmacogenetics

Name	Confidence	Status
Warfarin (Coumadin®) Sensitivity	★★★★	Increased
Abacavir Hypersensitivity	★★★★	Typical
Alcohol Consumption, Smoking and Risk of Esophageal Cancer	★★★★	Typical
Clopidogrel (Plavix®) Efficacy	★★★★	Typical
Fluorouracil Toxicity	★★★★	Typical
Response to Hepatitis C Treatment	★★★★	Typical
Pseudocholinesterase Deficiency	★★★★	Typical
Oral Contraceptives, Hormone Replacement Therapy and Risk of Venous Thromboembolism ♀	★★★★	Not Applicable
Caffeine Metabolism	★★★	Slow Metabolizer
Hepatitis C Treatment Side Effects	★★★	See Report
Metformin Response	★★★	Higher Odds of Positive Response
Antidepressant Response	★★	See Report
Beta-Blocker Response	★★	See Report
Floxacillin Toxicity	★★	Typical Odds
Heroin Addiction	★★	Typical Odds
Lumiracoxib (Prexige®) Side Effects	★★	Typical Odds
Naltrexone Treatment Response	★★	See Report
Postoperative Nausea and Vomiting (PONV)	★★	Higher Odds
Response to Interferon Beta Therapy	★★	Increased Odds of Responding
Statin Response	★★	See Report

The genotyping services of 23andMe are performed in LabCorp's CLIA-certified laboratory. The tests have not been cleared or approved by the FDA but

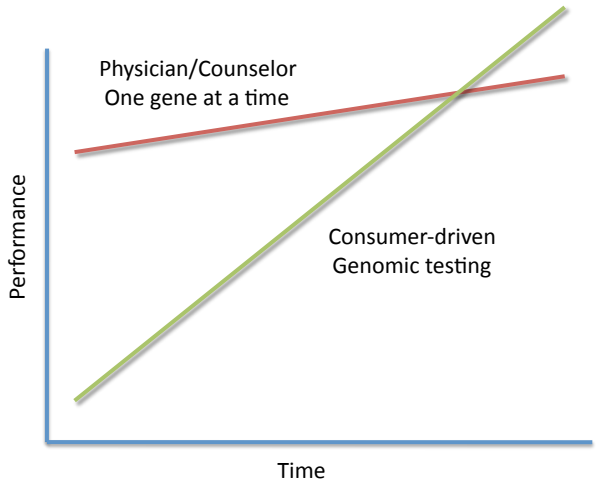


Personal Genomics: A Disruptive Technology?



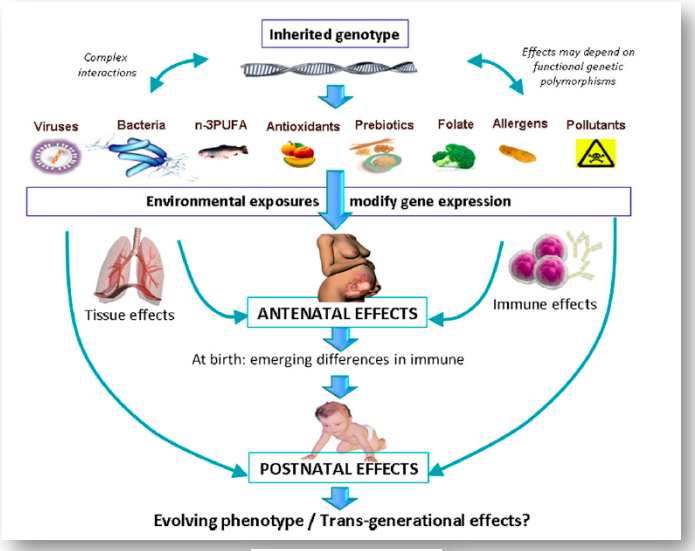
Modified from Christensen et. al. The Innovator's Prescription

Personal Genomics: A Disruptive Technology?



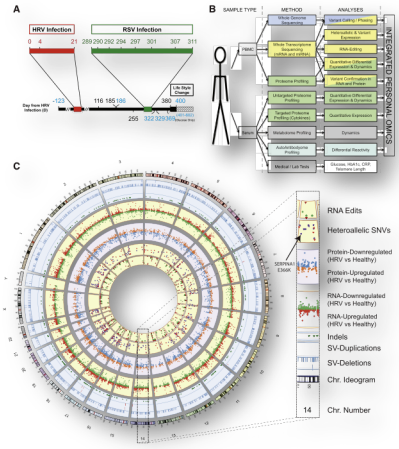
Modified from Christensen et. al. The Innovator's Prescription

Genomics and Epigenomics



David Martino and Susan Prescott
Chest 2011;139:640-647
DOI 10.1378/chest.10-1800

Personalized Genomics



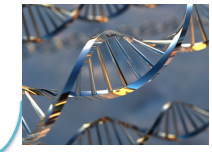
Chen R et al. Cell 2012;148:1293-1307.

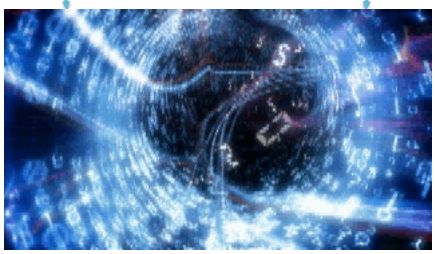
Sir Luke Fildes – The Doctor (1887)

Medicine in Transformation

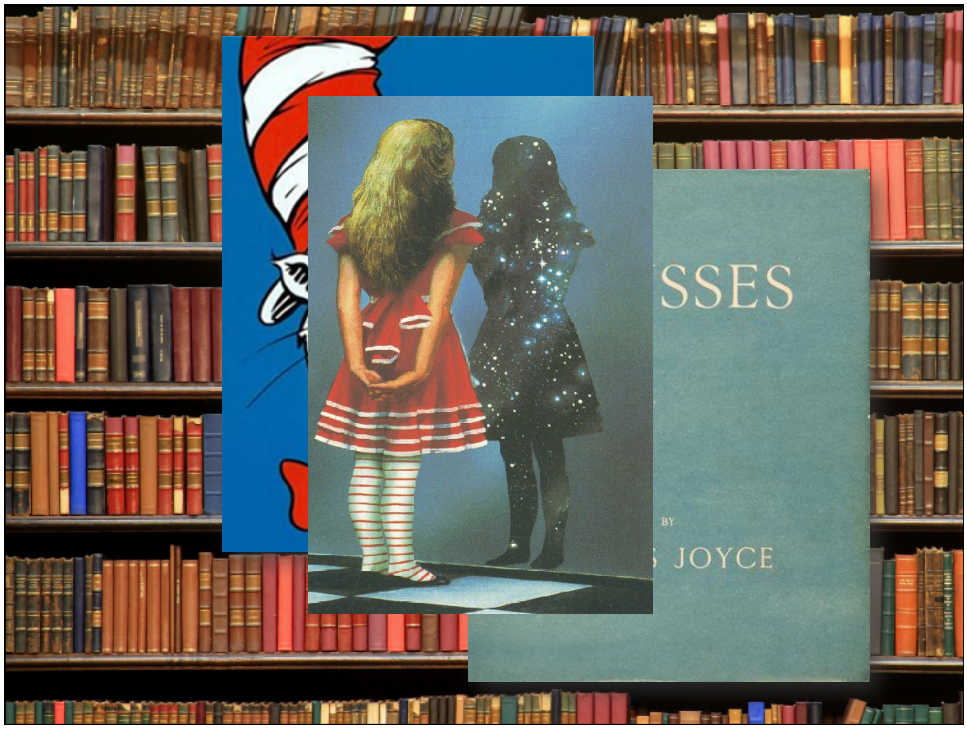
Information Technology

Genetics & Genomics

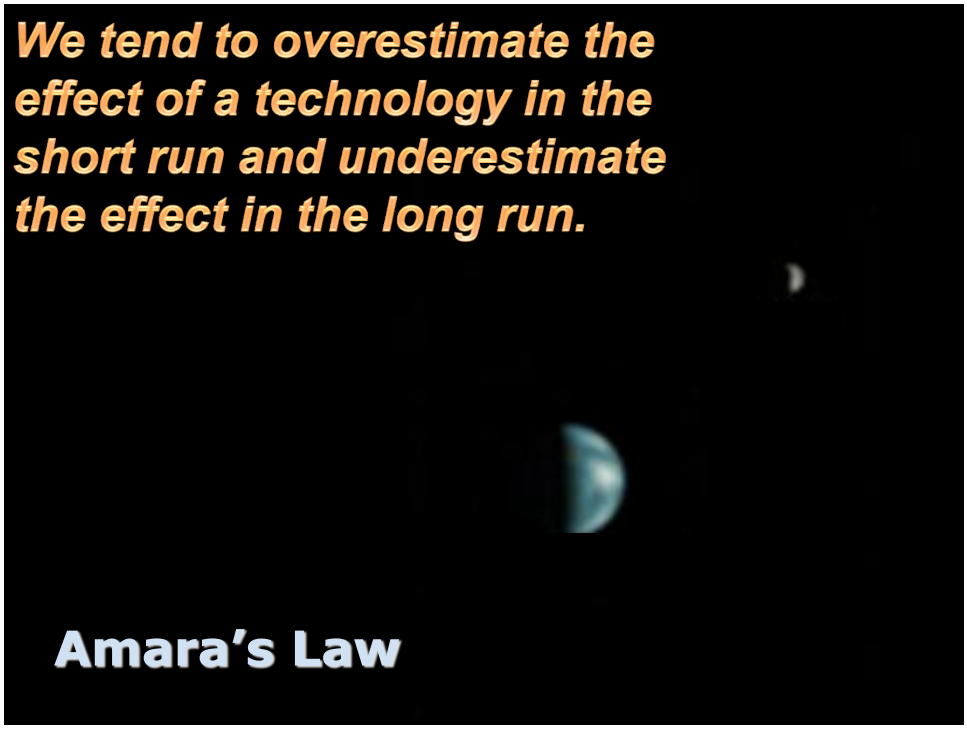




Where Will Personal Genomes Live?


SSES
BY
JOYCE


• Education of physicians and the general public
• Access to information
• Tools for screening, education
• Protection of individual rights and privacy
• Knowledge of outcomes
• Development of new prevention strategies and treatments
GBRB 2002


We tend to overestimate the effect of a technology in the short run and underestimate the effect in the long run.
Amara's Law


The best way to predict the future is to invent it.
Alan Kay
Computer Scientist