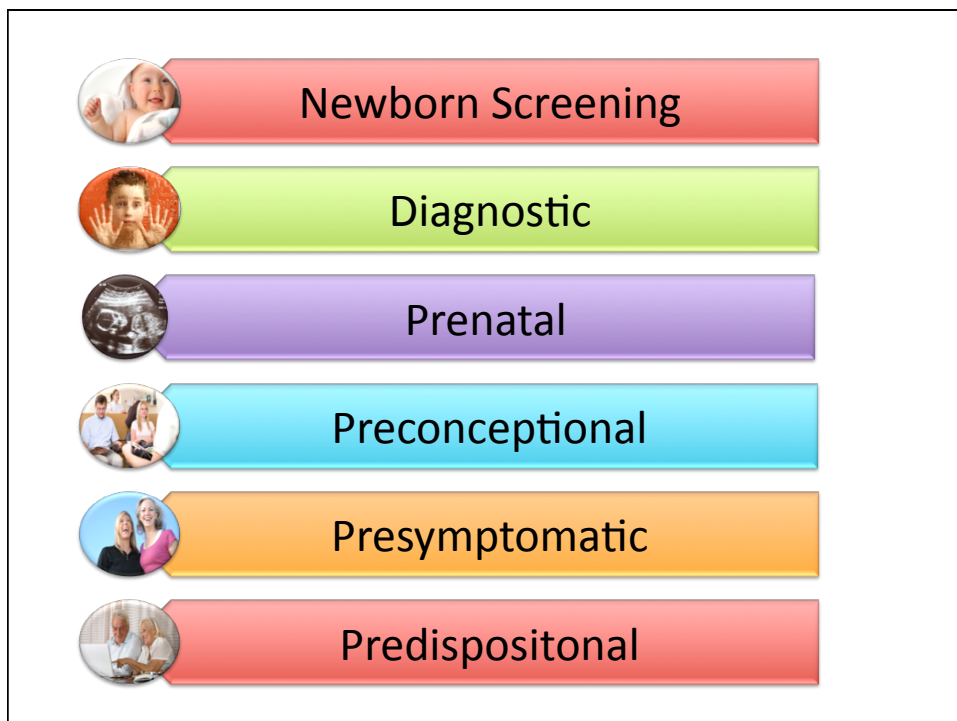
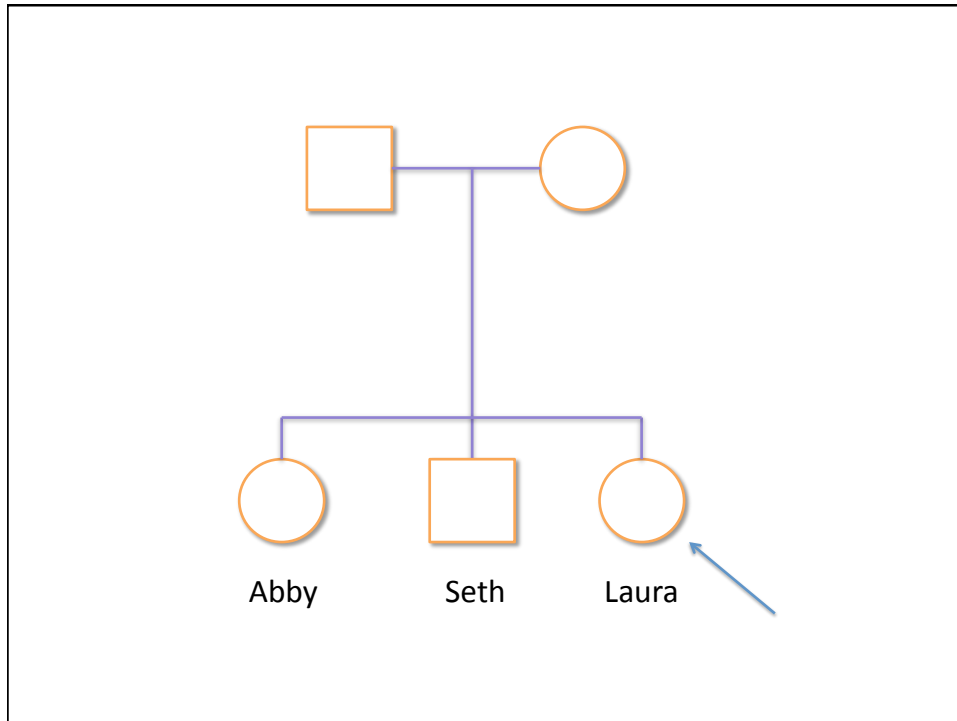


Disclosures

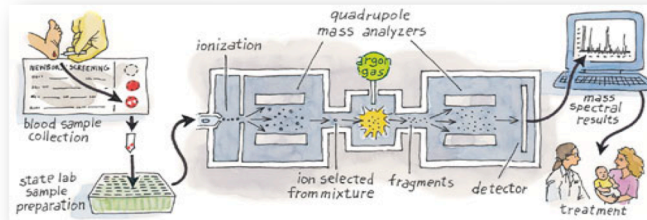
- Medical Director, UAB Medical Genomics Laboratory
- Chair, Medical Affairs Committee, Children's Tumor Foundation
- Grant Funding: NIH, Department of Defense, Novartis
- Advisory Boards: Novartis NF Advisory Board, March of Dimes



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 Shet
Gary P. Schroth,³ Ryan W. Kim,¹

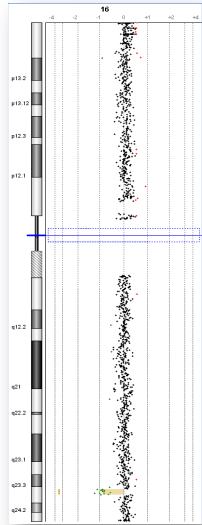
“We found an unexpectedly high proportion of literature-annotated disease mutations that were incorrect, incomplete, or common polymorphisms.”

Diagnostic Testing

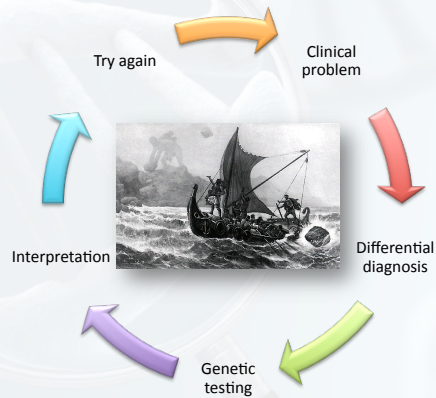


Laura is now 3 and her brother Seth is 5. Seth has been experiencing developmental problems, and is diagnosed as having autism

Genetic Evaluation in Autism



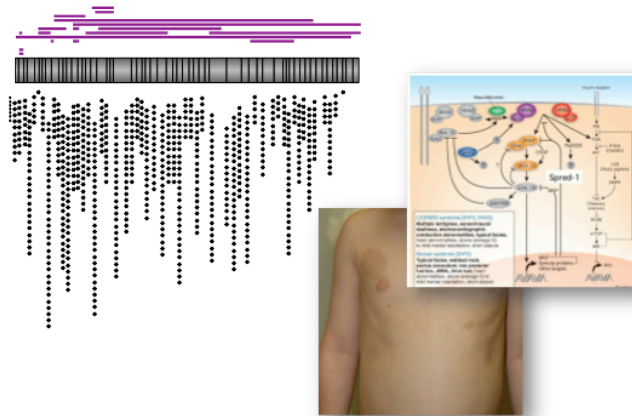
The Diagnostic Odyssey



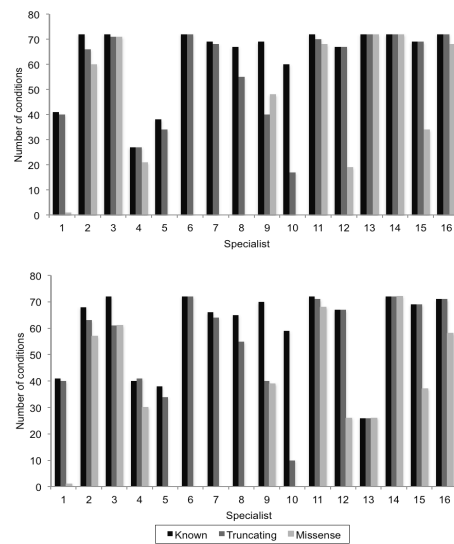
Making a definitive diagnosis: Successful clinical application of whole exome sequencing in a child with intractable inflammatory bowel disease

Elizabeth A. Worthey, PhD^{1,2}, Alan N. Mayer, MD, PhD^{2,3}, Grant D. Szymanski, MD², Daniel Hellberg, BS¹, Benedetta B. Bonucci, MS¹, Bryanna Decker, BS¹, James M. Scarp, BS², Trevoram Davis, PhD², Michael R. Tychanek, BS¹, Regan L. Veith, MS¹, Monica J. Bashford, PhD⁴, Ulrich Broeckel, MD, PhD^{2,5}, Amy Tomlin-Mitchell, PhD^{1,2}, Meghna J. Arora, MD^{2,6}, James T. Casper, MD^{2,7}, David A. Margolis, MD^{2,8}, David P. Bick, MD^{2,9}, Martin J. Hejblum, PhD², John M. Resnik, MD¹, James W. Verbsky, MD, PhD¹, Howard J. Jacob, PhD^{2,10}, and David P. Dimmock, MD¹¹

Genome Annotation



Secondary Findings



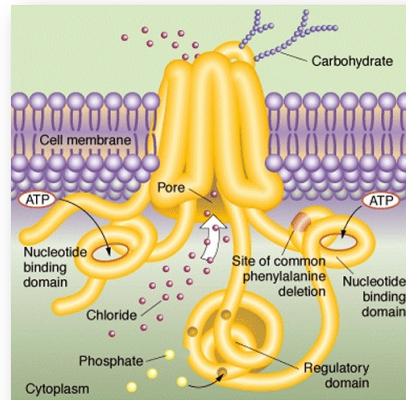
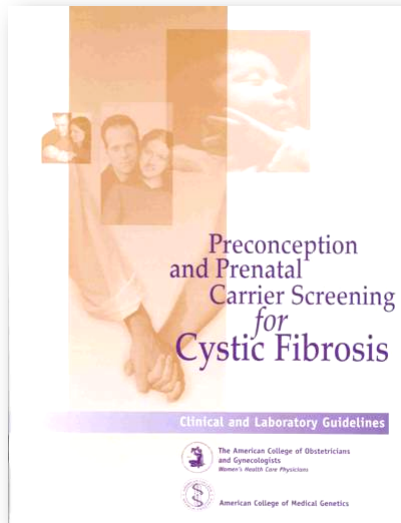
Green R, et al. *Genetics in Medicine* (2012) 14, 405–410

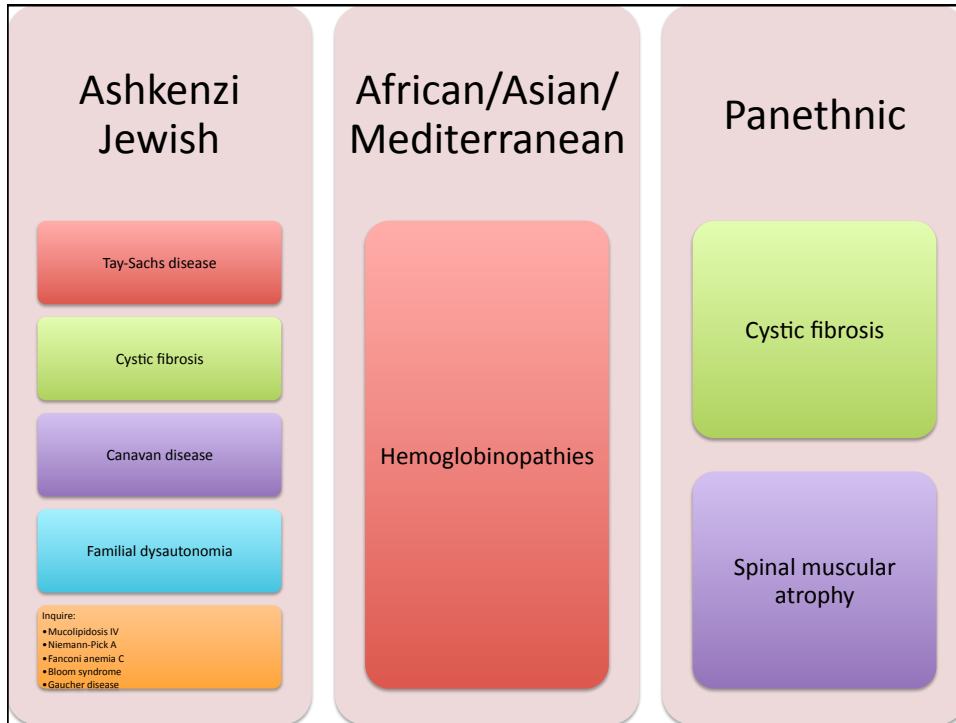
Preconceptional Testing



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





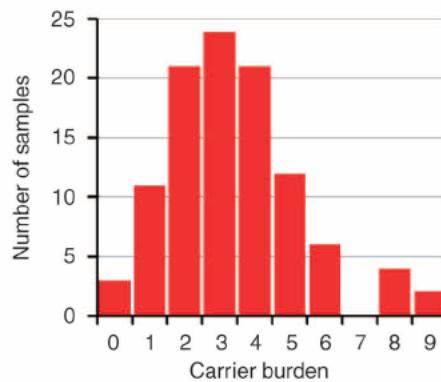
Genomic Carrier Testing

RESEARCH ARTICLE

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

Carrier Testing for Severe Childhood Recessive Diseases by Next-Generatic

Callum J. Bell,^{1*} Darrell L. Dinu
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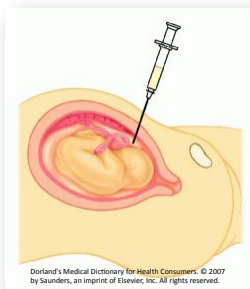


Prenatal Testing

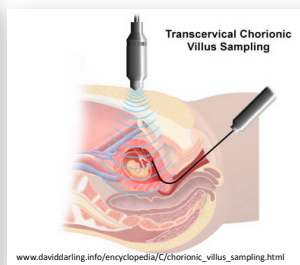


Laura and her Tom are indeed found to both be cystic fibrosis carriers. They elect to have prenatal diagnosis by amniocentesis at 16 weeks of pregnancy. The fetus is found to be a CF carrier.

Prenatal Diagnosis



amniocentesis



chorionic villus biopsy



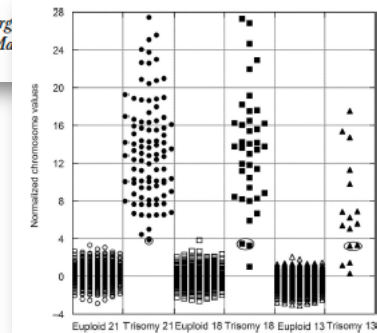
preimplantation diagnosis

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. Sehert, MD, and Richard P. Rava, PhD, on behalf of the Maternal Plasma Fraction Sequencing (MPFS) Study Group*

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

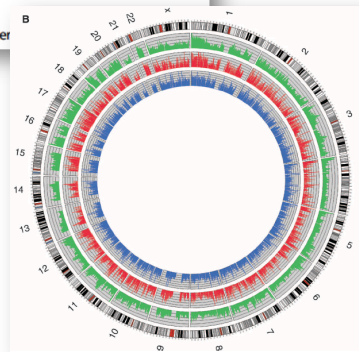


Genomic Prenatal Diagnosis

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}

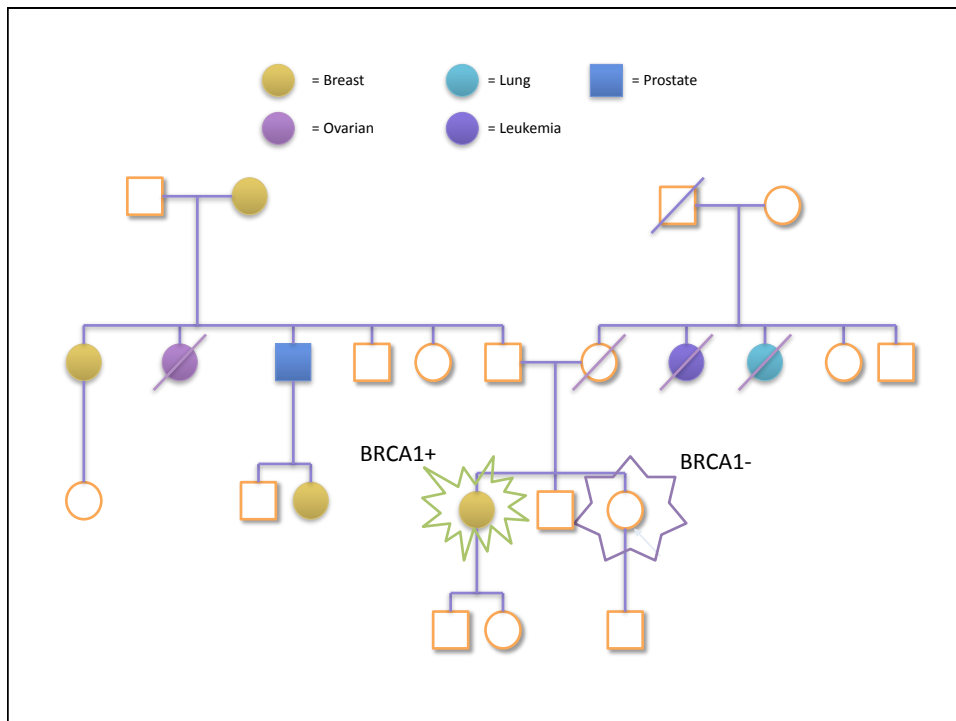
(Published 8 December 2010; Volume 2 Issue 61 61n91)
www.ScienceTranslationalMedicine.org 8 December

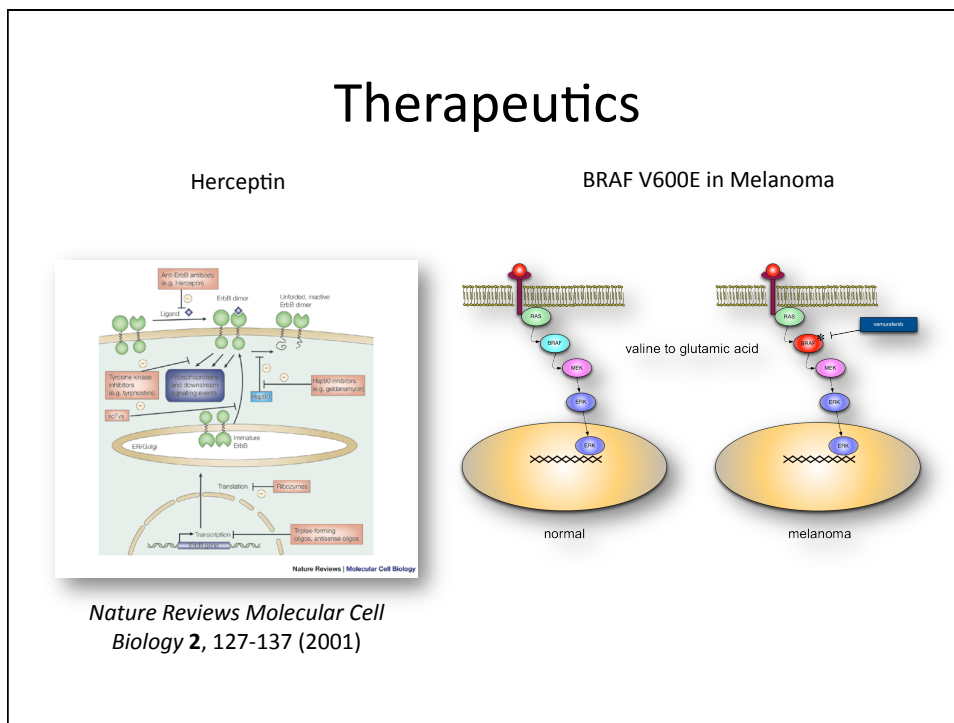
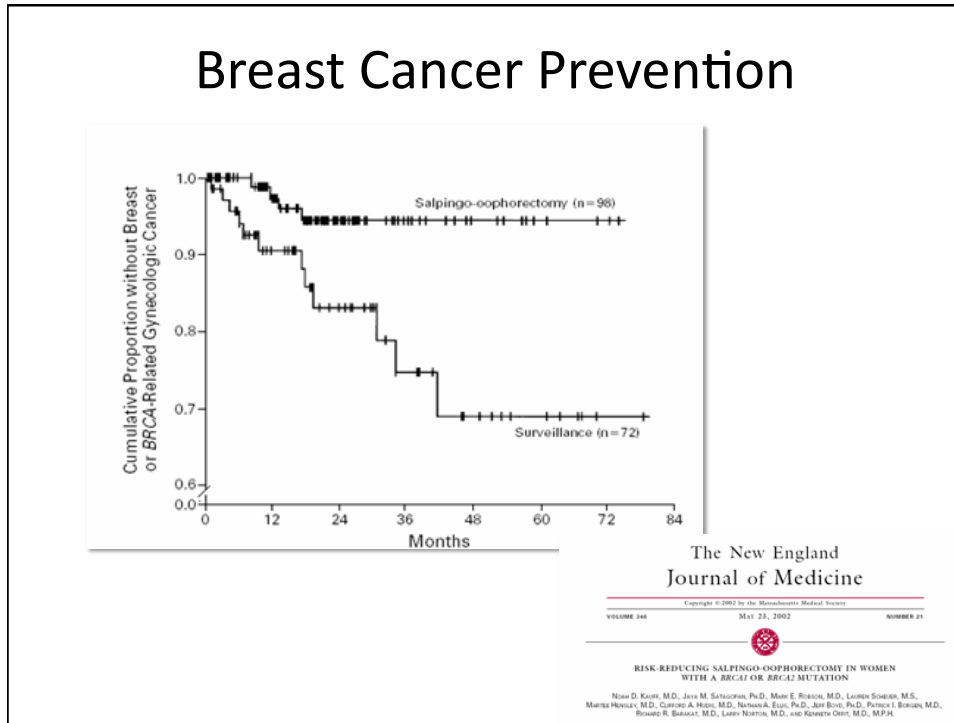


Presymptomatic Testing



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.





The Redactome

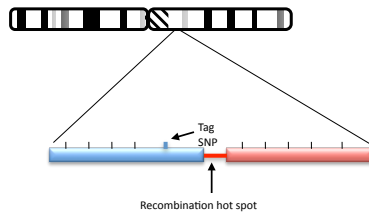
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Predispositional Testing



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.

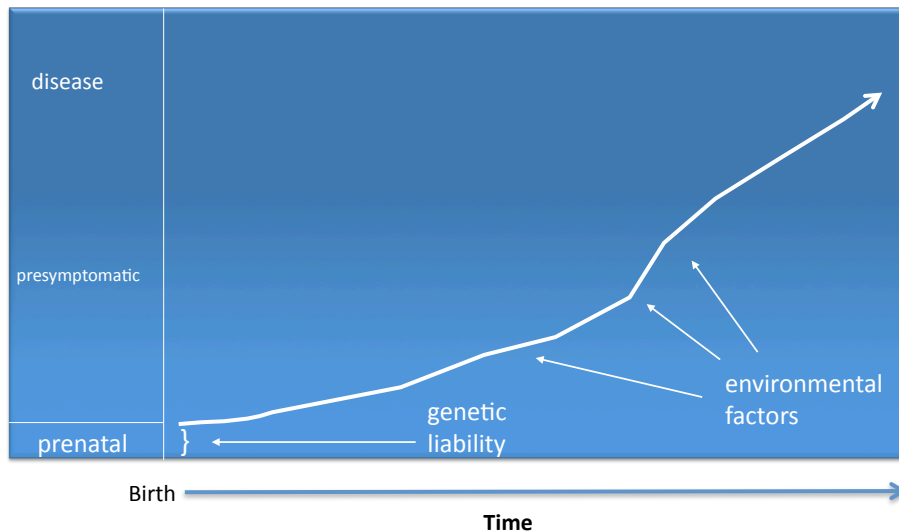
Genome-Wide Association Studies



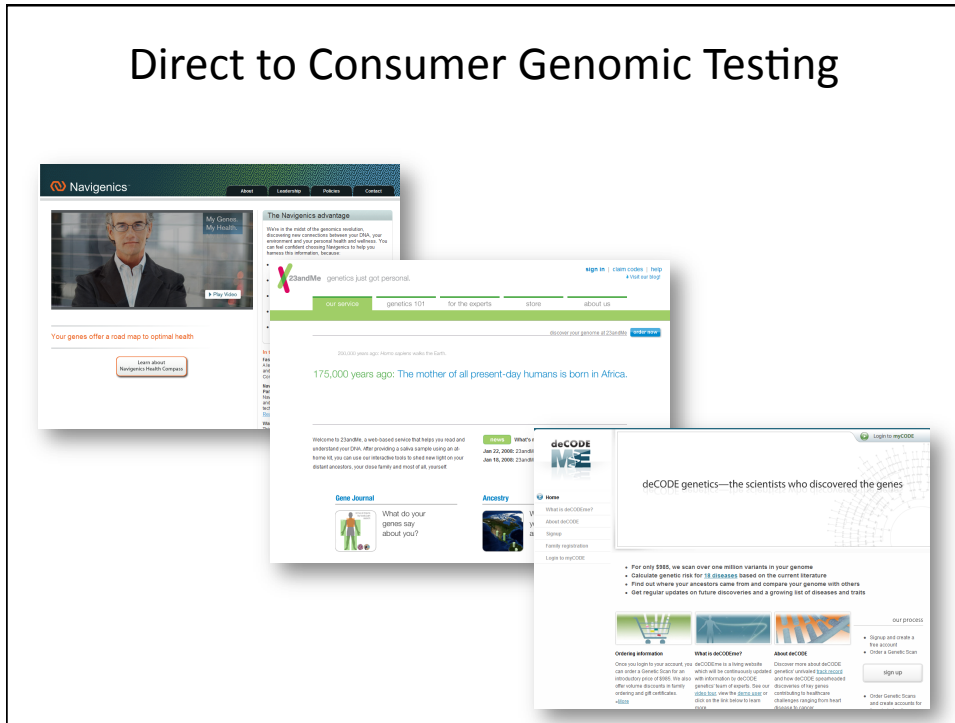
Gene	Symbol
Interleukin	<i>IL-4, IL-13</i>
Cluster of differentiation	<i>CD14</i>
β_2 -Adrenergic receptor	<i>B2AR</i>
Human leukocyte antigen DRB1, DQB1	<i>HLA-DRB1,</i> <i>HLA-DQB1</i>
Tumor necrosis factor	<i>TNF</i>
High-affinity IgE receptor β	<i>FCER1B</i>
Interleukin-4 receptor	<i>IL4RA</i>
Disintegrin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

Bierbaum, S., Heinzmann, A. *Resp Med*
[doi:10.1016/j.rmed.2007.01.018](https://doi.org/10.1016/j.rmed.2007.01.018)

Paradigm of Genetic Prevention



Direct to Consumer Genomic Testing



Your Genetic Data

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

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.

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](#))

What does the Odds Calculator show me?

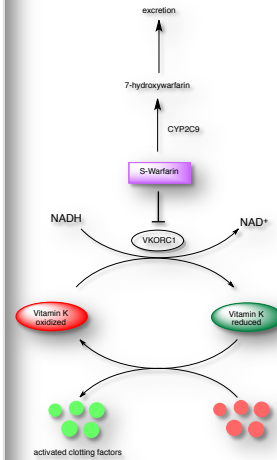
Use the ethnicity and age range selectors above to see the estimated incidence of Type 2 Diabetes due to genetics for men with **Bruce Korf's** genotype. The 23andMe Odds Calculator assumes that a person is free of the condition at the lower age in the range. You can use the name selector above to see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

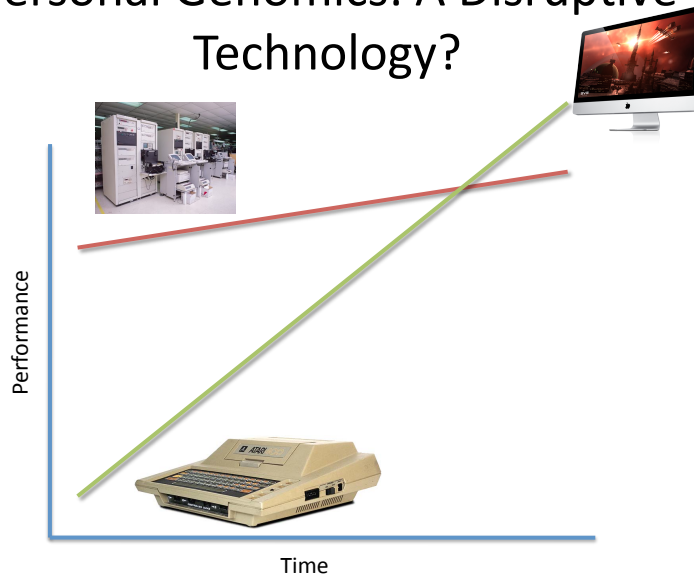
Pharmacogenetics

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
Pseudocholesterase 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
Floxacin 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

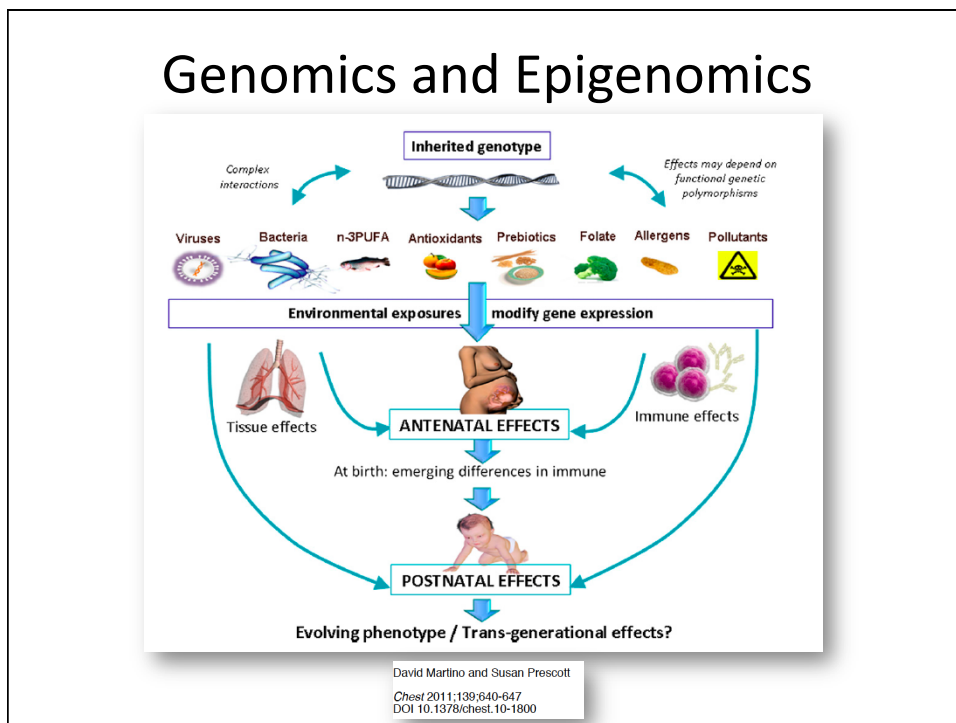
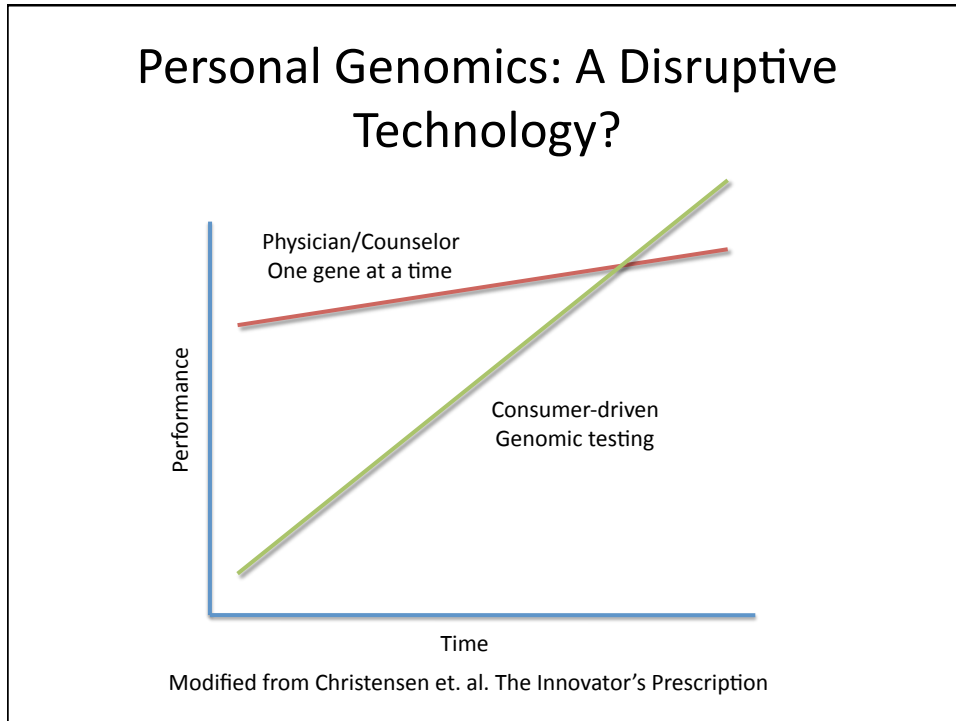
The genotyping services of 23andMe are performed in LabCorp's CLIA-certified laboratory. The tests have not been cleared or approved by the FDA but



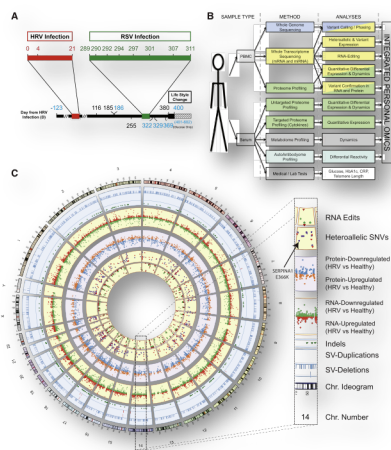
Personal Genomics: A Disruptive Technology?



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



Personalized Genomics



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



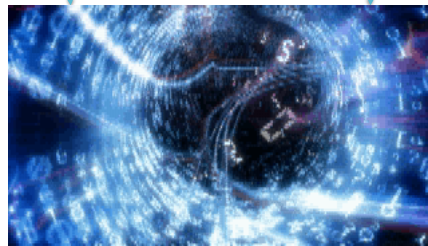
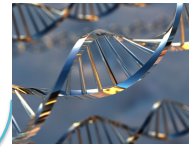
Sir Luke Fildes – The Doctor (1887)

Medicine in Transformation

Information Technology

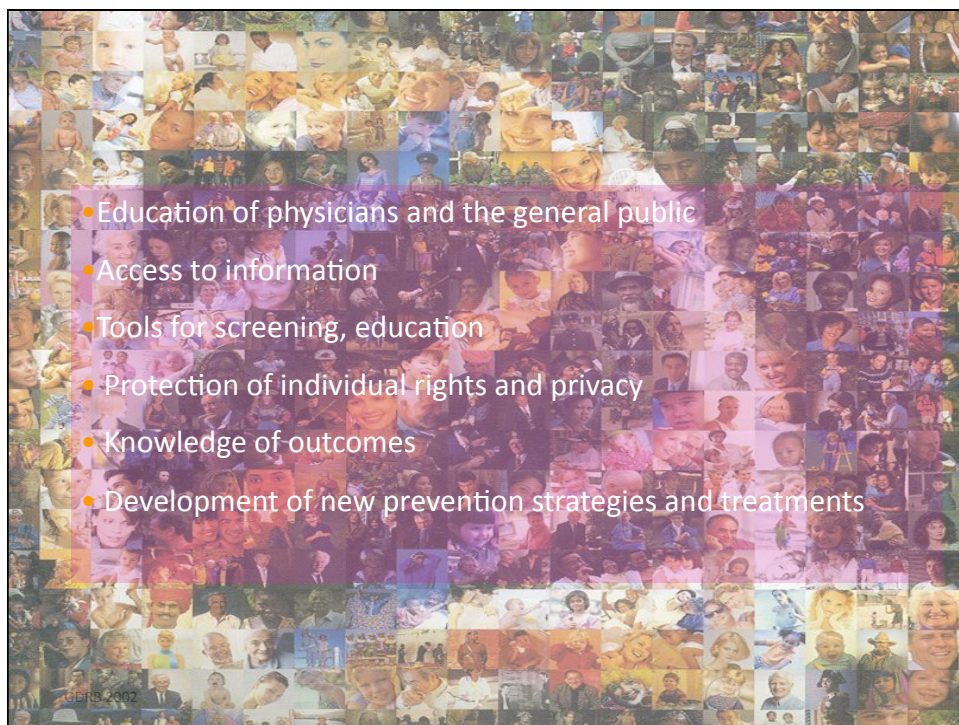


Genetics & Genomics



Where Will Personal Genomes Live?





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

Amara's Law

