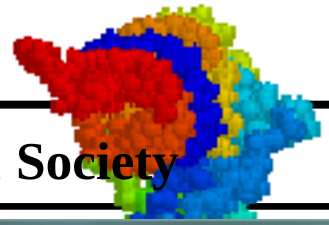
Personal Genomes Services : Research



8-Jul-08 Secretary's Advisory Committee on Genetics, Health, & Society

National Cancer Institute
U.S. National Institutes of Health | www.cancer.gov

genome.gov
National Human Genome Research Institute
National Institutes of Health

National Heart Lung and Blood Institute

NSF

GENOMES to LIFE
BIOLOGICAL SOLUTIONS FOR ENERGY CHALLENGES
U.S. DEPARTMENT OF ENERGY
INNOVATIVE APPROACHES ALONG UNCONVENTIONAL PATHS

BROAD INSTITUTE

molecular systems biology
A new type of online journal from EMBO and Nature Publishing Group

DARPA

Knome

CORIELL INSTITUTE for Medical Research

OrbiMed
Healthcare Fund Management

Google

23andMe

Roche

AFFYMETRIX

Agilent Technologies

Helicos
BioSciences Corporation

Applied Biosystems

enzymatics

DANAHER MOTION

illumina

CODON DEVICES

Personal Genome Project

BEIJING INSTITUTE OF GENOMICS
CHINESE ACADEMY OF SCIENCES

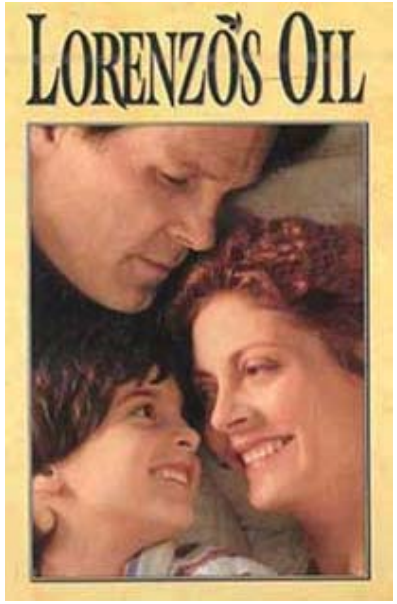
DIY DNA

DNA Explorer, $80
(Ages 10 and up)
www.discovery.com

Genographic Project $99

Genetics activism & research participation

(non-anonymous action to change currently incurable test results)



Adrenoleukodystrophy
Augusto Odone's son

Doug Melton's son, Sam, has **diabetes**

Huntington's Chorea
Nancy Wexler's family

ALS
Heywood family
PatientsLikeMe.org

Parkinson's
Michael J. Fox

Hugh Rienhoff
MyDaughtersDNA.org

Cancer, substance abuse
Betty Ford

Personal Genome Project

Is privacy in genomics realistic?

(10) Re-identification after "de-identification" using other public data.
Group Insurance Commission list of birth date, gender, and zip code was sufficient to re-identify medical records of Governor Weld & family via voter-registration records (1998)
(9) Hacking. A hacker gained access to confidential medical info at the U. Washington Medical Center -- 4000 files (names, conditions, etc, 2000)
(8) Combination of surnames from genotype with geographical info
An anonymous sperm donor was traced on the internet 2005 by his 15 year old son who used his own Y chromosome genealogy to access surname relations.
(7) Inferring phenotype from genotype Markers for eye, skin, and hair color, height, weight, racial features, dysmorphologies, etc. are known & the list is growing.
(6) Self-identification. An example of this at Celera undermined confidence in the investigators. Kennedy D. Science. 2002 297:1237. Not wicked, perhaps, but tacky.
(5) A tiny amount of DNA data in the public domain with a name leverages the rest.
This would allow the vast amount of DNA data in the HapMap (or other study) to be identified. This can happen for example in court cases even if the suspect is acquitted.
(4) Laptop theft. 26 million Veterans' medical records, SSN & disabilities stolen Jun 2006.
(3) Unauthorized access to DNA bearing samples (e.g. hair, dandruff, hand-prints, etc.)
(2) Identification by phenotype. If CT or MR imaging data is part of a study, one could reconstruct a person's appearance . Even blood chemistry can be identifying in some cases.
(1) Government subpoena. False positive IDs can be very disruptive.

Personal Genomics Service & Research Landscape

Individual access

23andMe *

The Genographic Project

Navigenics

Knome *

Coriell Institute for Medical Research *

deCODE me

DNAdirect *

Smart Genetics.

SeqWright DNA Technology Services

geneview

DNATraits Your Health. Your Right to Know.

GATC Biotech

Open-access DNA & traits

Personal Genome Project *

Research access

Multiplex Initiative

REVEAL

National Institutes of Health

ClinSeq

db GaP GENOTYPE and PHENOTYPE

Open DNA access

1000 Genomes
A Deep Catalog of Human Genetic Variation

International HapMap Project

PersonalGenomes.org Project Goals

1) **<$1000** for coding sequence + regulatory data
2) Full subject participation, informed redaction
3) **Avoid over-promising on de-identification**
4) **Exam** to assure informed consent
5) Multiple samples to assure identity
6) **Open access** (not just researcher subset)
7) **Trait** questionnaire, stem cell RNA, microbes
8) Cells available for personal functional genomics
9) **Scaleable** to 100,000 diverse research subjects

Personal Genome Project

Over 600 alleles of BRCA1

(Myriad/DNAdirect* sequencing, **not** chips)

How analyzing genes can indicate health risks and arm a person to take preventative measures.

The BRCA1 gene is a tumor suppressor gene

BRCA1 gene

Chromosome 17

In some people, there is hereditary mutation in the gene and the tumor suppressing functon does not work.

A normal BRCA1 sequence

AAA ATC TTA GAG TCT

A hereditary mutation that deletes two characters in the sequence...

GA

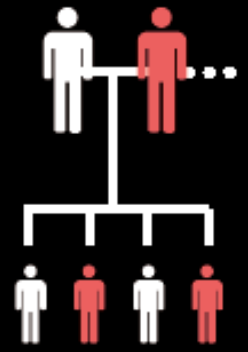
AAA ATC TTA _ _G TCT

...makes the rest of the characters move over to fill up the two spots

AAA ATC TTA GTC TCC

Mutated BRCA1 sequence

A woman with a mutated BRCA1 gene has a 60-80% chance of developing breast cancer and a 20-30% chance of ovarian cancer in her life and men have an increased risk of prostate cancer.



Mutated BRCA1 sequence

Offspring of those with this mutation have a 50% risk of inheriting the mutated gene.

What a person can do if they have the mutated gene

Surveillance
To be able to detect cancer as soon as possible

Avoiding risk
Exercise and limiting alcohol

Preventative chemotherapy
Drug therapy such as Tamoxifen

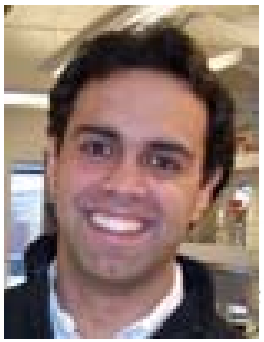
Preventative surgery
Mastectomy or removal of fallopian tubes and ovaries

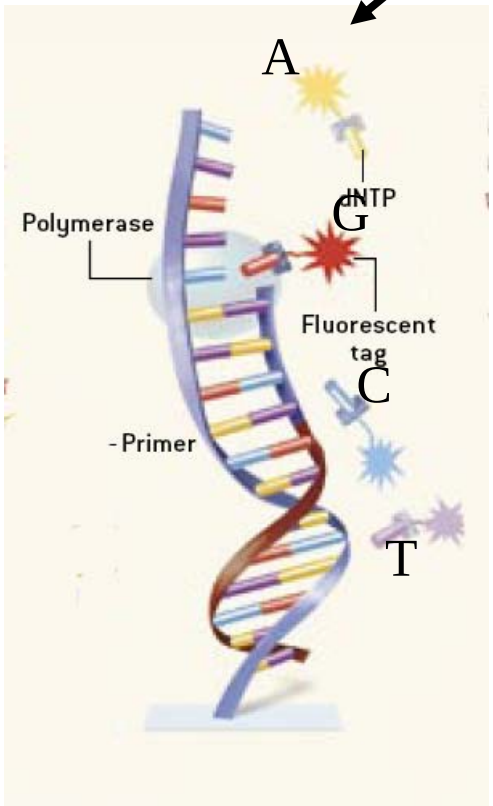
Next-generation Sequencing

Single instrument, multiplex chemistries: polonies on slides or beads

Polymerase -or- **Ligase**

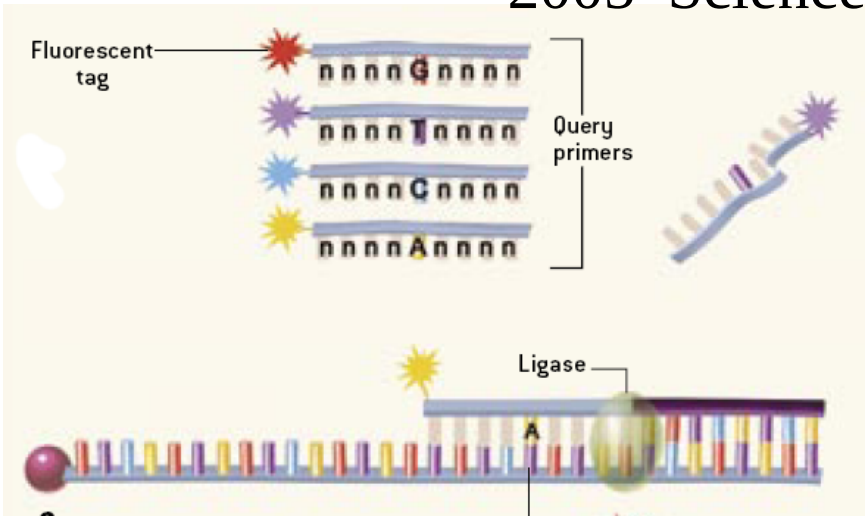
Mitra, et al. 2003 Analyt. Biochem. 1999 NAR





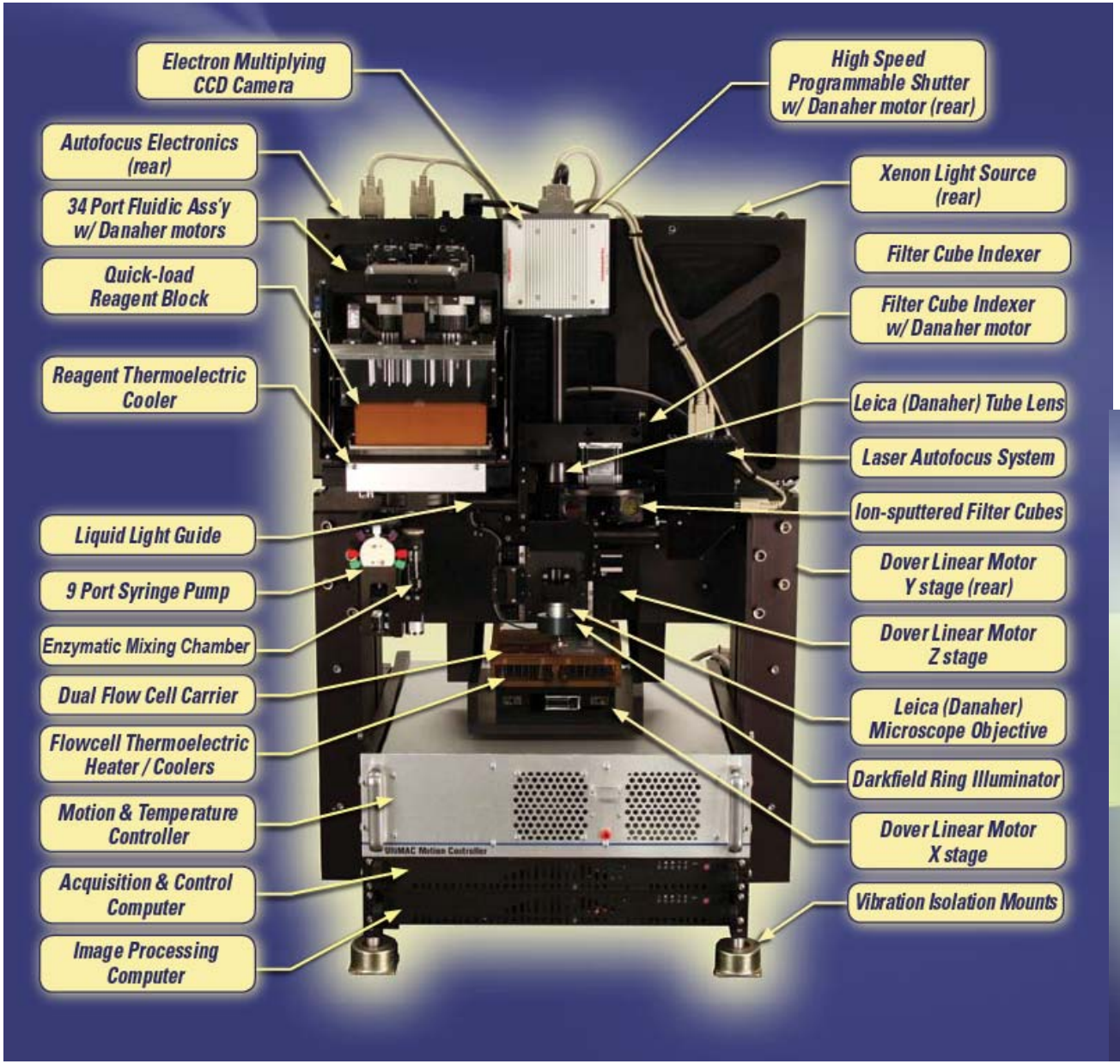
Illumina, IBS*

Shendure, Porreca, et al. 2005 Science



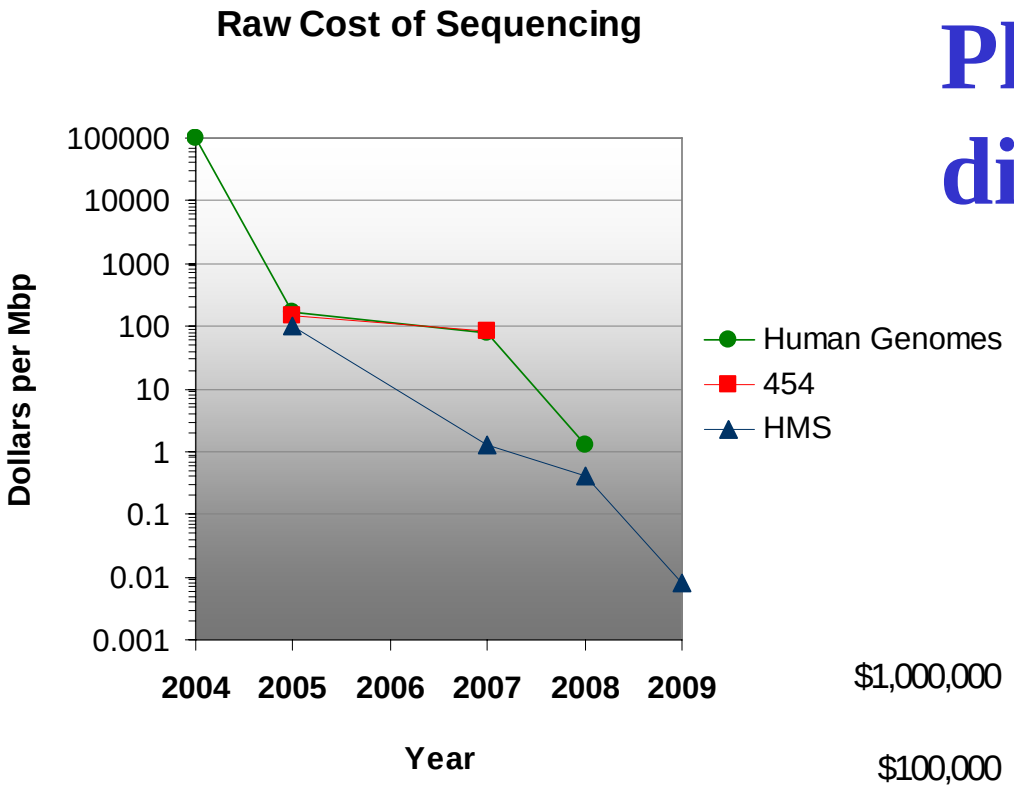
AB-SOLiD*, CGI*

Open-source hardware, software, wetware: Polonator G.007 (12TB images 10 to 400 Gbp /run)



Enzyme/oligo kits
Polymerase or Ligase chemistries
$150K including computer & 1 yr service, software, support
Dover Inc.

Plummeting costs & diversity of options

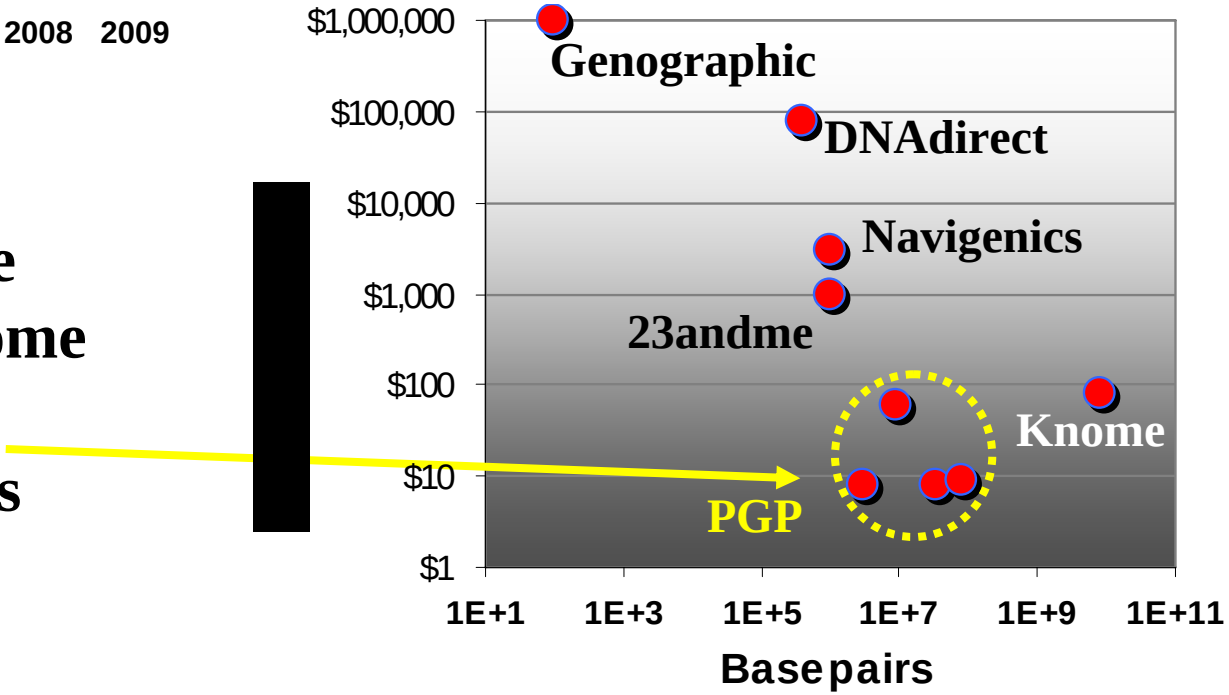


$1000 for one-time inherited PGP exome

+

$90 for yearly tests

VDJ-ome

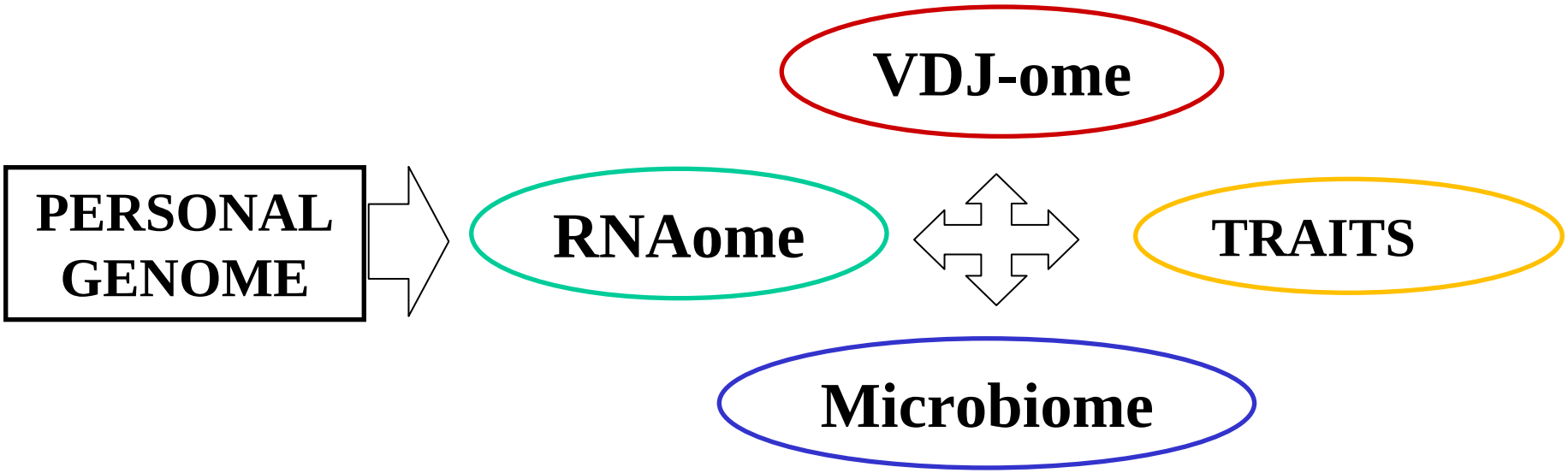


Personal Genome Project

Not just genomes but Environments of genomes too

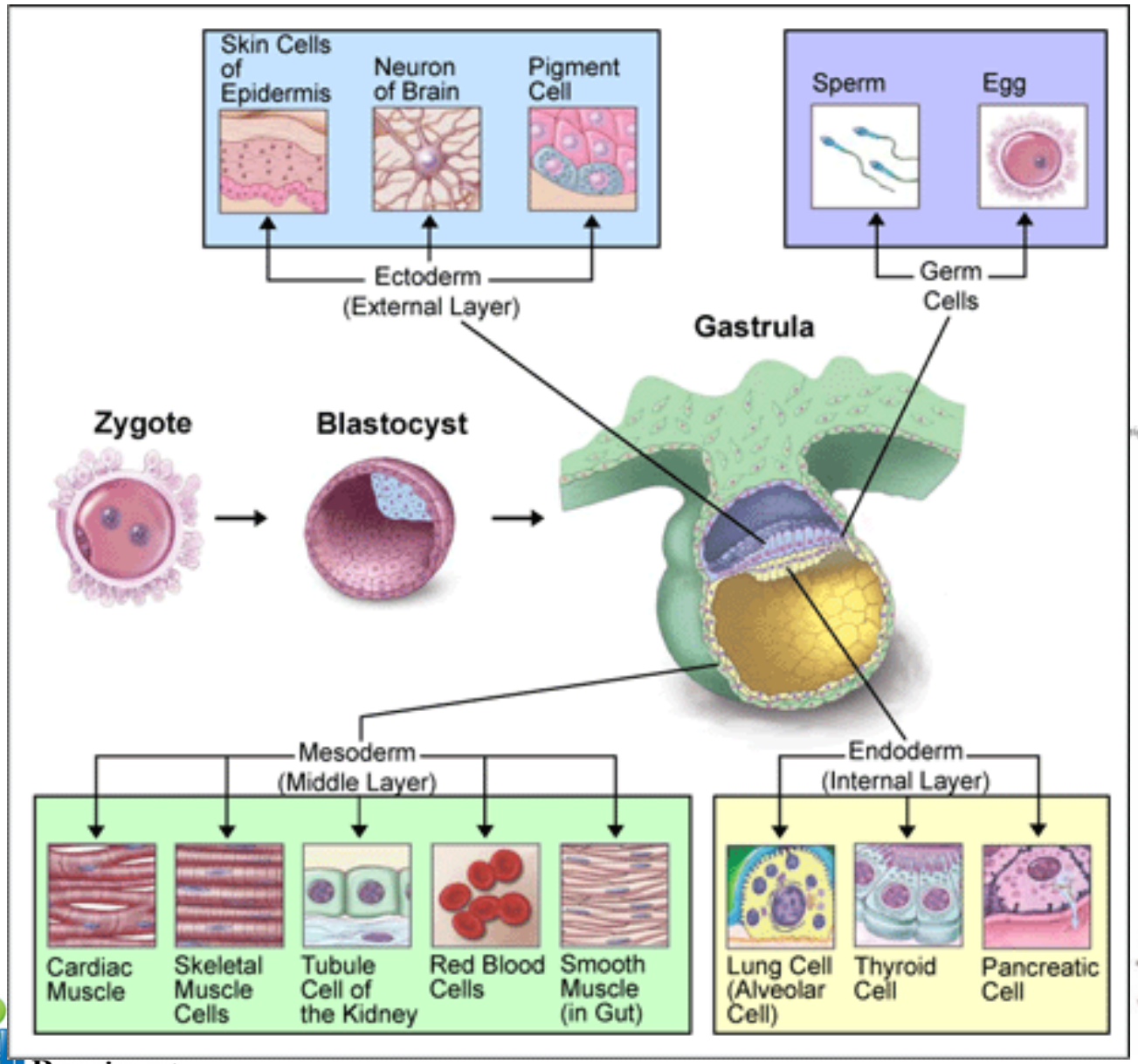
One in a life-time genome + yearly (to daily) tests

Bio-weather map : Allergens, Microbes, Viruses

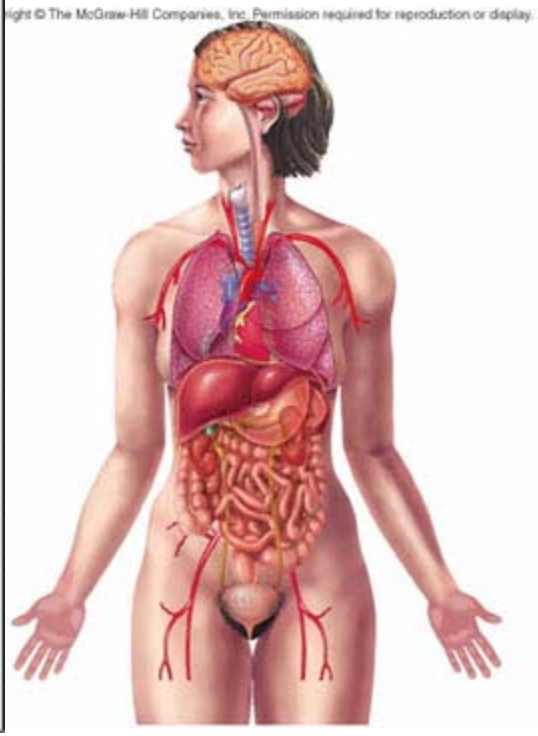


Personal Genome Project

Challenge: Multiple cell types from healthy adults



3mm skin sample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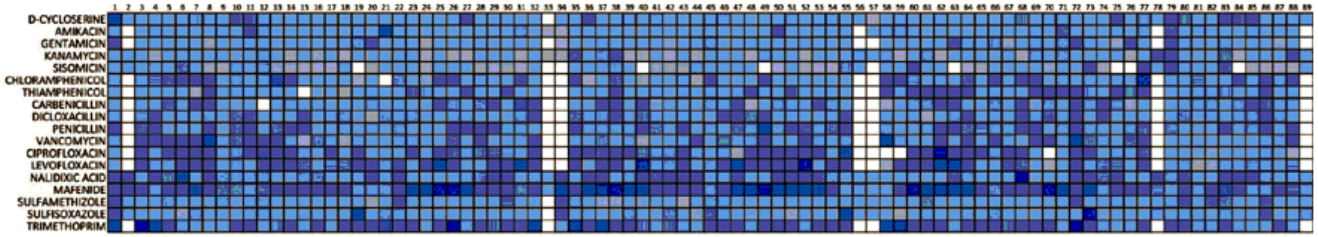
Project

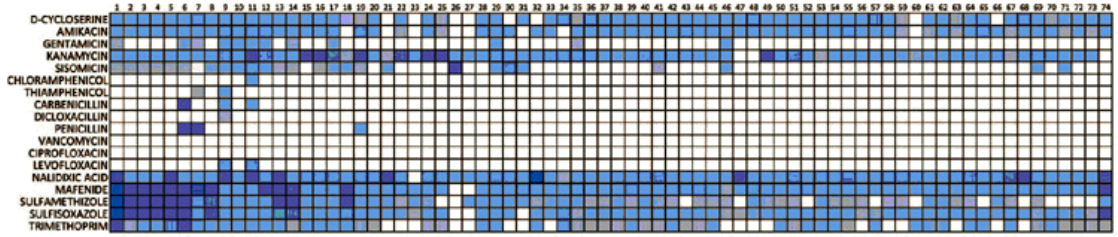
PGP Resistance to 18 Antibiotics

D-CYCLOSERINE
AMIKACIN
GENTAMICIN
KANAMYCIN
SISOMICIN
CHLORAMPHENICOL
THIAMPHENICOL
CARBENICILLIN
DICLOXACILLIN
PENICILLIN
VANCOMYCIN
CIPROFLOXACIN
LEVOFLOXACIN
NALIDIXIC ACID
MAFENIDE
SULFAMETHIZOLE
SULFISOXAZOLE
TRIMETHOPRIM

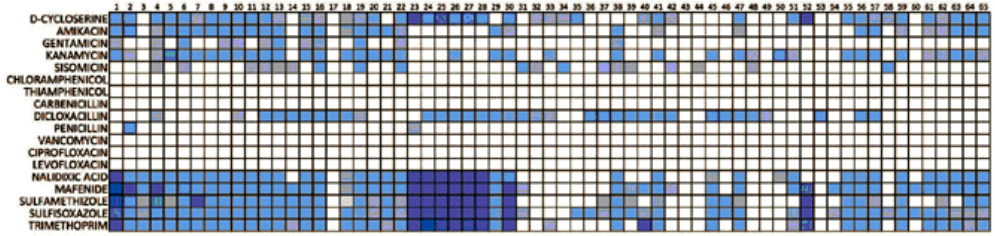
DAY 1



DAY 140



DAY 141



Dantas, Sommer, Church unpublished

Personal Genome Project

Personal Genomics SACGHS Pre-meeting Questions

1 Which diseases for risk assessments? **1288 tests @ Genetests.org**
Physician-ordered versus direct-to-consumer test? **PGP 5 MDs; research approved by DSMB & IRB since 2005.**
2 When is allele & phenotype association strong enough?
To educate: any level. To act: ideally QALY standards
3 Access to genetic counseling services & new discoveries?
Counselors included on PGP research team. Annual updates.
4 Analytically validated & clinical validity? **Multiple tissues for mosaicism & causal mechanisms.**
5 Value of services to consumers? **Research & education**
6 How are data stored & privacy protections ? **Entrance exam and consenting for public release.**
7 Beyond initial analysis, how will data be utilized? **Open research**
8 Requirements for research data access? **None**

Personal Genomics :Alternative Questions

1 How do we fund association studies & education? DTC role?

2 How do we celebrate/incentivize the best new protocols?
(not just scare the worst or reinforce the oldest)

3 What about do-it-yourself (DIY) genetics? and research?

4 Risks of gene info relative to other regulated DTC probabilistic personal research activities: internet, universities, news-media?

5 Risks of NOT educating in face of radical change?

6 Is the model constant & immediate-action (e.g. driving)
or hopefully-never-acting (e.g. accident insurance)?