



Precision medicine

BIO-698: The making of an innovative medicine

with Roger Clerc

Flavia Hodel

Traditional medicine

Doctors prescribe a medication and then wait to see how the patients respond

- » Some will respond positively
- » Some will not respond at all
- » Some will have a negative reaction and suffer side effects



Current "one-size-fits-all" prescribing approach

Every person has a unique variation of the human genome

Although most of the variation between individuals has no effect on health, an individual's health stems from **genetic variation** with behaviors and influences from the **environment**.

Every person has a unique variation of the human genome

Although most of the variation between individuals has no effect on health, an individual's health stems from **genetic variation** with behaviors and influences from the **environment**.

» Single nucleotide polymorphisms (SNPs) – a major source of variation

- Single base-change in DNA
- Arise as a consequence of “mistakes” during normal DNA replication
- Average frequency: 1/1'000 bp

AAGC**C**TA
AAG**T**TA

Other sources of variation: indels, translocations, duplications, repeats, etc.

Personalized medicine

The hope is that a doctor can test a patient's DNA and better predict how he or she might react to a drug.

» The ability to offer:

- The right drug
- To the right patient
- For the right disease
- At the right time
- With the right dosage



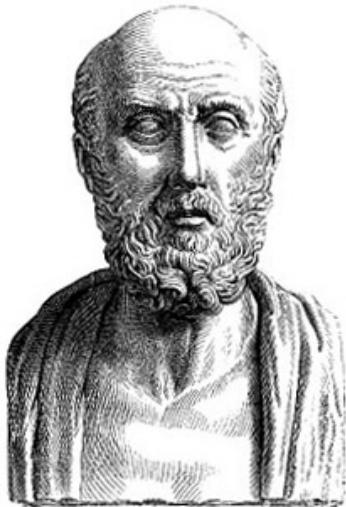
Genetically assisted prescribing approach

Where did it start?



Where did it start?

With Hippocrates? Or with the ambitious plan to sequence the first reference human genome?



It's far more important to know what person the disease has than what disease the person has.

Hippocrates (460-370 BC)



Human Genome Project (HGP) - \$3B

Launched in 1990

Completed in April **2003!**

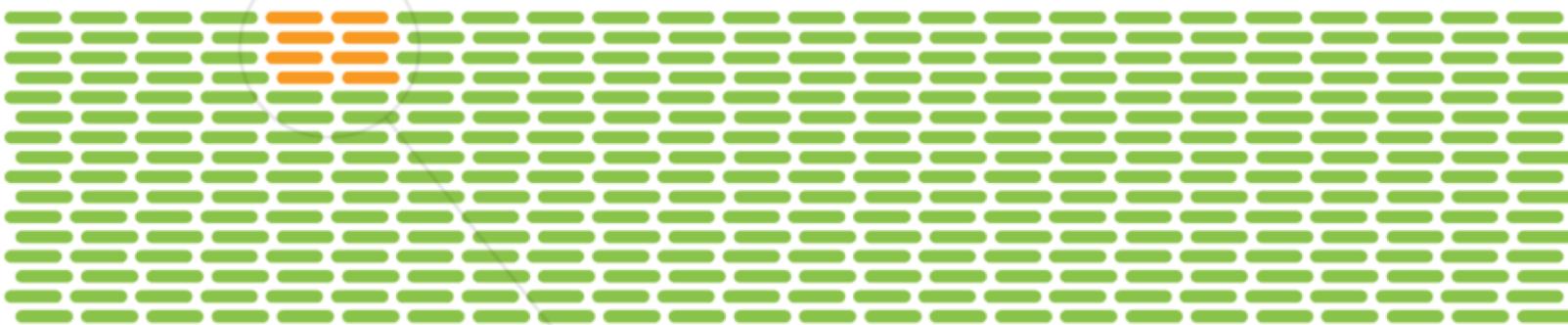
+ 50th anniversary of James Watson and Francis Crick's Nobel Prize winning description of the DNA double helix.

Today

\$ 1'000-2'000

Whole Genome Sequencing

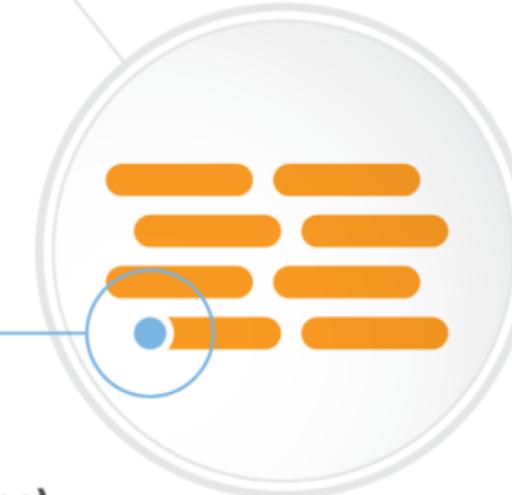
~300,000,000 bases (100% of human genome)



~ \$500

Whole Exome Sequencing

~60,000,000 bases
(~2% of human genome)



\$69

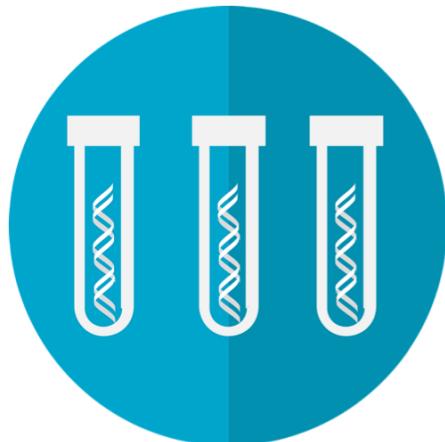
Large Scale Genotyping

~1,000,000 bases
(~0.03% of human genome)

One of the most promising areas: pharmacogenetics

How does a patient's genetic makeup influence treatment effectiveness?

» Genetic/biomarker testing before prescription writing (see *Tim's presentation*)



Biomarker	Application
Her-2/neu receptor	Select Herceptin (trastuzumab) for breast cancer
BRCA1/2	Breast and ovarian cancer inherited risk, prophylactic tamoxifen and surgery
Transcriptional profile – 21 genes	Avoid use of chemotherapy in breast CA patients with low risk of recurrence
CYP2D6/CYP2D19	Guide prescribing/ adjust dose of ~25% of commonly used drugs
VKOR/CYP2C9	Dosing of warfarin

Where is personalized medicine helping most?

Where is personalized medicine helping most?

In cancer!



THE RIGHT PATIENT. THE RIGHT TREATMENT.



Powerful Knowledge.
Personal Treatment.SM

But also: diabetes, Alzheimer's disease, obesity, infectious diseases, ...

23andMe

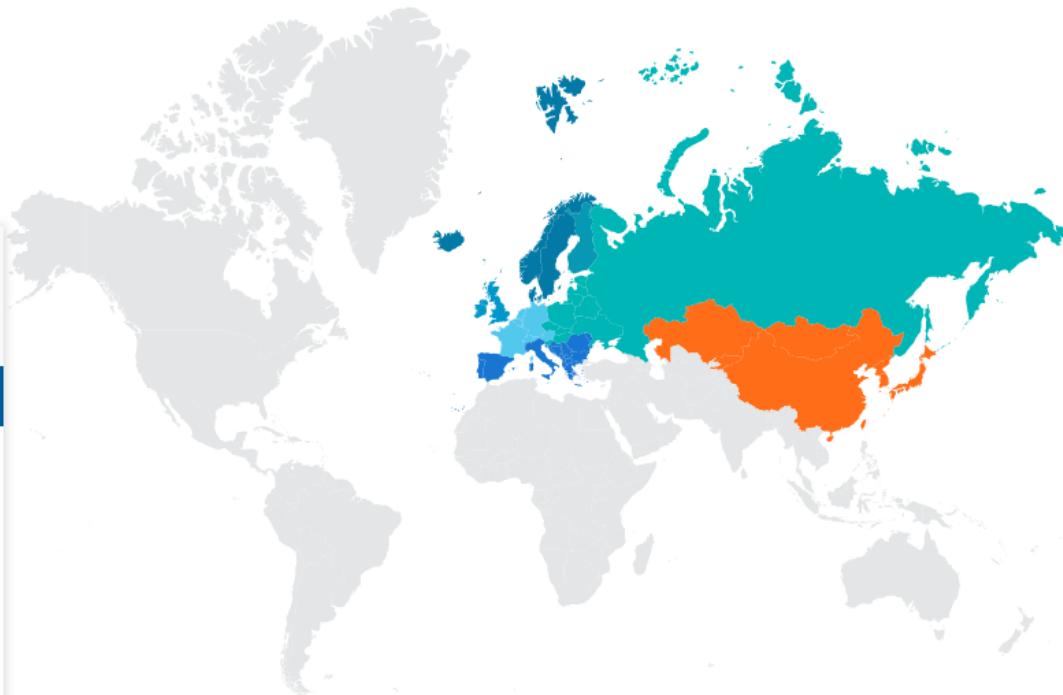
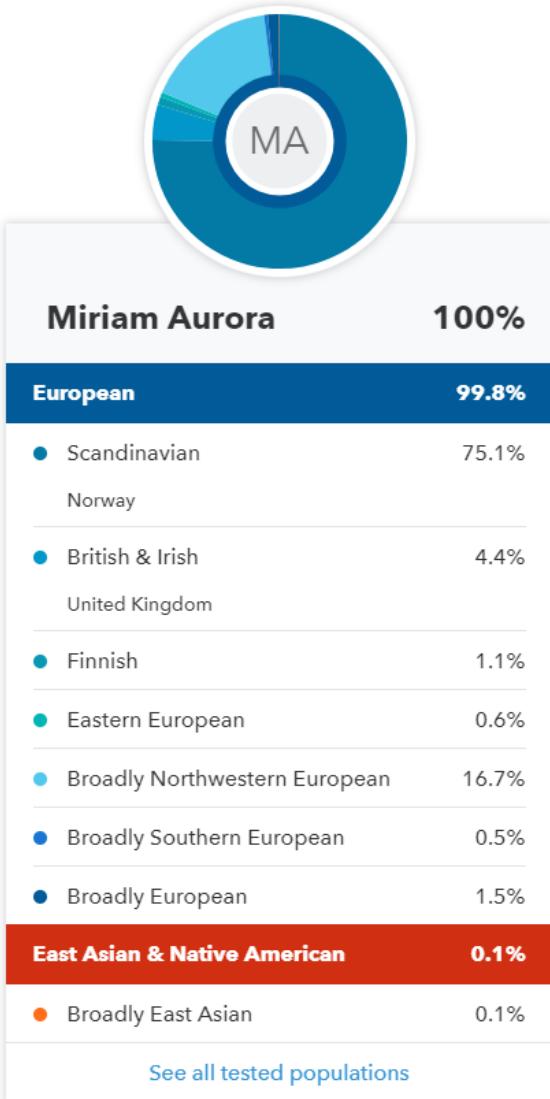


- **Founded in 2006**
- **Direct-to-consumer** genetic testing company
- Saliva-based
- Named “Invention of the Year” by *Time* magazine (2008)
- 2015: Approved by the FDA
- February 2018: > **3 Mo individuals** genotyped
- July 2018: partnering with GlaxoSmithKline (GSK) and will allow the pharmaceutical company to use the test results to design new drugs

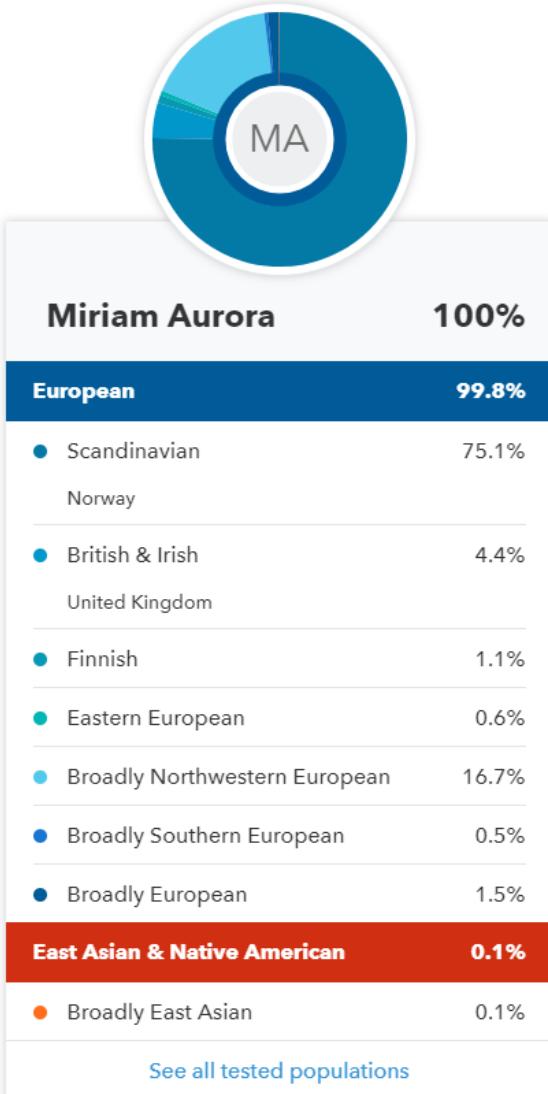


@ASHG in San Diego, October 2018

23andMe (ancestry)



23andMe (ancestry)



Matthew, you have **1188 DNA Relatives** in your 23andMe DNA Family.

You and each of your DNA Relatives share identical segments of DNA that were passed down to both of you from a shared ancestor. Close relatives share a lot of DNA with you, while distant cousins may share a single small segment.



Close Family to Second Cousins

Relationships may include: siblings, parents, children, grandparents, grandchildren, aunts, uncles, first and second cousins.

Third to Fourth Cousins

Relationships may include: third and fourth cousins, first to third cousins once or more removed.

Fifth to Distant Cousins

Relationships may include: fifth and distant cousins, closer cousins once or more removed. What is a fifth cousin? [Learn more.](#)

23andMe (health - Genetic health risk reports)

BRCA1/BRCA2 (Selected Variants)

[Learn more](#)

**Genetic risk based on a limited set of variants
for breast, ovarian and other cancers**

3 variants in the BRCA1 and BRCA2 genes;
relevant for Ashkenazi Jewish descent

Age-Related Macular Degeneration

**Genetic risk for a form of
adult-onset vision loss**

2 variants in the ARMS2 and CFH genes;
relevant for European descent

Alpha-1 Antitrypsin Deficiency

Genetic risk for lung and liver disease

2 variants in the SERPINA1 gene; relevant for
European descent

Celiac Disease

**Genetic risk for gluten-related
autoimmune disorder**

2 variants near the HLA-DQB1 and HLA-
DQA1 genes; relevant for European descent

Etc.

23andMe (health)

» **Genetic health risk reports:** BRCA1/BRCA2, celiac disease, late-onset Alzheimer's Disease, ...

» **Wellness reports:** Alcohol flush reaction, Caffeine consumption, Genetic weight, Muscle composition, Wake-up time, ...

» **Traits reports:** Ability to match musical pitch, asparagus odor detection, bitter taste, eye color, mosquito bite frequency, ...

Your Wellness Result

Jamie, your genes predispose you to weigh about 9% less than average.

This predisposition doesn't mean you will definitely weigh less than average. Keep in mind that your lifestyle and environment have a big impact on your weight.

Your Traits Result



Jamie, your genetics make you **unlikely to detect certain bitter tastes.**

Data privacy. Who owns the data?

These days, individual patients – and sometimes healthy people, too – can have their personal genomes genotyped or fully sequenced.



FAQs

Who has access to my data as a patient?

Solely the health professionals that are in charge of treating you has access to your data. Any other usage of your data requires your informed consent. In the case of a research project, the ethics commission of the respective canton of the research institution needs to additionally approve the usage of your data within the frame of the particular project.

How do you ensure data privacy and confidentiality?

Solely the health personnel in charge of you can access your data. Researchers will only work with encoded or anonymised data.

As a patient, is it possible for me to access my data?

Yes. According to the [Federal Act on Data Protection \(Article 8\)](#) every individual is entitled to request a copy of his/her data from the controller of a data file.

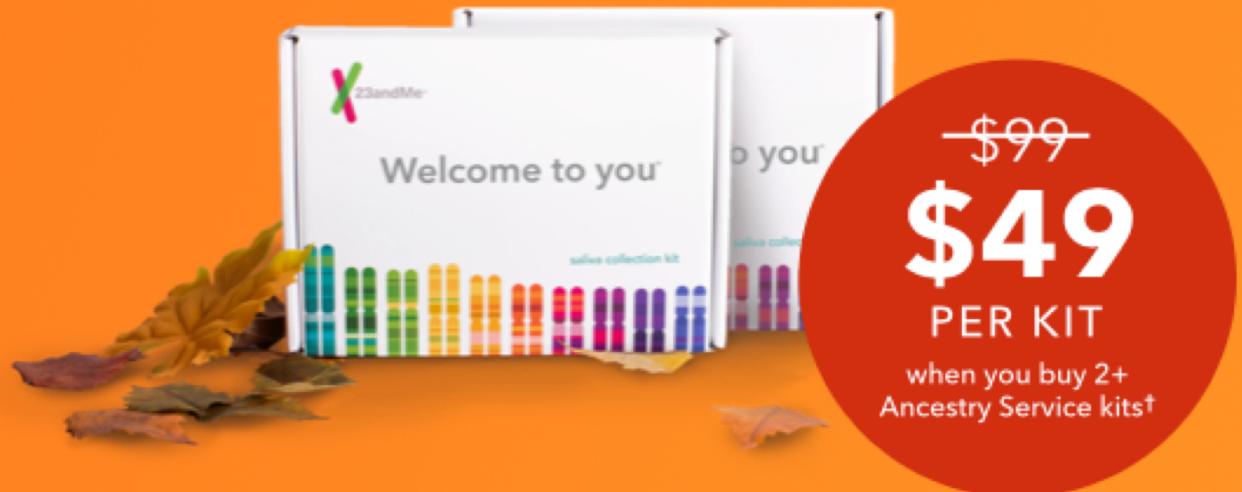


- **New diagnoses:** We may finally be able to identify genetic causes of diseases that were previously unknown.
- **Early diagnosis**
- **Prevention**
- **Drug development:** Therapies can be developed in a faster and more efficient way
- **Personalized treatments:** Treatments can be tailored to a patient's unique genetic aberration and we can avoid giving treatments to patients that we know may cause adverse reactions or that will fail to work.
- **Healthcare costs:** There's a potential to reduce healthcare costs if focus changes to prevention rather than treatment of disease and also if we can streamline drug development.



- **Data storage**
- **Privacy/Security**
- **Culture:** How do we prevent people from abusing this information and not using it to deny insurance coverage, denying jobs? How will this affect culture?
- **Ownership:** Who owns the data? Will it be the government?
- **Drug/device industry:** Genetic research and development of treatments has been very promising and productive in the private sector. How will government involvement affect research? Will our governmental agencies work cooperatively with them or competitively?
- **Healthcare costs:** there's also potential in greatly increasing costs. It's no small feat to genetically map a population, analyze the information, store it safely and securely, and develop recommendations and treatments.

Would you do it?



~~\$99~~
\$49
PER KIT
when you buy 2+
Ancestry Service kits†

Thanksgiving Family Offer

Discover, share and celebrate what connects you and your family.

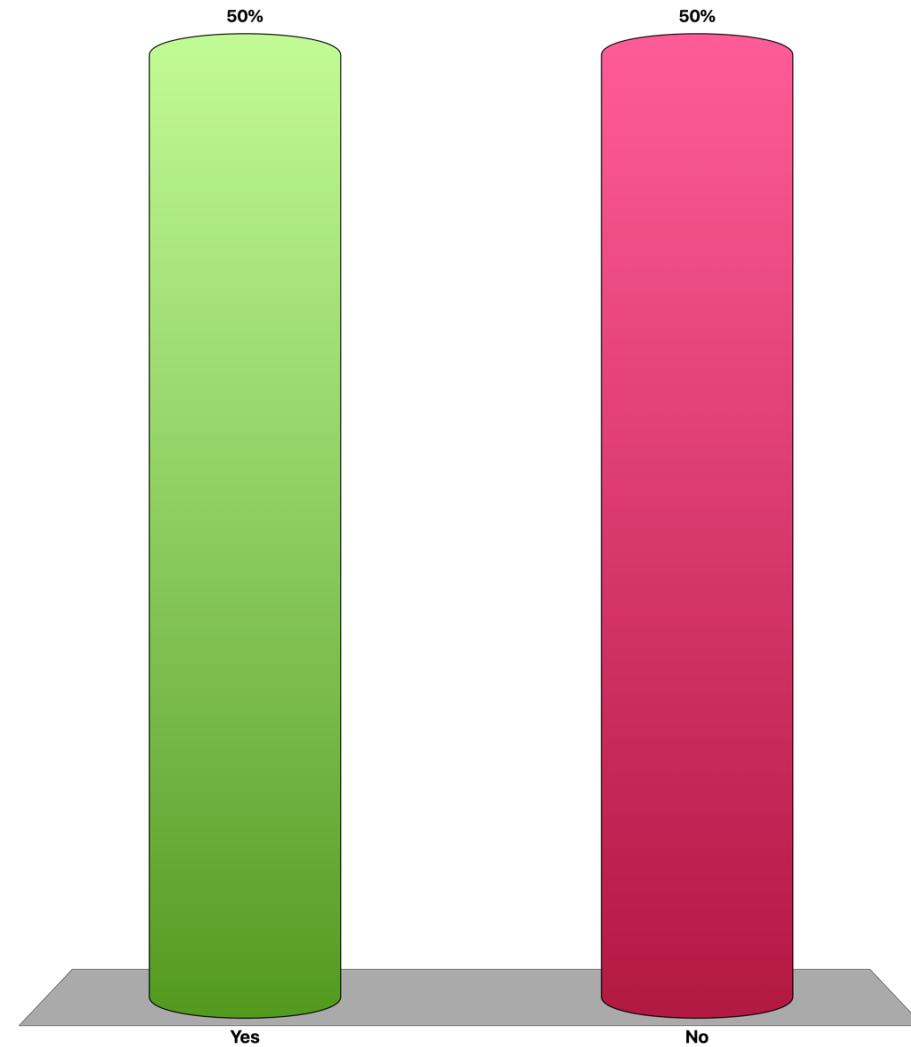
[order now](#)

† One kit for \$69 or two or more kits for \$49 each. Savings based on regular price per kit. Offer ends Nov 22.

Would you do it?



- A. Yes
- B. No





Thank you!

Flavia Hodel