Do You Want Fries With That?- The Pros and Cons of Direct to Consumer Genetic Testing

'Big Genetics' Sessions

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Disclosure Slide: Matthew Taylor (2018)

I have financial ties that may (or may not) relate to the content of this presentation that are disclosed to the University of Colorado:

- *Allomek*
- *American Board of Medical Genetics and Genomics*
- *American college of graduate medical education (ACGME)*
- *Arca Biopharma Inc.*
- *Array Biopharma*
- *Biomarin Pharmaceuticals, Inc.*
- *CU Medicine*
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- *Genzyme, a Sanofi Company*
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- *Rocket Pharma*
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Second Disclaimer

- Several commercial companies will be mentioned in this presentation
- It is not my intent to endorse or negative criticize any company(ies)
- I have had my DNA analyzed by 23andMe and have had whole genome sequencing completed by Illumina

Do You Want Fries With That?-

The Pros and Cons of Direct to Consumer Genetic Testing

Session Objectives

- Describe the current Direct to Consumer (DTC) Genetic Testing landscape
- Evaluate the positive aspects of DTC Genetic Testing (both purported and real)
- Appraise the potential drawbacks and limitations of DTC Genetic Testing
- **Choose how you will approach DTC Genetic Testing with your patients (…Discussion)**

Describe the current Direct to Consumer (DTC) Genetic Testing landscape

Definition of Direct To Consumer (DTC) Testing

- Commercial genetic testing companies
  - ancestry, traits, disease risk, pharmacokinetics, paternity
  - ~Target 'common', low/non penetrant variants
- Ordering provider ~not required
- Patient (consumer) driven:
  - decides whether to share results with providers
- $15M^{2010} \rightarrow \$130M^{2015} \rightarrow \$350M^{2020}$

Clinical vs. Direct To Consumer (DTC)

Clinical Genetic Testing

- Germline mutation(s) suspected
- Ordered by health provider with Gen Counseling
- Results shared with patient
- 'Interpreted' by health provider

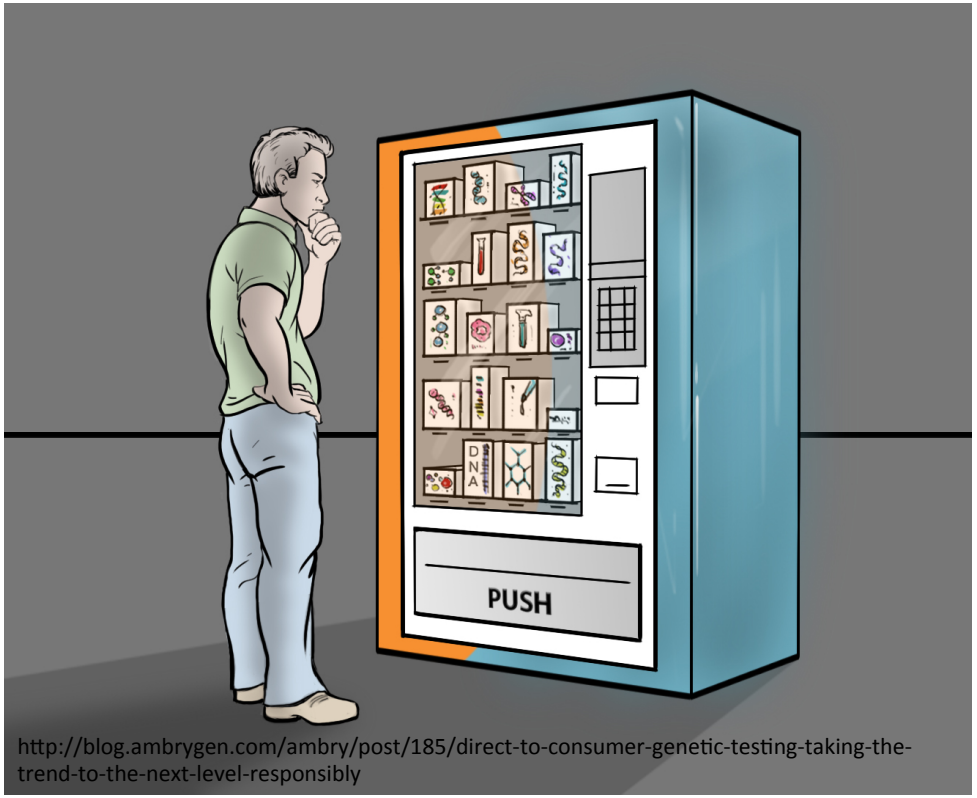
Direct To Consumer

- Specific mutation often not suspected
- Purchased by consumer w/o counseling
- Results received by person
- Interpretation by lab / company / website

Some DNA testing companies

- 23andMe)
- 23mofang
- 24 genetics
- African Ancestry
- AfricanDNA
- AncestrybyDNA
- AncestryDNA,
- Atlas Biomed
- Centrillion Biosciences
- Dante Labs
- DNA Ancestry and Family Origin
- DNA Consultants
- DNA Tribes
- DNA Worldwide
- Family Tree DNA)
- Full Genomes Corporation
- Gene by Gene
- Genebase
- GenoTek
- Genographic Project
- Genos Research Inc
- Helix
- iGENEA
- Living DNA
- MyHeritage DNA
- Oxford Ancestors
- Roots for Real
- Sorenson Genomics
- Sure Genomics
- TribeCode
- Veritas Genetics
- Xcode
- WeGene
- YSEQ
- Yoogene

International Society of Genetic Genealogy Wiki



http://blog.ambrygen.com/ambry/post/185/direct-to-consumer-genetic-testing-taking-the-trend-to-the-next-level-responsibly

Timeline

- 2010: >30 companies, > 400 tests[1]
- 2011: AMA sends letter to FDA suggesting that all genetic testing involve a physician[1]
- 2013: FDA halted 23andMe genetic health screening
- 2015: FDA lifted ban
- 2017: FDA approved DTC genetic testing (23andMe; 10 diseases)
- 2018: FDA approved DTC genetic testing (23andMe; BRCA1/2)

1) Bloss et al. Human Molecular Genetics, 2011

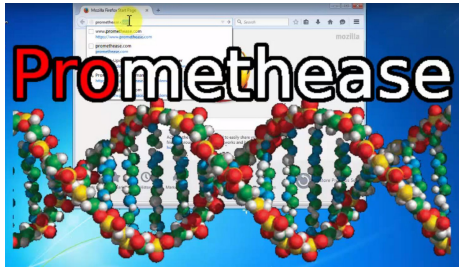
23andMe Genetic Health Risk

2017 FDA APPROVED

- **(2) Parkinson's disease** (LRRK2, GBA)
- **(1) Late-onset Alzheimer's** (APOE)
- **(2) Celiac disease** (HLA-DQB1 & DQA1)
- **Early-onset primary dystonia**
- **Factor XI deficiency**
- **Gaucher disease type 1**
- **(2) Alpha-1 antitrypsin deficiency** (SERPINA1)
- **(1) Glucose-6-Phosphate Dehydrogenase deficiency**
- **(2) Hereditary hemochromatosis** (HFE: C282Y, H63D))
- **(2) Hereditary thrombophilia**, (Factor II & V)

2018 SEPTEMBER

- **X(2) Age-related macular degeneration** (Y402H, A69S)
- **(3) BRCA1/2** (185delAG, 5382insC, 6174delT)
- ~~**Early-onset primary dystonia**~~
- ~~**Factor XI deficiency**~~
- ~~**Gaucher disease type 1**~~



XCODE LIFE

SNPedia

WatershedDNA .com

https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm551185.htm

https://permalinks.23andme.com/pdf/PN-20-0279.pdf

YouTube

9_African American DNA Results

Evaluate the positive aspects of DTC Genetic Testing (both purported and real)

Arguments Favoring Value of DTC

- Enhances individual autonomy / choice
- Denying access is paternalistic
  - Patient access tools exist (thermometers, BP & glucose monitors, pregnancy & HIV tests, fecal blood)
- Right to access one's own genetic information
  - Right to privacy for one's own genetic information
- Power to understand disease risks could motivate persons to improve their health

Patient / Consumer Comments

- *I think this is the early stages of the new medical era…although information is preliminary just knowing about yourself things you didn't know before I think is amazing. I just had my test done this week and looking forward to the results.*

- Carlos

CDC Genomics and Health Impact Blog: Direct to Consumer Genetic Testing: Think Before You Spit, 2017 Edition!

Patient / Consumer Comments

- *I received health risk assessment information from a DTC several years ago and have found it quite useful. Knowing that I was at higher risk for 2DM, I have been more careful of weight and diet. Knowing that I was at higher risk for macular degeneration, I've not skipped eye examinations and won't… It's good to have all the information you can get. Medical professionals will just have to be brought into the modern era and quickly and should not ignore or resent it when their patients are knowledgeable about genetics.*

- Jean

Appraise the potential drawbacks and limitations of DTC Genetic Testing

Arguments Concerning Risks of DTC

- Are consumers sufficiently informed / risking misinterpretation?
- Are the DTC tests all appropriate / have sufficient clinical utility?
  - Should results with low-predictive-indices be reported (GWAS variants)?
- Accuracy of results (false positives and false negatives)
  - Unnecessary worry/anxiety or inappropriate reassurance
- Inconsistent 'results' across different DTC tests?
- What are the privacy / confidentiality issues?
  - Commercialization (sale of genetic information / companies being bought/sold)

Patient / Consumer Comments

- *The average PCP does NOT have enough genetic education to be able to interpret the test results. My PCP…didn't understand enough about genetics to correctly access my health risk assessment based upon family health/medical history. My high school genetics from Canada turned out to be more genetic education then he received in medical school*

- Sheri

CDC Genomics and Health Impact Blog: Direct to Consumer Genetic Testing: Think Before You Spit, 2017 Edition!

Sara Altschule did DTC testing for ancestry purposes. Received email about BRCA1/2 testing being now available, chose to get those results → learned she had a BRCA mutation. Concerning, given she had a paternal cousin (once-removed) who had breast cancer and died of ovarian cancer.

If you would have told me at the beginning of this year that I would be writing a column on BRCA, I would have thought you'd got the wrong gal. But I like to think of myself as a "glass half full" kind of person. And currently, my glass is filled with hope — hope that I'm making decisions that may one day save my life.

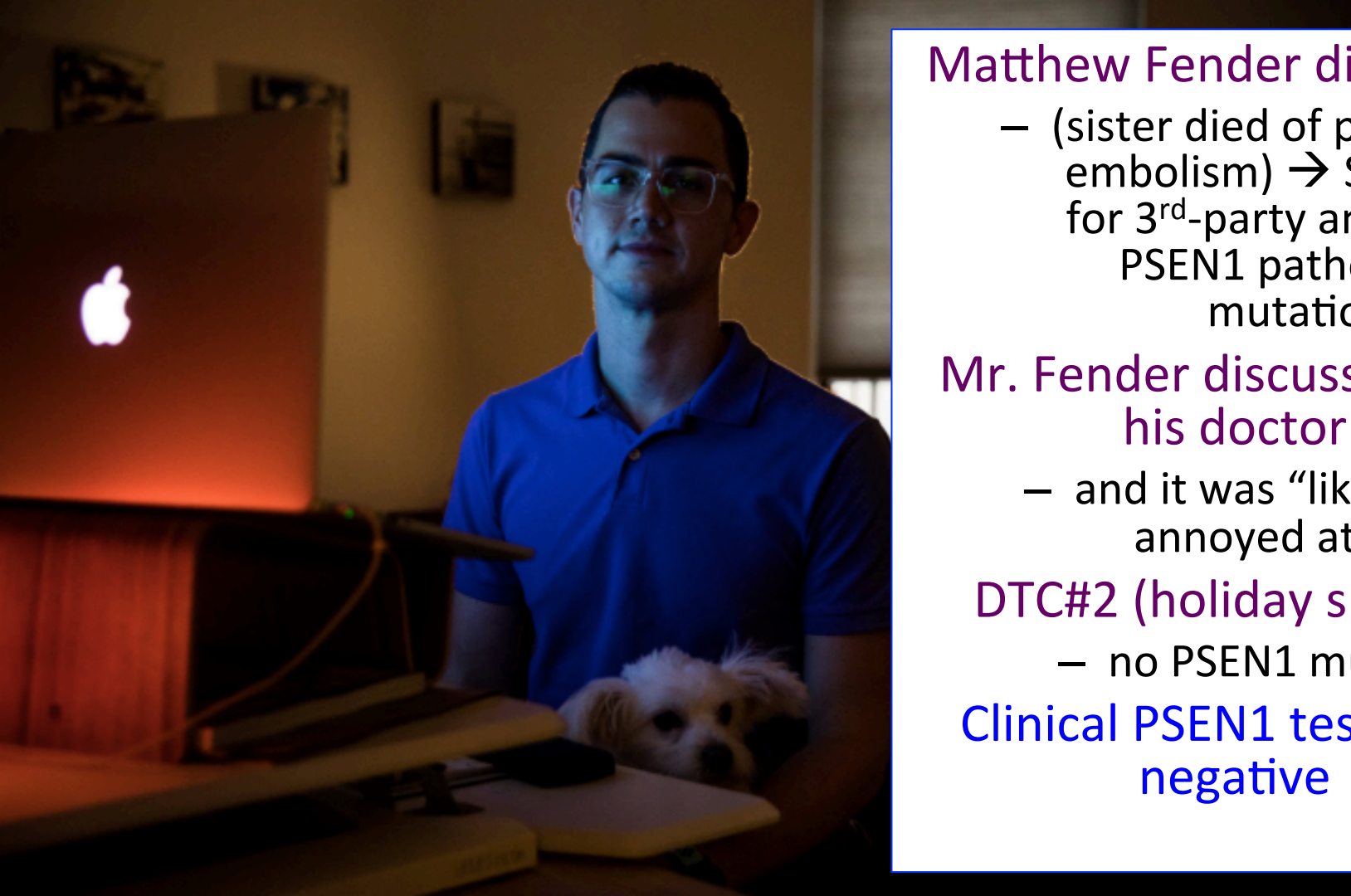
Dr. Josh Clayton, a 29 year-old radiology resident did ancestry testing. He then submitted results to online health analysis company, revealing he had a Lynch syndrome mutation.

Subsequent clinical Lynch syndrome testing proved the original results were a false positive.

NY Times

28 year-old woman DTC testing

- Submitted results for 3rd-party analysis → homozygous for pathogenic COL3A1 (vascular Ehlers Danlos syndrome)
- Previously seen by genetics → hEDS
  - (normal echocardiogram; non-concerning family history)
- Repeat clinical sequencing of hEDS → homozygous normal



Matthew Fender did DTC#1

- (sister died of pulmonary embolism) → Sent data for 3rd-party analysis → PSEN1 pathogenic mutation

Mr. Fender discussed with his doctor

- and it was "like he was annoyed at me,"

DTC#2 (holiday special)

- no PSEN1 mutation

Clinical PSEN1 testing → negative

62 year-old woman DTC testing

- MD contacted us with comment
  - *"…she had a [DTC] genetic test which says she is a male… Do you have any recommendations?*
- *DTC Company letter to patient*
  - *"Upon review of your data…it appears our formula classified your sex, based on your DNA, as male…if the results of our analysis are unexpected, we encourage you to consult your physician or a genetic counselor.*
- Clinical diagnosis → Androgen Insensitivity Syndrome

ORIGINAL RESEARCH ARTICLE | Genetics inMedicine

Open

False-positive results released by direct-to-consumer genetic tests highlight the importance of clinical confirmation testing for appropriate patient care

Results: Our analyses indicated that 40% of variants in a variety of genes reported in DTC raw data were false positives. In addition, some variants designated with the "increased risk" classification in DTC raw data or by a third-party interpretation service were classified as benign at Ambry Genetics as well as several other clinical laboratories, and are noted to be common variants in publicly available population frequency databases.

Conclusion: Our results demonstrate the importance of confirming DTC raw data variants in a clinical laboratory that is well versed in both complex variant detection and classification.

Genet Med advance online publication 22 March 2018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Thank you for your attention

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