Technologies,

Platforms &

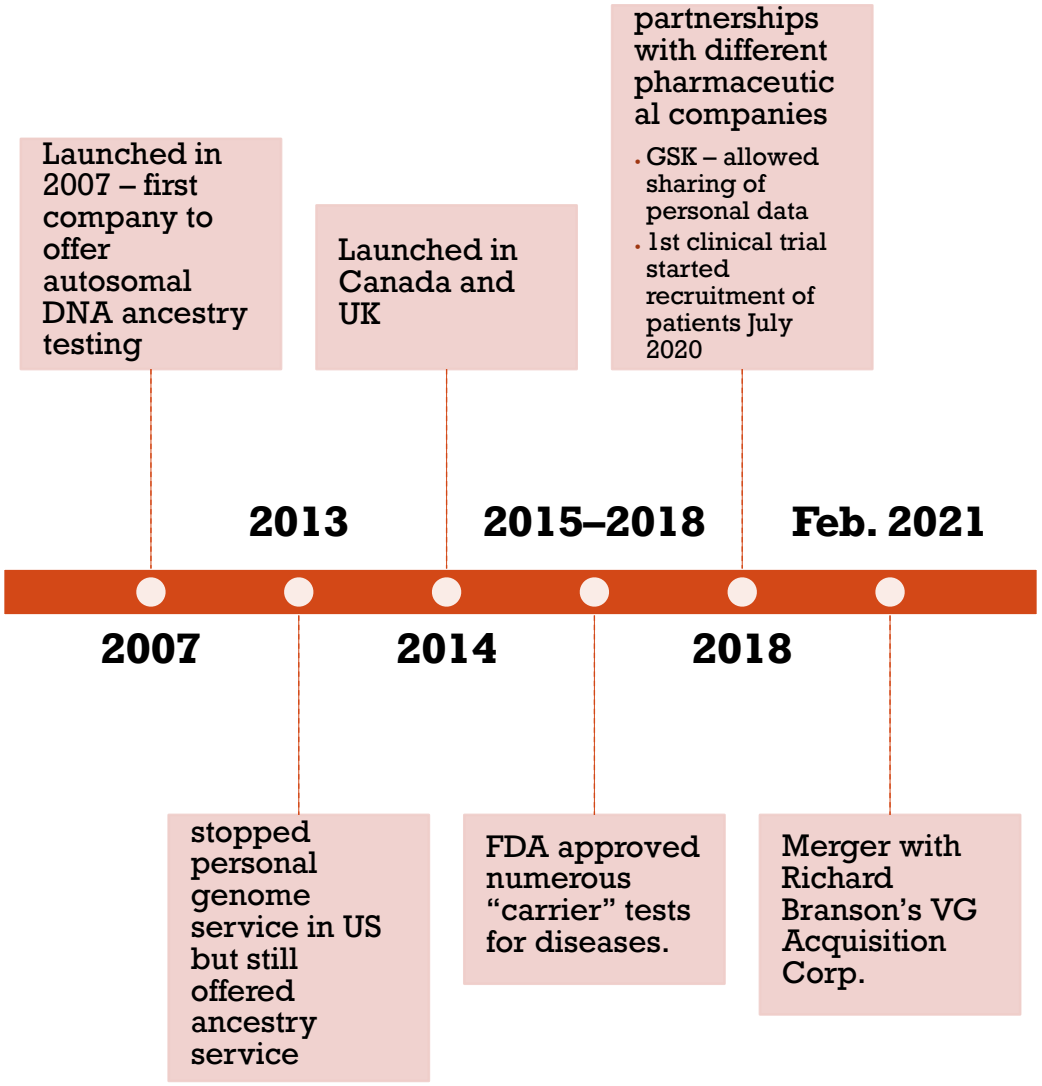
Tests

DIRECT TO CONSUMER TESTS

- Usually require a biological specimen (eg saliva) which is then sent to company for analysis

- Microbiome
- Toxins
- Ancestry
- Prediction of disease risk

- 23 & Me named as there are 23 pairs of chromosomes in a normal cell


Launched in 2007 – first company to offer autosomal DNA ancestry testing
Launched in Canada and UK
partnerships with different pharmaceutical companies
GSK – allowed sharing of personal data
1st clinical trial started recruitment of patients July 2020
2007
2013
2014
2015–2018
2018
Feb. 2021
stopped personal genome service in US but still offered ancestry service
FDA approved numerous "carrier" tests for diseases.
Merger with Richard Branson's VG Acquisition Corp.

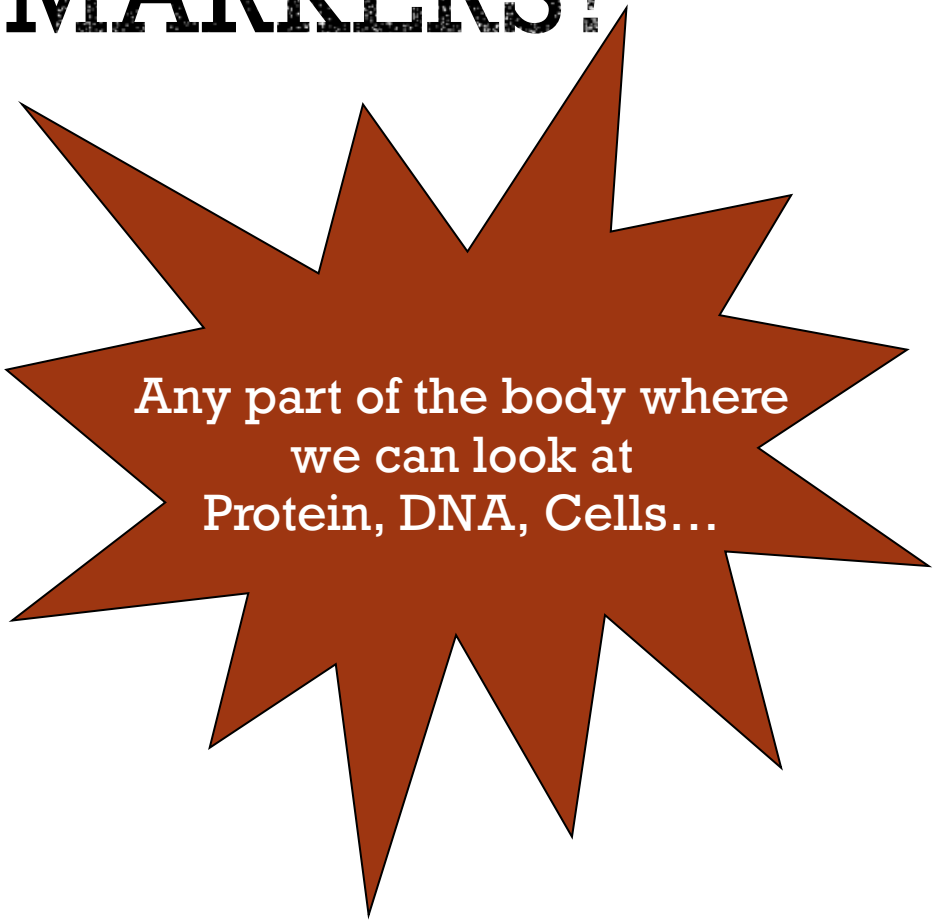
WHAT ARE WE TRYING TO DETECT?

Trying to detect a target or multiple targets that tell us about the disease

They can help with prediction, cause, diagnosis, progression, regression, or outcome of treatment of disease

WHERE DO WE DETECT THESE BIOMARKERS?

- Tissue
  - Normal
  - Diseased
- Blood
- Saliva
- Sweat
- Hair
- ….



COMMON TECHNOLOGIES EMPLOYED

- To identify DNA / Genetic biomarker(s) from patient:
  - DNA sequencing
  - PCR
  - Microarrays

- To identify protein biomarkers(s) from patient:
  - The enzyme-linked immunosorbent assay (ELISA)
  - Gel electrophoresis
  - Surface plasmon resonance (SPR)
  - Mass-sensing BioCD protein array
  - Surface enhanced Raman spectroscopy (SERS)
  - colorimetric assay; electrochemical assay; fluorescence methods

ONE OR MORE?

- We can look for the presence of
  - A single gene or protein or
  - Multiple individual genes or proteins or
  - Multiple variations in genes or proteins or
  - A signature which tells us how multiple gene/proteins/variations together contribute towards a disease

TESTING

- If more than one biomarker is known to be involved in a disease process, technology allowing identification of more than one biomarker at a time is far more beneficial for patient and health service

- Reduces costs of performing multiple single tests
- Reduces variability in test performance and accuracy
- Provides all results at one time

- ***Bundled Tests***: multiple independent tests from same sample
- ***Multiplexing***: measured from same analyte at same time and quantified at same time

Examples of different types of technologies and platforms and what their applications are

COMPANION DIAGNOSTICS (CDX)

- Zelboraf – CDx Cobas™ Platform (Roche)
- Detects BRAF V600E mutation
  - Via real time polymerase chain reaction
- CDx FDA approved and help accelerate product to market
- So, one process validated and approved
  - Good thing?

WHAT HAPPENS WHEN WE DON'T HAVE A CDX?

Gefitinib
Tyrosine kinase inhibitor

Used in non-small cell lung cancer (NSCLC) with EGFR-TK mutations that activate the growth factor

Promise of improved clinical outcome by stratifying population

Approval by NICE in 2010

>10 tests used to detect mutation – not validated as being equivalent

Clinical outcome limited / jeopardised?

Different tests need to be compared and linked to patient outcomes

ONCO*TYPE* DX

- Identifies the underlying tumour biology for breast cancer
  - 16 genes associated with breast cancer
  - 5 housekeeping genes
  - Detects these genes and uses a mathematical formula to calculate the Reoccurrence score®
  - Score 1-100 determines whether chemotherapy required
- Likely reoccurrence of tumour within next 10 years can also be checked

ONCO*TYPE* DX

- Used in patients that are positive for ER (oestrogen receptor) and negative for HER2
- Biopsy taken by pathologist; tissue sent to Genomic Health® Lab
- Costs $4175 (£2500 in UK)

AMPLICHIP CYP450 TESTS (ROCHE)

- Determines metabolic capacity of person
- Analysis of CYP2D6 and CYP2C19
  - Multiple SNPS and other variations
- Microarray-based test (Affymetrix)
  - Uses DNA purified from blood
  - FDA approved

PGX PREDICT CLOZAPINE

(GENAISSANCE PHARMACEUTICALS INC)

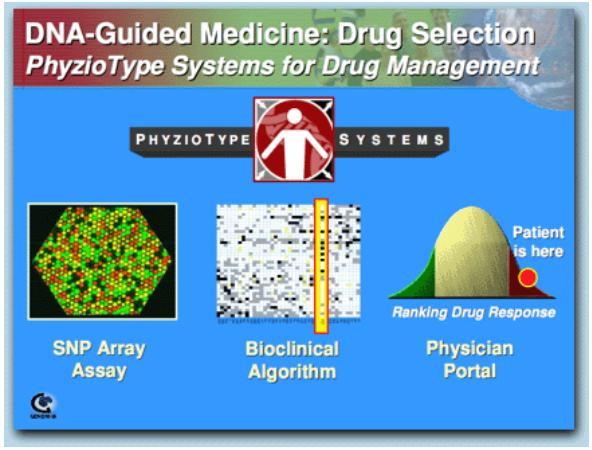
- Antipsychotic
  - Can cause agranulocytosis
  - Weekly blood monitoring
- Associated with variants in HLA complex (part of the immune system)
- Identifies 10 genes to give
  - Drug metabolism profile
  - Blood clotting factors
  - Metabolic genes
  - Blood clotting genes
  - P-glycoprotein
  - HLA variants

PGX PREDICT CLOZAPINE

- FDA approved
  - 21% sensitivity
  - 98% specificity
  - Lack of clinical take up so taken off market

PHYZIOTYPE (GENOMAS)

- Used to detect antipsychotic drug-induced metabolic changes
  - Weight gain
  - Hyperlipidemia
  - Diabetic risks



- Identifies SNPs in genes associated with
  - Antipsychotic pharmacology
  - Appetite control
  - Energy regulation
  - Endocrinology
  - Cholesterol homeostasis

- Signature used with biomathematical algorithm to determine risk profile

GENESIGHT PSYCHOTOPIC TEST

- DNA test looking for specific mutations in genes associated with:
  - Efficacy of antidepressants
  - Metabolism of antidepressants

- Allows for better dosing and drug selection for patients

- https://www.bloomberg.com/news/articles/2019-08-14/dna-test-for-depression-drugs-raise-fda-doubts-cratering-myriad

TELEMEDICINE & BIOSENSORS

- Mobile health (mHealth)

- Prolific market: measure tremor and freezing of gait most commonly

- DynaPort MiniMod Hybrid (worn on the lower back),
- Parkinson's Kinetigraph (a wrist worn logger),
- KinetiSense motion system (for dyskinesia measurements),
- ActivPAL, Stepwatch 3 (step activity monitor),
- Shimmer (records walking and turning),
- Mobi8Senior mobility monitor (SMM, Philips),
- SENSE-PARK system (for gait, hypokinesia, dyskinesia, sleeping),
- GAITrite (gait analysis systems),
- Opal (to asses quality of turning),

3D PRINTING

- 3D printing of pills
  - Allows polypills to be formed
  - Change dose according to patient specific age, weight, organ function
  - Change in dissolution rate of tablets (eg Spritam for epilepsy) http://www.computerworld.com/article/3048823/3d-printing/this-is-the-first-3d-printed-drug-to-win-fda-approval.html

- 3D printing of organs and tissues
- Fripp Design, Sheffield

3D PRINTING

Advantages

- Highly adaptable
- On-demand
- Fast prototyping
- Cost effective
- Allows complex and intricate design
- Scalability

Disadvantages

- Sustainability: plastics used; energy used
- Inconsistency
- Cyber Risk
- Copyright
- Low throughput

CONCLUSION

- Lots of potential exciting avenues
- Still a lot of work for most to make benefits clear
- What happens when genetics don't underlie the disease or are too complicated?