How can we generate economic value from personalized medicine and big data analysis?

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Past and Future Practice of Medicine

The past 1000s of years
Diagnosis and treatment based on what could be seen, smelled, tasted, palpated or intuited (anatomical)

The last 10-100 years (clinical insight)
Diagnosis and treatment based on increasing knowledge about biochemistry and cellular processes (cellular)

Today (generalised guidelines)
Diagnosis and treatment increasingly based on rapidly growing insights into molecular biology, genetics and molecular imaging. (molecules, genes and pathways)

Tomorrow (back to personalised)
Patient management based on individualized computer prediction of optimal therapies for individual patients.
How to create Economic Value in Health

1. More effective health care provision at the same cost
2. The same health care for lower cost
3. Innovative Products and Services to allow others to do 1 and 2.
4. More research funding from International Sources
5. Real world data for clinical trials and registration studies
Science "the precursor of chemical pharmacology and therapeutics and the most original medical thinker of the sixteenth century."

Studied alchemy, surgery, and medicine at the University of Basel

Thrown out! Forced to leave the city hurriedly after trouble over his studies in "necromancy". Developed new antibiotics in Middle East

Returned to Basel to take a professorship of physics, medicine, and surgery offered to him at the insistence of Erasmus.

Thrown out! The medical faculty were infuriated at their authority being undermined and he was forced to leave Basel once again

Auroleus Phillipus Theostratus Bombastus von Hohenheim 1493-1541
Healthcare pressures

More effective drugs and treatments required

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Safety</th>
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<tr>
<td><strong>Drug Response Rate, %</strong></td>
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- **Stratified**
- **Analgesics**
- **Cancer**

Spears et al., Trends Mol Med, 2001; Lazarou et al., JAMA, 1998
Response to V Raf inhibition in 15 weeks followed by resistance

B = 15 weeks Rx (Zelboraf®)
C = 23 weeks Rx and emergence of MEK1C1215 mutant (Wagle et al. (2011))
Non-responders to Oncology Therapeutics Are Highly Prevalent and Very Costly

Avastin
$3.059B
Responder
Non-responder

Rituxan
$2.466B

Herceptin
$1.526B

Revlimid
$1.373B

Gleevec
$1.285B

Taxotere
$1.042B

Alimta
$975M

Gemzar
$723M

Tarceva
$661M

Femara
$650M

Erbitux
$646M

Velcade
$598M

Xeloda
$508M

Arimidex
$494M

Leuplin
$483M

Rethinking Clinical data and its impact on Medical relevance

- Phase three clinical trial data are not often closely related to the real world
- Can we run clinical trials in the real world of medical practice?

- Observational data is now used as control for orphan diseases approval studies

- Requires new statistical approaches to analyze Complex multi-dimensional data

- Prospective studies on existing ongoing extensive data sets may become the most effective way to make progress in medicine as blinded prospective studies become too long and cumbersome
Towards Personalized cancer testing and therapy: How can genetics help focus Diagnostics and Therapies to patients who benefit?

1. DNA test for genetic risk
2. Environmental risk
3. Blood tests - Circulating Tumour DNA Exosomes etc.
4. Physical tests – Mamography etc
5. Biopsy - Immunoscore
6. Full panel test on tumor sample
7. Best Treatment with available technologies and agents
Caris Molecular Intelligence™ (CMI) matches patient-specific biomarkers to potential therapies to help doctors individualize cancer treatment.

**Sophisticated Tumor Interrogation & Analysis**
- Microdissection of tumor samples by pathologist
- Polymerase chain reaction (PCR) and next-generation sequencing (NGS) – identify mutations
- Fluorescence (FISH) and chromogenic (CISH) in situ hybridization – detect gene rearrangements and gene copy number variations
- Immunohistochemistry (IHC) – determines a biomarker’s level of protein expression
- Sanger Sequencing, Pyro Sequencing, Fragment Analysis

**Extensive Clinical Literature Assessment**
- Maintain an up-to-date repository of the world’s most relevant clinical literature
- Caris has reviewed over 120,000 clinical literature publications
- Creates recommendations based on the strength of clinical evidence supporting associations between biomarkers and treatments
- Performed by disease-specific clinical advisory boards and a team of Ph.D. scientists, oncologists, and pathologists
- Most relevant evidence is assembled into each MI Profile report
Caris Molecular intelligence:
Companion diagnostics & NCCN-Guidelines require a multi-technology approach to connect biomarkers to medicines

For illustrative purposes. For a complete list of therapies assessed by Caris, please view the profile menu.
Caris Clinical Research Activities

Leadership in Oncology Research

Collaboration with Vector Oncology Solutions

- For patients treated with therapies consistent with CMI recommendation
- Track therapeutic response and outcomes for patients with the following tumor types: Sarcoma, Pancreatic, Breast, Lung, Ovarian and Rare tumors

Research Case Study: CMI for Ovarian Cancer

- Median survival was 2.5 years longer after disease recurrence
- Results published at ASCO 2014

Caris Prospective Observational Study

- Multi-center, observational outcomes database
- Launched December 2009
- Collects data on the demographics, presentation, diagnosis, treatment, resource use, and outcomes of eligible patients
• More research Funding
Innovative Medicines Initiative (IMI)

• Public-private partnership between the European Commission and the European Pharmaceutical industry (28 companies)

• Currently the biggest European PPP initiative (over 2 billion Euros)

• Promote innovation in R&D

• IMI 2 now - Budget 3.5 Billion Euros

Horizon 2020
Drug Screening on Leukemia Patient samples: FIMM, Helsinki

Drug sensitivity and resistance testing (DSRT ex vivo)

Individual cancer samples & clinical data

Integrated cancer drug sensitivity and molecular profile database

Compendia of responses to drugs

Genomics & Molecular profiling (in vivo)

Genomics & cell signalling

Driver signals and pathways for cancer

Patient-specific treatment recommendations

Patterns of response highlighting MOA, new drugs and biomarkers
Genetic Risk

• How can we use genetics to redefine human disease?

• Schizophrenia - “autoimmune or neurodegeneration”

• Redefinition of classes of “Alzheimer’s”

• Autoimmune and Inflammatory Disease (MS)
Redefinition of Alzheimer’s disease

- Multiple mechanisms may be responsible
- Well characterized patients essential (sleep, activity ...)

Diagram:
- Insulin insensitivity (diabetes)
- Vascular
- Synaptic malfunction
- Tau and Amyloid
- Inflammation
How can genetics help focus Diagnostics and Therapies to patients who benefit?

Cardiovascular disease

- Genetic risk
- Environmental/lifestyle risk
- Incentives for lifestyle changes (it worked for smoking!!)

- Focused testing – ECG, ultrasound,
- Therapy
How can we use Genetic risk manage incipient disease
A Finnish Cardiovascular study?
The Cardio Compass study, Finland

- **N = 120 people**
- Systems wellness health check-up, coaching and monitoring
  - Health questionnaire
  - Health check-up
  - Clinical lab tests
- Biobanking
- Genome sequence analysis
- Metabolomics & biomarkers for inflammation
- Gut microbiome
- Quantified self sensors (exercise, sleep, pulse)
- Other health data (digital footprints)
- Daily monitoring (QS sensors) + laboratory data at 4 mo intervals
- Health and wellness advice and coaching
- Research database
- Personal health account dashboard
  - Data mining
  - Time trends
  - Correlations
- Researchers
- Clinicians
- Participants
Summary

• Personalized Health Care is essential for further progress in medicine.
• Economic Value is generated by running health care more effectively now only possible with Personalized approaches.
• Clinical data generation must move on from classical blinded studies to the new paradigm of ongoing observational studies with “big data”.
• Change the success metrics of health care to support pilot studies to show Cost Effectiveness and patient benefit.
• This will create a market nationally and internationally for systems approaches to provide cost effective Personalized Health.

• Break at least one orthodoxy : and it will be challenging