Data for personalized health(care): time for quality, not quantity

IHE NL jaarcongres 2016
Bussum, 11 Nov 2016

Prof Alain van Gool
Alain’s path 1989-now

- Basis in molecular biology
- Academia, pharma, medical center, applied research institutes
- Biomarkers / Omics / technologies
- Mechanisms of disease
- Translational medicine
- Personalized healthcare

Professor of Personalized Healthcare
Head Radboud Center for Proteomics, Glycomics & Metabolomics
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Senior Scientist Integrator Biomarkers

Scientific lead DTL-Technologies

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Radboud umc

TNO innovation for life

DTL | eatris

European infrastructure for translational medicine
Consider individual differences in life science research
Principle of Personalized Medicine

- The **right drug** for **right patient** at **right dose** at **right time**
- = Precision medicine or Targeted medicine

Source: Chakma, Journal of Young Investigators, 16, 2009
Personalized medicine in melanoma

B-RAF\textsuperscript{V600E} mutation

- B-RAF\textsuperscript{V600E} cells always grow and become cancer cells
- RAF inhibitors will block pathway, block cell growth and inhibit cancers that have a B-RAF\textsuperscript{V600E} mutation
- 60% of melanoma patients have B-RAF\textsuperscript{V600E} mutation
- Basis for a personalized medicine!
Personalized medicine in melanoma

B-RAF inhibitor
Treat patients with B-RAF\textsuperscript{V600E} mutation
Inhibit growth of cell

Cells stop growing
Tumors disappear
Patients live longer

Alain van Gool, IHE jaarcongres, Bussum. 11 Nov 2016
Emerging Personalized / Precision / Targeted Medicine

2010:

5% of drugs in pipeline had companion diagnostic biomarker test

2015:

AstraZeneca 80%

Roche 50%
Optimal Personalized / Precision / Targeted Medicine
Moving to personalized health(care)

- People are more than linear pathways
- Different systems and networks
- Different risk factors
- Different preferences

(Source: Barabási 2007 NEJM 357; 4)
Personalized health(care) in a systems view

**BIODATA**

- Metabolites
- RNA
- Protein
- DNA
- Biochemical process
- Enzymatic activity
- Imaging
- mDNA
- Nutrition
- Environment
- Social network
- Attitude in life
- Stress work/private

**RISK FACTOR PATTERN**

**PERSONALIZED INTERVENTIONS**

- PHARMA
- LIFESTYLE
- NUTRITION

**MULTIPARAMETER PERSONAL PROFILES**

Statistics
Selection
Ranking
Societal need in efficient personalized health(care)

Towards cost effective care, less cure

(Source: prof Jan Kremer)
Highest need in efficient personalized health(care)

It’s personal!

‘I want to stay healthy.’

‘If not, how do I get healthy?’
Translating Personalized Health(care) in society
Metaphor: a route planner
Analogy: GPS route planner

GPS to a location

Route 1

= Default

Traffic jam near Utrecht

Route 2

Alternative route

Alain van Gool, IHE jaarcongres, Bussum. 11 Nov 2016
Personalized Health(care) model

GPS to health

Route 1
= Default

First signs of disease risk

Route 2

Alternative route
We need a personalized data-driven GPS for health

- Monitor (biomarkers) on background
- Alert when you are at risk
- Advice what to do
3 key aspects of personalized health(care)

‘I want to stay healthy. If not, how do I get healthy?’

1. **What** to measure?
2. **How much** can it change?
3. **What should be the follow-up for me?**
Exponential technology developments in laboratories

• Next generation sequencing
  • DNA, RNA
  • Risk analysis and therapy selection

• Mass spectrometry
  • Proteins, metabolites
  • Monitoring of disease and treatment effects

• Imaging
  • Non invasive images, real time
  • Spatial view of intact organs and organisms
Advances in mass spectrometry

- Mass spectrometry analysis of glycoproteins in human plasma
- 0.05 microliter analysis: detection of 1,000,000 signals in one scan (1.4 Gb)
- ~40,000 peptides of which >80% contain sugar modification
- Diagnose patients and identify new biomarkers

Proof of principle study:

{Hans Wessels, Monique van Scherpenzeel, Dirk Lefeber, Alain van Gool}
System biology

Disruption circadian rhythm → Sleep disturbance

Inflammatory response → Chronic Stress

Endorphins → Worrying, Fear

Physiological inactivity → Caloric excess

Visceral adiposity → dyslipidemia

Rosiglitazone, Pioglitazone → Muscle metabolic inflexibility

Adipose IR → Low glycemic index, Sitagliptin, Anthocyanins

Fenofibrate → Adipose IR

Carnitine, choline → Adipose IR

Gut activity → Adrenalin

Beta-cell Pathology

Risk factor

Source: Ben van Ommen TNO

11 Nov 2016, IHE jaarcongres, Bussum.
A changing world: Getting digital

2005

2013
New data!
(generators, owners)
Live a healthier lifestyle with the new S Health!

S Health is a personal health management application that helps you track your daily activities more easily, and achieve your health and exercise goals.

Check your activity level, goal achievement rate, and recent health stats in one spot.

- Record health data easily using trackers such as Steps, Running, and Hiking.
- Be more active. Eat healthier, and Feel more rested, check all three GOALS for healthier habits in one spot.

Set Steps goals with your friends and compete with each other. It's more fun to walk together.

- Invite friends, compete with them, check each other's scores, and cheer each other on.
- Check your rank among ALL USERS.

Read up-to-date health news every day. Find general information and specialist content covering a variety of topics, such as fitness tips, diet tips, health management suggestions, and the latest news.
New Smartphone App 'Detects' Skin Cancer

Written by Sarah Glynn

Published: Friday 22 March 2013

A new smartphone app that claims to detect warning signs of skin cancer has just been launched in the UK market following a two year beta in the U.S.

The novel app, called Mole Detect Pro, provides its users with a remote professional diagnosis within 24 hours. To do so, it safely stores pictures of moles and uses an advanced algorithm to grade the probability of a possible melanoma based on the ABCDE method of detection.

Dermatologists frequently bring up this acronym during check-ups and ask their patients to keep an eye on symptoms at home.

The ABCDE method stands for:

- Asymmetry - irregular shape
- Border - ragged, notched, or blurred
- Color - more than one in an individual mole
- Diameter - bigger than 6mm
- Evolution - changing size, color, or shape

Leading dermatologist in the UK, Dr. John Ashworth, has shown a lot of interest in this new app, which has been created by the same experts from the U.S. who are responsible for the award-winning instant smartphone webcam known as Eva Nota.
HEALTH TECH

Cogito and MGH test voice app to monitor moods

Cogito’s Companion app uses the company’s voice analysis software to detect emotions in your speaking voice.

A Boston company has developed a smartphone app that can decipher emotions in the human voice, an early-warning system that could bring timely help to those with mental illness.

Cogito has been developing its voice analysis software for more than a decade and since last fall has been working with the US Department of Veterans Affairs to monitor the moods of service members through the app.
A smartphone app that can tell if users are in danger of having a heart attack by the tone of their voice is being considered for use by the NHS.

Clinical trials of the software showed it accurately predicted admission to hospital for people with congestive cardiac failure one week before they were taken gravely ill.

The app is one of a wealth of gadgets and systems under review by the health service with the aim of revolutionising personalised healthcare.
Ongoing: translate laboratory to society

- 1.000.000 signals per proteomics analysis
- Point-of-care analysis of few biomarkers
Manchester shoppers offered scans to spot lung cancer

13 June 2016 | Manchester

Shoppers at Harpurhey Market will benefit from the mobile scanning unit for a month before it moves to Wythenshawe Forum and Gorton Tesco

Shoppers are being offered scans in north Manchester in a bid to spot lung disease in smokers.
What does my DNA tell me?

23% chance blond hair

3.1% Neanderthal DNA
What does my DNA tell me?

Genetic risk lung cancer → don’t smoke!

No expected adverse reaction to Warfarin
Een revolutionaire nieuwe manier om glucose te controleren zonder routinematig vingerprikken

U hoeft niet meer routinematig te testen met lancetten, teststrips en bloed*

**FreeStyle Libre** - Een revolutie voor diabetespatiënten

FreeStyle Libre is een makkelijke manier om glucose te controleren met een pijnloze scan van 1 seconde in plaats van een pijnlijke vingerprik*

**BESTEL VANDAAG NOG UW STARTPAKKET**
Smartphone App Detects Bacteria, Diseases

Thu, 04/02/2015 - 11:58am by Florida Atlantic University

Thin, lightweight and flexible materials developed by researchers at Florida Atlantic University, Stanford University and Harvard University, integrate cellulose paper and flexible polyester films as new diagnostic tools to detect bioagents in whole blood, serum and peritoneal fluid. Image credit: Florida Atlantic University.
App-icalisering

De belangrijkste drager van de digitale revolutie in de gezondheidszorg is de smartphone. De DigitaleZorgGids - waa
medische apps worden geregistreert - vermeldt momenteel meer dan 9000 medische apps.
De gemiddelde waardering is 3,4 op 5. Ku
blunt is er dan nog veel ruimte te maken.
(www.DigitaleZorgGids.nl)
... but not all data is useful data!
Data for personalized health(care)

time for quality, not quantity
Need for optimal quality in health biomarker analyses

Test, interpret, advice

“Post-traumatic Test Syndrome”? 
Need to change our focus

NIET OMDAT HET MOET MAAR OMDAT HET KAN

omdathetkan.nl
Biomarker innovation gaps!

- Too much biomarker discovery
- Too little development to application
Biomarker innovation gaps: some numbers

Eg Biomarkers in time: Prostate cancer
May 2011: 2,231 biomarkers
Nov 2012: 6,562 biomarkers
Oct 2013: 8,358 biomarkers
Nov 2014: 10,350 biomarkers
Oct 2015: 11,856 biomarkers
11 Nov 2016: 14,481 biomarkers

Discovery
Clinical validation/confirmation
Diagnostic test

Gap 1
Gap 2

~ 5 biomarkers/working day
1 biomarker/1-3 years
1 biomarker/2-10 years
Choice for clinical researchers: discover or confirm?
Good example of multi-laboratory biomarker validation

3 biomarkers:
- Aβ42
- T-Tau
- P-Tau
Good example of multi-laboratory biomarker validation

Potential sources of variability

Participating laboratories

Data

Conclusions

Adoption of best biomarker practice ???
Share negative outcomes
Need to build biomarker validation pipelines

Standardisation, harmonisation, knowledge sharing needed in:

1. Assay development
2. Clinical validation
3. Application
Join forces among Europe’s major academic infrastructures + industry to:

1. **Establish “Good Biomarker Practice” guidelines**
   - on translational research, biomarker technologies, biobanking, data stewardship.

2. **Efficiently execute high quality biomarker projects**
   - work together in clinical validation and development of probable biomarkers.
Critical component in personalized healthcare: Data

- Data capture
- Data stewardship

“data is the new oil for the digital age”

DATA IS CRUCIAL NOWADAYS

Neelie Kroes, Vice-President of the EC. Responsible for the Digital Agenda for Europe

FAIR data stewardship

Comment: The FAIR Guiding Principles for scientific data management and stewardship

Mark D. Wilkinson et al.

{Wilkinson et al, Nature Scientific Data, 2016}

Prof Barend Mons

Leiden University Medical Center
Dutch Techcenter for Life Sciences
Netherlands eScience Center
'We support appropriate efforts to promote open science and facilitate appropriate access to publicly funded research results on findable, accessible, interoperable and reusable (FAIR)'}
FAIR data stewardship working model

Services

Exchange layer

Data

minimal protocols
Translation is key in Personalized Healthcare!

“I’m afraid you’re suffering from an increased IL-1β and an aberrant miR843 expression”

Adapted from:
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glasbergen.com
Think big, start ‘small’

Radboudumc Technology Centers

- Molecule
  - Flow cytometry
  - Stem cells
  - Animal studies
  - Translational neuroscience
  - Microscopy
  - Imaging
  - Image-guided treatment
  - 3D lab
  - Investigational products
- Population
  - Genomics
  - Mass Spectrometry
  - Bioinformatics
  - Health economics
  - Data stewardship
  - Statistics
  - EHR data analysis
  - Human performance
- Man
  - Biobank
  - Clinical studies
Think big, start ‘small’

Ruben Kok

Barend Mons

Alain van Gool

Jaap Heringa

National Technology Infrastructure (collective of 40+ partners in DTL)
www.dtls.nl
Joining forces in Netherlands

To drive personalized medicine & health research
https://youtu.be/MpMSkbu9YQg
Health-RI Congress

1 December 2016
De Flint in Amersfoort
Register: www.nlhealthresearch.nl
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