Parallel tussen personalized medicine en precisielandbouw

Ctgb Relatiedag
Ede, 15 June 2017

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
Coordinator Radboud Technology Centers

Senior Scientist Integrator Biomarkers

Scientific lead DTL-Technologies

Head EATRIS Biomarker Platform

Alain's path 1989-now

Consider __individual__ differences in life science research

Alain van Gool, Ctgb Relatiedag 2017, Ede, 15 June 2017
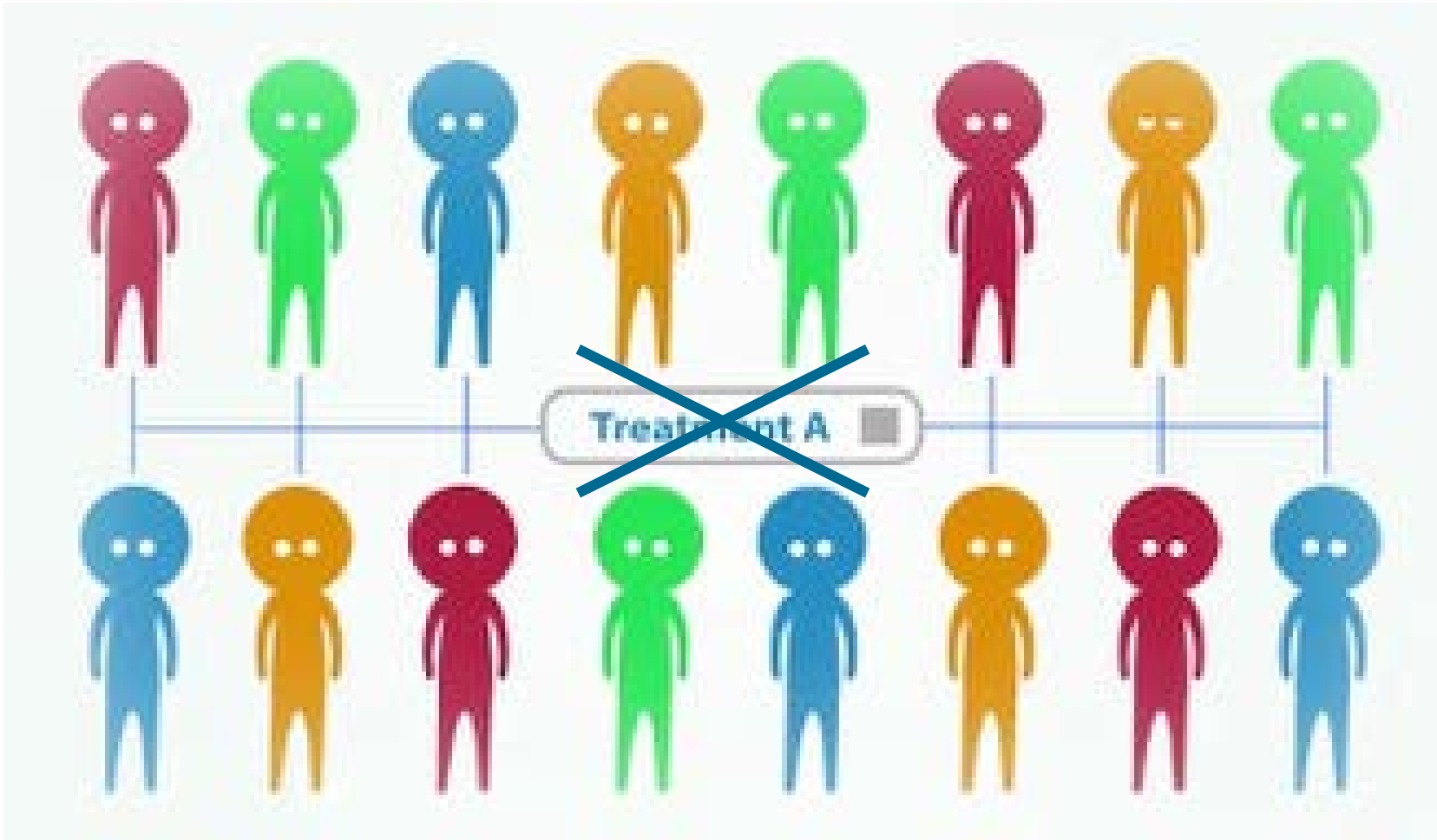
Principle of Personalized Medicine
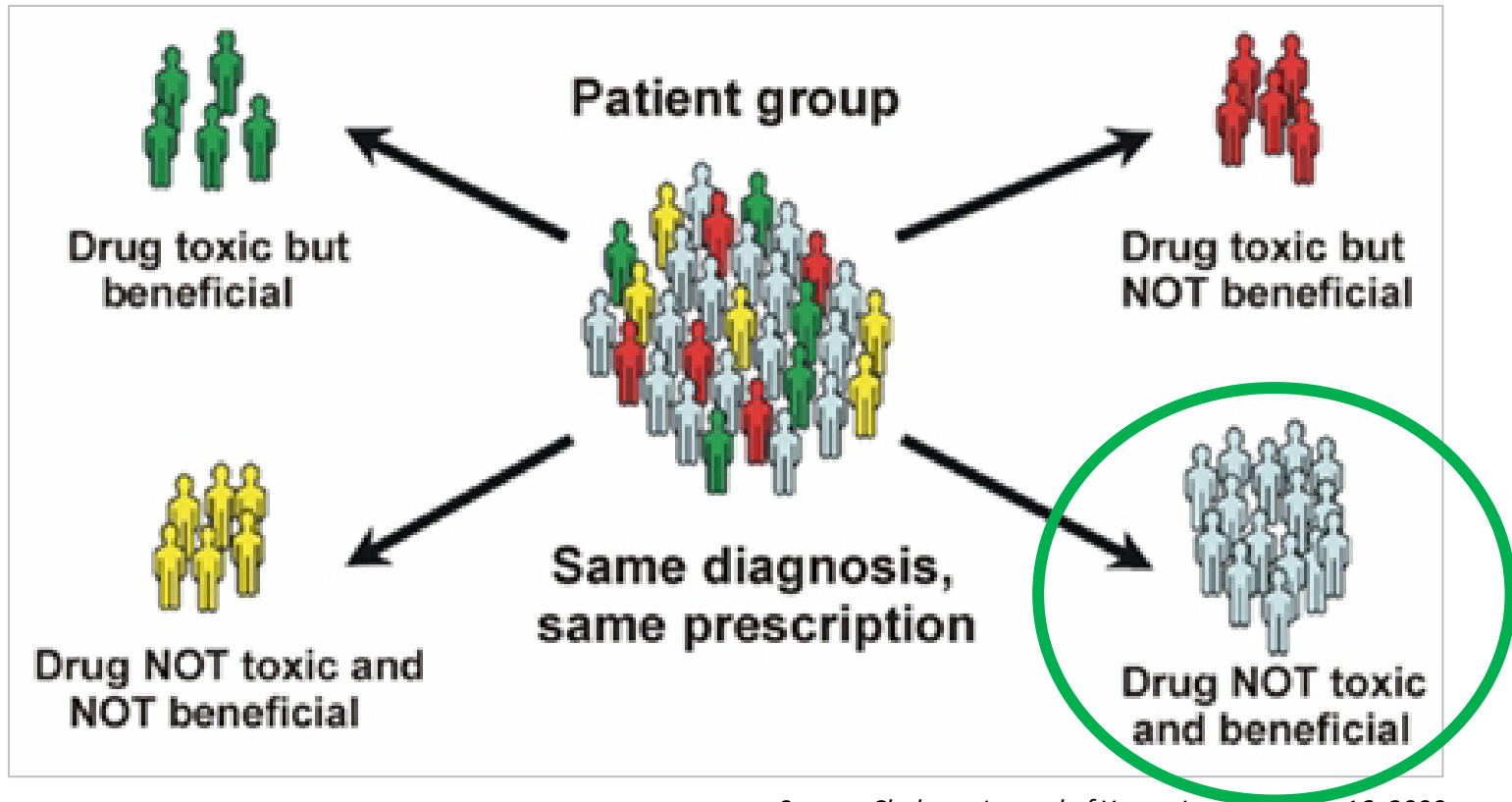
Source: Chakma, Journal of Young Investigators, 16, 2009

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

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Crash course in molecular biology

DNA, protein, cell, tissue, system biology

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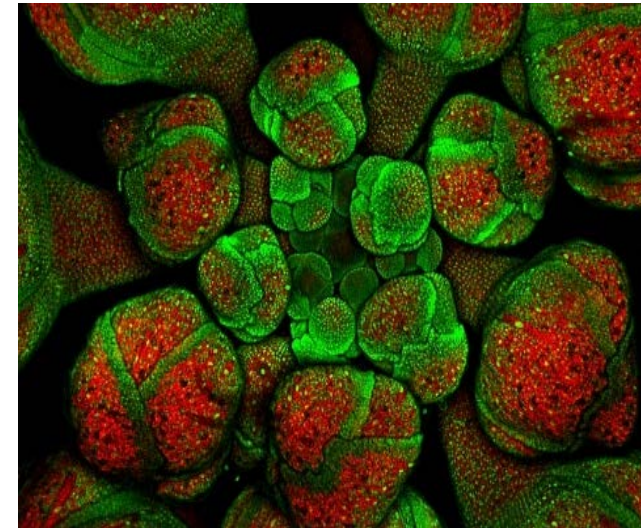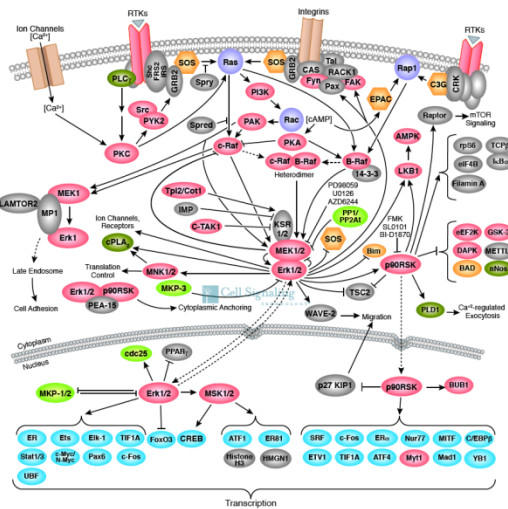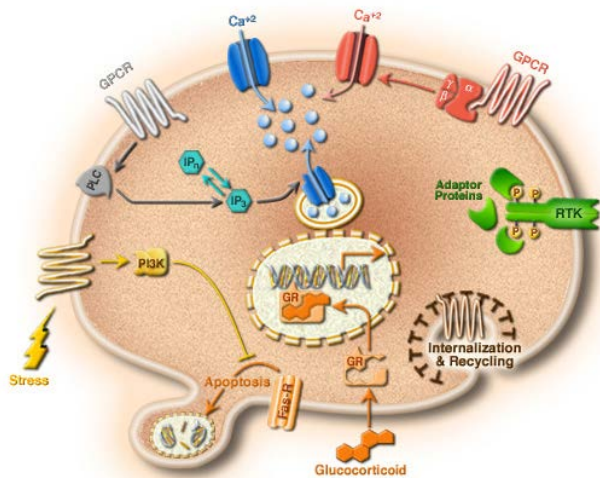
Personalized medicine in melanoma
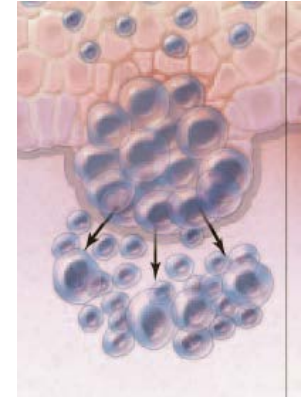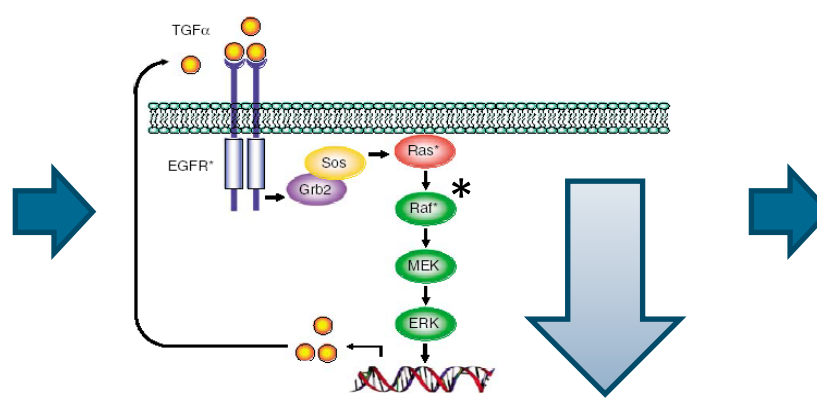
B-RAF^{V600E} mutation

Strong growth of cell

Growth of tumor
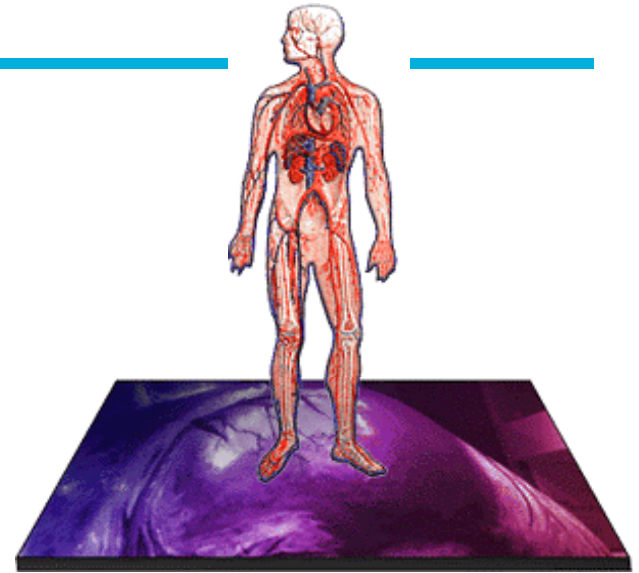
- B-RAF^{V600E} cells always grow and become cancer cells

- RAF inhibitors will block pathway, block cell growth and inhibit cancers that have a B-RAF^{V600E} mutation

- 60% of melanoma patients have B-RAF^{V600E} mutation

- Basis for a personalized medicine !

Personalized medicine in melanoma

ZELBORAF™ (vemurafenib) tablets

Zelboraf (vemurafenib)

B-RAF inhibitor

Treat patients with B-RAF^{V600E} mutation
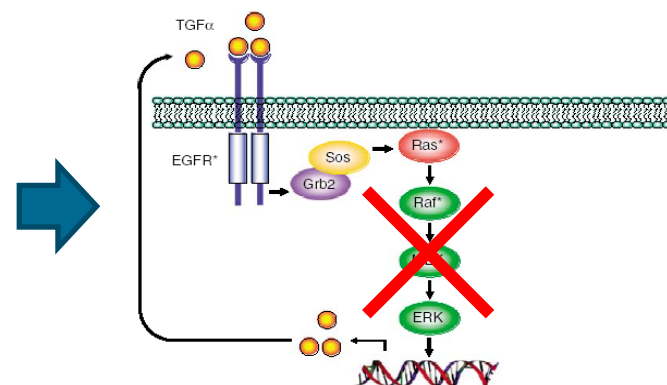
Inhibit growth of cell
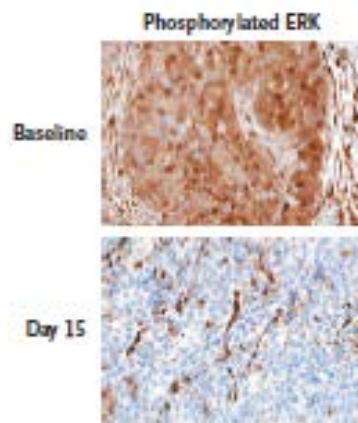
Cells stop growing
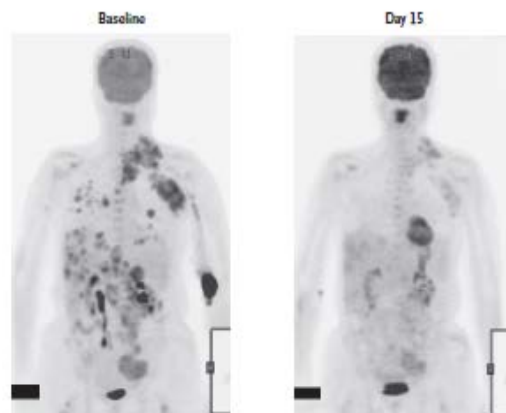
Tumors disappear

Patients live longer

Phosphorylated ERK — Baseline, Day 15

Baseline — Day 15

A Progression-free Survival — Hazard ratio, 0.26; 95% CI, 0.20 to 0.33; $P<0.001$; Vemurafenib (N=275); Dacarbazine (N=274)

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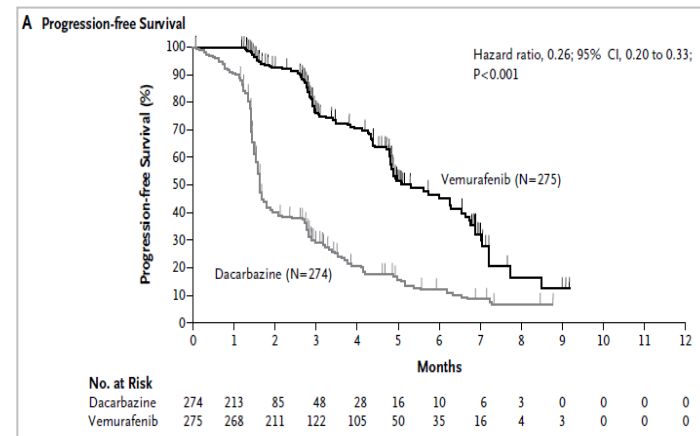
Emerging Personalized / Precision / Targeted Medicine

2010:

5% of drugs in pipeline had companion diagnostic biomarker test

2015:

AstraZeneca   80%

Roche   50%

Optimal Personalized / Precision / Targeted Medicine

People are more than linear pathways

Moving to personalized health(care)
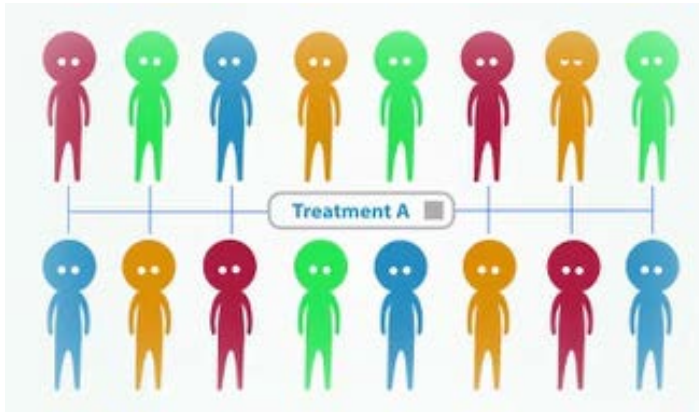
- People are more than linear pathways
- Different systems and networks
- Different risk factors
- Different preferences
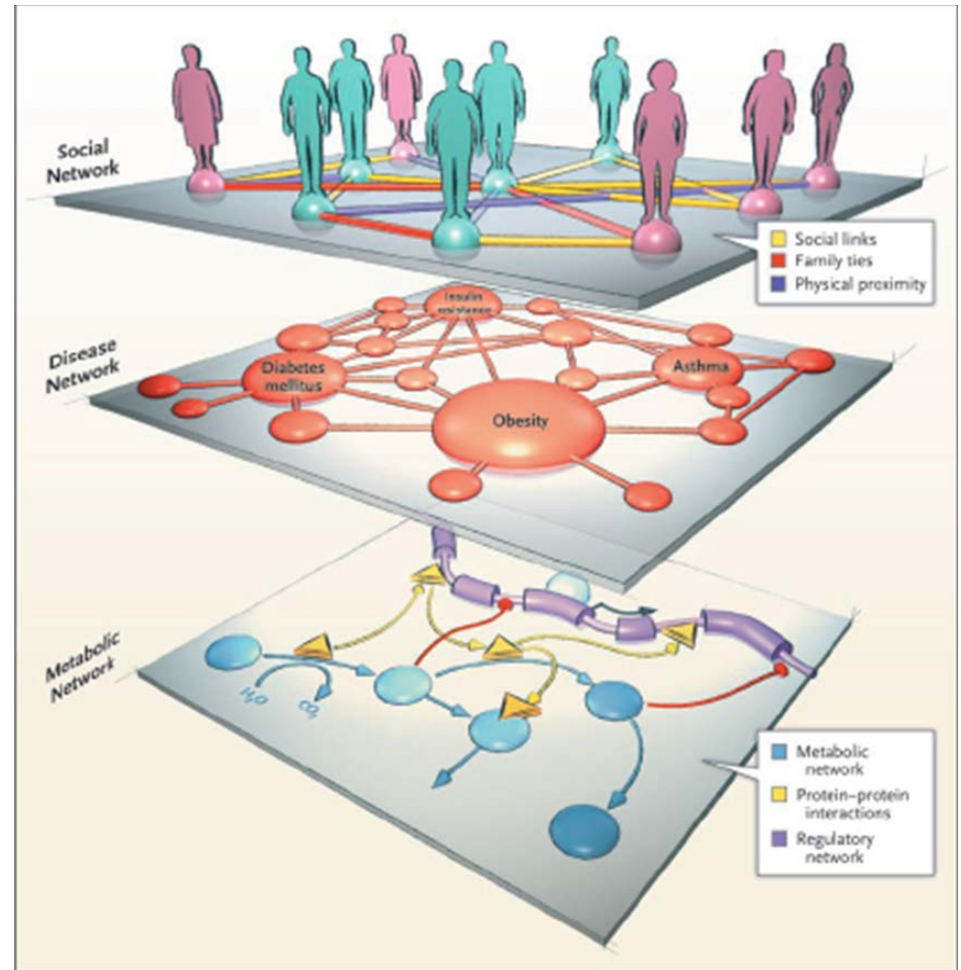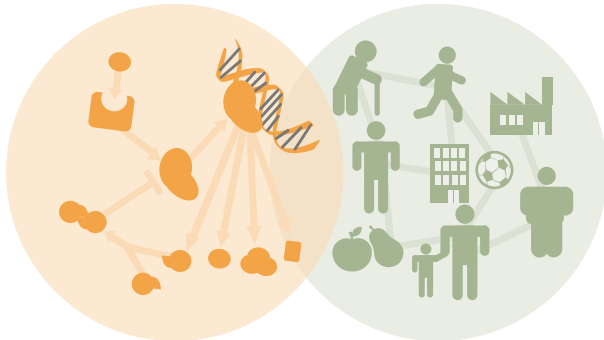
{Source: Barabási 2007 NEJM 357; 4}

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

MOLECULAR   LIFESTYLE / ENVIRONMENT

Statistics
Selection
Ranking

PERSONALIZED INTERVENTIONS

PHARMA

LIFESTYLE

NUTRITION

MULTIPARAMETER PERSONAL PROFILES
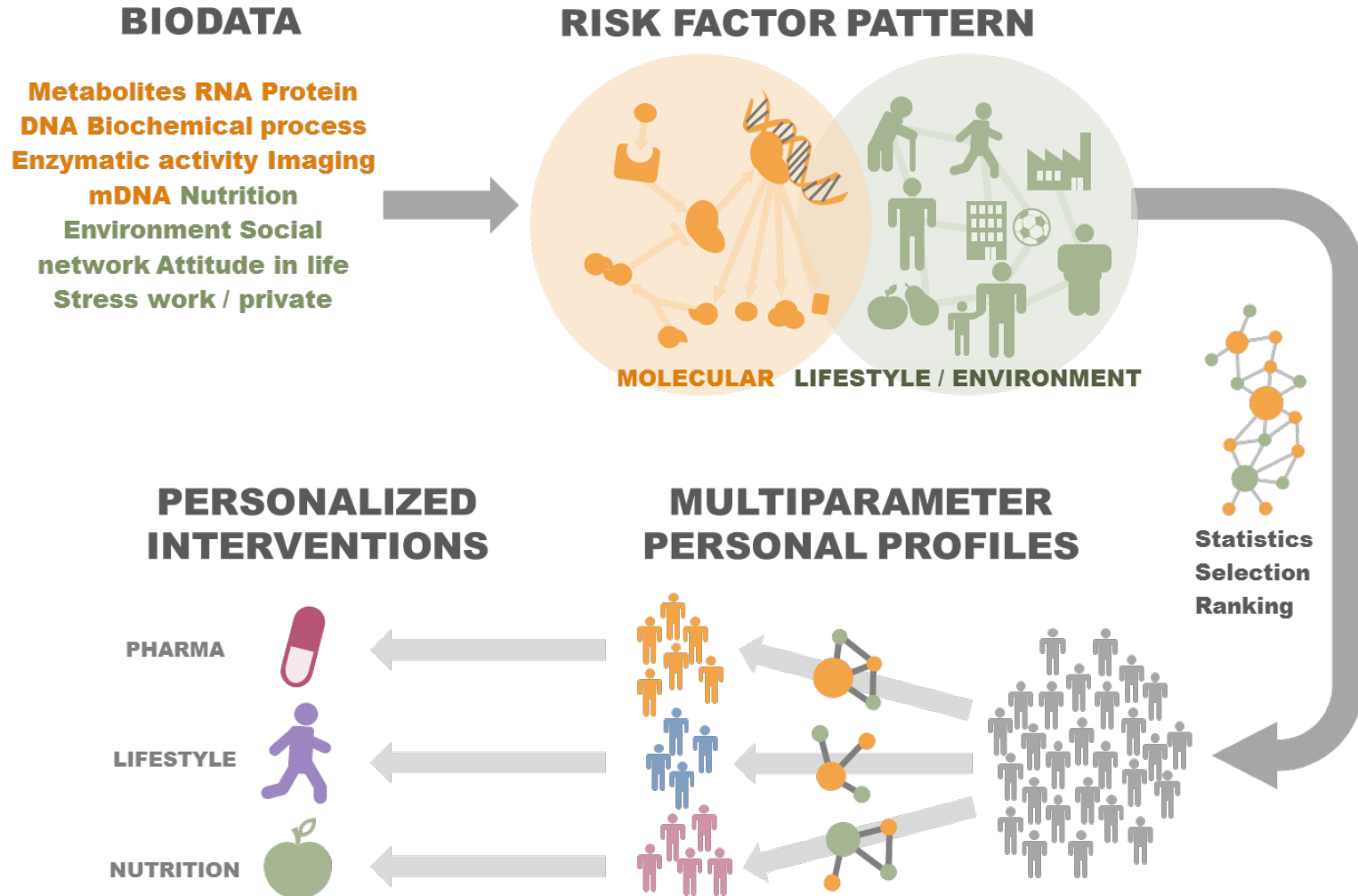
Societal need in efficient personalized health(care)
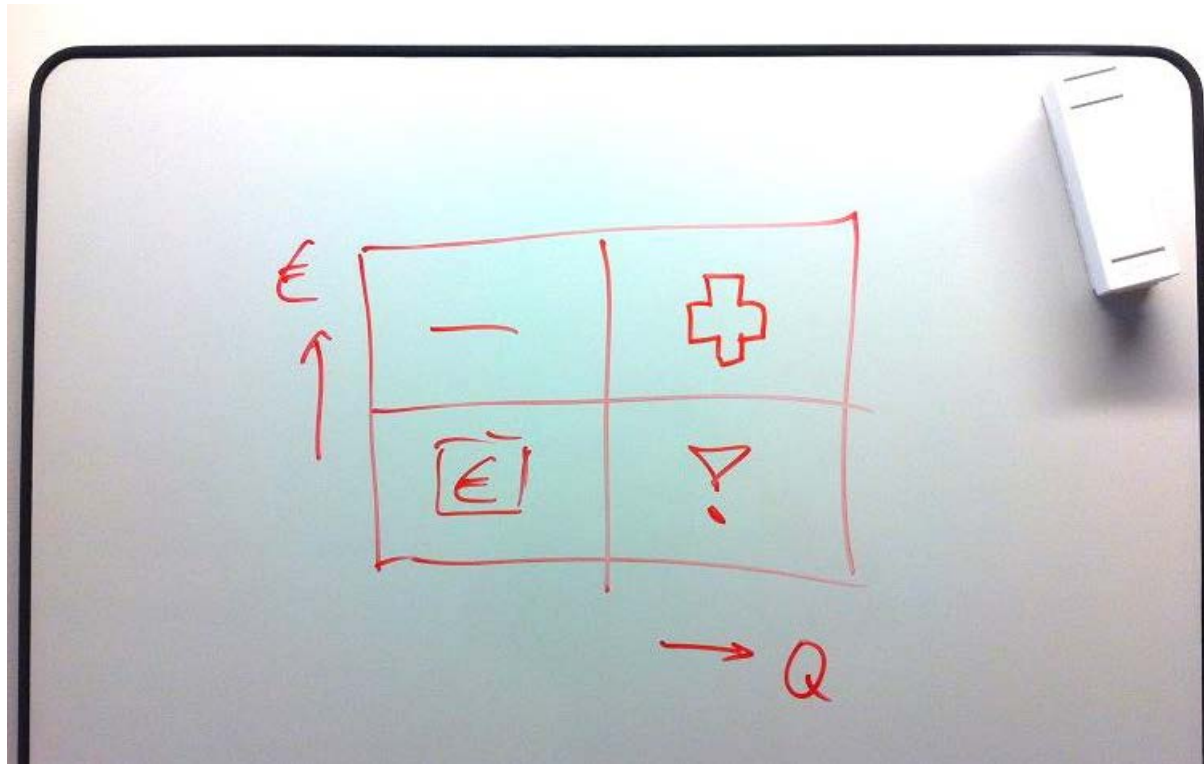
{Source: prof Jan Kremer}

Towards cost effective care, less cure

Highest need in efficient personalized health(care)

It's personal !

'I want to stay healthy.'

'If not, how do I get healthy?'

Focus on the end user: the patient / citizen
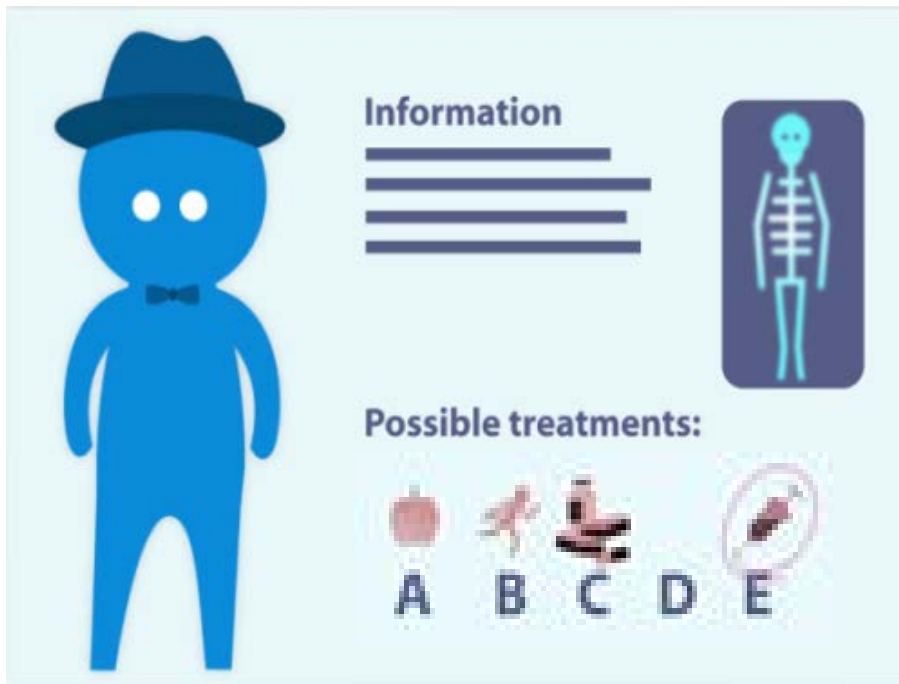
Moving to Personalized Health(care)

"The term "personalized medicine" is often described as providing "the right patient with the right drug at the right dose at the right time."

More broadly, "personalized medicine" may be thought of as the tailoring of medical treatment to the individual characteristics, needs, and preferences of a patient during all stages of care, including prevention, diagnosis, treatment, and follow-up."

(FDA, October 2013)

OCTOBER 2013

Paving the Way for Personalized Medicine

FDA's Role in a New Era of Medical Product Development
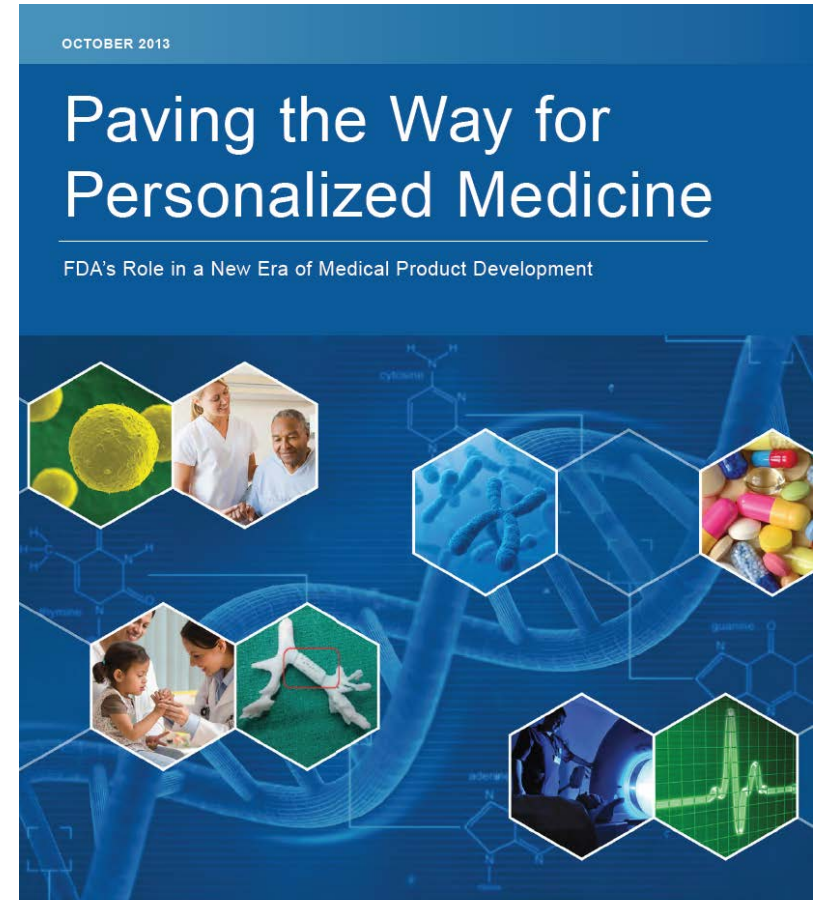
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
U.S. FOOD AND DRUG ADMINISTRATION

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

Alain van Gool, Ctgb Relatiedag 2017, Ede, 15 June 2017
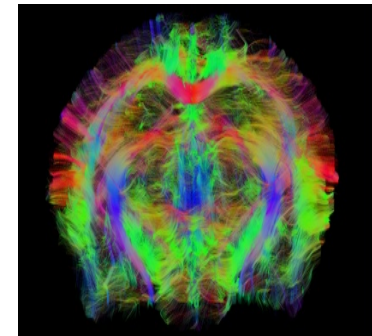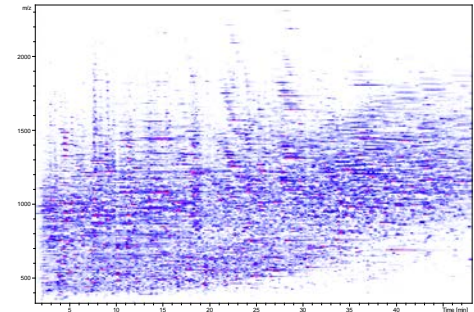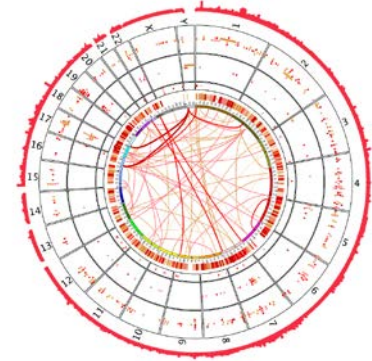
System biology
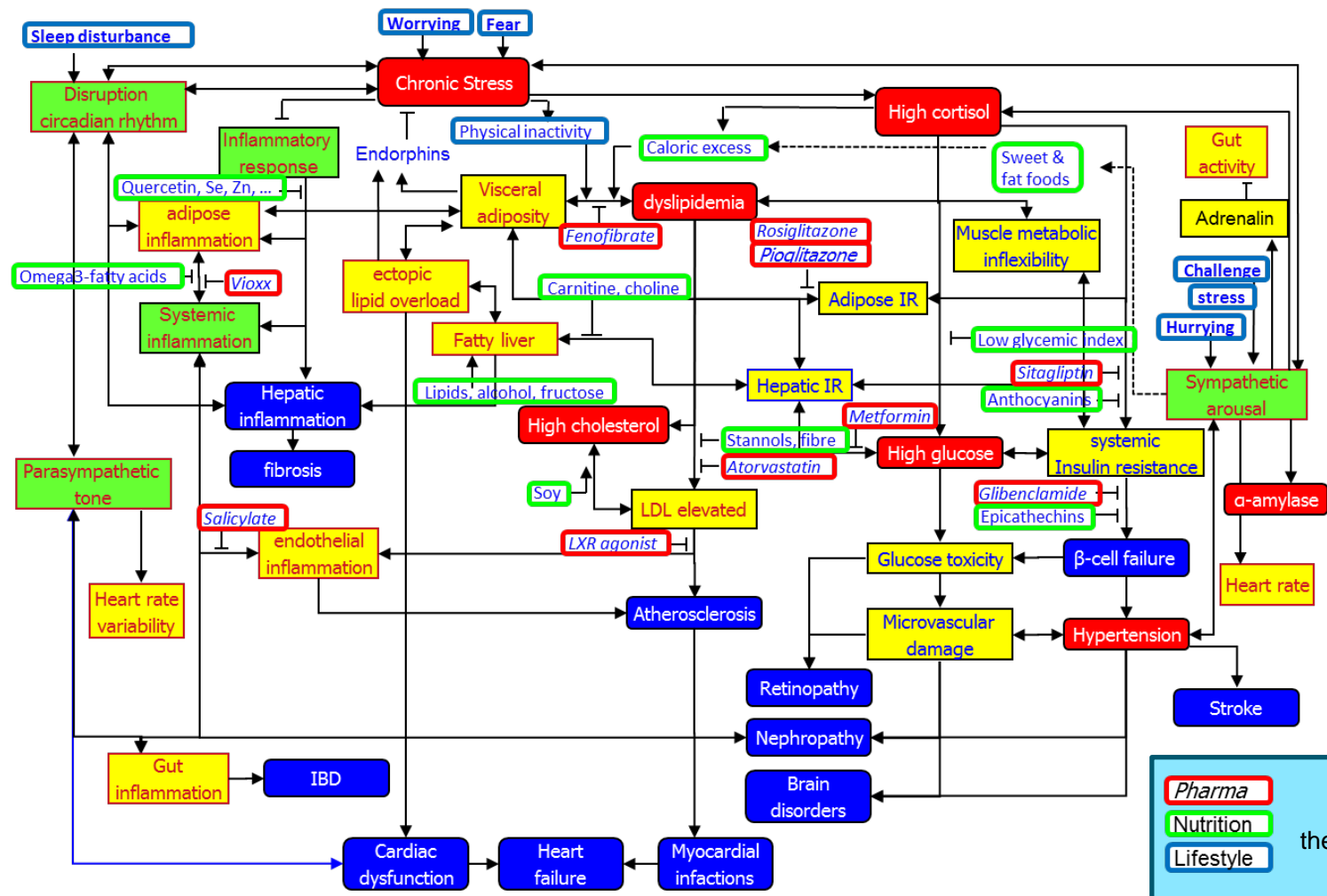
A changing world: Getting digital

New data !

(generators, owners)

App-icalisering

De belangrijkste drager van de digitale revolutie in de gezondheidszorg is de smartphone. De DigitaleZorgGids – waar medische apps worden gereviewd – vermeldt momenteel meer dan 9000 medische apps. De gemiddelde waardering is 1,4 op 5. Kwalitatief is er dus nog wel een slag te maken. (www.DigitaleZorgGids.nl)

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🏠 › News

Phone app that can detect heart attack a week out considered by NHS

f share 🐦 ✉

The smartphone app tracks changes in tone of voice to warn of heart attacks CREDIT: ALAMY

By **Henry Bodkin**

9 JUNE 2016 • 12:20AM

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.

NEWS MOST VIEWED

Ongoing: translate laboratory to society

- 1.000.000 signals per proteomics analysis

- Point-of-care analysis of few biomarkers

Manchester

Manchester shoppers offered scans to spot lung cancer

🕐 13 June 2016 | Manchester

MACMILLAN CANCER SUPPORT

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

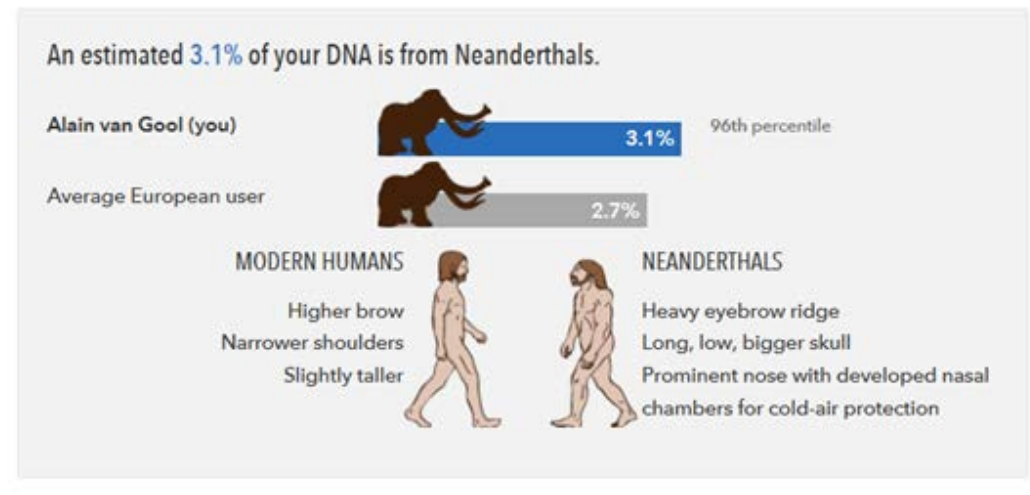Shoppers are being offered scans in north Manchester in a bid to spot lung disease in smokers.

23andMe

uBiome

ORIG3N

and many many many more ...

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What does my DNA tell me?

FIND OUT WHAT YOUR DNA SAYS ABOUT YOU.

only $99

23andMe

HEALTH OVERVIEW
- HEALTH RISKS
- DRUG RESPONSE
- INHERITED CONDITIONS
- TRAITS
- HEALTH TOOLS

ANCESTRY OVERVIEW
- ANCESTRY COMPOSITION
- MATERNAL LINE
- PATERNAL LINE
- NEANDERTHAL ANCESTRY
- ANCESTRY TOOLS

Your Results

Who	Genetic Result
	Has 5 or more varia... blond hair in peopl... ancestry. Approximately 53% of 23andMe customers with this result report having blond hair.
Alain van Gool	Has 3-4 variants associated with blond hair in people with European ancestry. Approximately 28% of 23andMe customers with this result report having blond hair.
	Has 1-2 variants associated with blond hair in people with European ancestry.

Got Neanderthal DNA?

An estimated 3.1% of your DNA is from Neanderthals.

Alain van Gool (you) — 3.1% — 96th percentile

Average European user — 2.7%

MODERN HUMANS
- Higher brow
- Narrower shoulders
- Slightly taller

NEANDERTHALS
- Heavy eyebrow ridge
- Long, low, bigger skull
- Prominent nose with developed nasal chambers for cold-air protection

23% chance blond hair

3.1% Neanderthaler DNA

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- ANCESTRY TOOLS

Alain van Gool
11.6 out of 100
men of European ethnicity who share Alain van Gool's genotype will develop Lung Cancer between the ages of 20 and 79.

Average
8.5 out of 100
men of European ethnicity will develop Lung Cancer between the ages of 20 and 79.

Your Results

Who	Genetic Result
	Likely to be more sensitive to warfarin based on genetics. Genetic information may only be useful when determining an initial dose of warfarin. Many other factors also influence warfarin sensitivity. If you are taking warfarin, keep taking it as directed by your doctor.
	May be more sensitive to warfarin based on genetics. Genetic information may only be useful when determining an initial dose of warfarin. Many other factors also influence warfarin sensitivity. If you are taking warfarin, keep taking it as directed by your doctor.
Alain van Gool	Likely to have typical sensitivity to warfarin based on genetics. Genetic information may only be useful when determining an initial dose of warfarin. Many other factors also influence warfarin sensitivity. If you are taking warfarin, keep taking it as directed by your doctor.

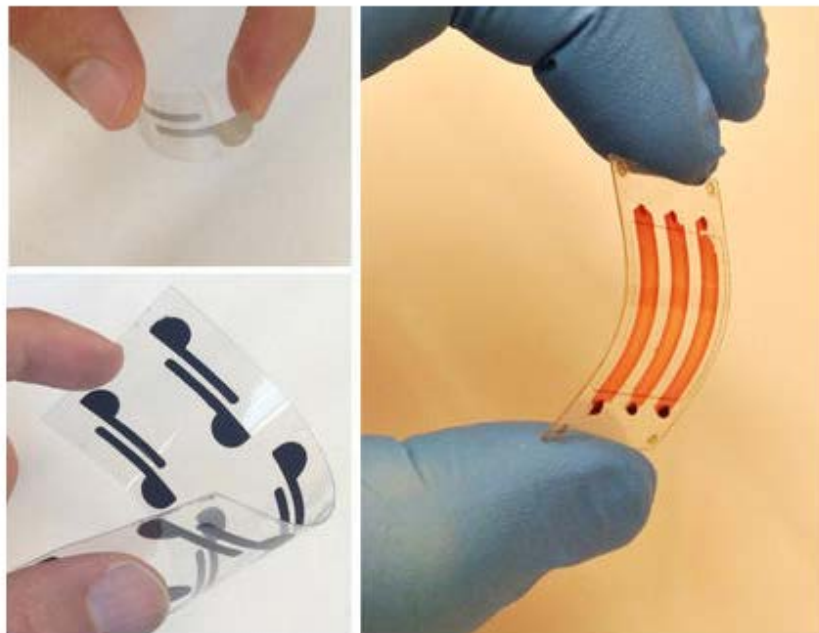Genetic risk lung cancer
→ don't smoke !

No expected adverse reaction to Warfarin

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Browser address bar: https://www.pddnet.com/news/2015/04/smartphone-app-detects-bacteria-diseases

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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

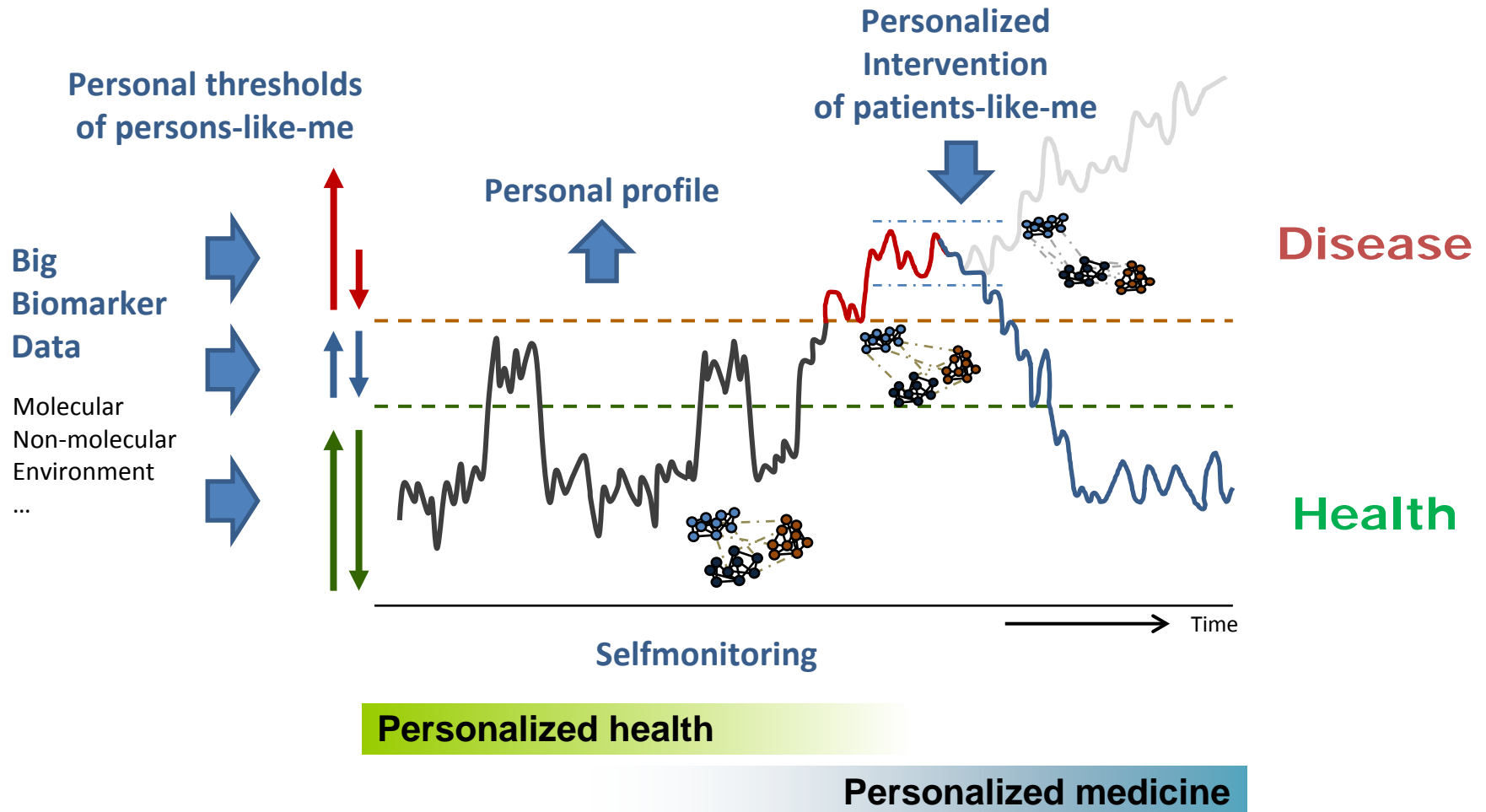29 Alain van Gool, Ctgb Relatiedag 2017, Ede, 15 June 2017

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?

Personalized health(care) model

P4 Medicine
●PREDICT ●PREVENT ●PERSONALIZE ●PARTICIPATE

Personal thresholds of persons-like-me

Personalized Intervention of patients-like-me

Personal profile

Big Biomarker Data

Molecular
Non-molecular
Environment
…

Disease

Health

Time

Selfmonitoring

Personalized health

Personalized medicine

Adapted from Jan van der Greef, TNO

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Personal Omics Profiling Reveals Dynamic Molecular and Medical Phenotypes

Cell

Rui Chen,[1,11] George I. Mias,[1,11] Jennifer Li-Pook-Than,[1,11] Lihua Jiang,[1,11] Hugo Y.K. Lam,[1,12] Rong Chen,[2,12] Elana Miriami,[1] Konrad J. Karczewski,[1] Manoj Hariharan,[1] Frederick E. Dewey,[3] Yong Cheng,[1] Michael J. Clark,[1] Hogune Im,[1] Lukas Habegger,[6,7] Suganthi Balasubramanian,[6,7] Maeve O'Huallachain,[1] Joel T. Dudley,[2] Sara Hillenmeyer,[1] Rajini Haraksingh,[1] Donald Sharon,[1] Ghia Euskirchen,[1] Phil Lacroute,[1] Keith Bettinger,[1] Alan P. Boyle,[1] Maya Kasowski,[1] Fabian Grubert,[1] Scott Seki,[2] Marco Garcia,[2] Michelle Whirl-Carrillo,[1] Mercedes Gallardo,[9,10] Maria A. Blasco,[9] Peter L. Greenberg,[4] Phyllis Snyder,[1] Teri E. Klein,[1] Russ B. Altman,[1,5] Atul J. Butte,[2] Euan A. Ashley,[3] Mark Gerstein,[6,7,8] Kari C. Nadeau,[2] Hua Tang,[1] and Michael Snyder[1,*]
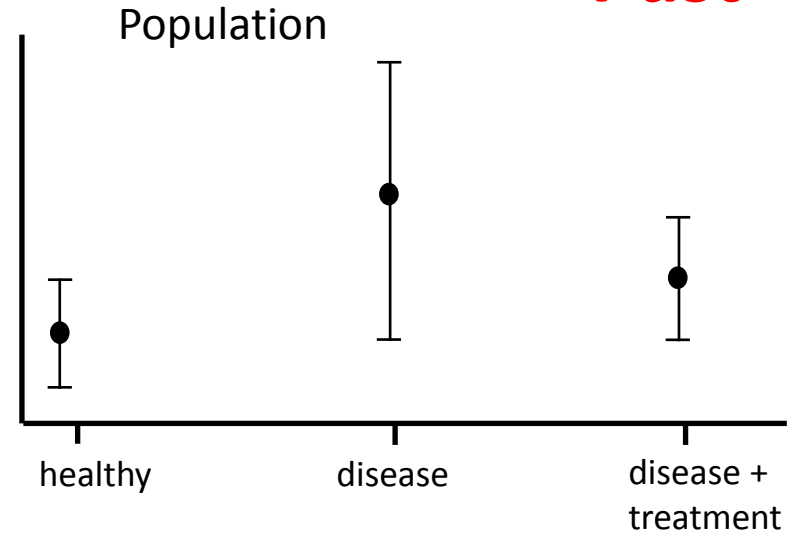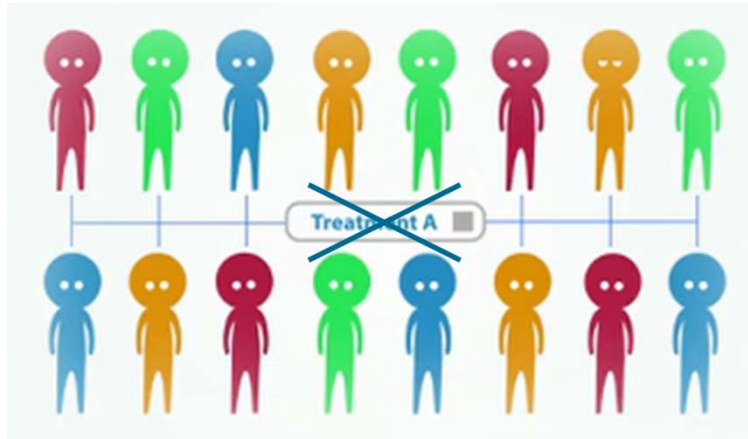
{Chen et al, Cell 2012, 148: 1293}

Concept:
- Continuous monitoring (n=1)
- Routine biomarkers to alert
- Omics to explain
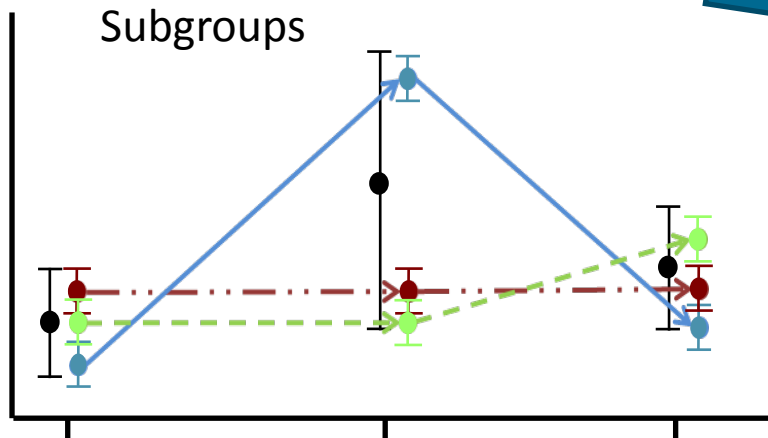- Early intervention
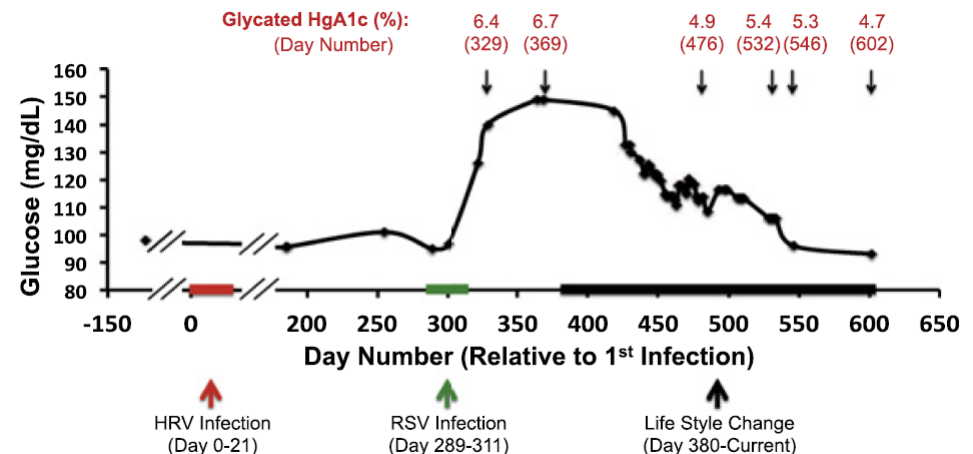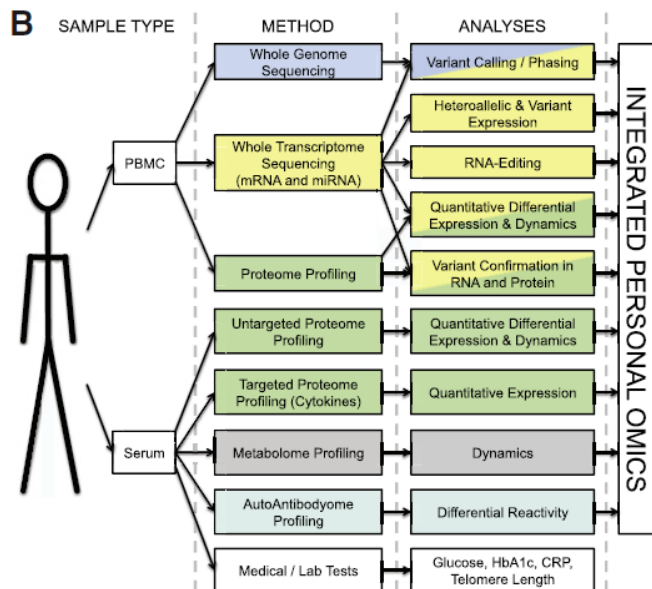
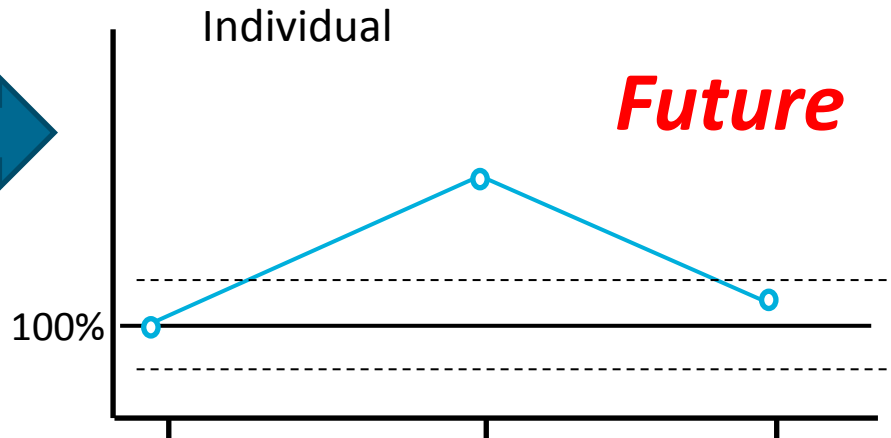# Moving to truly personalized monitoring
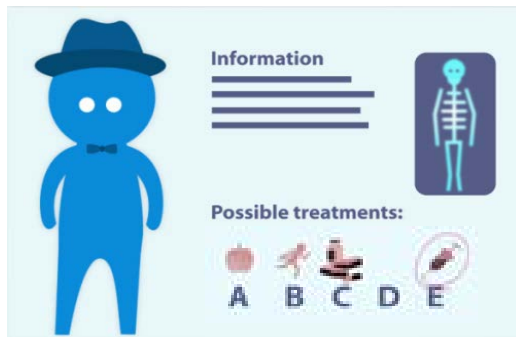
Past

Present

Future

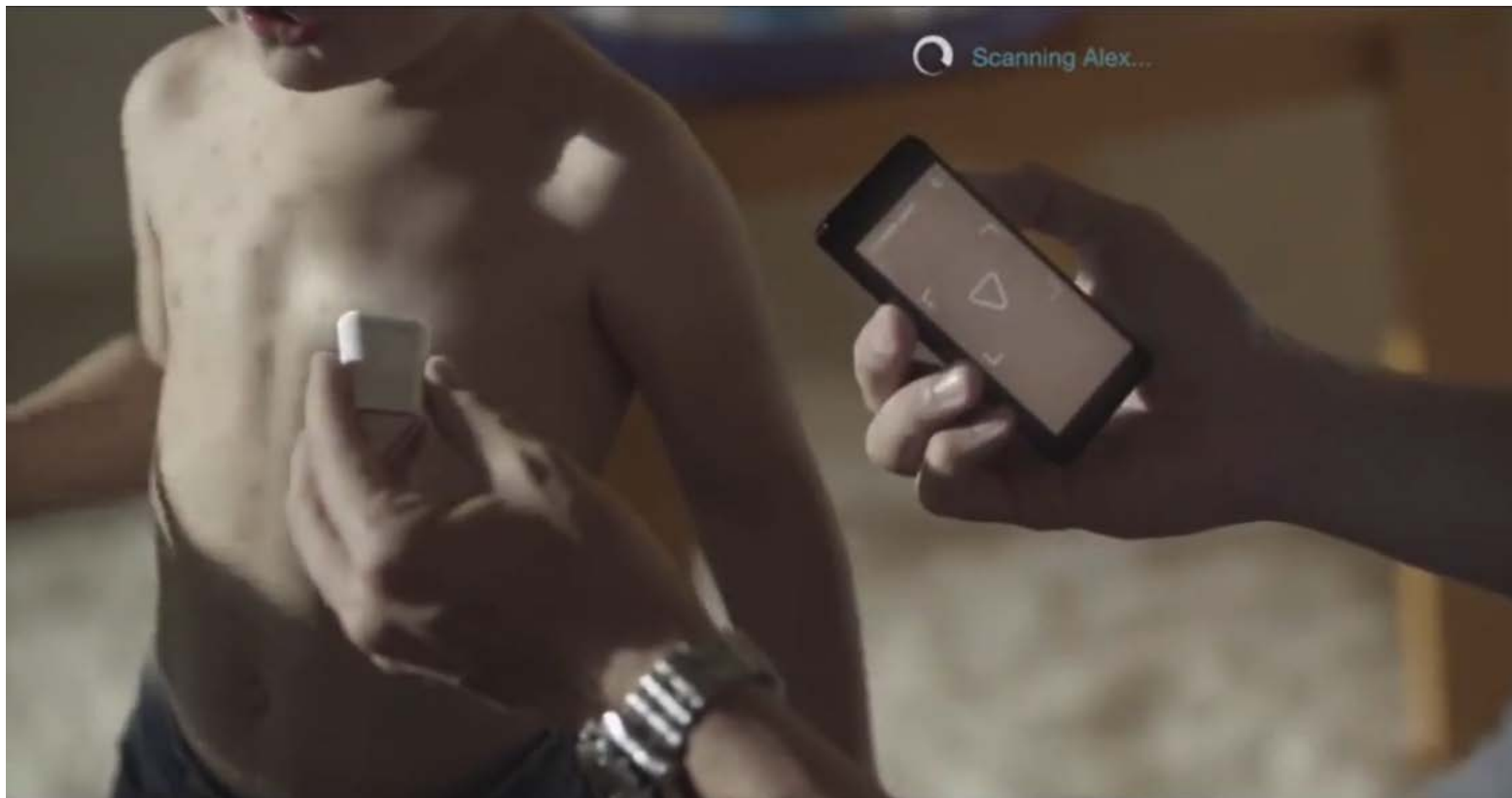# Personalized health(care) monitoring as part of our lives

- Monitor on background

- Alert when <u>you</u> are at risk

- Advice what to do

Examples from car dashboard:

- Empty gas tank

- Traffic jam ahead

View in the (very near) future

Acknowledgements

Many collaborators and funders

Radboud umc

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the Radboudumc Technology Centers	
and many others	

DTL

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many others	

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Lars Verschuren	Marjan van Erk
Suzan Wopereis	Heleen Wortelboer
Wessel Kraaij	Ronald Mooi
Peter van Dijken	Cyrille Krul
and many others	

eatris
European infrastructure for translational medicine

Anton Ussi	Florence Bietrix
Laura Bermejo	Andreas Scherer
Sulev Koks	Marian Hajduch
Giovanni Migliaccio	
and many others	

Radboudumc Technology Centers

www.radboudumc.nl/personalizedhealthcare
www.radboudumc.nl/research/technologycenters
www.radboudresearchfacilities.nl

CarTarDis

Biomarker Development Center

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HealthValley Netherlands

provincie Gelderland

HORIZON 2020 LE PROGRAMME DE RECHERCHE ET D'INNOVATION DE L'UNION EUROPÉENNE

STW Perspectief Nieuwe technologie mogelijk maken in de topsectoren