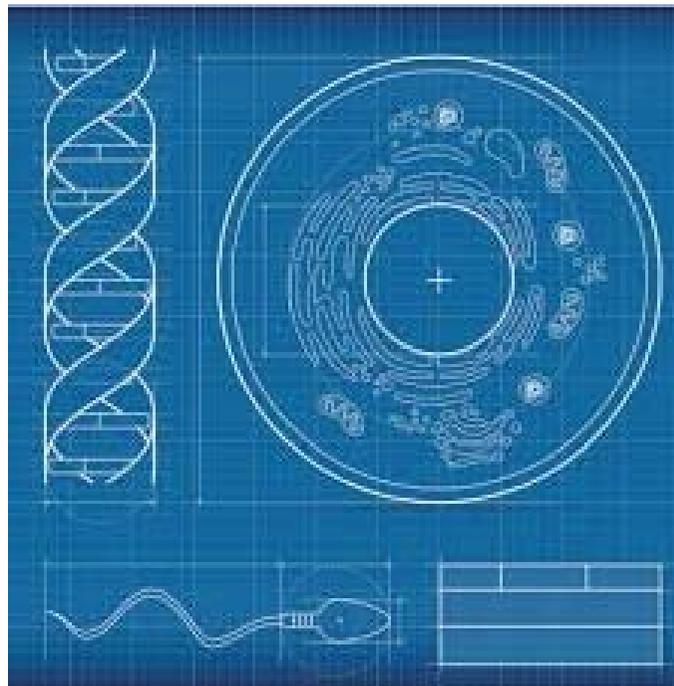

Von der Blaupause zur Therapie

Molekulare Medizin als Herausforderung

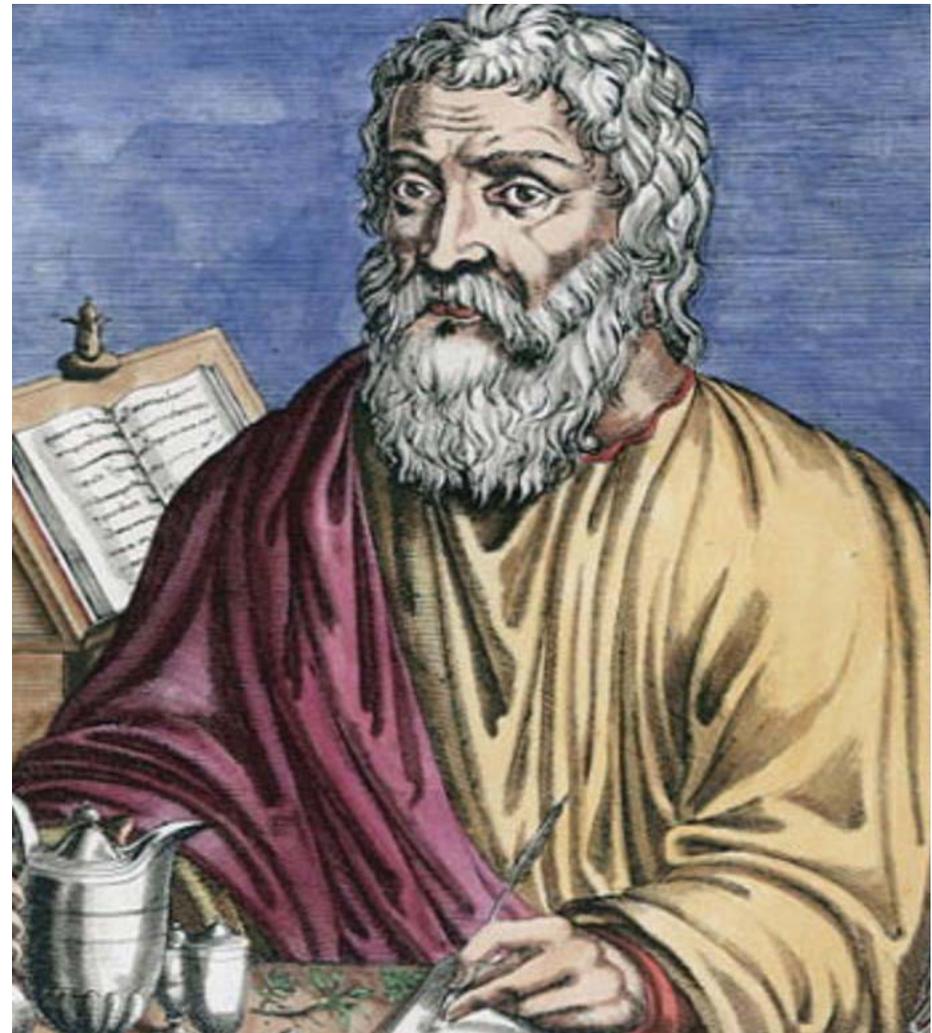


Thomas D. Szucs

18.02.15

Hippokrates (466-377 v. Chr.)

„Es ist wichtiger zu wissen, welche Person eine Krankheit hat, als zu wissen, welche Krankheit eine Person hat.“



Wo stehen wir heute?



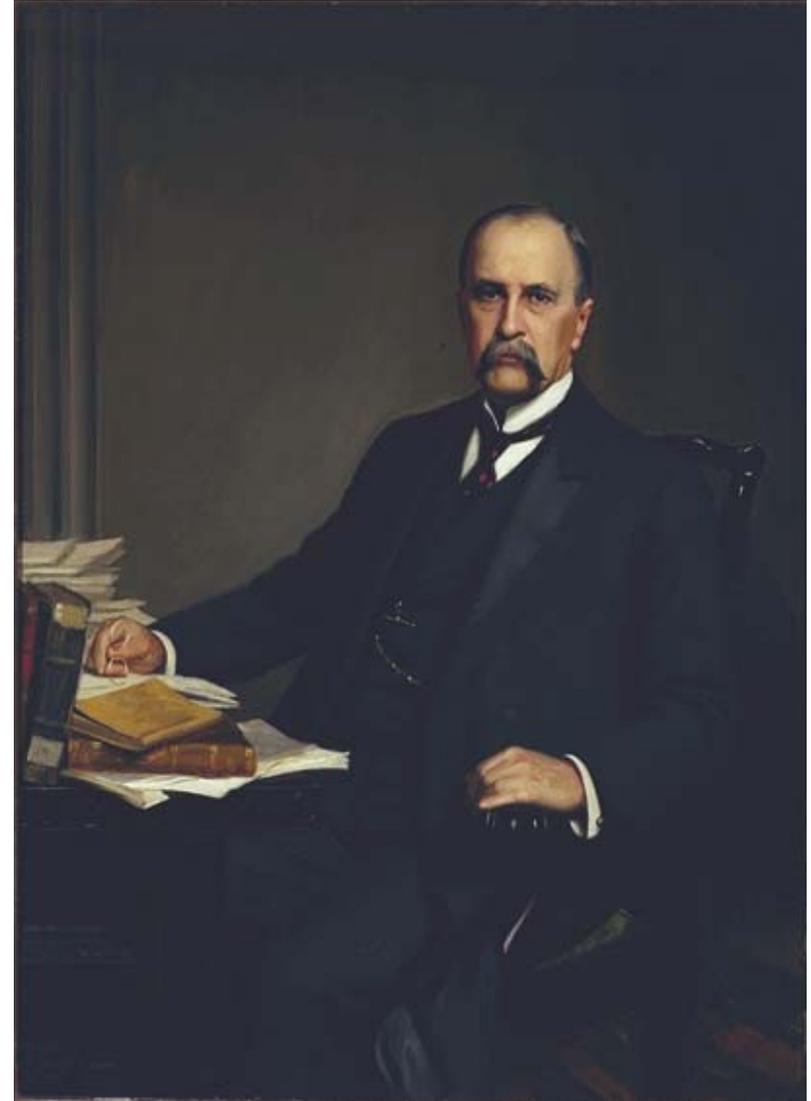
Genetische Forschung im Wandel



Wir sind alle verschieden



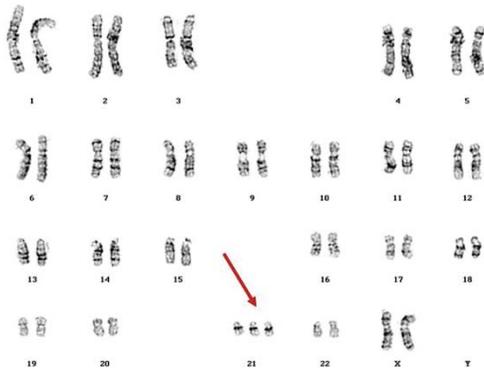
Sir William Osler



Genetik und Krankheit

Chromosomenstörungen

Down Syndrom



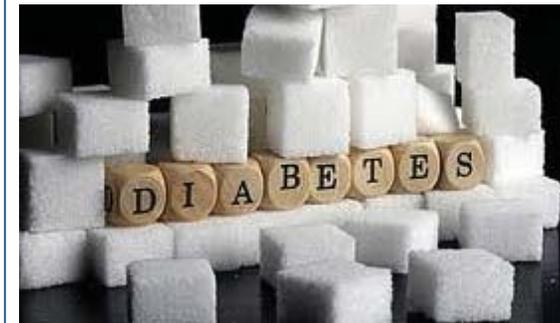
Monogene Erkrankungen

Bluterkrankheit



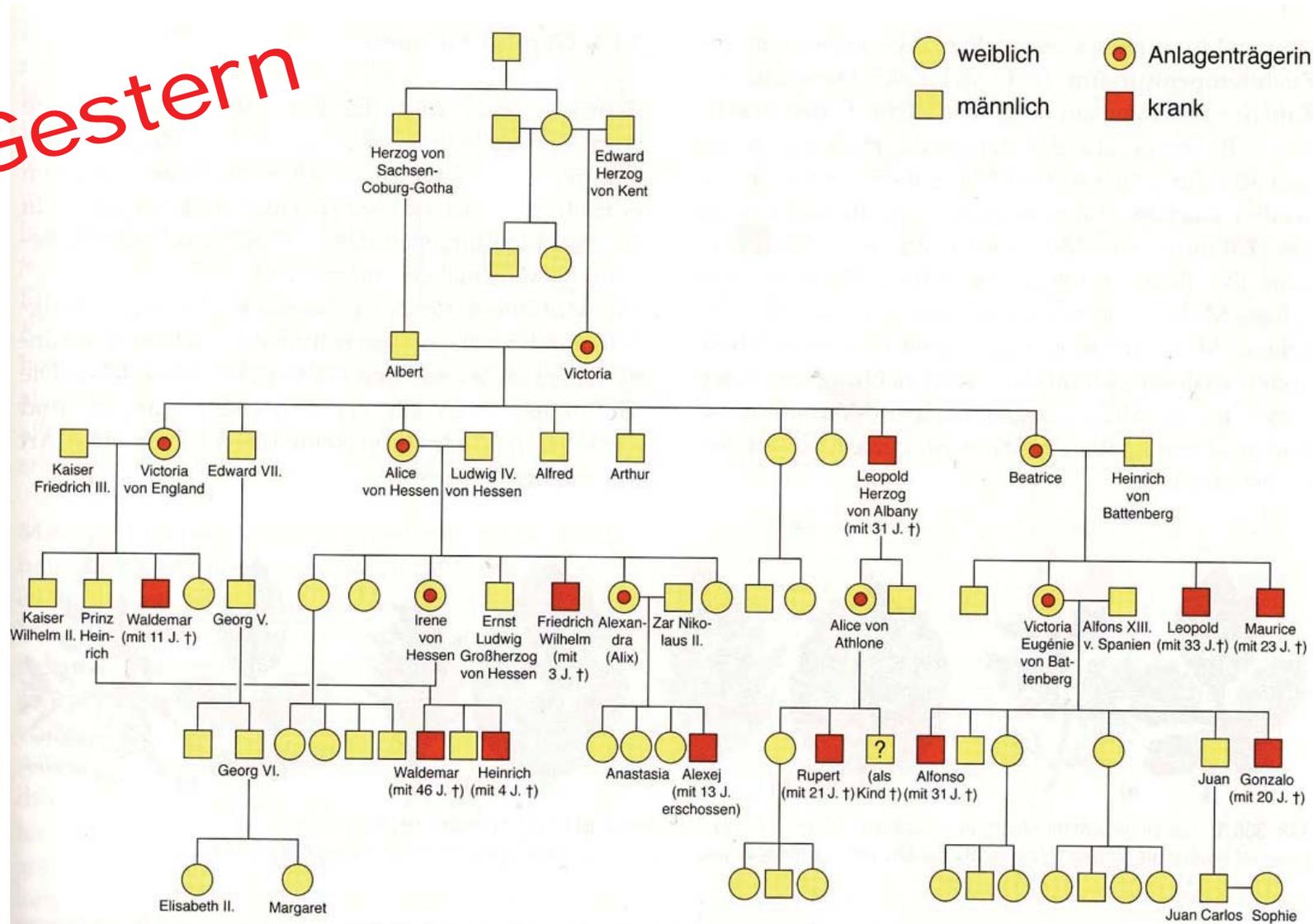
Multifaktorielle Erkrankungen

Zuckerkrankheit



Stammbaum europäischer Fürstenhäuser mit Bluterkrankheit

Gestern



Russische Zarenfamilie Romanow (1913)

Gestern



Zwillingsstudien

Gestern

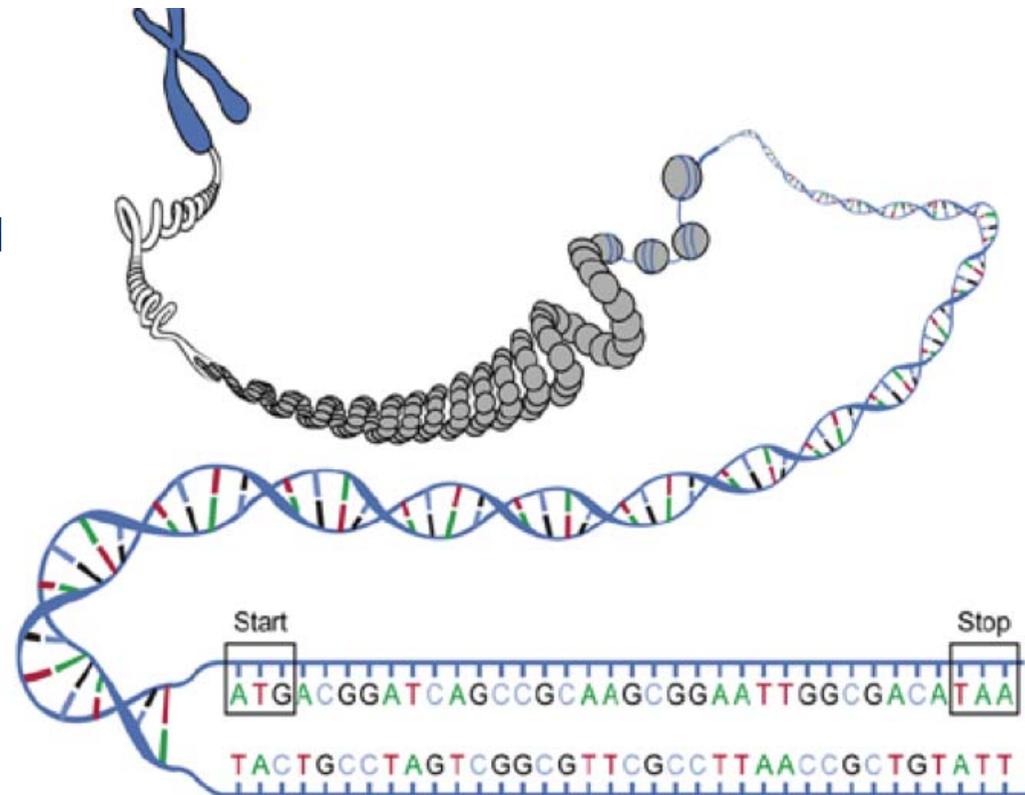


Die Blaupause

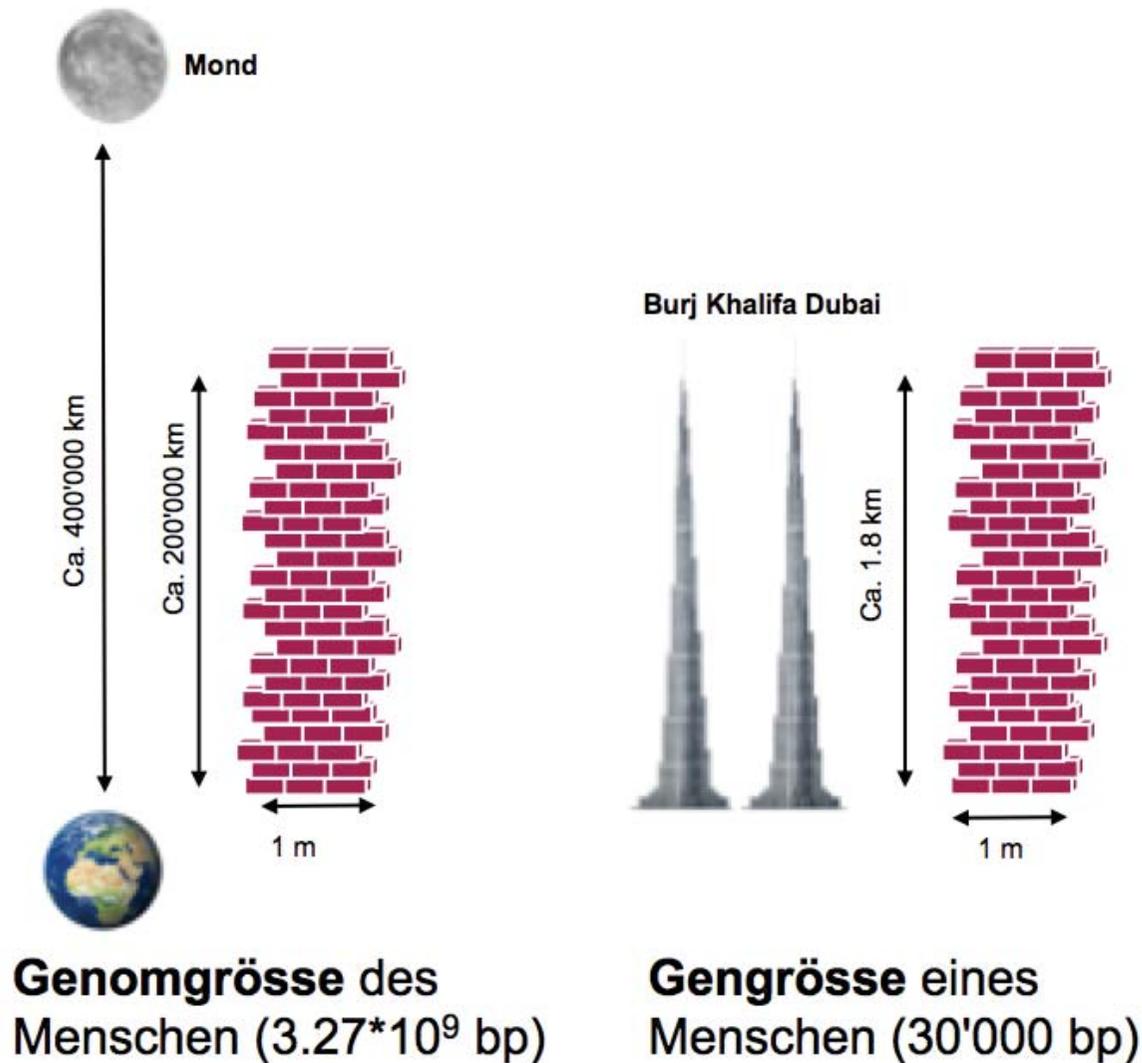


DNA = genomische Blaupause

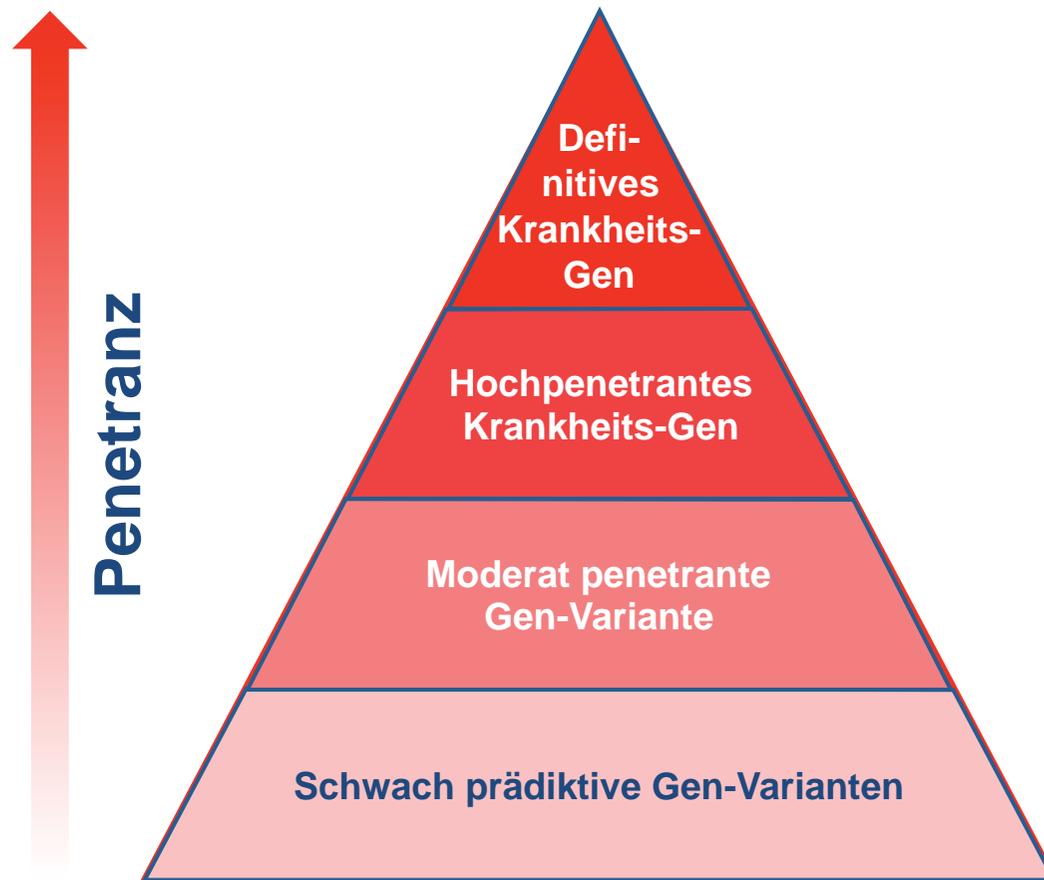
- 3 mrd Basenpaare
- 46 Chromosomen
- 30'000 Gene in 2 Kopien
- 2-3 mio Unterschiede zwischen individuellen Genomen
- 300 mrd Zellteilungen/Tag
- 40'000 Schäden pro Zelle/Tag



Dimensionen von Basenpaaren



Nicht jede Genvariante macht krank



Jeder wird krank

Die **meisten** werden **nicht** krank

Was kostet die Genom Sequenzierung und wie lang dauert sie?

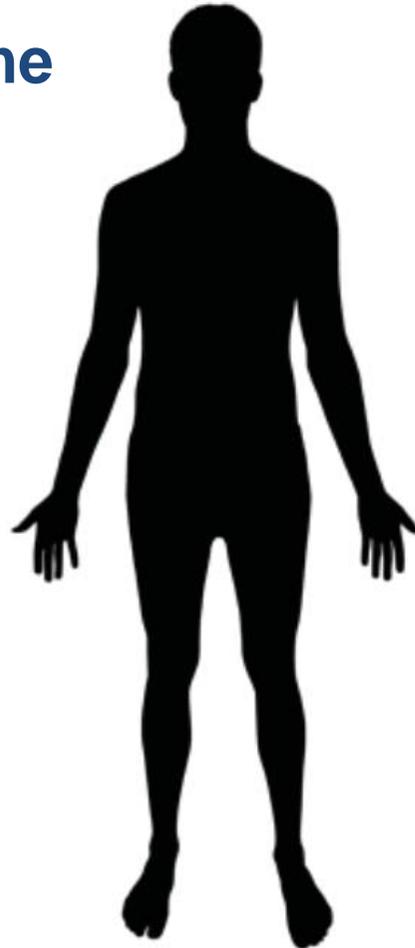
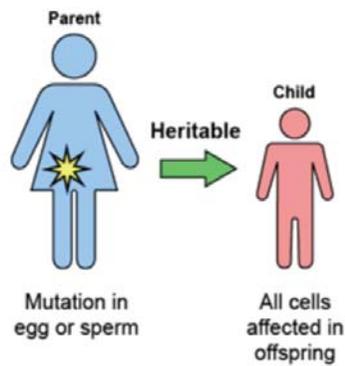
Wann?	Wie lange?	Kosten (?)
2001	15 Jahre	1 mrd USD
2015	10 Tage	30'000 USD
Bald	1 Stunde	1'000 USD



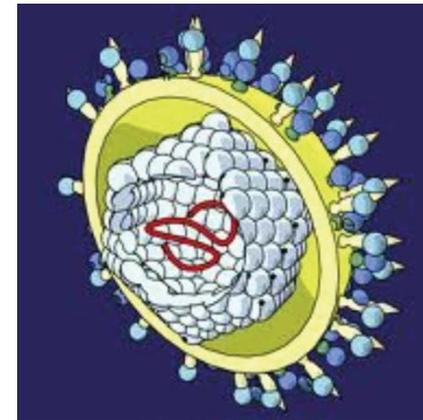
Humangenom Projekt: 2.5 mrd USD

Welche Gene interessieren?

Keimbahn Genome



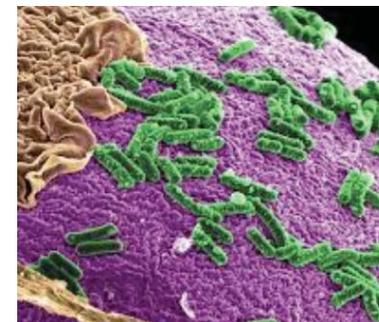
Infektionserreger Genome



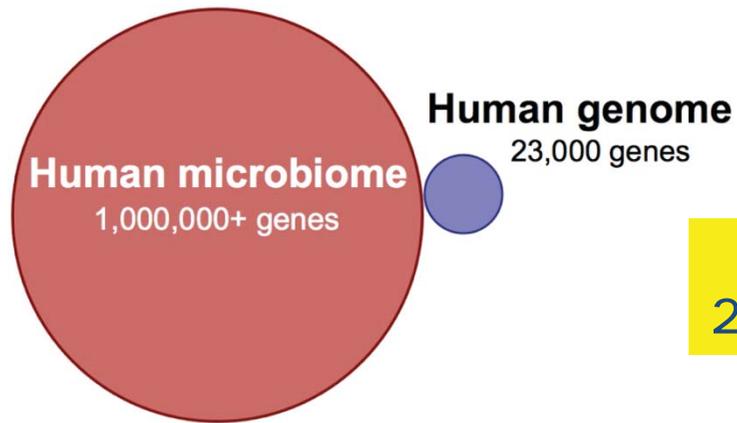
Tumor Genome



Mikrobiome

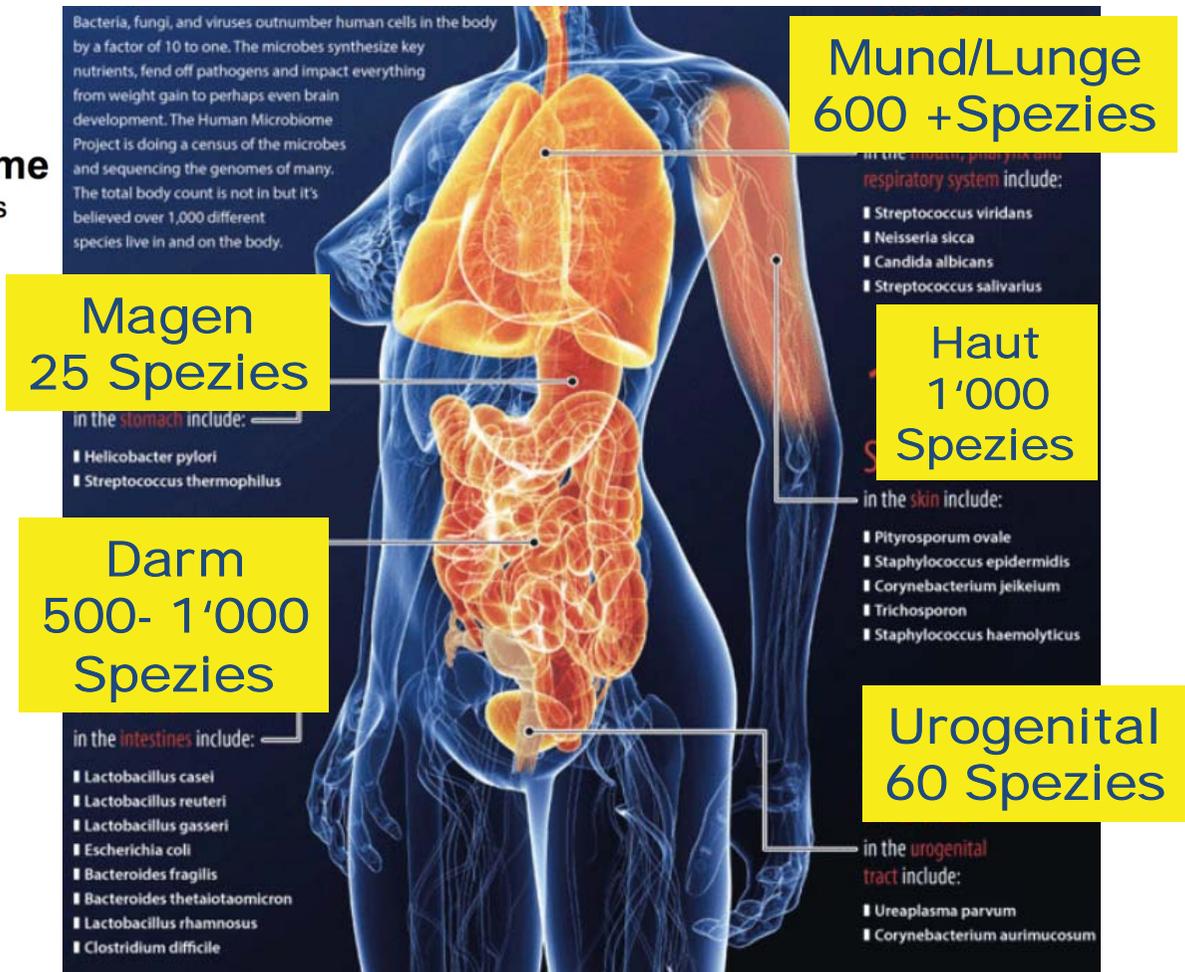


Mikrobiom: 10'000 Spezies (2kg)



Körperzellen: $1 \cdot 10^{13}$

Mikroben: $9 \cdot 10^{13}$



5P - Medizin



Präzise

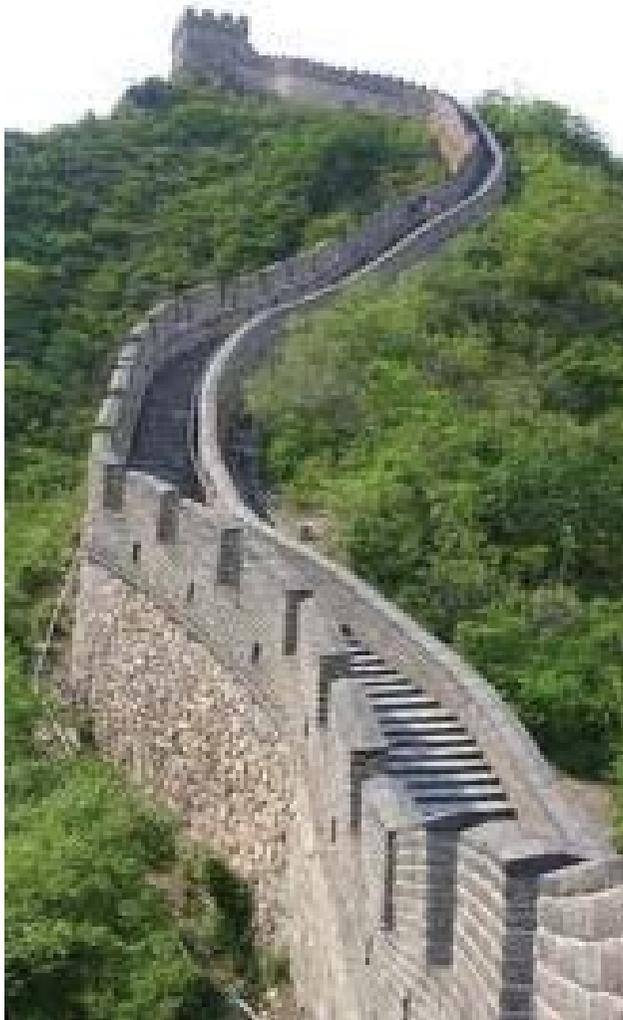
Prädiktiv

Präventiv

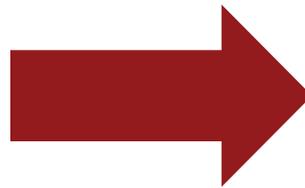
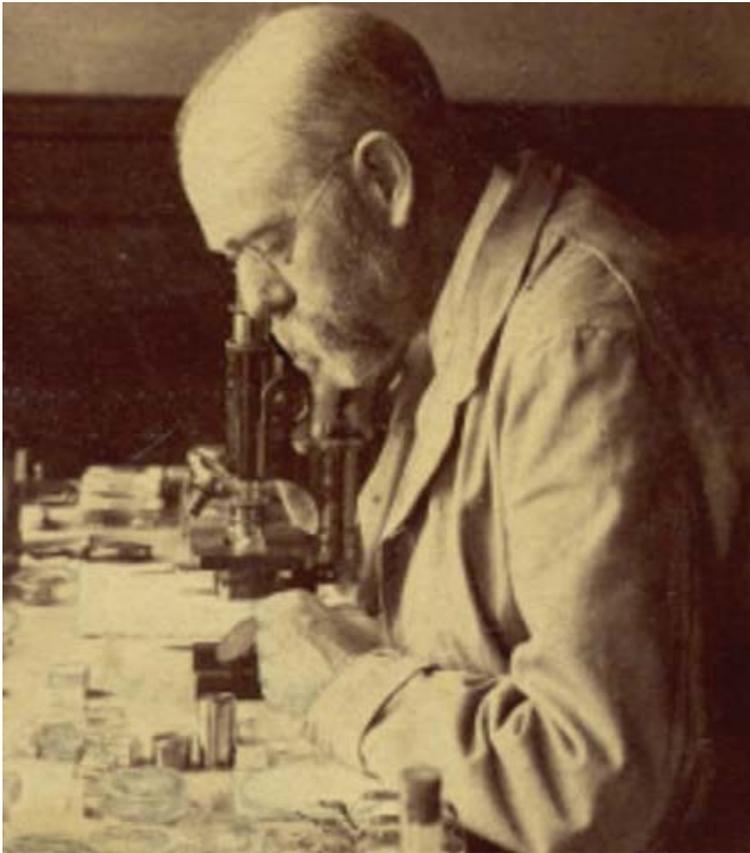
Personalisiert

Partizipativ

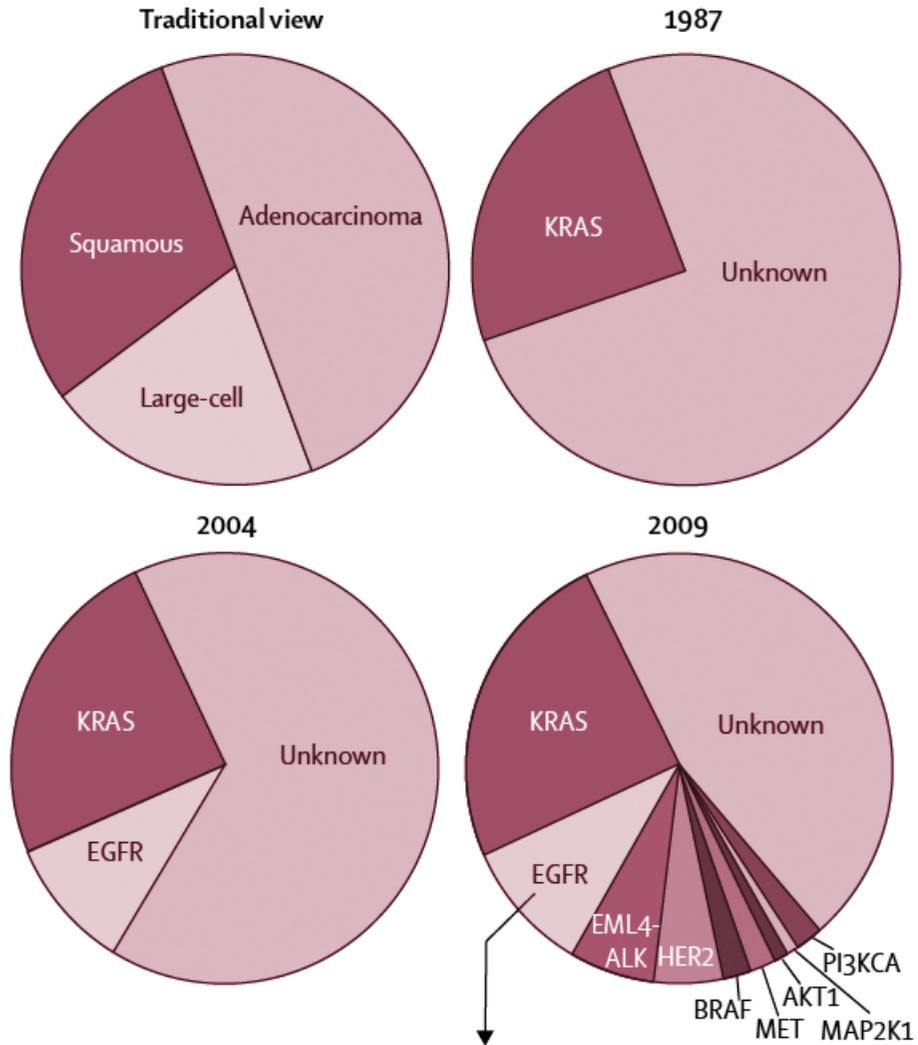
Diagnosen im Zeitalter der molekularen Medizin



Pathologie wird digital



Erkenntnis 1: Neue molekulare Klassifikationen (z. B. Lungentumore)



Pao W. Lancet Oncology 2011



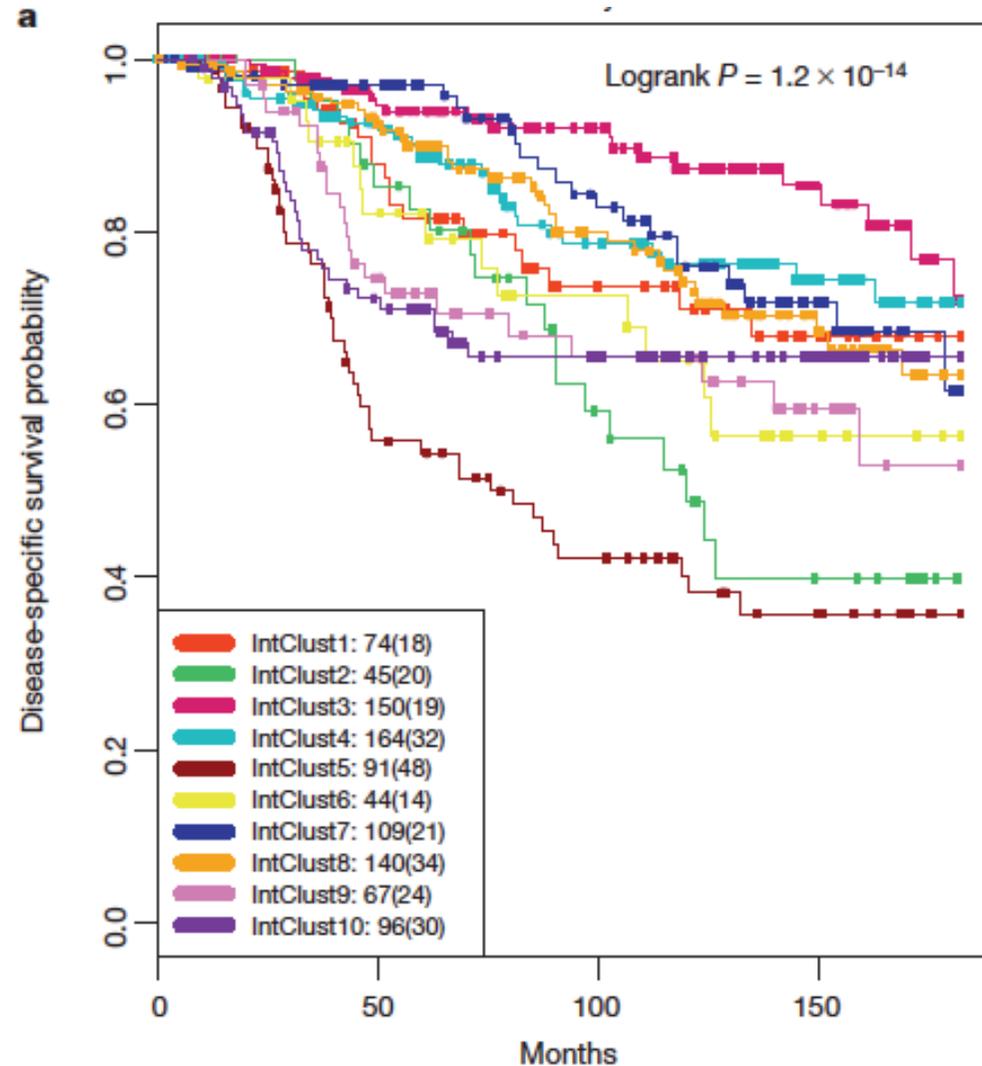
Erkenntnis 2: Molekulare Klassifikation hat auch Konsequenzen für Therapie und Prognose

ARTICLE

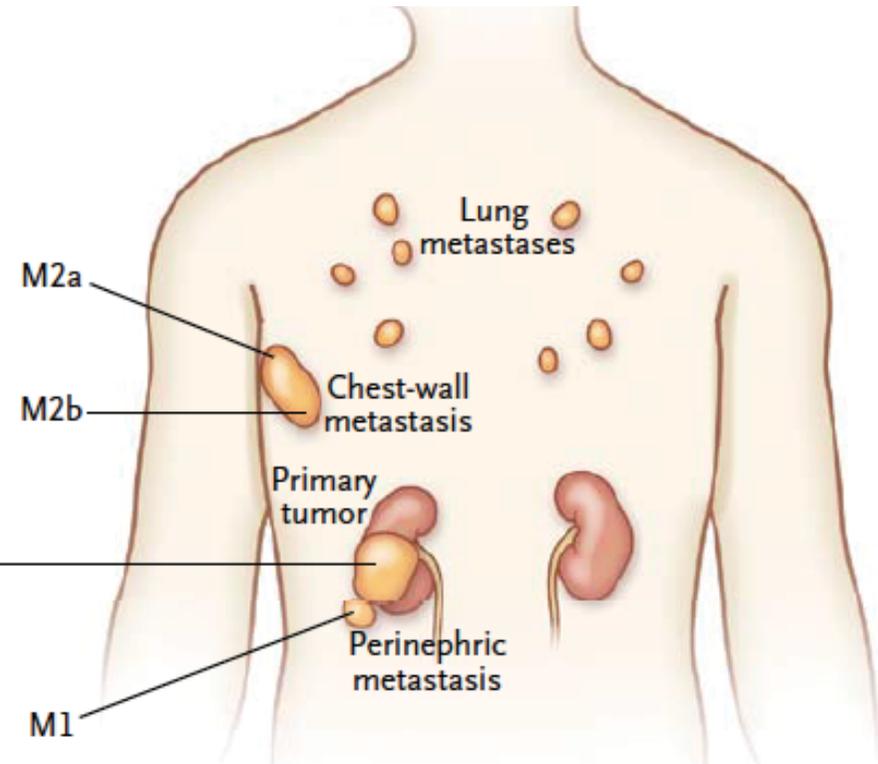
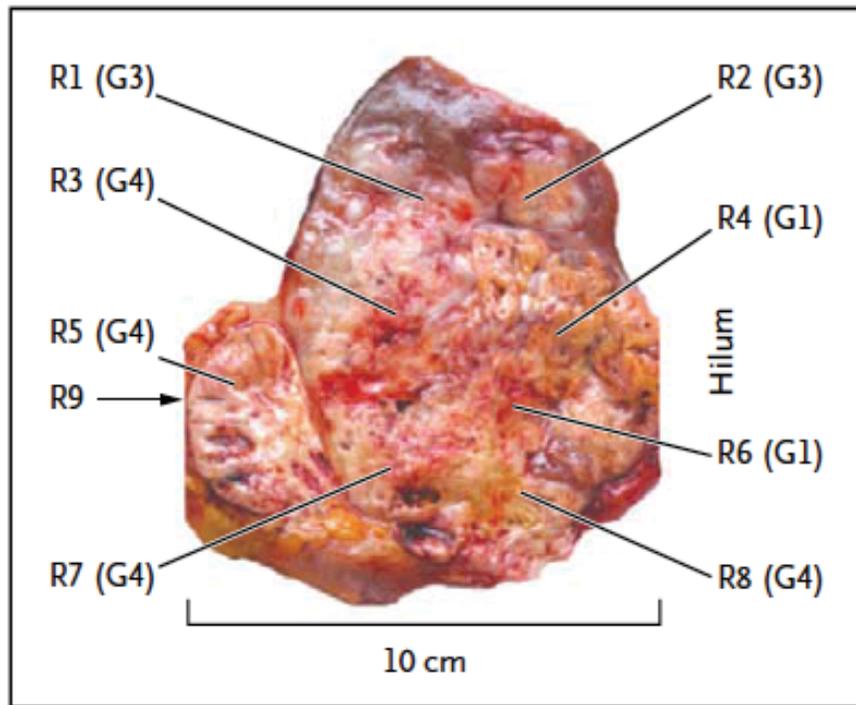
doi:10.1038/nature09003

The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups

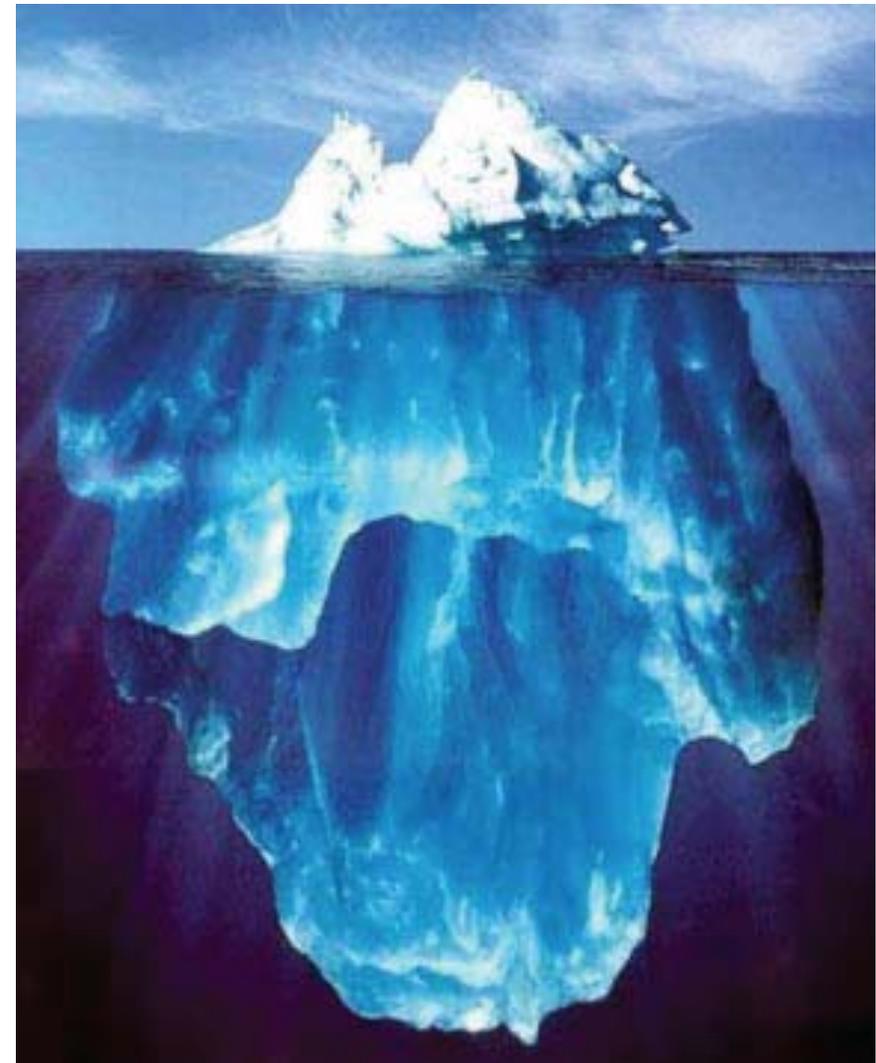
Christina Curtis^{1,2}, Laura J. Chin^{3,4}, Ingrid A. Olsson^{5,6}, P. Shih^{7,8*}, Scott-Peng Chin^{9,10*}, Galina Ivancheva^{11,12,13*}, Oscar M. Rueda^{14,15}, Mark J. Dunning¹⁶, Doug Speed^{17,18}, Michael J. Lynch^{19,20}, Shamith Samanthi^{21,22}, Yinyin Yuan²³, Stefan Geis²⁴, Gordon Ho²⁵, Cholanzena Hallam²⁶, Ali Raza²⁷, Sushant Kulkarni²⁸, Steven McKay^{29,30}, METABRIC Group¹, Anders Lauritzen³¹, Andrew Gown³², Elena Provenzano³³, Gordon Wilson³⁴, Sarah Pinjar³⁵, Peter Wikman^{36,37}, Florian Markowitz³⁸, Leigh Murphy³⁹, Ian Ellis⁴⁰, Arnie Purushotham^{41,42}, Anne-Lise Skov⁴³, John Doble⁴⁴, James D. Brenton⁴⁵, Simon Tavernier^{46,47,48}, Carlos Caldas^{49,50,51} & Samraa Aparicio⁵²



Erkenntnis 3: Molekulare Heterogenität ist eher die Regel als die Ausnahme

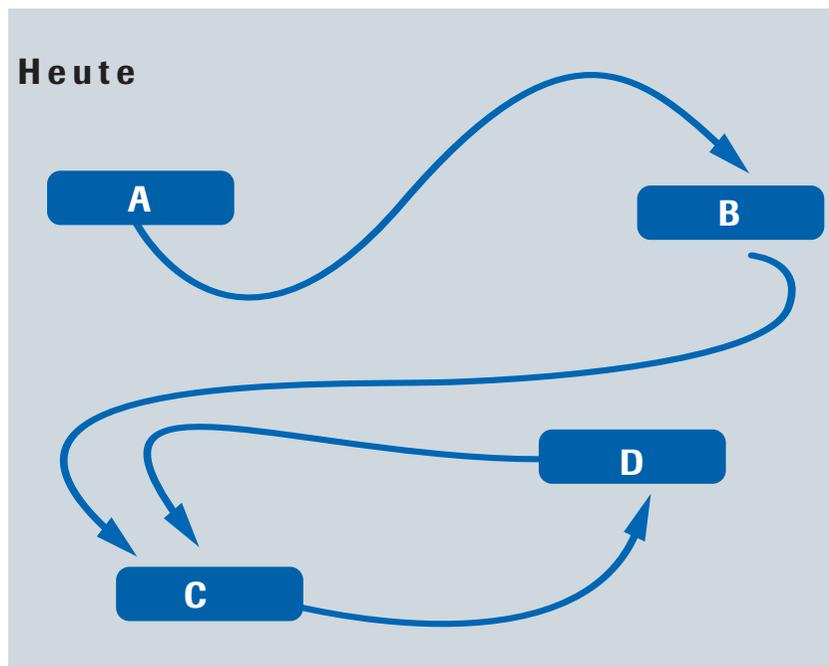


Diagnosen im Zeitalter der molekularen Medizin

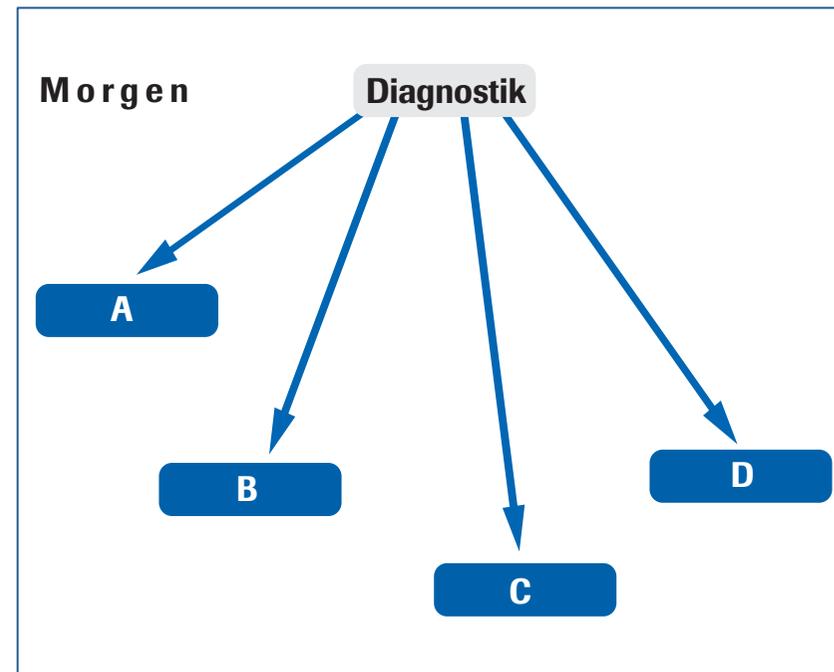


Therapieprozesse im Wandel

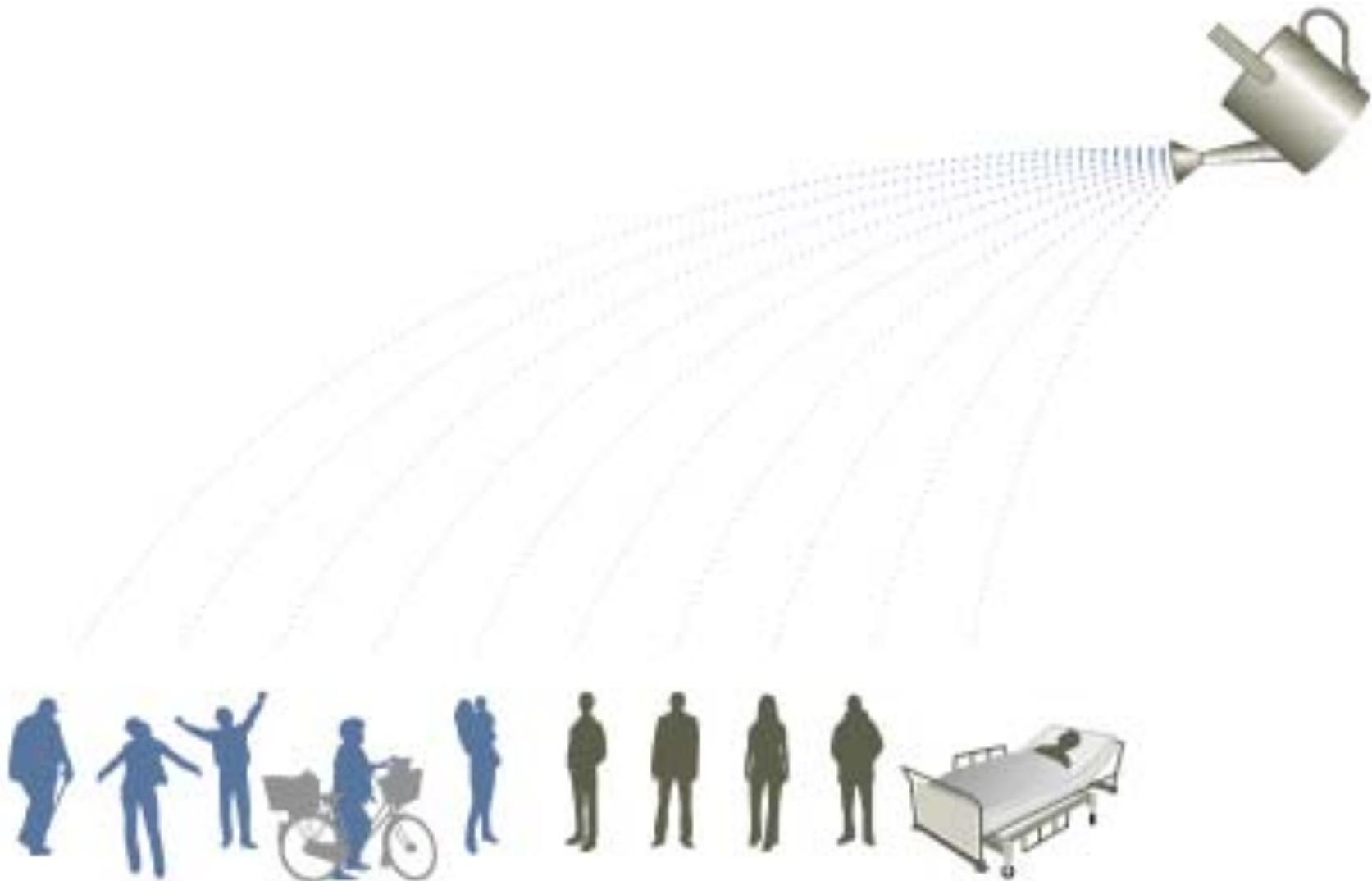
Alt



Neu



Personalisierte Medizin: Abschied vom Giesskannenprinzip

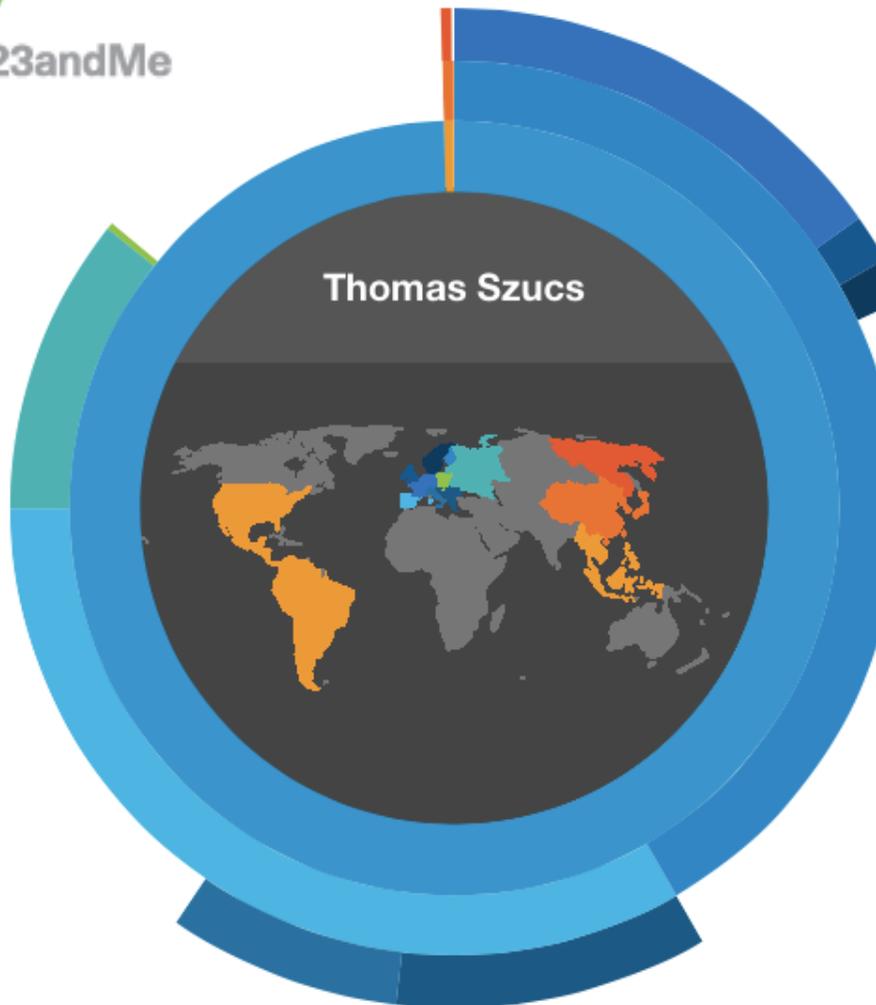


Wer soll Gentests in Auftrag geben? Mediziner UND/ODER Laien?



Abstammungsanalysen

LIFESTYLE



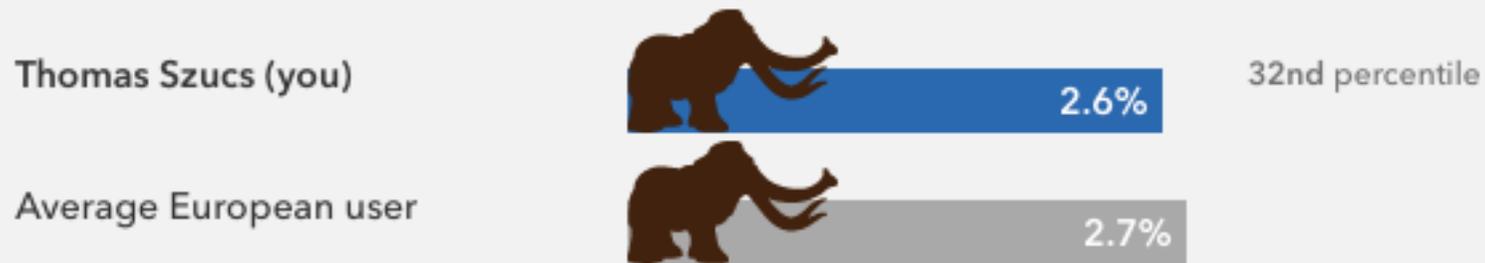
99.6%	European
	<ul style="list-style-type: none"> Northern European French & German British & Irish Scandinavian
15.2%	Broadly Northern European
1.6%	Southern European
1.4%	Balkan
23.5%	Italian
10.2%	Broadly Southern European
7.6%	Eastern European
15.5%	Ashkenazi
10.8%	Broadly European
0.3%	East Asian & Native American
13.6%	East Asian
	<ul style="list-style-type: none"> Yakut
0.4%	Broadly East Asian
0.3%	Unassigned
0.1%	
< 0.1%	
100%	Thomas Szucs

Neanderthal Genanteil

LIFESTYLE



An estimated **2.6%** of your DNA is from Neanderthals.



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



rs53576(G;G)

LIFESTYLE

Promethease Report

Version: 0.1.157

Generated: 2013-09-07 09:25

Infile: /Users/Thomas/Downloads/genome_Thomas_Szucs_Full_20130907000438.txt

Reference Population CEU

18331 genotypes annotated

- **... Optimistisch und empathisch**
- **... Besser im Erkennen von Emotionen anderer Menschen durch Beobachtung ihrer Gesichter**
- **... Erschrickt weniger beim Ertönen eines lauten Lärms**

Wer mag Koriander?

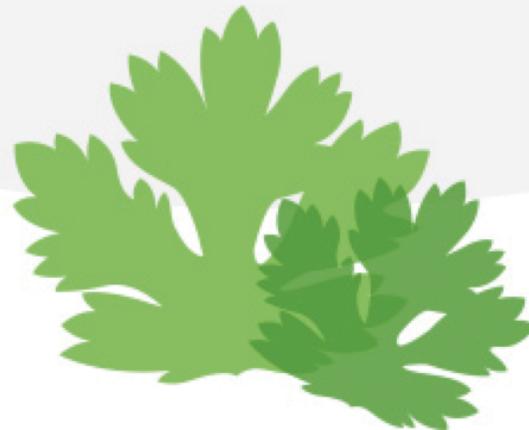
LIFESTYLE



23andMe

December 2014

**Your Genes
May Affect Whether
You Love or Hate Coriander**

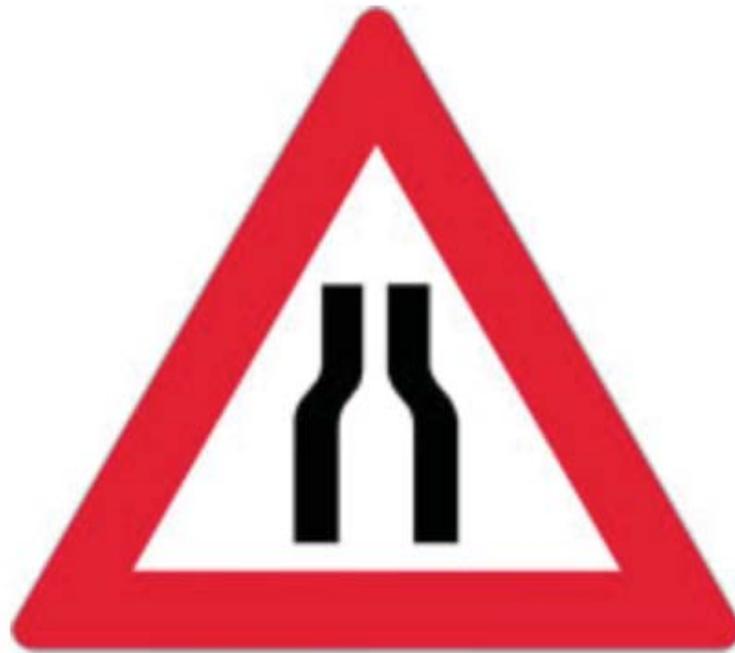


Herausforderungen und Chancen



Technologiekonvergenz

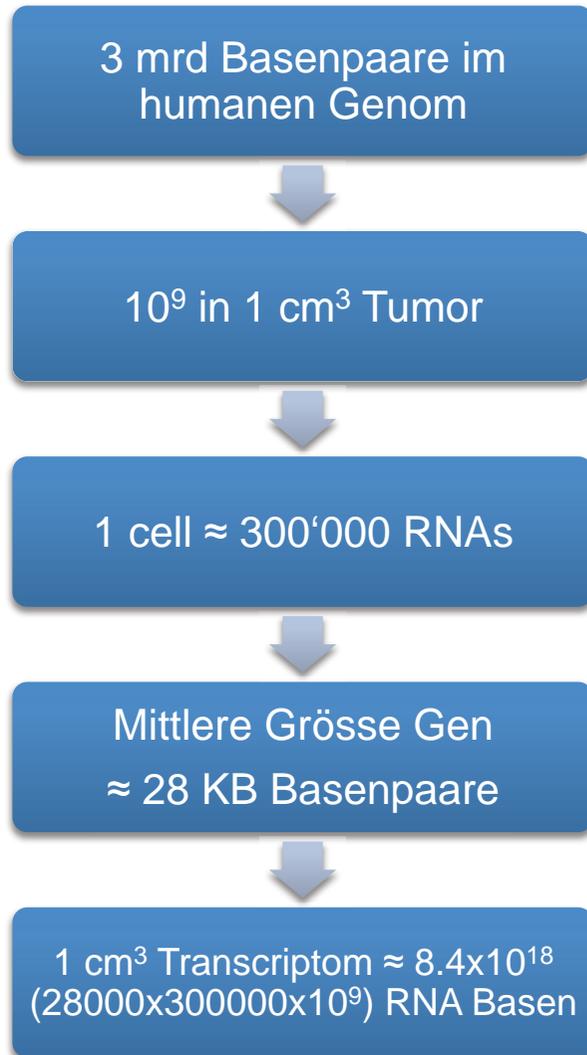
Medizin



Biologie

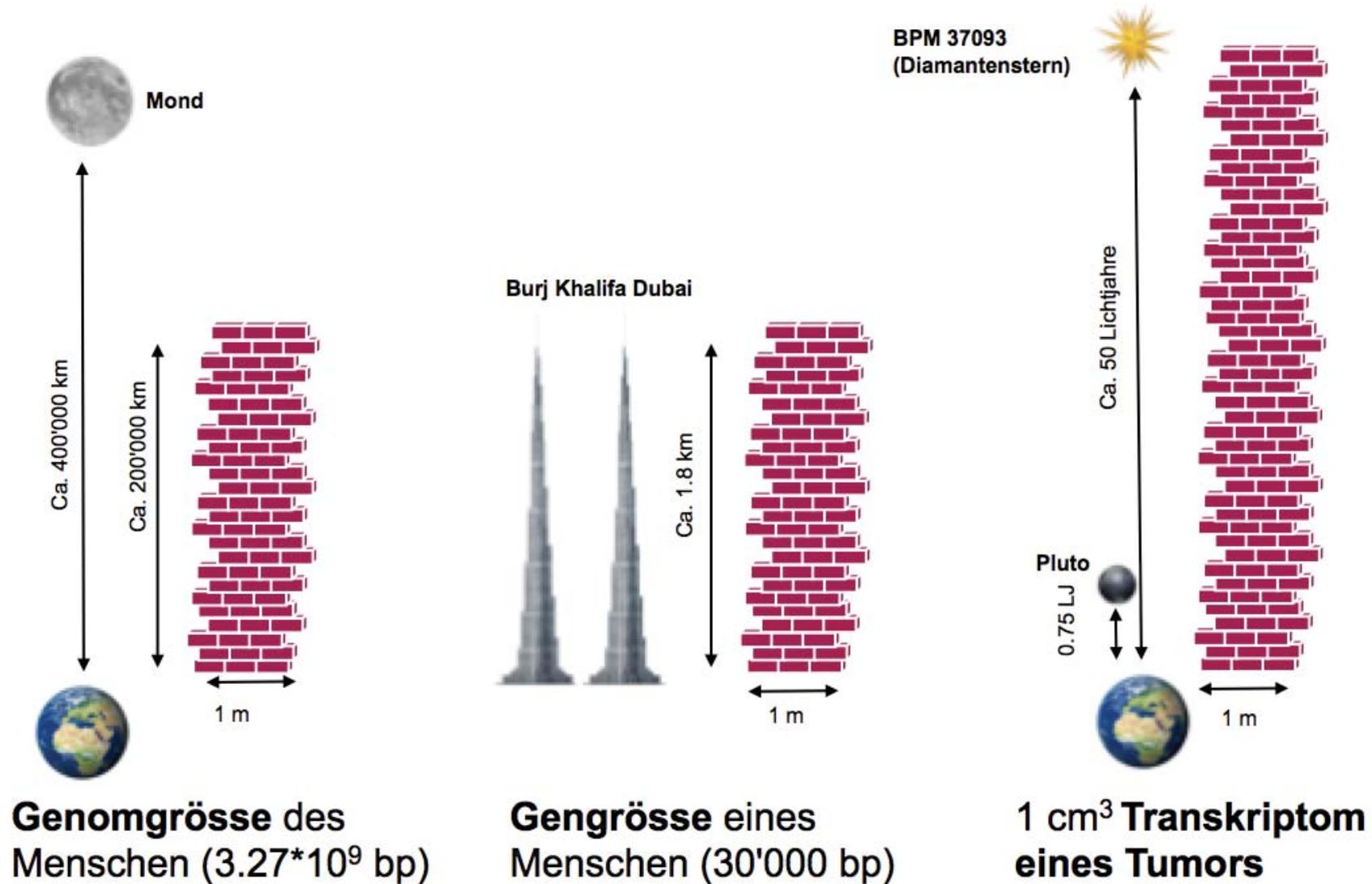
Informatik

Bioinformatik: Riesendatenmenge zur Analyse von 1 cm³ Tumor



- **8.4 Exabytes**
- **Vergleich: 5 Exabytes = Text aller je von der Menschheit gesprochenen Worte**

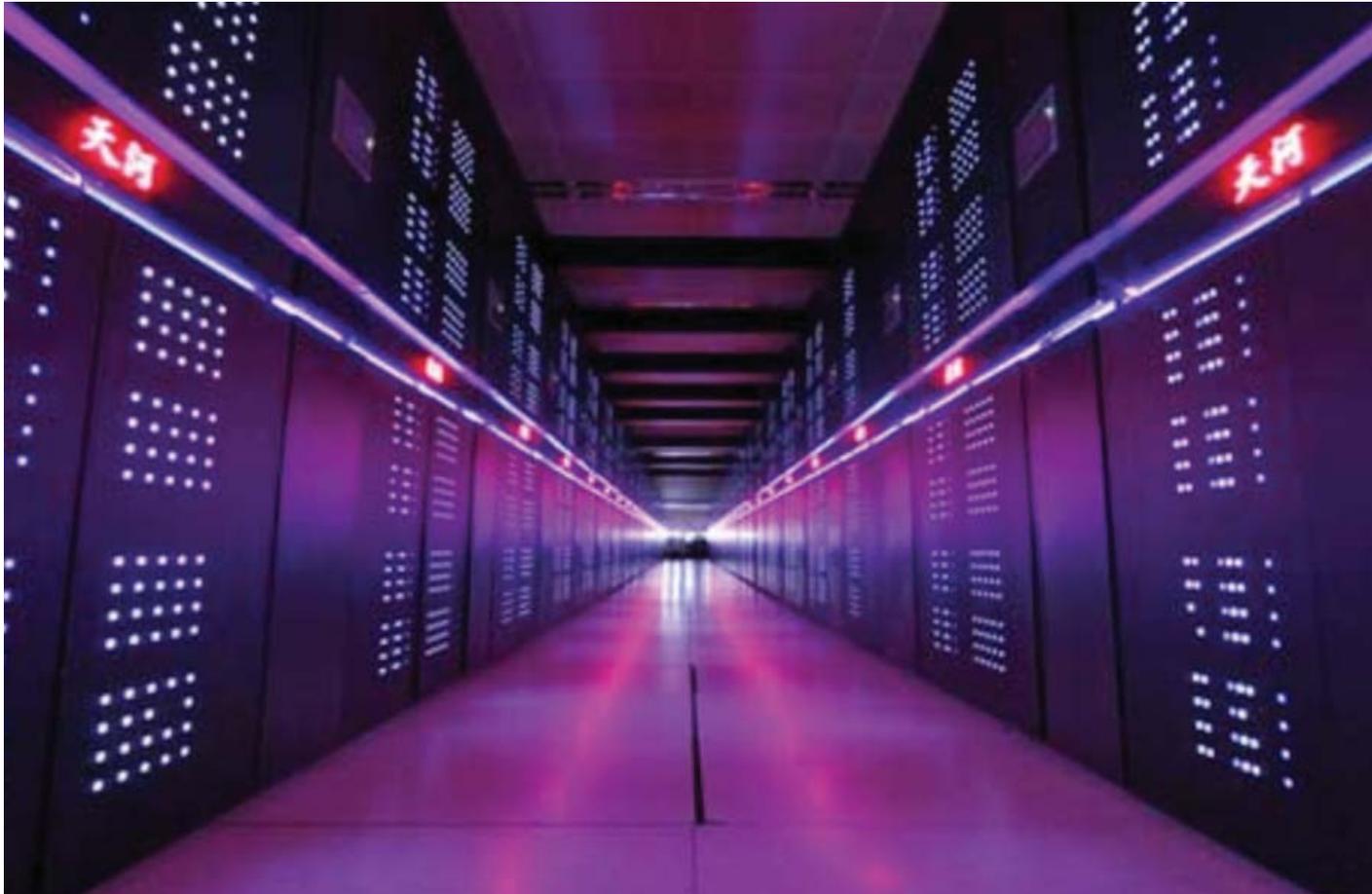
Dimensionen



Physische Biobanken



Digitale Biobanken

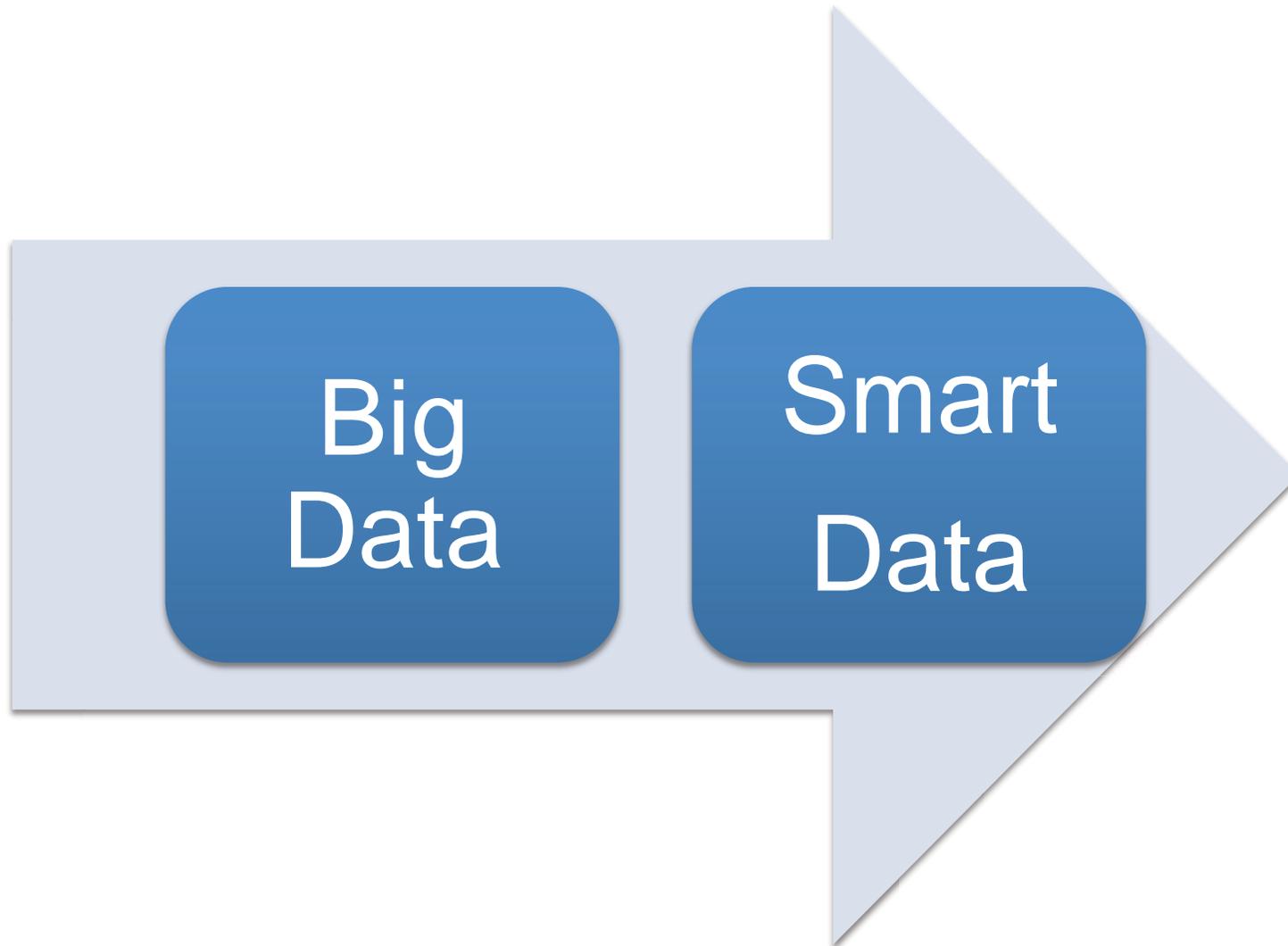


**National Super Computer Center
Guangzhou, China**

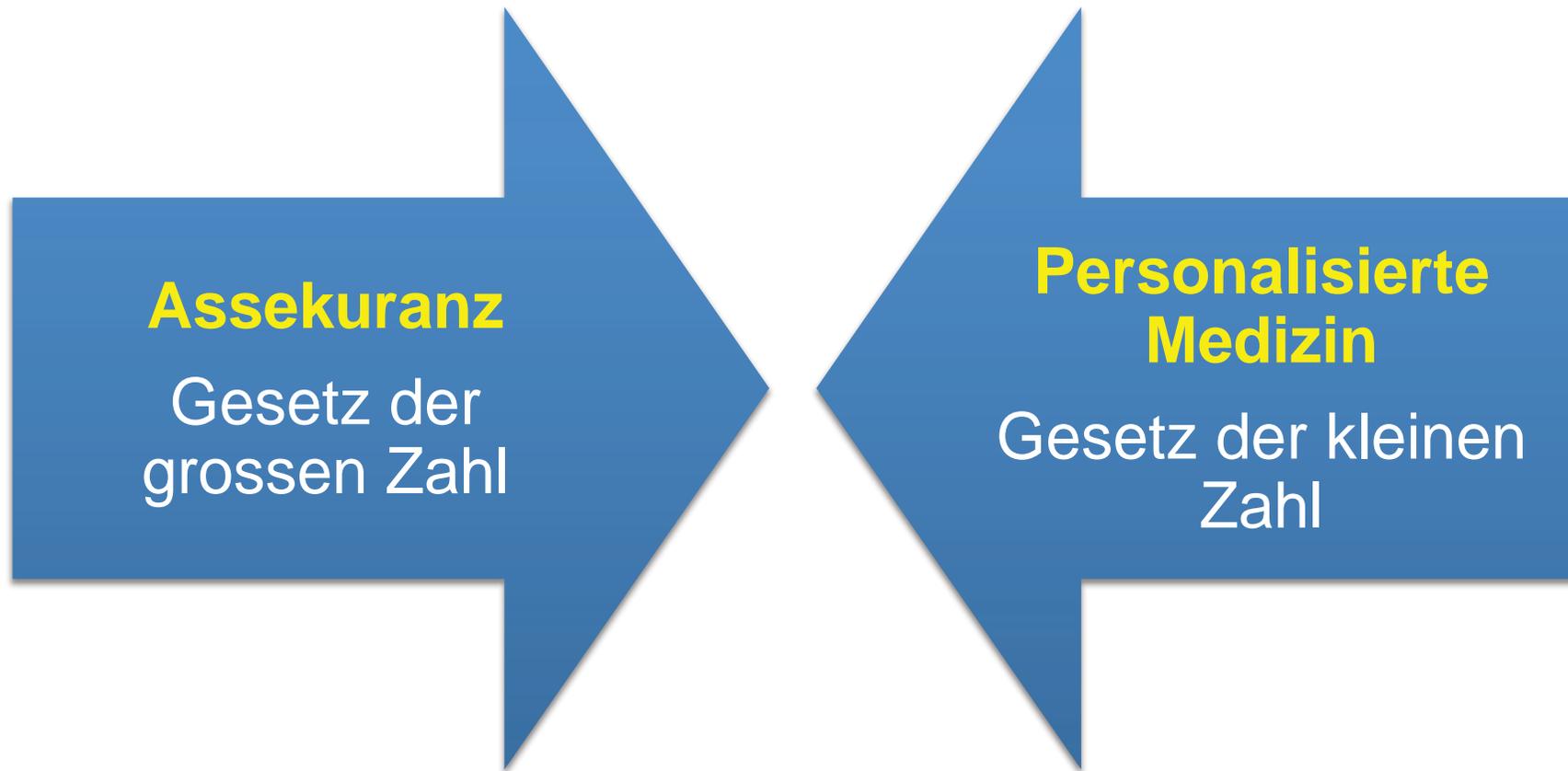
**33.8 Petaflops/s Rechenleistung
12.4 Petabytes Speicher**

(Oak Ridge Laboratory, Titan Supercomputer: 17 PFLOPS/s, 20-30 PBytes)

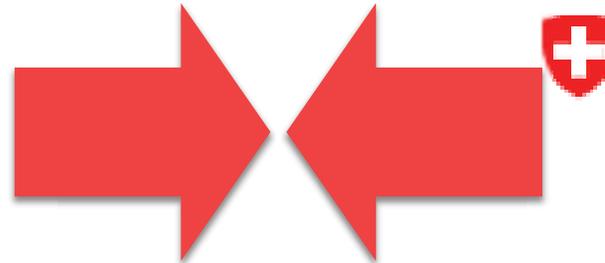
Wichtiges Ziel



Pricing: Zwei gegensätzliche Sichtweisen



Regulatorische Widersprüche



Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Eidgenössisches Departement des Innern EDI
Bundesamt für Gesundheit BAG



„Es gibt ein wichtiges Gen“

„Der Gentest wird nicht erstattet“

Patentrechtliche Aspekte



Ärztliches Haftungsrecht



Morgen ist heute schon gestern



Warum war bisher die Diffusion von genomischen Technologien langsam?



Gensequenzierung der gesamten Bevölkerung

SCIENCE FOR THE CURIOUS
Discover

FROM THE JULY/AUGUST 2013 ISSUE



Faroe Islands Aim to Sequence Genes of Entire Country

The country is offering whole genome sequencing to every citizen who wants it — a project that will chart the way for the future of genomic medicine.

By Brendan Borrell | Wednesday, December 11, 2013

Neues Genomik Programm in den USA



U.S. developing large-scale genomics project

The Obama administration is planning a new, large-scale genomics project that could be formally announced in the State of the Union speech on Tuesday, according to administration sources. NIH Director Francis Collins proposed the project to the White House. NIH will lead the project, which will include FDA and other federal agencies.

The project will include sequencing of up to a million human genomes. It will incorporate a push to develop new tools to analyze large genomics databases and make the data useful for research and medicine. [Back](#)

State of the Union Address 20.1.2015

Tonight, I'm launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes—and to give all of us access to the personalized information we need to keep ourselves and our families healthier.

1 mio Menschen

Gesundheit 2020 (Wo sind die Gene?)



Gentestung – Die „neue Normalität“

Geregelter Markt für Gentests

Expertenkommission des Bundes empfiehlt Zulassung unter strengen Auflagen

Gefahrengut Transport Heute



Gefahrengut Transport **Morgen**

Land A



Telekommunikation

Land B



Medikamenten Re-Positionierung

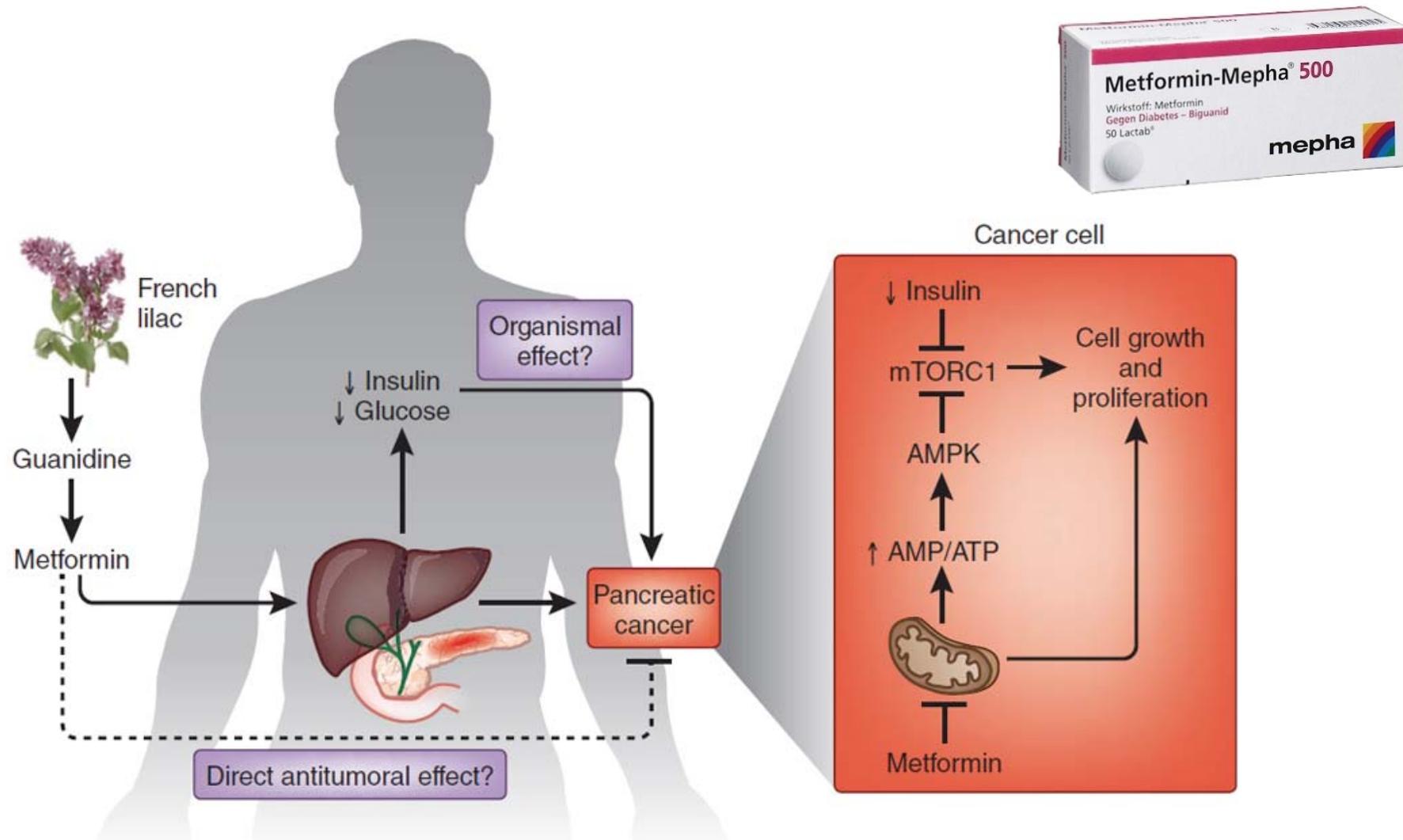
- **Alter Wein in neuen Schläuchen!**



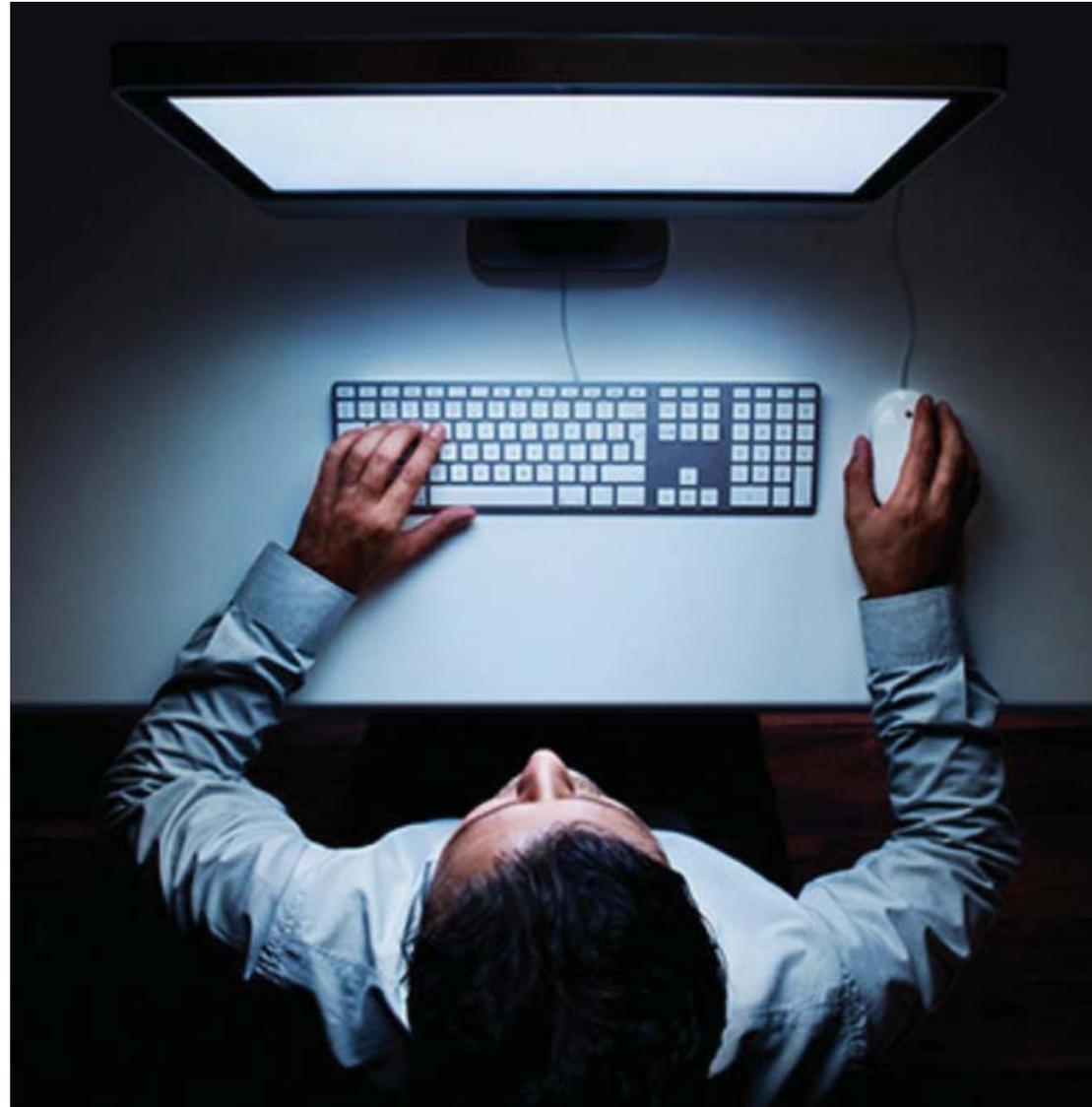
Konzept von molekularen Pfaden



Metformin – ein altes Diabetes Medikament als Tumorthherapie



Repositionierungen: Labor = Computer (*in silico*)



Unsere Riesenchance



Elite controllers
Super heroes
Exceptional responders



