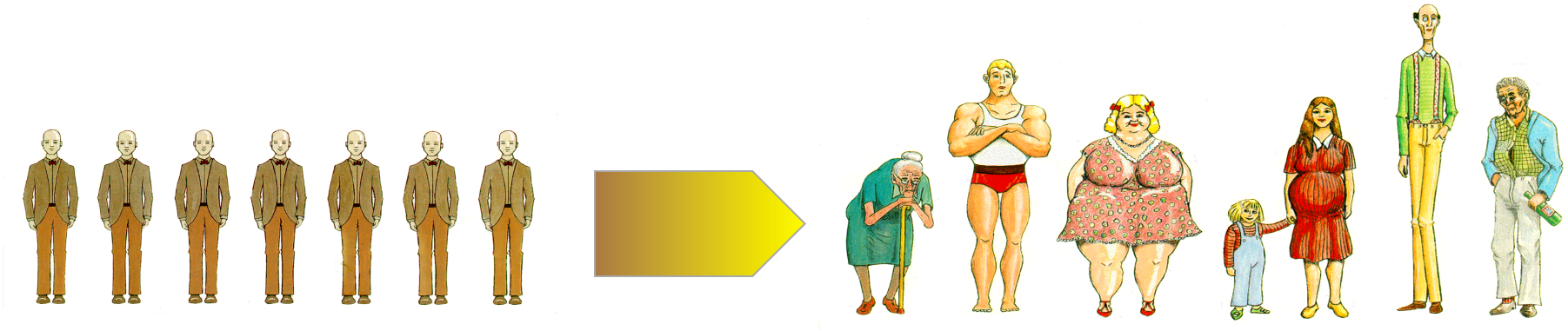
Gibt es individualisierte Medizin auch ohne Genotyping?

Jochen Maas

Personalisierte Medizin – was ist das?



Personalized medicine is a medical model emphasizing in general the customization of healthcare, with all decisions and practices being tailored to individualized patients in whatever ways possible. Recently, this has mainly involved the systematic use of genetic or other information about an individual patient to select or optimize that patient's preventative and therapeutic care[1]

- … um die **Effektivität** von Arzneimitteln zu verbessern
- … um die **Sicherheit** von Arzneimitteln zu erhöhen
- … um die **Dosis** von Arzneimitteln zu optimieren

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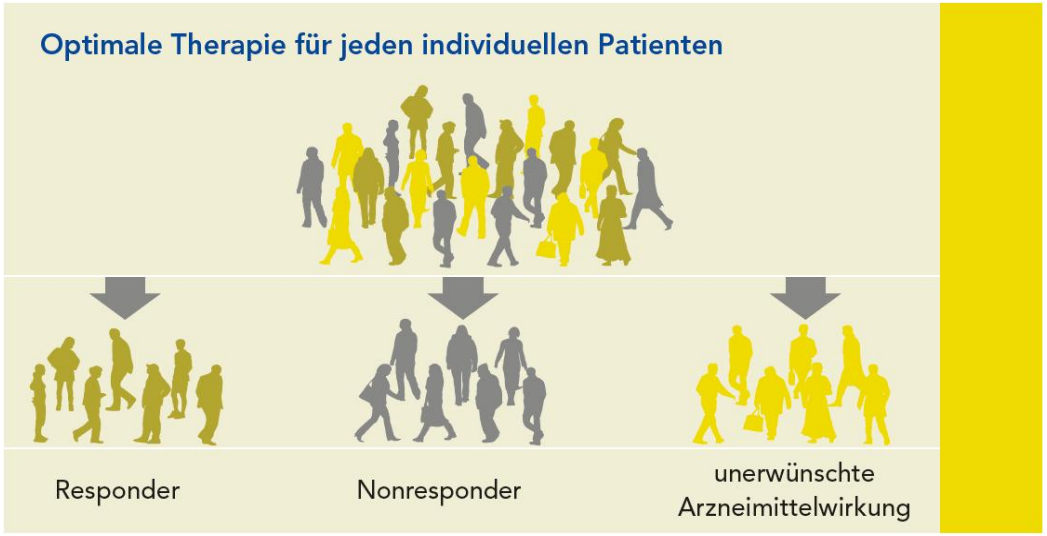
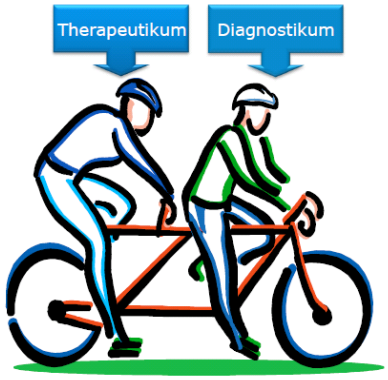
Voraussetzung für alle personalisierten Ansätze

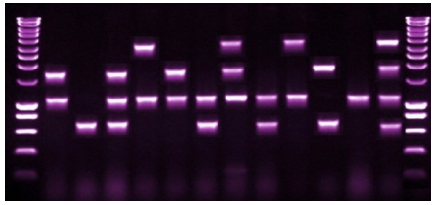
O: Patient stratification – Optimized therapy for each individual patient

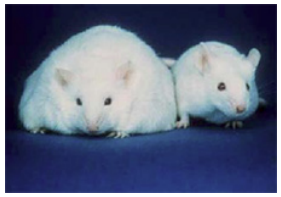


Quelle: Johann Wolfgang Goethe-Universität, Frankfurt am Main



P: Diagnosis: Genotyping and Phenotyping





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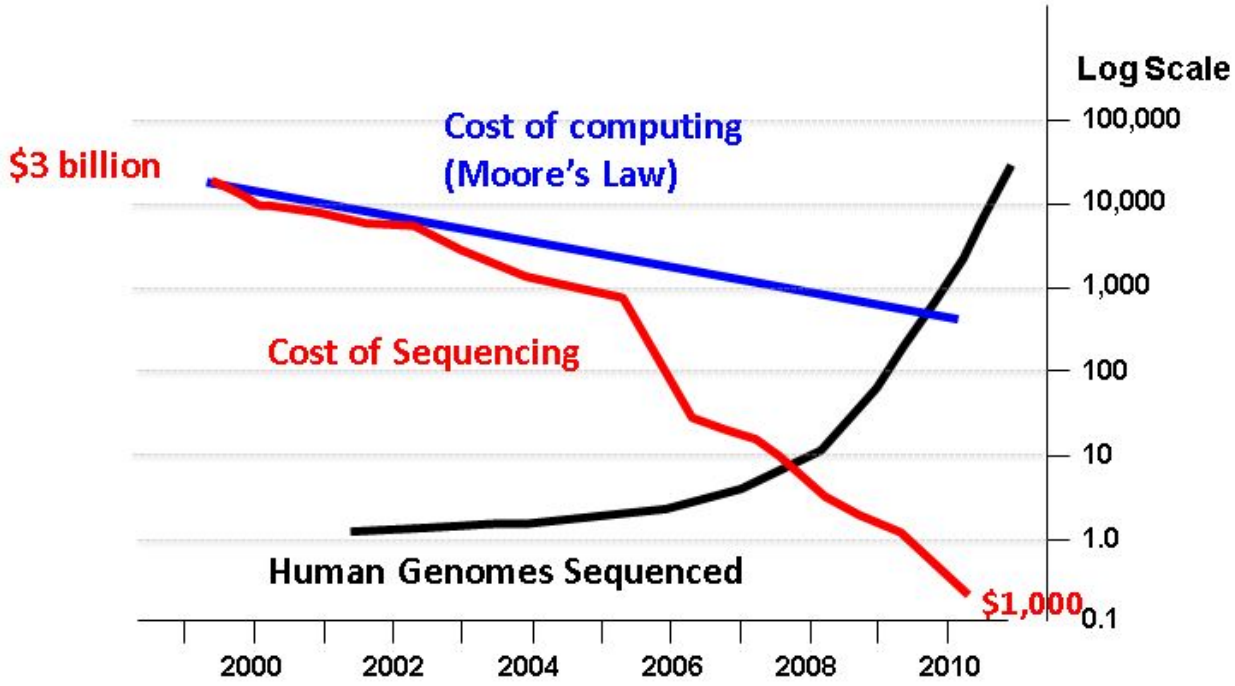
Wo kommt der „Hype“ her?

Adapted from The Economist

The Sequencing Explosion



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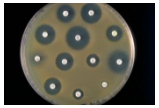
Beispiele außerhalb Genotyping / Onkologie

Personalisierte Medizin gibt es schon lange….



Antibiogram: Ist das nicht auch personalisierte Medizin?

Implantate: Ist das nicht auch personalisierte Medizin?

Zahnmedizin: Ist das nicht auch personalisierte Medizin?

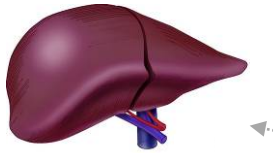
Überall: Ist eine exakte Anamnese nicht auch personalisierte Medizin?

.... und wie sieht es bei den großen Volkskrankheiten aus ?
(z.B. Herzinfarkt, ZNS-Erkrankungen, Diabetes)?

Heterogenität von Diabetes (*ohne irgendeine Genanalyse*): Beteiligung vieler Organe und Gewebe

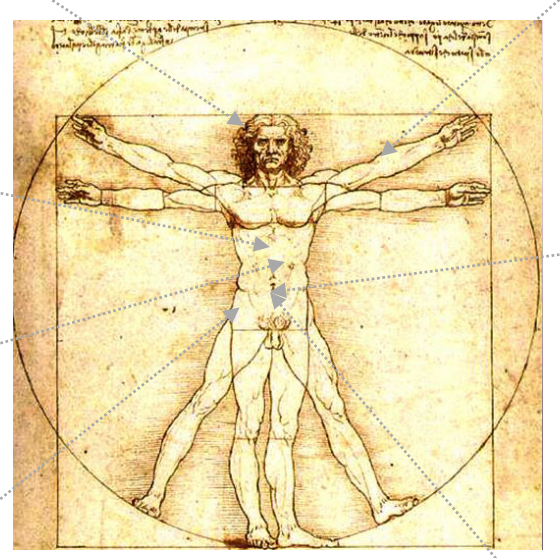
<u>Brain</u>
Regulation of food intake

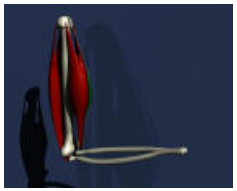
<u>Liver</u>
Glucose production/ storage
Lipid metabolism



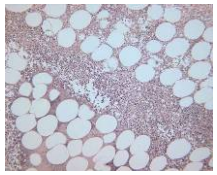
<u>Pancreas</u>
Secretion of Insulin, SST, Glucagon, PP

<u>Kidney</u>
Glucose reabsorption





<u>Muscle</u>
Glucose uptake



<u>Adipose tissue</u>
Glucose uptake
NEFA and adipokine release

<u>Gut</u>
Enteroendocrine hormone secretion (e.g. GLP-1, Ghrelin, PYY)
Nutrient uptake
Microbial metabolism

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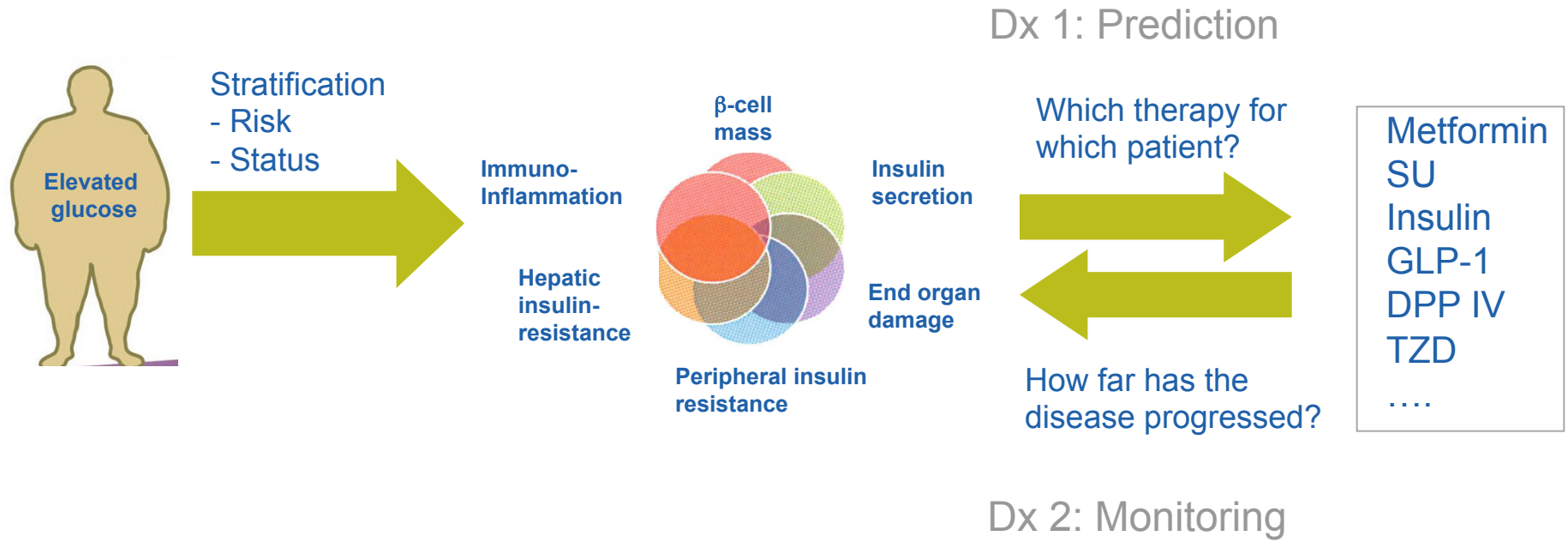
Personalisierung durch Kombination von Biomarkern (1)

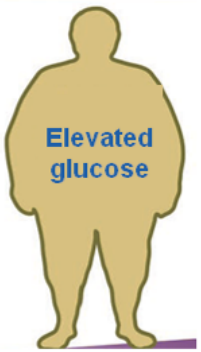


Personalisierung durch Kombination von Biomarkern (2)

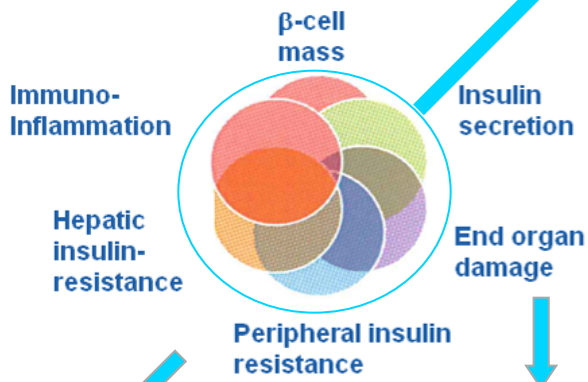
Detect genetic predisposition to T2D
Ca. 38 common genetic risk factors from GWA studies

β-cell status
- β-cell mass by noninvasive imaging
- Assess function by quantitative models

Prognose and monitor T2D by scores
- Branched chain (I,L,V) and aromatic (Y, F) amino acids - Wang, Gerszten)
- 5-year risk of developing diabetes based on glucose and 6 proteins (Lyssenko, Groop, Ordea)
- (Pre-)diabetes status by multiple proteins (Biophys corp)
- Cardiometabolic status by Proinsulin, Adiponectin, CRP (Pfützner)



Stratification
- Risk
- Status



Prognose CV events
- Troponin, NT-proBNP, IL6, CRP

Insulin resistance
-Detect IR, prognose progression of IGT by 3 metabolites (α-HB,L-GPC,oleate – Gall, Ferannini et al)
- Liver-specific IR-markers (Fetuin-a, SHBG, Selenoprotein P - Häring, Fritsche et al)

Prognose progession to DN
- Urinary proteomes (Mischak)
- TNFR, macrophage marker YKL-40, tubular damage markers L-FABP, NGAL, KIM-1

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Fazit

Genotypisierung ist ein wichtiger…….

… aber bei weitem nicht der einzige Aspekt der individualisierten Medizin