March 23rd, 2022
Pharmaforum Wiesbaden

Medizin nach Corona – Neue Technologien für die Gesundheitsindustrie

Jochen Maas

Megatrends of Medical Research

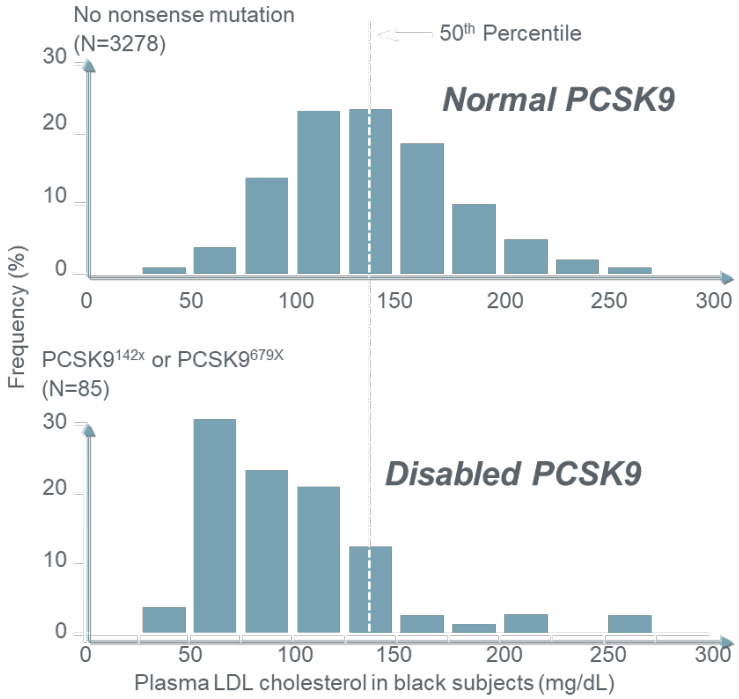
Technologien *und Denkweisen*

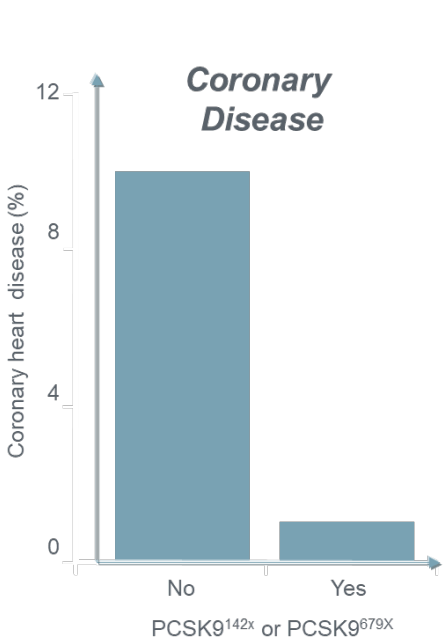
- Translational medicine
- Solutions, not longer only Drugs
- Digitalisation incl. self-medication and tele-medicine
- Modulation of immune-system
- Individualisation of medicine
- Gene-therapy
- (Vaccines)

- *… and what about ethics?*

Translational medicine – The PCSK-9 example (1)

The "translational" aspect: Disabled PCSK-9 results in significantly lowered LDL



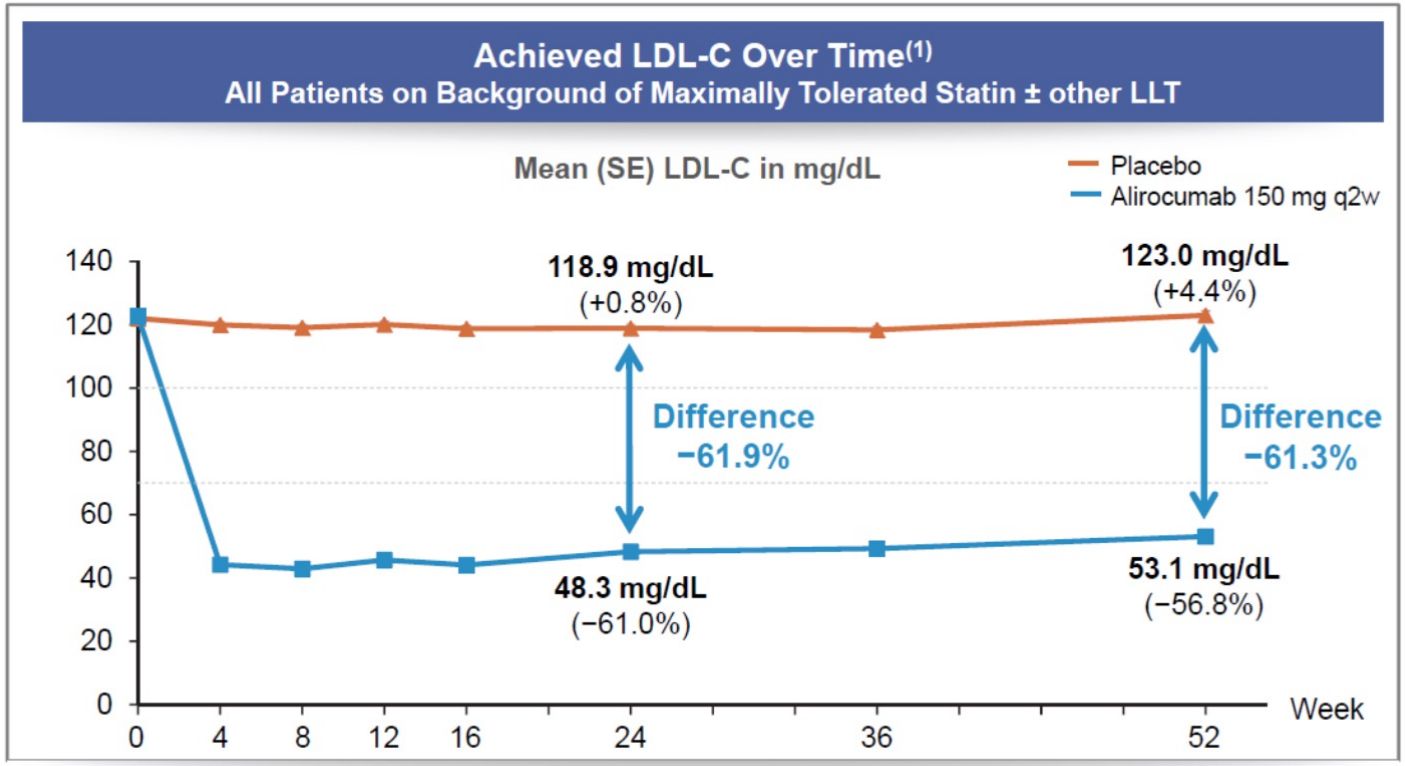


From an (clinical) observation to a product

… in 12 years

Cohen JC. *N Engl J Med* 2006;354(12):1264-72

… and it works – The PCSK-9 example (2)



Solutions for Patients – not longer only drugs (1)

Digitalisierung

Patient von morgen: Nicht mehr nur ein Arzneimittel, sondern eine individuelle Lösung für ein individuelles Problem

Apps

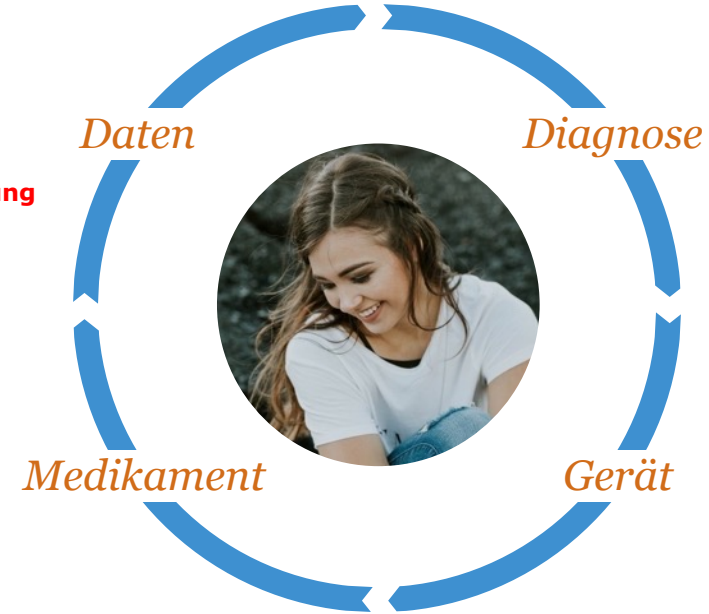
Krankheits-Management
Patientenportale
Patientenbindung
Patienten-Weiterbildung
Infektionsketten-Nachverfolgung

Big Data

Analytik und Mining
Mustererkennung
Modelling

Services

Fitnessprogramme
Online-Beratung
Telemedizin



Monitoring

Vital-Parameter
Schlafmuster
Ernährung
Körperliche Aktivität
Genomanalysen

Technik I

Tracker/Wearables
Sensoren (Tatoos)
Smarte Kleidung

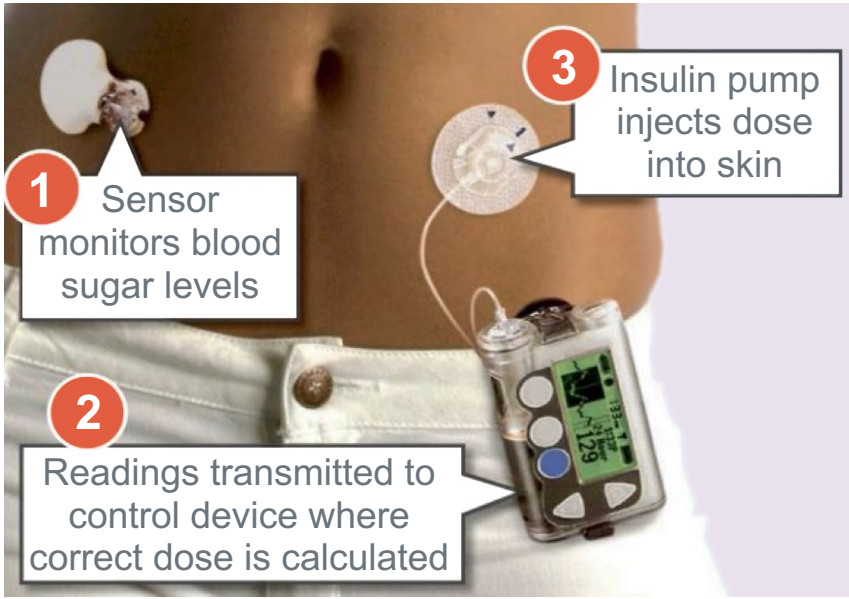
Technik II

Pens
Pumpen
Implantate
Smarte Tabletten
3-D-Prints

→ *Bessere Ergebnisse, zielgerichtetere Behandlung, bessere Prävention, geringere Kosten, Lebensstiländerungen*

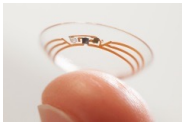
Solutions for Patients – not longer only drugs (2)

Diagnostic / Drug / Device / (Data): The ***digital*** artificial pancreas



Artificial pancreas
works already well during the night,
but has some optimisation potential:

- Implanted sensors and pumps
- Two hormones (Glc/Ins)
- More rapid response times
- etc.



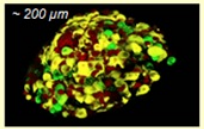
Solutions for Patients – not longer only drugs (3)

Diagnostic / Drug / Device / (Data): The ***biological*** artificial pancreas

In vitro **differentiation of human stem cells into islet like clusters**

"hSC islet-like cluster"

evotec



hSC islet-like cluster

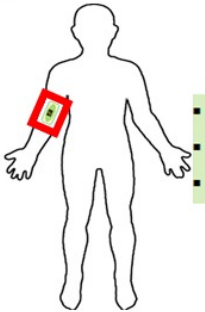
Bio-artificial Pancreas

Device

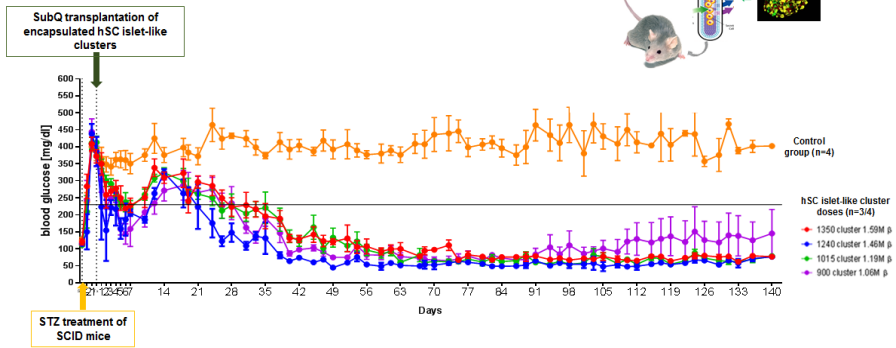
Encapsulation Device

- Immunoisolating
- Adequate cell load & size
- Minimal invasive implantable
- Cell longevity
- Adequate response rate
- Anytime retrievable

Cure !!!!!

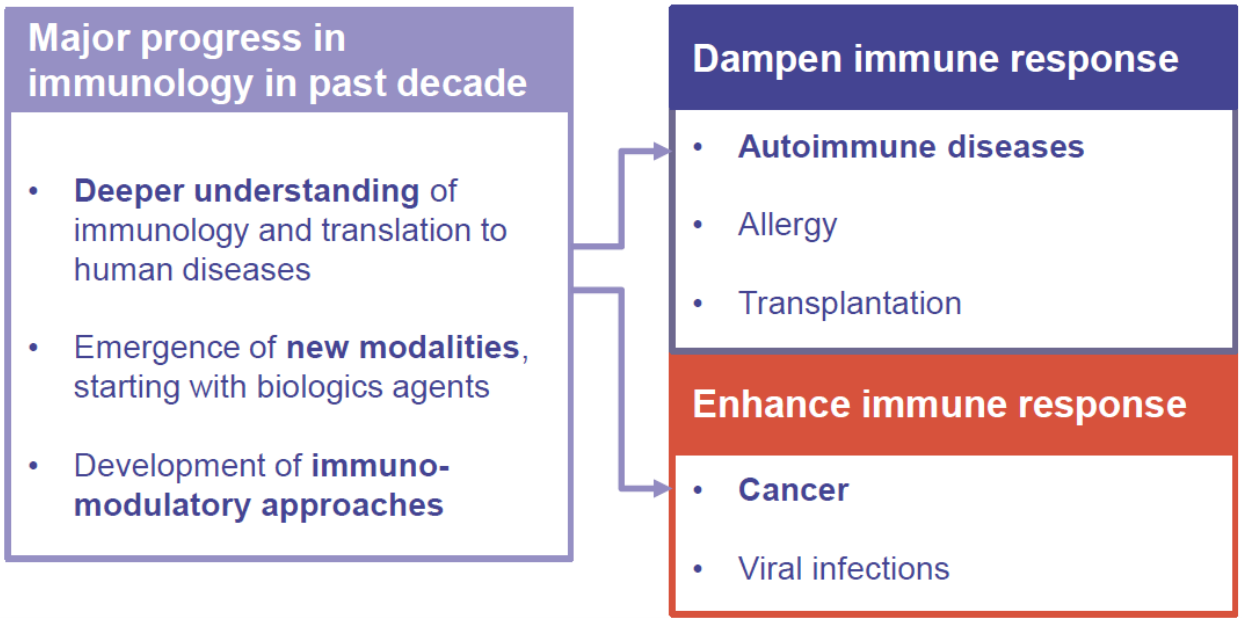


- **T1 Diabetics**
- Pancreoprivic Diabetics
- T2 Diabetics



Modulation of Immune system

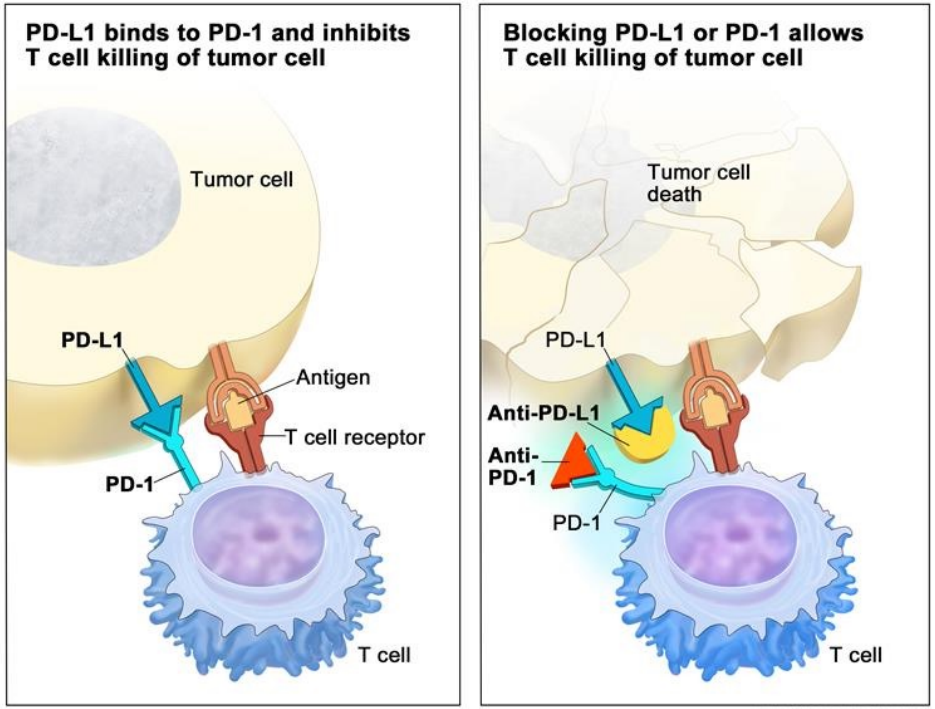
We’re learning how to “switch on” or “switch off” the human immune system in order to better control diseases like cancer



Modulation of Immune system: Immune checkpoint therapy

A new weapon against cancer

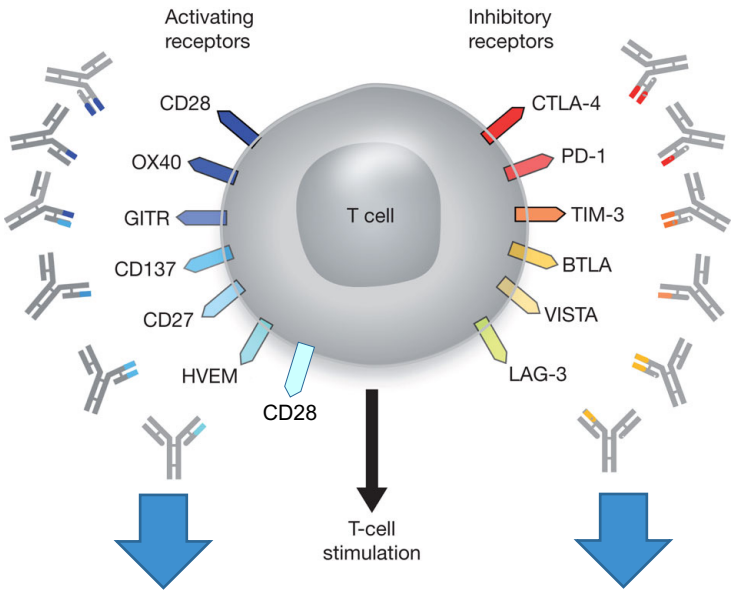
- **T cells have a major role in immune defense**
  - T-cells recognize tumor antigens, consequently become activated, and, ultimately, eliminate cancer
- **Immune checkpoints**
  - Multiple co-stimulatory and inhibitory ligand-receptor interactions to regulate T cell response
- **Cancer cells are invisible to the immune system**
  - Escape from immune attack by dysregulating immune checkpoint
- **Immune checkpoint therapy**
  - Tumor is not targeted directly but lymphocyte receptors or their ligands to enhance endogenous antitumor activity
  - Agonists for co-stimulatory receptors or antagonists of inhibitory signals resulting in amplification of antigen-specific T-cell response

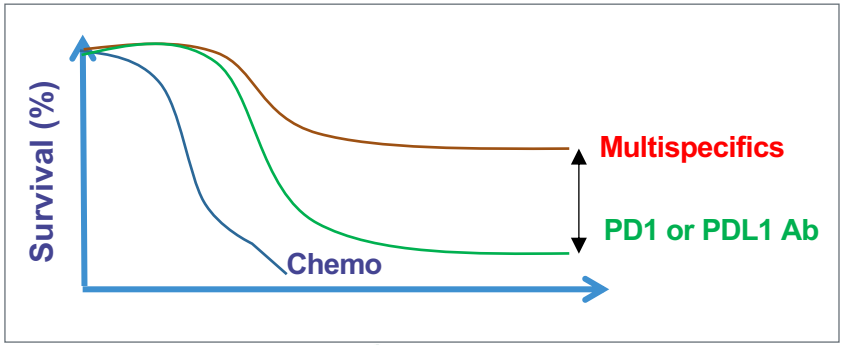


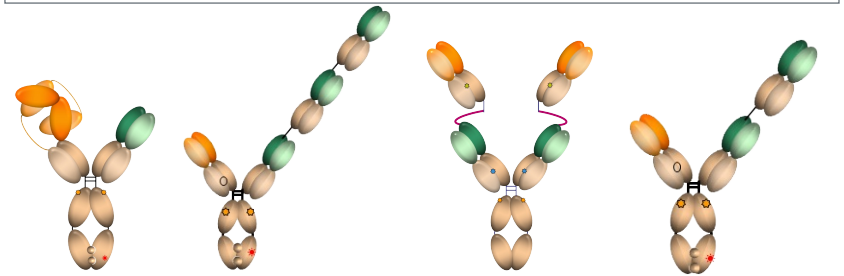
Science, **2015**, *348*, 56-61; *Nature Rev.* **2012**, *12*, 252-264

Modulation of Immune system: Next generation

- **Combination therapies or multi-specific molecules to enhance anti-tumor immunity**





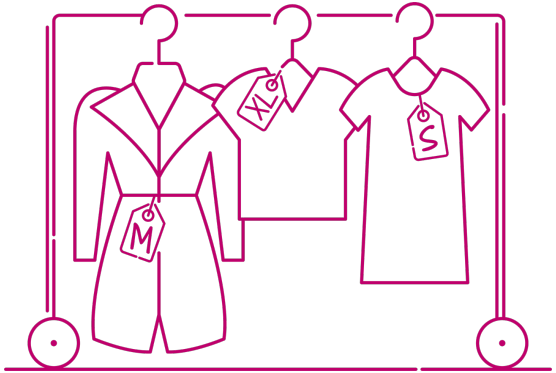


Agonist antibody + **Blocking antibody may enhance T-cell stimulation to promote tumor destruction**

Nature, **2011**, *480*, 480-489

Individualisation of medicine – where we are (1)

Wo wir herkommen …
(and where we still are –
at least in some areas)



… wo wir stehen
(but only in some areas)

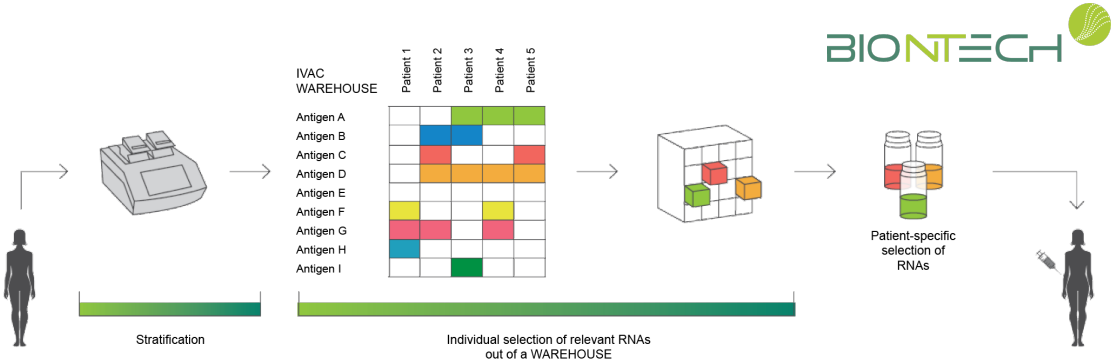
Wo wir hin möchten
(but haven‘t reached it)

Individualisation of medicine – where we are (2)

mRNA‘s – A personalized concept to fight cancer

RNA based vaccines that targeting shared tumor-associated antigenes

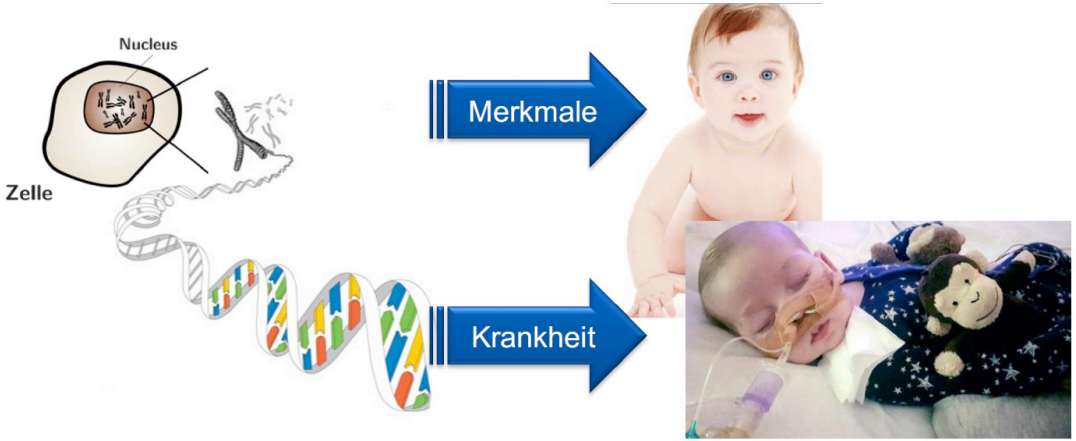
- Tumor profiled by RT-qPCR for specific antigen expression profile
- Patient receive individual combination of RNAs from warehouse that corresponding to antigen-expression profile



RNA based vaccines targeting unique antigens that result from tumor-specific mutations

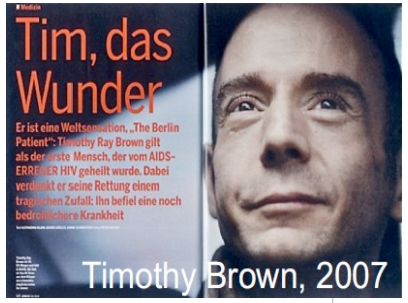
- Tumor-specific mutations determined, patient-individual immune status investigated
- Sequences in healthy and cancerous tissue compared to determine patient specific tumor mutanome
- Patient receive truly personalized combination of RNAs produced de novo based on mutation profile

Individualisation of medicine – Gene Therapy



A few concrete examples:

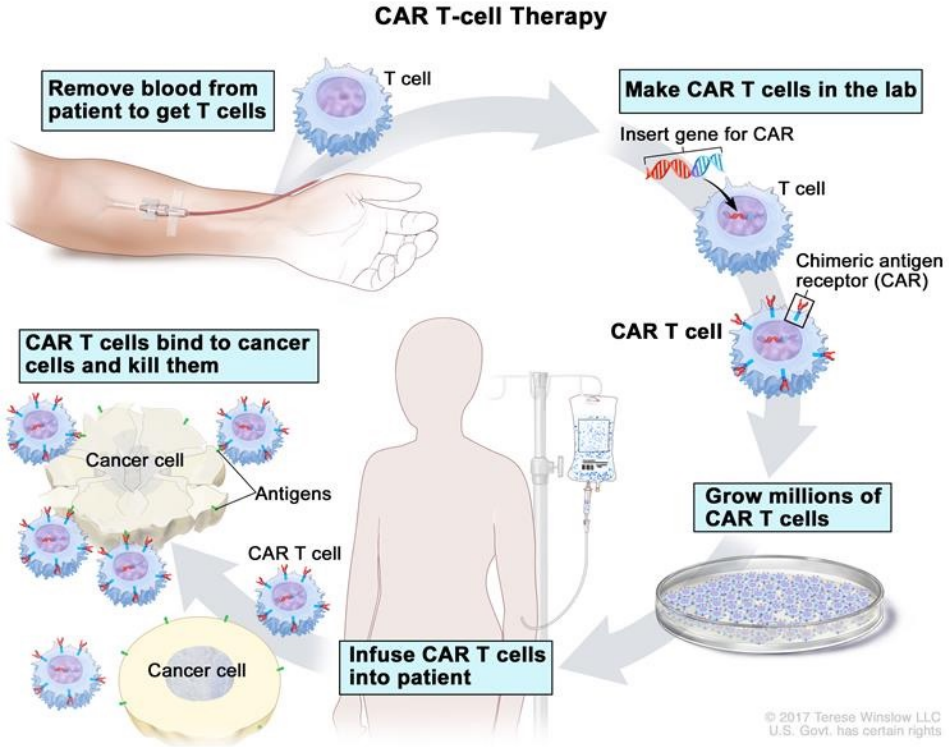
- Emily Whitehead
- Jameson Golliday
- Steve Crohn
- Timothy Brown



Gene Therapy – **Emily**: CAR-T – cell Therapy

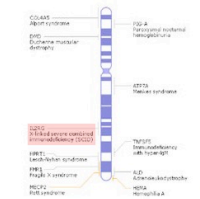
CAR-T – Souped-up killers against blood cancer

- Kymriah (Novartis, B-cell acute lymphoblastic leukemia) and Yescarta (Kite Pharma, acquired by Gilead, non-Hodgkin's lymphoma approved by FDA
- Extracted patient T-cells are genetically altered to produce a protein called chimeric antigen receptor (CAR) which directs the T cells to target and kill leukemia cells with a specific antigen on their surface.
- Costs: Approx $ 480.000/patient
- Significant site effects

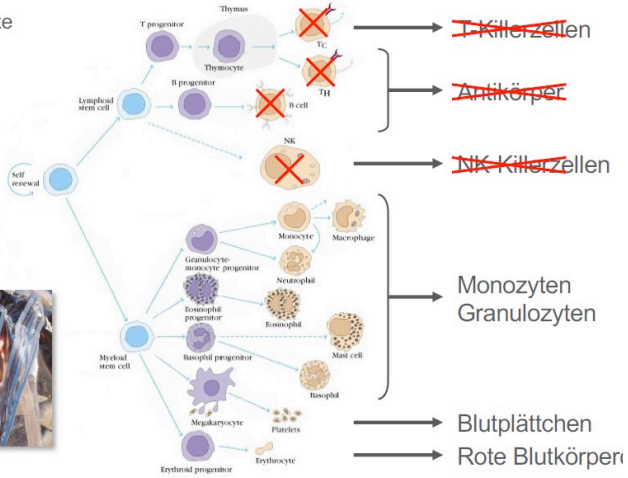


Gene Therapy – **Jameson**: Virus-Vektoren

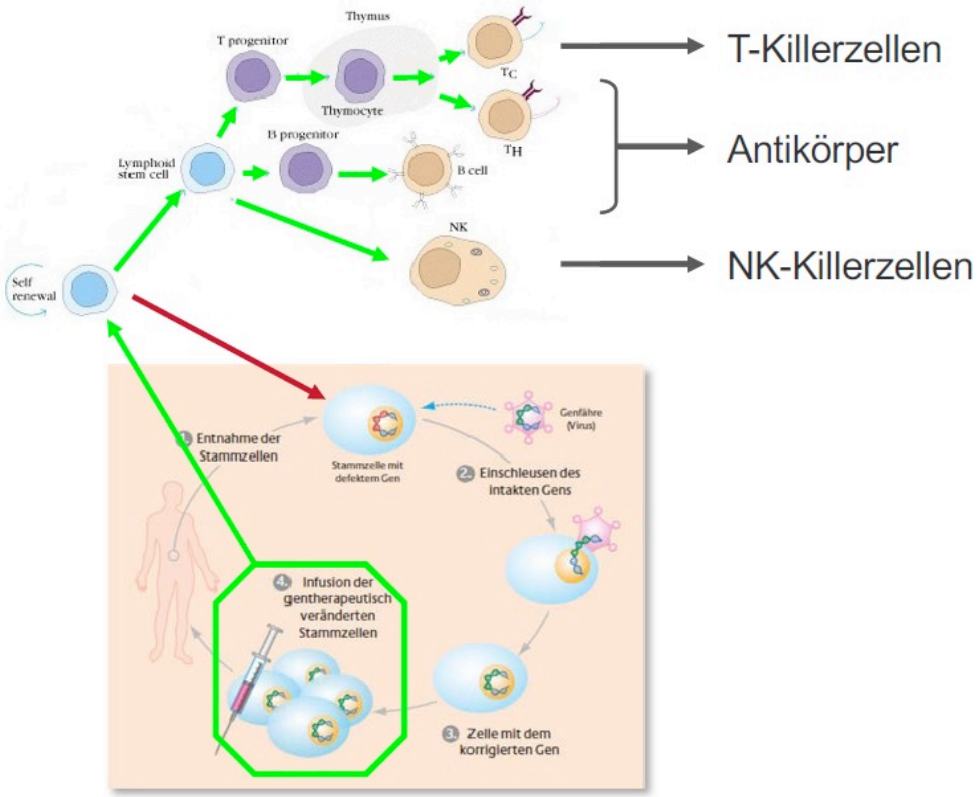
Mutation in der γc-Kette



Jameson Golliday



Jameson Golliday
Quelle: The Atlantic

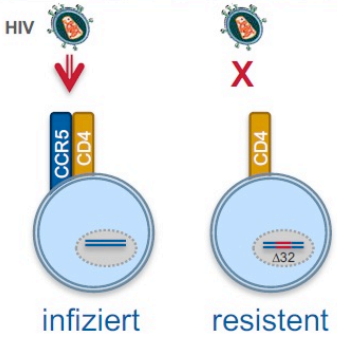


Quelle: BMBF

Gene Therapy – **Steve and Tim** - HIV

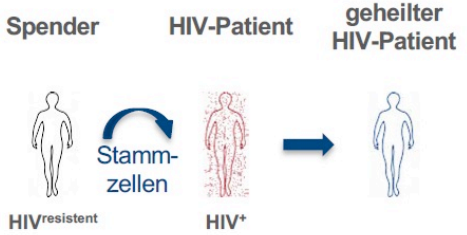
Therapie der HIV-Infektion

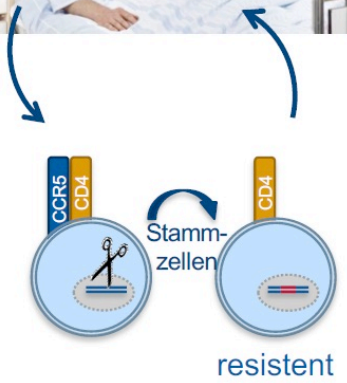
The man who can't catch AIDS



Ein Gen ausschalten

The Berlin patient





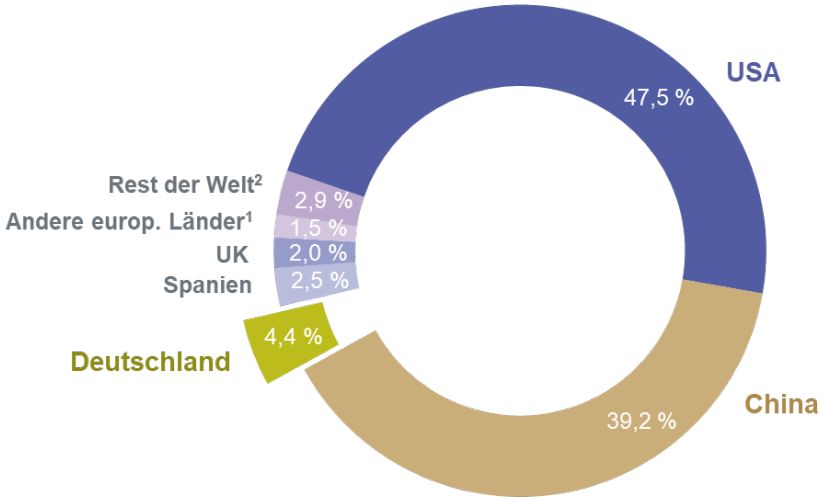
…but not “in his way”

He Jiankui

New technologies: Chancen und Risiken

Chancen	Risiken
Krankheiten heilen	Langzeitfolgen? Genscheren, Virusvektoren
Einmalige Therapie	Kosten? Ethische Bedenken

Weltweite Gentherapie-Studien nach Ländern



1 Italien, Tschechien, Frankreich
2 Japan, Südkorea, Australien, Russland
Anmerkung: Studien, die im Jahr 2018 genehmigt bzw. begonnen wurden
Quelle: The Journal of Gene Medicine

A last word regarding ethical considerations…

Don‘t condemn the technology, condemn the individuals misusing them….

Das „Petos-Paradoxon“

Tumorsuppressor p53
mit „Genschalter“ LIF6

Science **2018**, *359*, 1-10