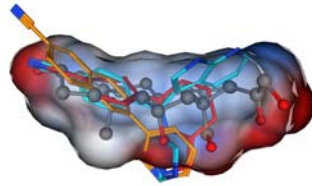
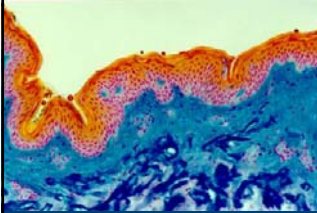


Nanomedizin

Für den Arzneistofftransport über biologische Barrieren

Prof. Dr. Claus-Michael Lehr



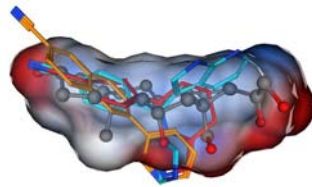
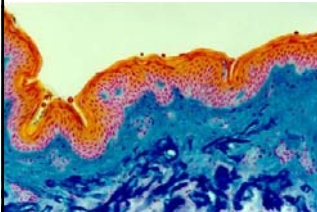
Helmholtz Institute for Pharmaceutical Research Saarland (HIPS)
Department of Drug Delivery (DDEL)

claus-michael.lehr@helmholtz-hzi.de
www.helmholtz-hzi.de



NEW since September 2009:

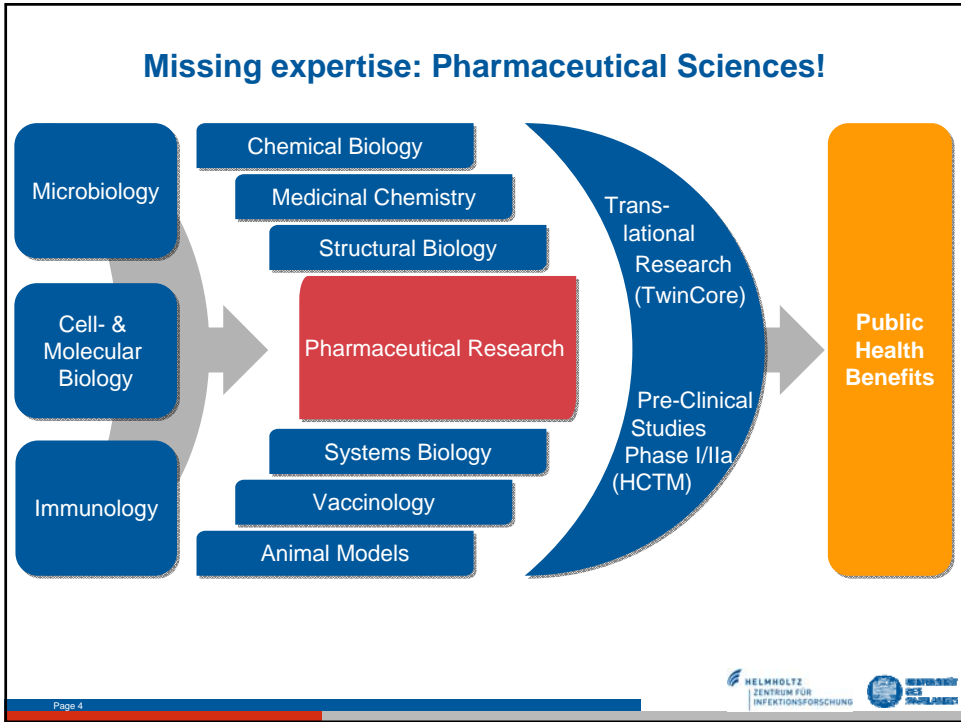
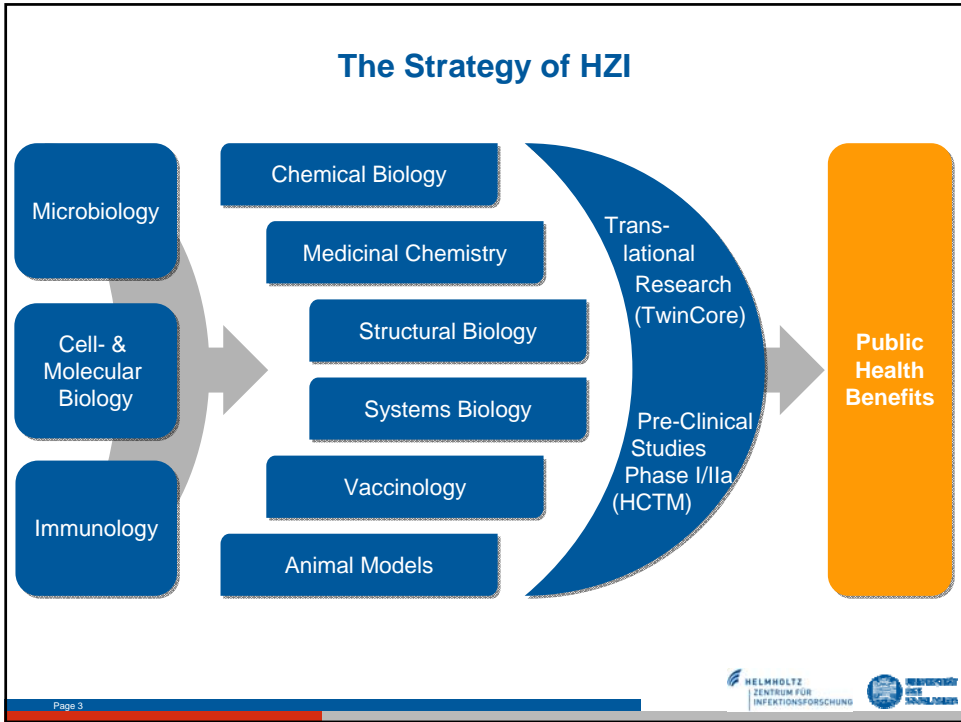
**Helmholtz Institute
for Pharmaceutical Research Saarland
(HIPS)**

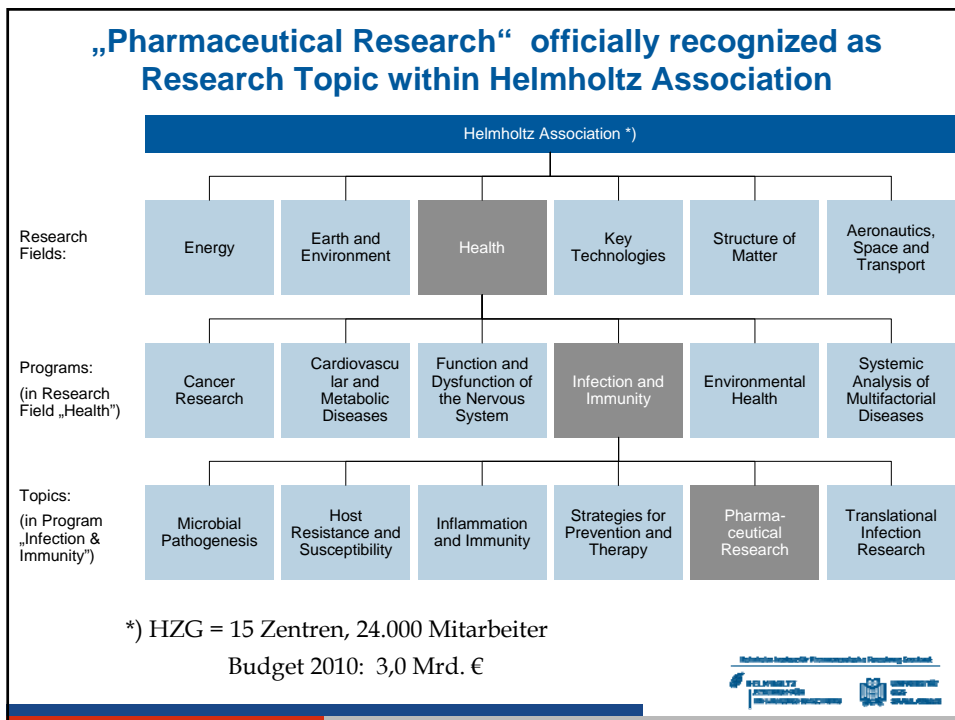
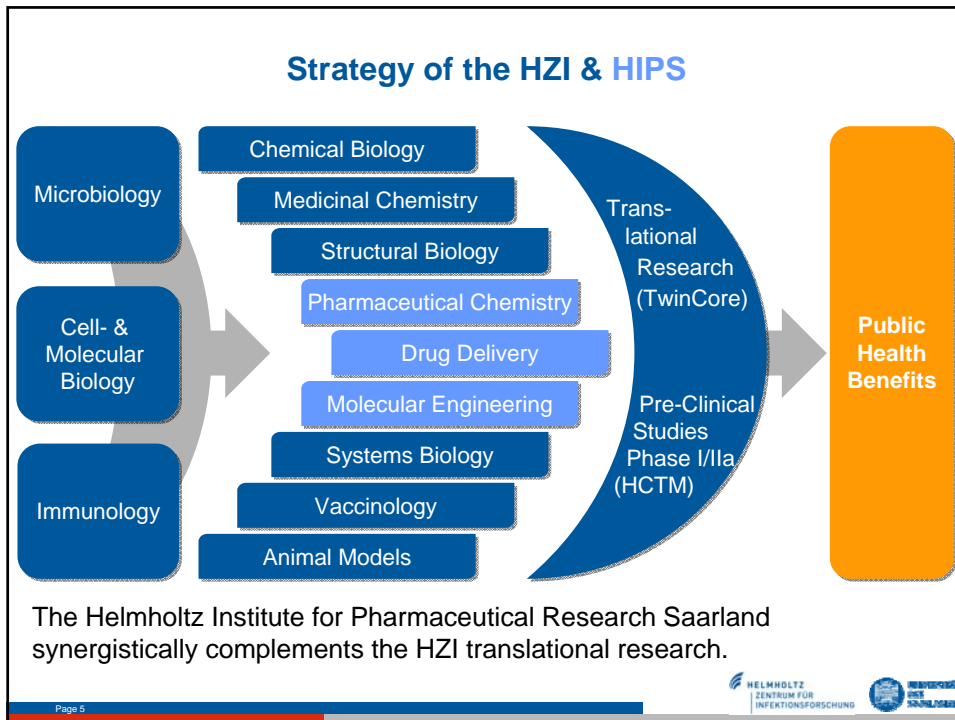


Departments:

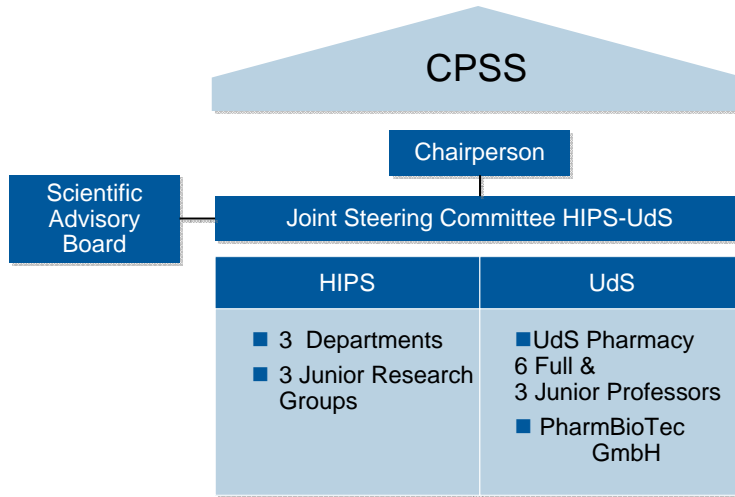
- Molecular Engineering (R. Müller)
- Med. Chemistry (R.W. Hartmann)
- Drug Delivery (C.-M Lehr)







HIPS, UdS and PharmBioTec are forming the “Center of Pharmaceutical Sciences Saarland”



Page 7

“Drug Delivery Research”



Central Research Theme: „Biological Barriers“

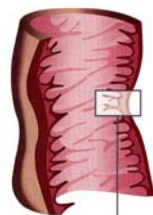
Cell & tissue based in-vitro models

- intestinal mucosa
- skin
- lung

Drug delivery technologies

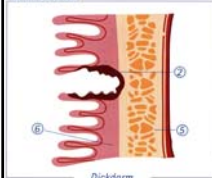
⇒ Explore new ways to overcome these barriers,
e.g. with NANOMEDICINES
(i.e. Nanoparticles for pharmaceutical applications)

Entzündliche Darmerkrankungen

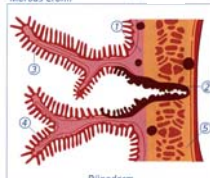


- ① Schleim
- ② Entzünd
- ③ Darmrot
- ④ Darmfalt
- ⑤ Muskelschicht
- ⑥ Schleimhaut mit Saamepithel

Colitis ulcerosa



Morbus Crohn



Formen:
Colitis Ulcerosa,
Morbus Crohn

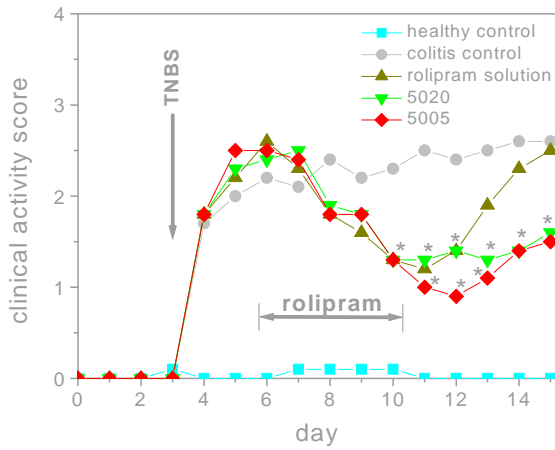
⇒ **Unklare Ätiologie, aber ähnliche Symptomatik:**

Schmerzen,
Durchfälle,
Blutiger Schleim...

⇒ **Therapie nur symptomatisch, und überdies schwierig:**

- häufige und höhere Dosierung
Systemische Nebenwirkungen

Rolipram NP: clinical activity

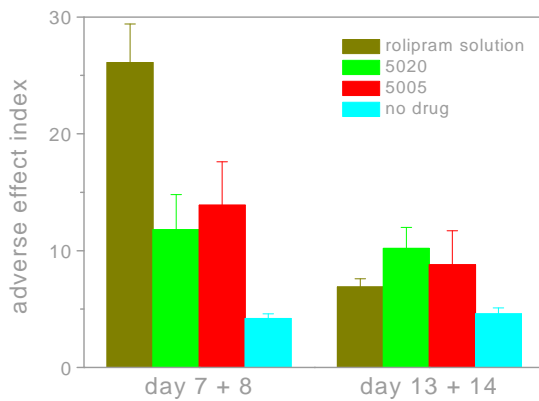


- Improvement by rolipram became significant on day 10
- rolipram solution showed a relapse after 3 days without drug

Lamprecht et al., JPET 2001



Rolipram NP: adverse effects



- rolipram solution group showed highest adverse effect index
- adverse effects after nanoparticles were reduced

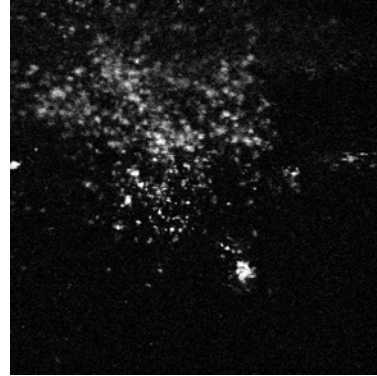
Lamprecht et al., JPET 2001



Visualisation of particle accumulation at inflammatory areas in Colitis patients



Moderately inflamed mucosa

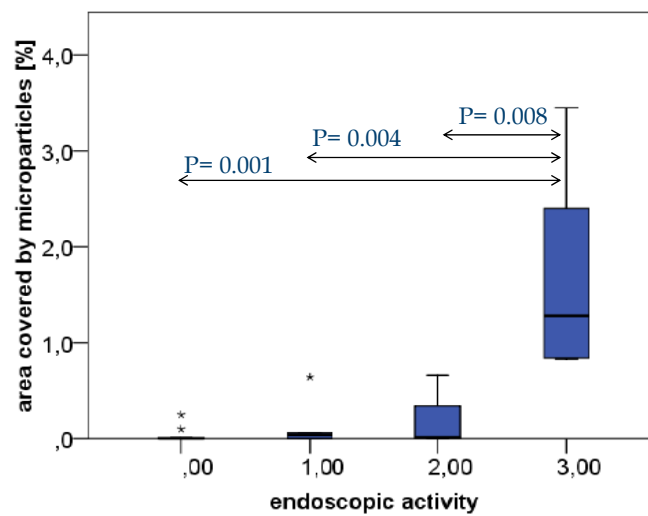


Inflamed mucosa with flat ulcerations

Dr. C. Schmidt, Prof. Dr. Andreas Stallmach, Jena



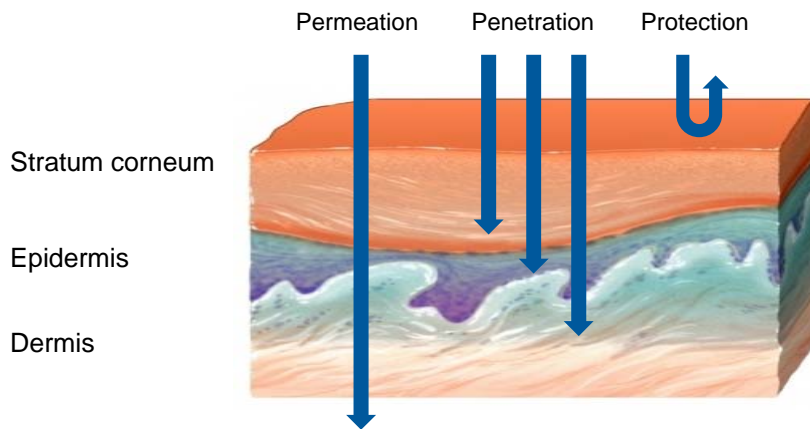
Accumulation of microparticles in rectal mucosa of patients with UC and CD, resp.



Data by C. Schmidt & A. Stallmach, Jena

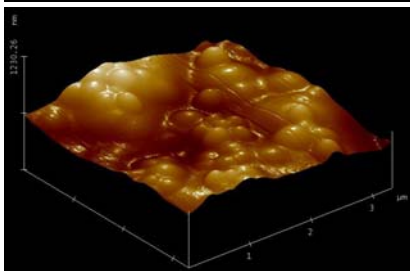
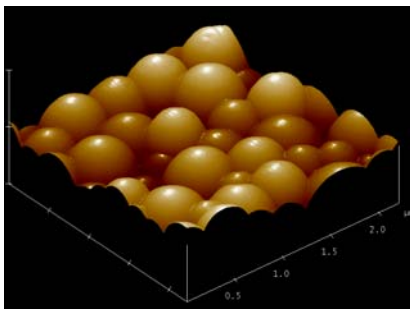


Skin drug delivery



Pharmazie-Institut für Pharmazeutische Technologie/Strahlentherapie
FACULTÄT FÜR PHARMAZIE
UNIVERSITÄT WÜRZBURG

Nanoparticles for skin drug delivery



Can nanoparticles enhance percutaneous transport into and across the skin barrier when administered topically?

PLGA nanoparticles

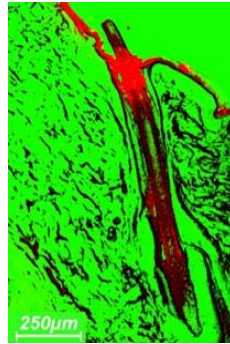
Nanoparticles in hydroxy(ethyl)cellulose gel

Luengo, Weiss, et al.,
Skin Pharmacol. & Physiol., 2006

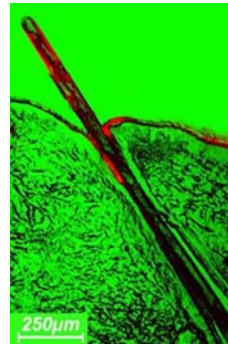
Pharmazie-Institut für Pharmazeutische Technologie/Strahlentherapie
FACULTÄT FÜR PHARMAZIE
UNIVERSITÄT WÜRZBURG

NP may use the follicular pathway to penetrate into skin

pig ear skin (in vitro), after massage
PLGA NP's (320 nm)



particles

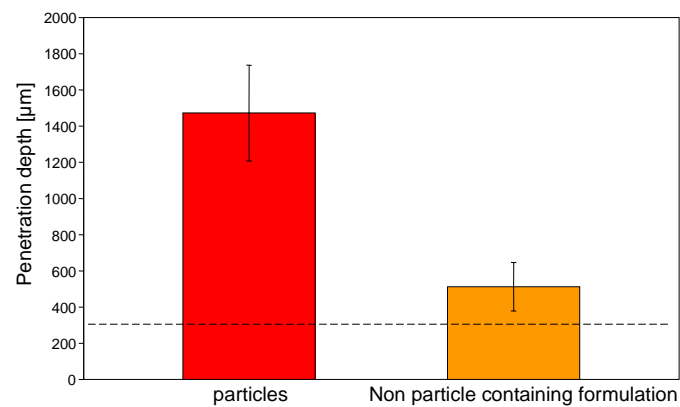


Non particle containing formulation

Lademann et al., *Eur J Pharm Biopharm*, 2007, 66, 159

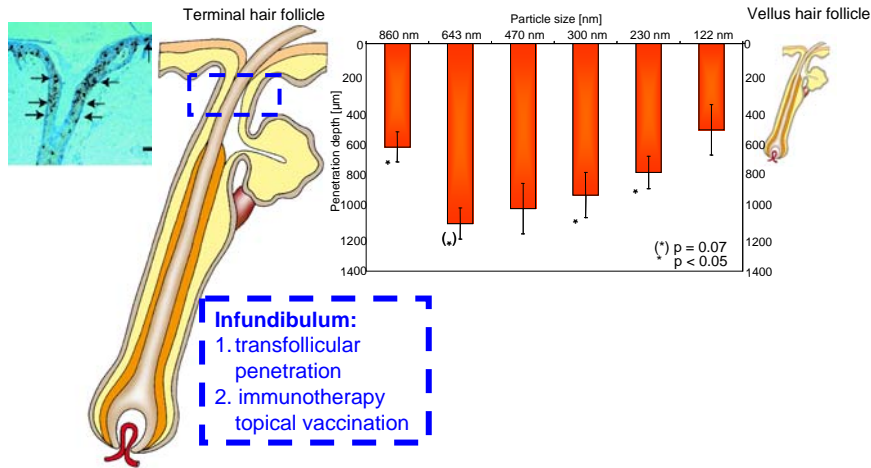
Determination of the penetration depth

pig ear skin (in vitro), after massage
PLGA NP's (320 nm)



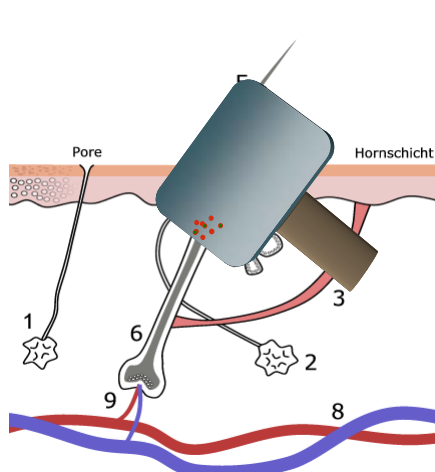
Lademann et al., *Eur J Pharm Biopharm*, 2007, 66, 159

Size dependence of follicular penetration (pig ear)

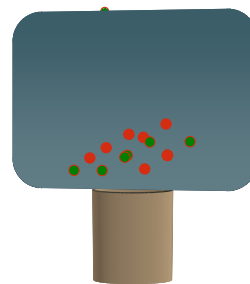


Slide courtesy of J. Lademann, Charité Berlin

New project idea: „Pollen-mimetic vaccine carriers“



BILL & MELINDA
GATES foundation



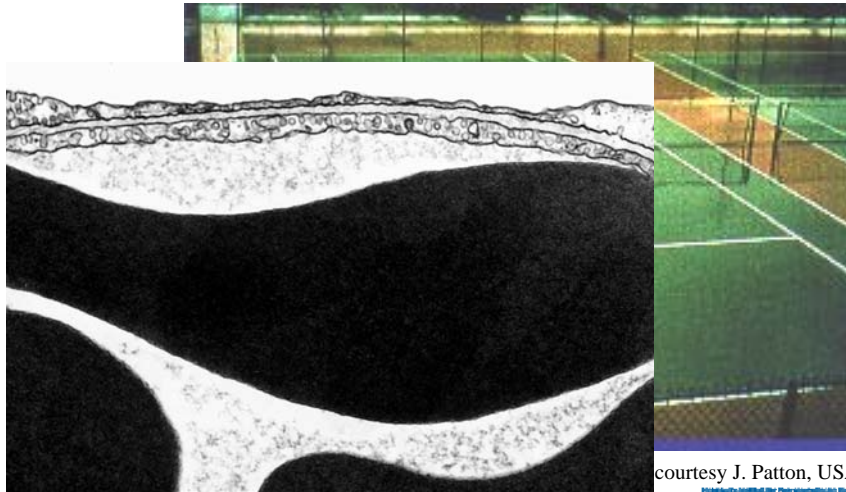
Sweat

- 80-185 mosmol/kg
- pH 5-6.5

Sebum

- Triglycerides, Wax monoesters, Free Fatty Acids, Squalene

Pulmonary Drug Delivery A promising new area for Nanomedicines

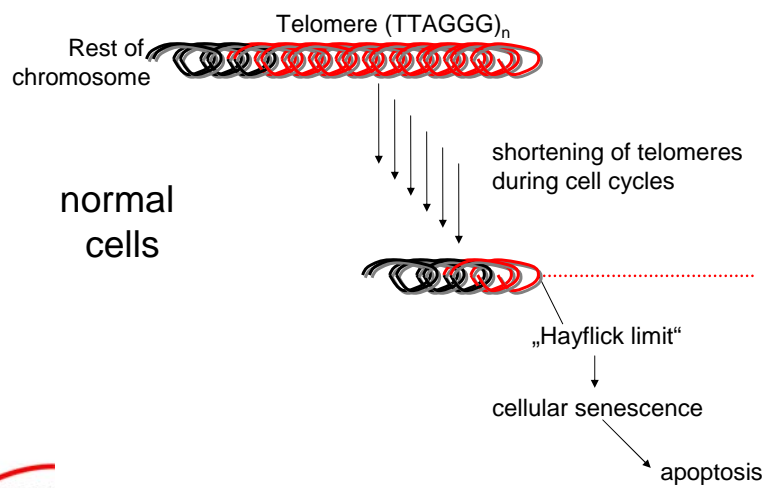


courtesy P. Gehr, Bern

courtesy J. Patton, USA



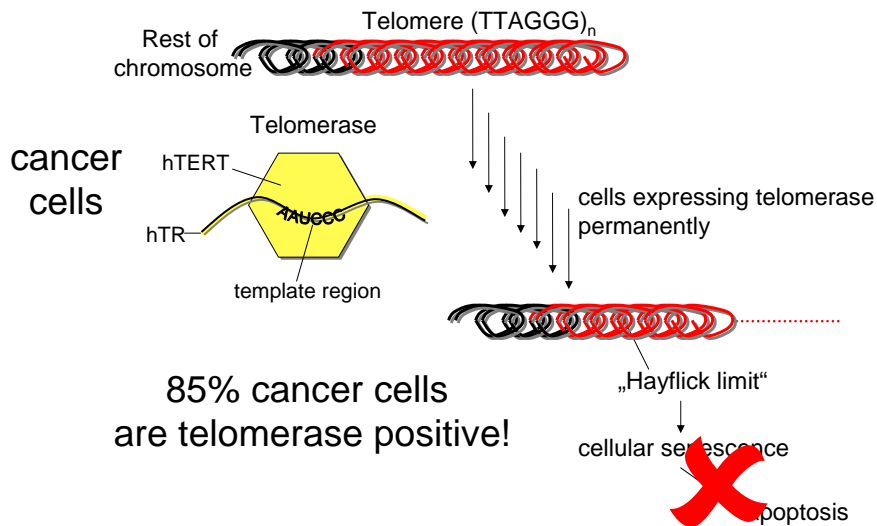
Telomerase-Hemmer als neuartige Krebs-Medikamente



Funding: DEUTSCHE KREBSHILFE



Telomerase-Hemmer als neuartige Krebs-Medikamente



Antisense-Oligonukleotide als Telomerase Inhibitoren

Wirkstoff = sog. Antisense - Nukleotid

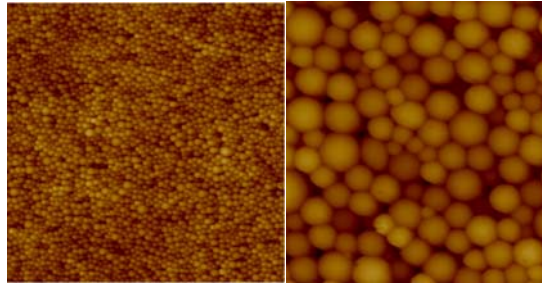
(“antisense 2'-O-Methyl-RNA”, 2OMR)

Probleme :

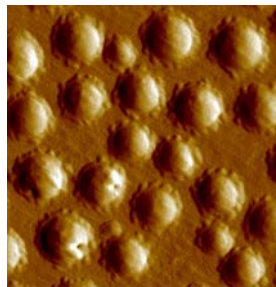
- großes Molekül
 - hohe negative Ladung
- => gelangt kaum in die Zelle
oder gar in den Kern!

Chitosan coated PLGA Nanospheres

Nanospheres
< 200 nm



Surface
Morphology

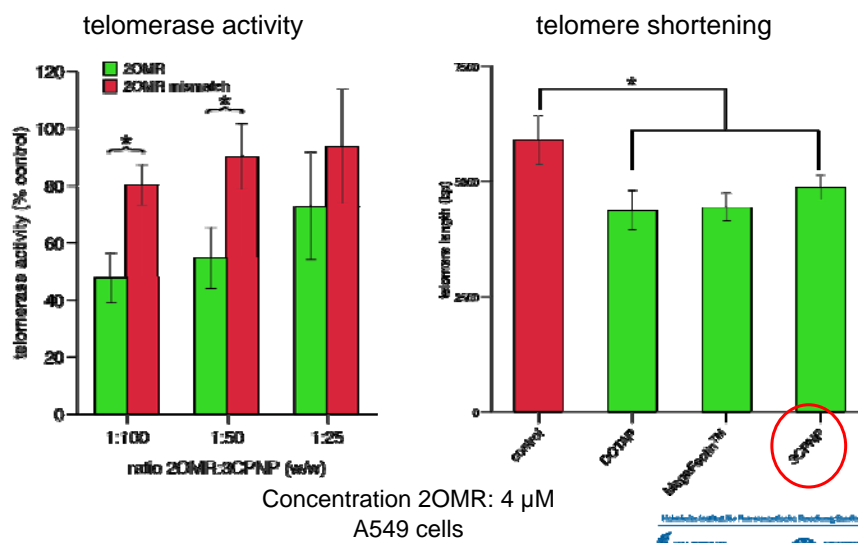


Nanosphere-DNA
Complexes

Kumar et al,
Biomaterials 25 (2004)
1771-1777



Efficacy in-vitro



The next step: animal experiments

Effect on tumor growth , NCI-H460 (=HTB-177) cells in nude mice

Control group

Nanoplex treatment

Mouse Nr	Left side (mm)	Right side (mm)	Mouse Nr	Left side (mm)	Right side (mm)
1	8,17 x 8,82	14,42 x 5,57	5	2,45 x 2,51	1,77 x 1,89
2	4,95 x 8,29	9,36 x 9,82	6	1,97 x 1,92	1,79 x 1,55
3	8,44 x 5,88	10,43 x 6,97	7	2,28 x 2,46	2,16 x 1,96
4	+	8,79 x 10,84	8	1,54 x 1,92	1,52 x 1,52

B. Loretz, C. Philippi, et al.
In cooperation with Dr. Matthias W. Laschke
Prof. Dr. Michael D. Menger, Homburg



Acknowledg

Helmholtz Institute for Pharmaceutical Research Saarland

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SAARLANDES



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Forschungsgemeinschaft
DFG

Bundesministerium
für Bildung
und Forschung

BfR
Risiken erkennen – Gesundheit schützen

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